Society for Epidemiologic Research

2025 Annual Meeting

Abstract Book

June 10-13, 2025

Cancer

Predicting risk of fatal ovarian cancer using a novel two-stage model Mary Townsend* Mary Townsend Shelley Tworoger Bernard Rosner

Background: Identifying risk factors for the most aggressive forms of ovarian cancer is important to guide prevention. We used a multi-state model to capture the additive effects of ovarian cancer risk factors on disease risk and death among those with ovarian cancer.

Methods: We used prospectively collected data from the Nurses' Health Studies (three 12-year risk periods, 1980-2017). Putative risk factors assessed at baseline of each risk period included age at menarche, pre- and post-menopause duration, reproductive/hormonal factors, smoking, early life body mass index (BMI), family history of breast and ovarian cancer, and race. We used Fine-Gray models to estimate HRs and 95% CIs for risk of incident ovarian cancer among at-risk individuals and risk of mortality among those with ovarian cancer adjusted for competing risks. Estimates were combined using weights for incidence and mortality based on baseline hazard (incidence) and survival (mortality) functions over follow-up to estimate the log relative risk of fatal ovarian cancer over 12 years in cancer free individuals.

Results: We had 197,690 eligible participants, with 1678 confirmed cases of ovarian cancer and 693 deaths due to ovarian cancer. A SD increment in age at menarche (1.4 years), premenopausal (5.9 years) and postmenopausal (7.0 years) duration, duration of estrogen only hormone therapy (4.1 years), and BMI at age 10 (3.0kg/m2) as well as nulliparous vs. parous and 20+ pack-years vs. never smoking were associated with increased risk of fatal ovarian cancer (HRs 1.11-1.92, $p<0.05$). Duration of oral contraceptive use was associated with lower risk of fatal ovarian cancer (10+yr vs. never use HR=0.64, 95%CI=0.43-0.96).

Conclusion: Our results support that pre-diagnostic factors can predict risk of developing and dying of ovarian cancer. Model refinement and validation could identify high-risk populations who would benefit from intensive screening and possibly prophylactic bilateral salpingo-oophorectomy.

Cancer

Social factors and prostate cancer survival in Quito-Ecuador, between 2000 and 2019

Harold Alexander* Harold Alexander María Fernanda García Yunqi Yu Liu

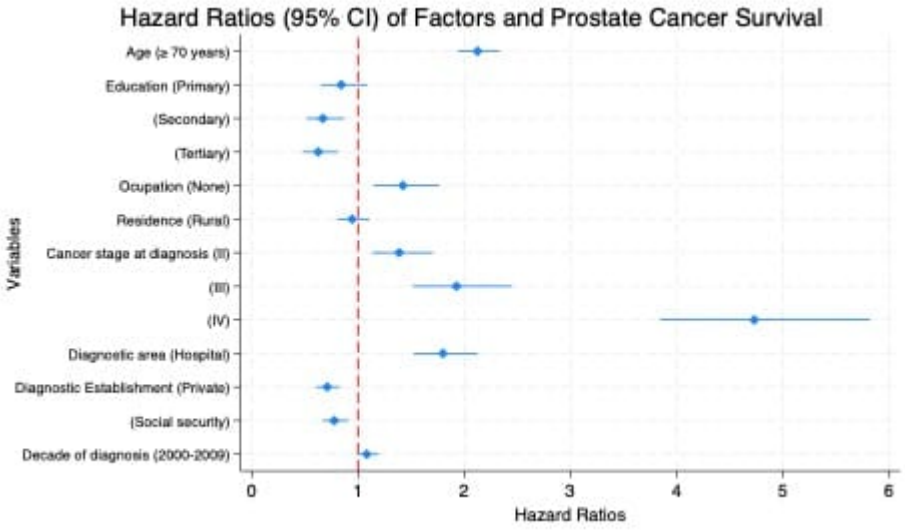
Introduction: Prostate cancer is a global health concern, the second most diagnosed cancer among men, and a leading cause of cancer-related mortality in Ecuador. While genetic and biological factors have been studied, the impact of social factors on survival remains unclear in Quito, where inequalities in healthcare access and education persist. Lower educational levels and unemployment are linked to limited healthcare access and worse survival. This study assessed the association between social factors (education, residence, occupation, and healthcare access) and survival in prostate cancer patients in Quito from 1989 to 2019.

Methods: A secondary, retrospective cohort study was conducted using data from the National Tumor Registry of Solca-Quito. Men diagnosed with prostate cancer between 2000 and 2019 were included (with follow-up until August 14, 2024). Survival was compared across social groups using multivariate Cox regression, adjusting for clinical and social variables.

Results: Of 4,595 patients, most were diagnosed at stage II (53.9%) or stage IV (26.7%). Median survival was 7.51 years (IQR 4.73–11.35). Advanced age (≥70 years) increased mortality risk (HR = 2.13; 95% CI: 1.94–2.33; $p < 0.001$). Higher education showed a protective effect (secondary: HR = 0.67; tertiary: HR = 0.63; $p < 0.01$). Stage IV cancer strongly increased mortality (HR = 4.73; 95% CI: 3.84–5.82; $p < 0.001$). Hospital-based diagnosis versus laboratory diagnosis raised mortality risk (HR = 1.80; 95% CI: 1.52–2.13; $p < 0.001$), while private or social security-based healthcare was protective (HR = 0.71 and 0.78; $p < 0.01$).

Conclusions: Social factors influence survival in prostate cancer. Advanced age and late-stage diagnosis increase mortality, while higher education and better healthcare access improve survival. Policies addressing social disparities and healthcare access are essential to improve outcomes.

Keywords: Prostate cancer, education, mortality, survival, Ecuador.



Cancer

Sugar-sweetened soda consumption and mortality risk in Mexican: A target trial emulation
Ana Rodríguez* Ana Rodríguez Nancy López Liliana Gómez Marion Brochier Martín Lajous Dalia Stern

Numerous studies have shown that higher consumption of sugar-sweetened beverages (SSBs) is associated with increased disease risk and mortality. However, a more critical public health question is whether reducing SSB consumption can lower disease risk. While a randomized trial would be ideal to answer this question, it may be infeasible. This study uses the target trial framework to estimate the effect of reducing sugar-sweetened soda consumption on mortality risks.

Methodology: Using observational data from 115,527 women in the Mexican Teacher Cohort. Eligibility criteria included Mexican women aged >25 y who were current consumers of sugar-sweetened soda. Mortality data were obtained through probabilistic linkage with national death records. We estimated the observational analog of the intention-to-treat effect. To adjust for confounding, we used the parametric g-formula to estimate the effect of reducing sugar-sweetened soda to one serving/month versus no intervention on the risk of all-cause and cause-specific mortality over 13 years. Bootstrap resampling (500 iterations) was used to calculate confidence intervals.

Results: A total of 87,529 women met the eligibility criteria. During 13 years of follow-up, 1,480 deaths occurred, including 563 from cancer, 234 from CVD, and 91 from liver diseases. The median consumption of sugar-sweetened soda was 3 servings/week (IQR:0.5-4.0). The 13-year RD (95% confidence interval) for all-cause mortality with reduced soda consumption versus no intervention was -0.06%(-0.23%,0.13%) and the corresponding RR was 0.97 (95% CI:0.90,1.06). The RD for cancer mortality was -0.07%(-0.17%, 0.03%), and a RR of 0.92(0.80, 1.04).The RD for liver disease mortality was -0.03%(-0.06%,0.00%) and an RR of 0.79(0.56,1.03). For CVD mortality, the RD was 0.04%(-0.04%,0.16%) with a corresponding RR of 1.10(0.89,1.37).

Conclusion: In the Mexican context, reducing sugar-sweetened soda consumption may reduce the risk of cancer and liver disease mortality.

Cancer

A prospective analysis on adult weight change and risk of colorectal cancer incidence and mortality in the NIH-AARP Diet and Health Study Wen-Yi Huang* Wen-Yi Huang Kathryn Hughes Barry Steven C. Moore Semi Zouiouich Rashmi Sinha Erikka Loftfield Sonja I. Berndt

Obesity has been rapidly increasing worldwide. Although obesity is a risk factor for colorectal cancer (CRC), the influence of weight change over adult lifetime on risk of CRC incidence and mortality is unclear.

With >20 years of follow-up, we prospectively evaluated the risk of CRC incidence (n=9,255) and mortality (n=2,934) in relation to adult weight change among men and women (n=292,238) in the NIH-AARP cohort. Participants reported their weight and height at age 18, age 50, and enrollment (aged 50-71), and their maximal adult weight. Hazard ratios (HRs) and 95% confidence intervals (CI) were computed using multivariable-adjusted Cox proportional hazard models.

Compared with individuals whose BMI never exceeded 25 kg/m2 over their lifetime, those who first exceeded a BMI of 25 kg/m2 at either age 18, age 50, or enrollment all had a 20% higher risk of CRC (HR=1.2, all P-values <0.05). Participants who had a lifetime maximal BMI between >25 to 30 kg/m2 had a 10% increased risk (95% CI:1.1-1.2) and those with a maximal BMI exceeding 30 kg/m2 had a 30% increased risk (95% CI:1.2-1.4). Moreover, compared with stable weight from age 18 to 50 years, weight gain of >4, >2-4, and >1-2 kg per 5 years was associated with a 30% (95% CI:1.2-1.4), 20% (95% CI:1.1-1.3), and 10% (95%CI:1.0-1.2) increased risk of CRC incidence, respectively. We observed similar risk patterns for CRC mortality. For example, weight gain of >4, >2-4, and >1-2 kg per 5 years from age 18 to 50 years, compared with stable weight, was associated with a 70% (95% CI:1.5-1.9), 30% (95% CI:1.2-1.5), and 20% (95%CI:1.0-1.3) increased risk of CRC mortality, respectively.

In conclusion, our study demonstrates that exceeding a normal weight at any age and weight gain from early to middle adulthood are associated with an increased risk of both CRC incidence and mortality. These findings highlight the importance of maintaining healthy weight throughout the adulthood.

Cancer

Comparison of enzalutamide, abiraterone, and apalutamide for prostate cancer outcomes: a target trial emulation using data from the IRONMAN Registry Connor Grady* Connor Grady Jordan Tuai Xabier García-Albéniz Emma McGee Philip Kantoff Lorelei Mucci Barbra Dickerman

The clinical landscape for men with advanced prostate cancer is rapidly evolving, with the introduction of several new therapies over the past decade – including androgen receptor signaling inhibitors (ARSIs) – that have been shown to improve survival. However, further evidence to inform the optimal selection and sequencing of these agents is needed.

In this study, we will use observational data from the IRONMAN registry, an international, prospective cohort of >4,300 men with advanced prostate cancer, to emulate a target trial of ARSIs (enzalutamide, abiraterone, apalutamide) and risk of progression and death among individuals with metastatic prostate cancer. We will use inverse-probability weighted pooled logistic regression models to estimate intention-to-treat and per-protocol effects of dynamic treatment strategies, adjusting for baseline and time-varying confounders. To identify potential subgroups of individuals for whom the treatment strategies may be most beneficial, we will conduct analyses separately in subsets of the population defined at baseline according to demographic and clinical features. These findings will help to inform clinical recommendations for individuals with metastatic prostate cancer, as well as the design of future studies aimed at evaluating different selections and sequencing of cancer treatments.

Substance Use

The Impact of Gentrification on Fatal Opioid Overdoses in Chicago Gabrielle Zuckerman*
Gabrielle Zuckerman Kechna Cadet Elizabeth Nesoff

Background: Neighborhood contextual factors (e.g., socioeconomic disadvantage, structural racism) significantly influence fatal opioid overdose (OOD) disparities. Few studies have examined the association between fatal OOD and gentrification, where socioeconomic forces transform urban neighborhoods, often displacing earlier, usually poorer residents. This study assessed whether gentrification impacted neighborhood-level fatal OOD rates at two time points, enabling a cross-sectional analysis of neighborhood socioeconomic stressors.

Methods: Cook County Medical Examiner records of fatal OODs from 2019 (n=793) and 2022 (n=1264) were aggregated to Chicago Census tracts. Census tracts were classified as non-gentrifiable, gentrifiable, or gentrifying using the Freeman method with American Community Survey 5-year estimates (2014, 2017). We used negative binomial regression to estimate tract-level associations between gentrification status and neighborhood fatal OOD rate, adjusting for segregation and population density via complete case analysis.

Results: The neighborhood fatal OOD rate for gentrifying tracts was 37% higher than for non-gentrifiable tracts in 2019 and 24% higher in 2022 (2019: IRR=1.37, 95% CI=1.06-1.77; 2022: IRR=1.24, 95% CI=1.00-1.55). Neighborhoods with larger proportions of non-Hispanic Black residents experienced higher fatal OOD rates in both years (2019: IRR=0.48, 95% CI=0.41-0.55; 2022: IRR=0.37, 95% CI=0.32-0.42). Fatal OOD rate was not significantly associated with being gentrifiable in either year.

Conclusions: Gentrifying neighborhoods and neighborhoods with higher proportions of non-Hispanic Black residents experienced higher fatal OOD rates, emphasizing the role of structural inequities. Addressing neighborhood contextual factors and socioeconomic stressors, including gentrification and segregation, is critical for mitigating fatal OOD disparities.

Substance Use

Fentanyl Test Strip Use and Homelessness among People Who Use Drugs in Rhode Island

Leah Shaw* Julia Noguchi Yu Li Carolyn J. Park Jacqueline Goldman Leah C. Shaw Jane A. Buxton Scott E. Hadland Susan G. Sherman Katie B. Biello Brandon D.L. Marshall

Background

People experiencing homelessness (PEH) have been disproportionately affected by the overdose crisis in the United States. Housing insecurity and associated structural factors have been shown to pose barriers to engaging in harm reduction practices. Fentanyl test strips (FTS) can help people who use drugs (PWUD) avoid accidental overdose. This analysis assessed the association between recent homelessness and FTS use over 12 months among a cohort of PWUD who were part of the The Rhode Island Prescription Illicit Drug Study (RAPIDS).

Methods

We recruited 505 participants from September 2020-February 2023. Baseline data assessed correlates of past-month FTS use through bivariable and multivariable analyses. We used generalized estimating equations (GEE) to estimate the longitudinal association between past-month homelessness and FTS use at six time points.

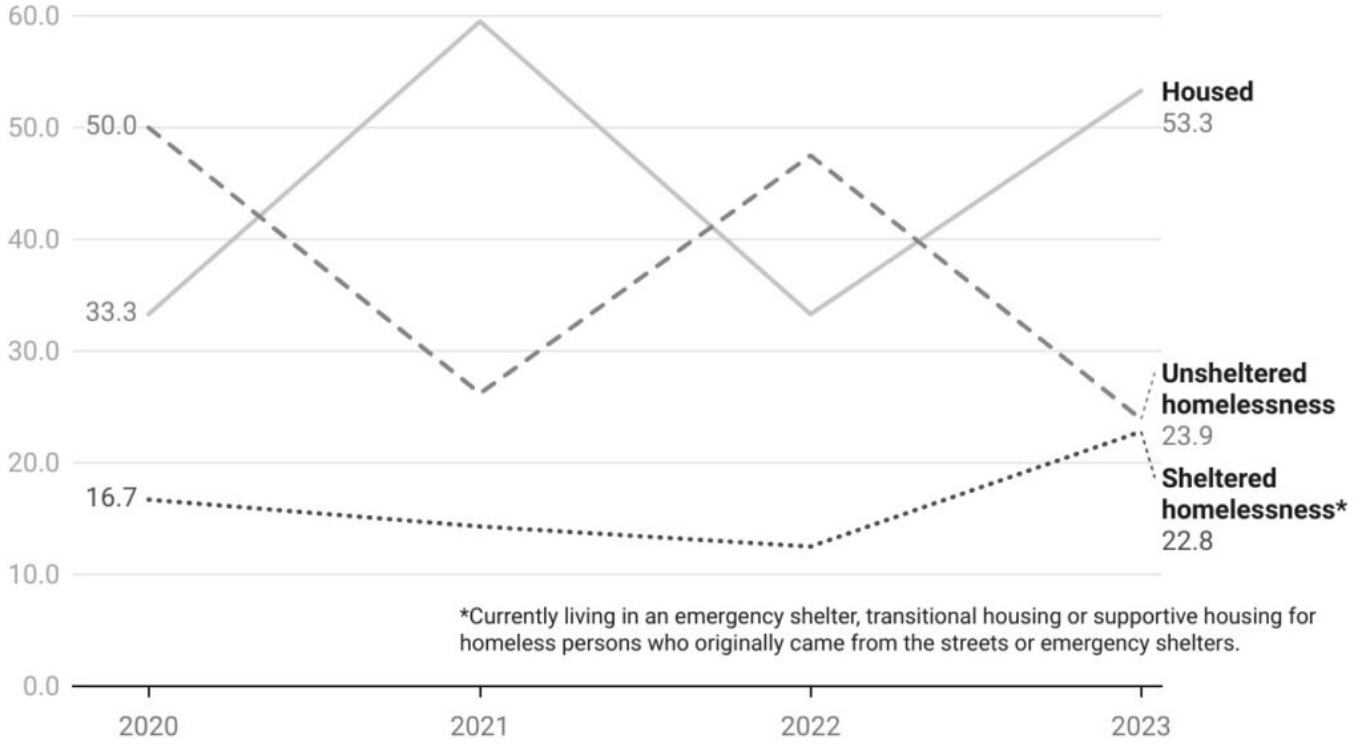
Results

At baseline, 297 (59%) participants had experienced past-month homelessness. Of those, 67 (22.6%) reported recent FTS use compared to 30 (14.4%) of those who were housed. In bivariable analysis, homelessness was positively associated with FTS use ($p<0.05$). A sensitivity analysis showed that people living in homeless shelters had consistently lower rates of FTS use across all four years. In multivariable GEE analysis, homelessness was not associated with FTS use, but regular use of crystal meth was positively associated with FTS use (aOR=2.12, 95% CI 1.43–3.13; p <0.001). The odds of FTS use in the entire sample in 2023 increased by 158% (aOR=2.58, 95% CI 1.27-5.25; $p<0.001$) compared to 2020.

Conclusions

We found that FTS use was feasible and acceptable among PEH, and that FTS use was positively associated with crystal meth use. Increased FTS use over time may be due to ongoing community-based education about FTS, improved access to harm reduction tools, and increased awareness of the proliferation of synthetic drugs in the illicit drug supply. Interventions tailored to people who are unstably housed, particularly those staying in shelters, and people who use stimulants are needed to help prevent fentanyl-involved overdoses.

Figure 1. Rates of FTS use among RAPIDS participants by housing status, 2020-2023 (Copy)



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Substance Use

Drug-induced homicide laws and drug overdose mortality in the United States, 2000-2022: A synthetic control analysis Bennett Allen* Bennett Allen Cale Basaraba Corey Davis Seungha Um Katherine Wheeler-Martin Samrachana Adhikari Magdalena Cerdá

Background: Drug-induced homicide laws (DIHLs) are a prominent and controversial criminal-legal response to the overdose epidemic. DIHLs target individuals who provide drugs that resulted in the unintended death of another person. Proponents of DIHLs often argue that they may reduce overdose death by deterring drug distribution. Critics argue that they may discourage help-seeking, mostly target people who use drugs and low-level drug sellers, and amplify racial inequities. Despite the increasing adoption of DIHLs, there is limited evidence of their impact on overdose mortality. From 2000-2022, 13 states enacted DIHLs.

Methods: We examined the effects of DIHLs on overdose mortality in 5 states—Alaska, Delaware, Kansas, Michigan, and Vermont—that enacted these laws from 2000-2022. Using an augmented synthetic control method, we analyzed state-level overdose mortality, demographic and economic data, and co-occurring policy data. Statistical inference was derived through permutation-based placebo testing and conformal inference to estimate effects across 5 post-DIHL years for each state. Sensitivity analyses considered traditional synthetic control methods and robustness to enactment dates. Analyses remain in progress for the 8 other states that enacted DIHLs from 2000-2022.

Results: DIHL enactment was not significantly associated with overdose mortality in any of the five states during the five years post-implementation. Estimated treatment effects were small, with acceptable pre-intervention model fit (RMSPE < 3.0). Preliminary sensitivity analyses confirmed these null findings.

Conclusions: DIHLs were not associated with changes in population-level overdose mortality in the states analyzed. Ongoing work will examine DIHL impacts in additional states. Future research should explore local-level effects of prosecutions under DIHLs and assess broader societal and equity implications to inform public health and criminal justice responses to the overdose crisis.

Substance Use

Overdose mortality among those engaged in opioid use disorder treatment in New York City Sean Locke* Sean Locke Gail Jette Nicole DAnna Hannah Johnson Jason Graham Chinazo O Cunningham

Overdose death risk is extremely high for those with opioid use disorder (OUD). Medication treatment is first-line OUD treatment, reducing the risk of overdose death by >50%. Other forms of OUD treatment vary in reducing overdose death. Few studies have examined the impact of different treatment modalities on overdose death. We assessed overdose death risk among those in OUD treatment using a retrospective cohort design.

We matched individuals receiving NYC-based OUD treatment data from the NYS Office of Addiction Services and Supports to overdose death records from the NYC Chief Medical Examiner (study period: 01/01/16-07/31/19). Target trial emulation was adopted to address preexposure covariates and align key time points. Cox proportional hazard model was used to estimate crude (cHRs) and adjusted hazard ratios (aHRs) with 95%CIs. Sex, age, race/ethnicity, housing, and employment were covariates in the adjusted model based on evidence from the literature and subject knowledge.

We identified 73,125 individuals receiving OUD treatment in NYC with 538 died of overdose during treatment. The annual overdose death rate was 39.6-48.5 per 10,000 individuals in the study period. Those reporting problematic alcohol use (cHR 2.2, 95%CI:1.8, 2.7) were more likely to experience overdose death compared to those without problematic alcohol use. In the adjusted model, those receiving medication-based treatment were significantly less likely to experience overdose death compared to other treatment modalities (aHR: 0.36 95%CI:0.3, 0.5).

We found that individuals engaged in medication-based OUD treatment had the lowest overdose death rate compared to other treatment modalities. Overdose prevention interventions and medication-based treatment may be particularly important for those with OUD and problematic alcohol use. Strategies to expand equitable access to medication-based OUD treatment are crucial to reducing overdose death risk among populations with OUD.

Substance Use

Association of non-fatal overdose surveillance data with concurrent and future overdose deaths in Rhode Island Alexandra Skinner* Alexandra Skinner Yu Li Benjamin D. Hallowell Claire Pratty William C. Goedel Bennett Allen John C. Halifax Alexandria Macmadu Jennifer Ahern Magdalena Cerdá Brandon D.L. Marshall

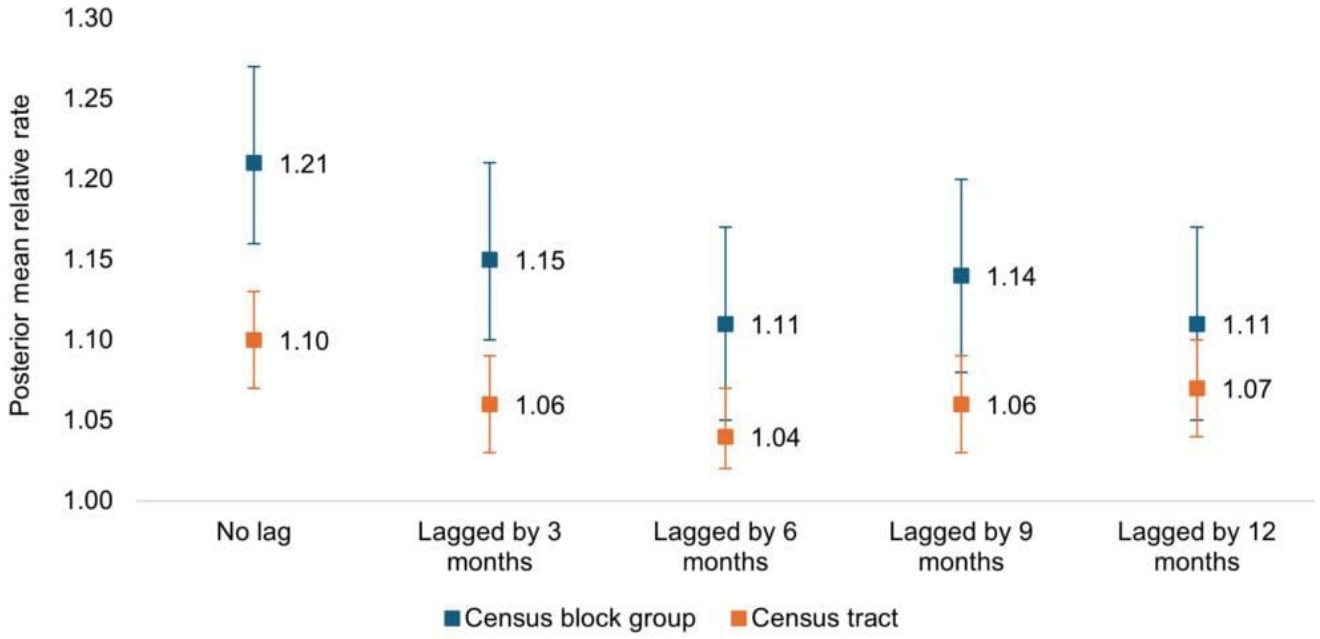
Given substantial reporting delays in overdose deaths, state health departments typically rely on non-fatal overdose data to inform rapid overdose response efforts. For instance, the Rhode Island (RI) Department of Health monitors emergency medical services (EMS) responses to suspected overdose events in near-real time to detect increases in overdose activity and to direct public health resources to the corresponding neighborhoods. However, there is limited understanding about whether EMS-attended non-fatal overdoses serve as a reliable proxy for fatal overdoses. We sought to evaluate the extent to which non-fatal overdose data were associated with concurrent and future overdose deaths in RI.

We aggregated non-fatal overdose data from EMS records (2019–2022) and fatal overdose data from the RI State Unintentional Drug Overdose Reporting System (2020–2022) in 3-month intervals at both census block group (CBG) and census tract (CT) levels. We estimated rates of fatal overdose, relative to non-fatal overdose lagged by 0, 3, 6, 9, and 12 months, using negative binomial regression models offset by population size. We applied integrated nested Laplace approximation, a Bayesian spatiotemporal approach that allows for spatial autocorrelation and small area estimation.

At the CBG level, each additional EMS-attended non-fatal overdose was associated with rates of fatal overdose that were 11–21% higher than expected in concurrent or future 3-month intervals. However, at the CT level, we observed diminished predictive utility; each additional non-fatal overdose was associated with fatal overdose rates just 4–10% higher than expected (**Figure 1**). Forthcoming analyses will explore these associations at town and regional levels and in monthly intervals.

Spikes in non-fatal overdoses were most strongly associated with elevated overdose mortality in concurrent and near-concurrent periods. At small geographies, non-fatal overdose activity may be indicative of fatal overdose burden.

Figure 1. Posterior mean relative rates between EMS-attended non-fatal overdose, lagged by 0–12 months and aggregated in 3 month intervals, and fatal overdose rates, Rhode Island census block groups and census tracts, 2020–2022

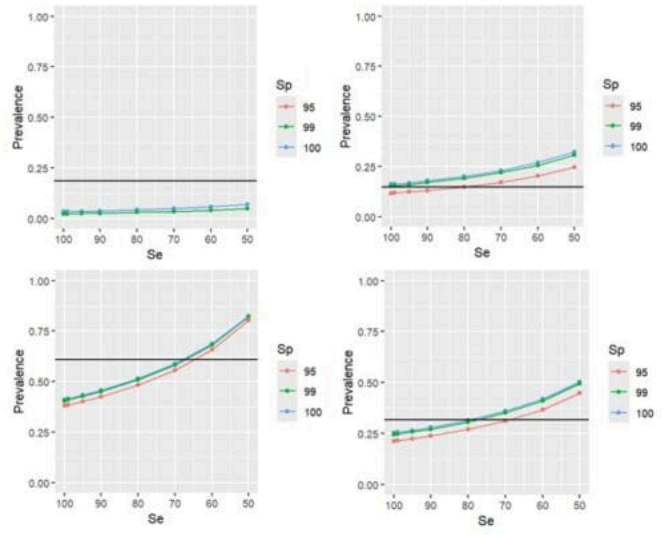


Injuries/Violence

Addressing measurement error in IPV self-report data using multiple overimputation and multidimensional quantitative bias analysis Irina Bergenfeld* Irina Bergenfeld Cari Jo Clark Robin A. Richardson Regine Haardörfer Alexandria R. Hadd Charis Wiltshire Timothy L. Lash Angela M. Bengtson

Intimate partner violence (IPV) is an important global health issue for which measurement error, including underreporting, limits public health action. Although most national IPV prevalence estimates come from general health surveys like the Demographic and Health Surveys (DHS), such data are presumed to underestimate prevalence compared to violence-focused surveys (VFS). Using VFS conducted in the same country and year (±1) as validation data, we explored two methods of bias adjustment to address measurement error in DHS prevalence estimates. In multidimensional bias analysis (MBA), we directly adjusted summary prevalence estimates, using a range of possible sensitivities (10%-100%) and specificities (95%-100%) to elucidate their reasonable bounds. In multiple overimputation (MO), we probabilistically overimputed all IPV observations, incorporating prior information on measurement error, and combined prevalence estimates over 50 MO iterations. MBA revealed that an assumption of 95% specificity resulted in negative prevalence estimates in some cases, confirming that false positives are likely negligible (Figure). Reasonable sensitivities varied considerably across countries and IPV types, likely due to differences in the number of items used to assess IPV. MO-adjusted estimates were similar to VFS estimates, except when unadjusted DHS estimates were <5% and highly discrepant. In surveys assessing physical IPV using several items, DHS and VFS estimates were comparable, while DHS estimates for sexual and emotional IPV were lower. Past-year estimates were less discrepant than lifetime estimates, suggesting that recall bias may be a factor in underreporting. This study examines the nature and scope of measurement error due to IPV underreporting in specific contexts where external information exists, highlighting the need for more accurate IPV assessment using multiple items per domain and for internal validation studies to be incorporated into large-scale surveys.

Figure. Adjusted prevalence estimates for lifetime physical IPV vs sensitivity at 95%, 99%, and 100% specificity (clockwise from top left: Albania, Cambodia, Peru, Egypt)



Black horizontal lines are prevalence estimates from violence-focused surveys

Injuries/Violence

Assessing the role of mental health symptoms in the relationship between sexual minority status and intimate partner violence in women Megan Souza* Megan Souza

Despite evidence that sexual minority women—lesbian, bisexual, queer or otherwise not heterosexual—experience higher rates of intimate partner violence than heterosexual women, research has only begun to explore the mechanisms for this violence. The Minority Stress Model as a theoretical framework can help to explain these higher rates, suggesting that sexual minority women experience stress caused by structural homophobia and sexism that makes them more vulnerable to perpetrating or experiencing intimate partner violence. To explore this theory further, we will utilize causal inference methods to simulate the impact of reducing mental health symptoms on the relationship between sexual minority status and intimate partner violence victimization. Using the National Longitudinal Study of Adolescent to Adult Health data, we will conduct a mediation analysis with controlled direct effects. First, we will analyze a model measuring the impact of a 100% reduction in adolescent depression and anxiety symptoms on the relationship between sexual minority status and intimate partner violence in young adulthood. We will also analyze models using stochastic mediation analysis, exploring the impact of a 15% and 30% reduction in symptoms—simulating a more realistic opportunity for prevention. We hypothesize that a reduction in symptoms will be associated with a reduction in intimate partner violence victimization for sexual minority women and that a smaller reduction in symptoms will be associated with a smaller reduction in violence. This study will provide insight into the causal role that mental health symptomology may play in the pathway between marginalized identity and violent victimization. Results may provide evidence for enhancing mental health services for sexual minority women as means of reducing the risk of intimate partner violence.

Injuries/Violence

Within-Person Associations Between Experiences of Violence and Victimization with Alcohol and Marijuana Use Among College Students Chloe Wilson* Marie-Claude Couture Chloe Wilson Erin Grinshteyn Rayna E Gasik Katherine P Theall

Background: Experiences of victimization and violence have been associated with substance use among young adults, but the literature assessing causal associations is limited. We aim to assess within- and between-person associations between daily experience of victimization and violence with alcohol and marijuana use among college students.

Methods: An ecological momentary assessment (EMA) study was conducted among 218 college students aged 18-25. Daily experiences of victimization (discrimination, bullying, microaggressions), violence (verbal threats, physical threats, or sexual assault), alcohol and marijuana use were assessed three times a day for 28 days. Mixed-effects logistic regression models were used to examine the effects of victimization and violence on alcohol and marijuana use, controlling for race, gender, sexuality, and time of week.

Results: Within-person results indicate that students experiencing bullying on a given day were at a greater risk of using marijuana that day (1.48; 95% CI: 0.09-2,86). Experiencing microaggressions on a given day was associated with an increased risk of drinking (0.82; 95% CI: 0.33-1.30) and marijuana use (1.07; 95% CI: 0.27-1.87). Those who experienced discrimination on a given day had an increased risk of drinking only (1.25; 95% CI: 0.39-2.1). Experiencing any form of victimization on a given day was associated with increased alcohol use (1.61, 95% CI: 0.98-2.24) that day. Those who experienced any form of violence on a given day were more likely to drink alcohol (0.89, 95% CI: 0.45 -1.33) and use marijuana (0.98, 95% CI: 0.24-1.73). Between-person associations were not statistically significant for any of the above models.

Conclusion: Young adults are more likely to use alcohol and marijuana on days when they experience certain forms of violence and victimization. Better understanding the consequences of experiencing violence or victimization on substance use could help target interventions for young adults.

Injuries/Violence

Social network analysis on sexual violence attitudes and behaviors among socially connected youth from communities across California Sabrina C. Boyce* Sabrina C. Boyce Holly Shakya Anna Hazlett Ricardo Vera Monroy Emma Jackson Jay G. Silverman

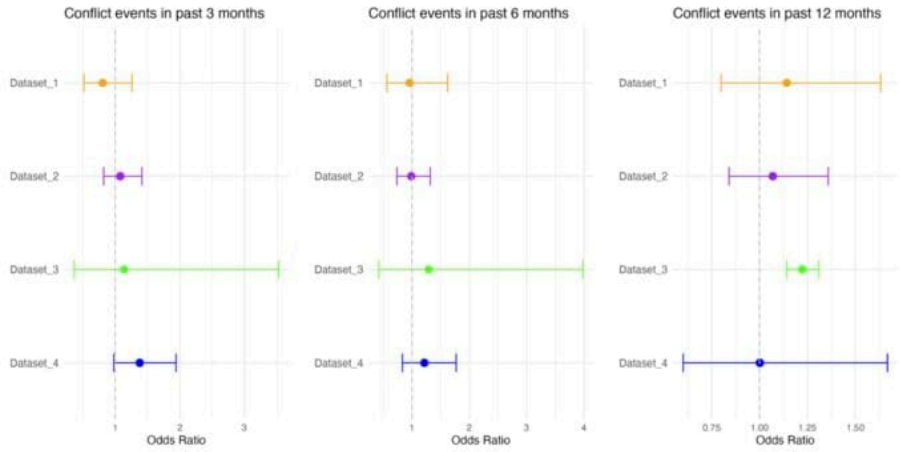
This research aims to illuminate how sexual violence (SV)-related attitudes and behaviors cluster among socially connected youth to understand the utility and potential importance of social network-based violence prevention. Social network data were collected from diverse youth program participants from 22 community-based organizations across California, 11 of which were implementing a community-led, community mobilization SV prevention program called Close to Home and 11 of which were implementing 4-H Youth Development Programs, and two layers of their social networks (n=1001; ages 14-24). These data were collected for the purposes of baseline assessment of a 24-month cluster-matched control evaluation of the Close to Home model, funded by CDC and undertaken in collaboration with the California Department of Public Health. Using this cross-sectional baseline data from program participants and their nominated peers, we used dyadic generalized estimating equations to understand the level to which socially connected peers hold attitudes and behave in similar ways related to SV. On average, nominating youth successfully recruited 1.6 of their close peers to participate in the survey. Statistically significant associations exist between nominators and their nominated peers across the full range of SV attitudes ($\beta=0.29$, $p=0.001$), positive bystander behavioral intentions ($\beta=0.59$, $p<0.001$), positive bystander behaviors ($\beta=0.22$, $p=0.01$), engagement in SV prevention ($\beta=0.58$, $p<0.001$). Results provide evidence of clustering of SV attitudes and behaviors across socially connected peers, suggesting that peer attitudes and behavior is influential on individual attitudes and behavior and that the effects of SV intervention may transit across peer networks. These results suggest that youth social networks and the normative attitudes and behaviors within them could be strategic to target for efficient and effective SV prevention.

Injuries/Violence

Population health in armed conflict: How to conceptualize and measure a prominent threat to global health Maya Luetke* Maya Luetke Signe Svallfors Elizabeth Heger Boyle

The humanitarian impact of armed conflict remains a significant international issue, with an estimated 2 billion people residing in fragile or conflict-affected settings. Despite growing research on armed conflict and its impact on human populations, few studies have explicitly considered the methods necessary to assess such relationships (i.e., how to use disaggregated and granular conflict data, measure and operationalize conflict, and other potential considerations). In this study, we identify key methodological considerations for conducting research on the effect of armed conflict on population health, including how data structures, study design, and methodological decisions might impact conclusions. First, we discuss particular characteristics of existing armed conflict datasets, such as identifying and dealing with the spatial and temporal imprecision of conflict events within such datasets. We demonstrate how different data and measurement choices may result in spatial misclassification, bias, and spurious conclusions. Lastly, we provide an empirical example using armed conflict data from the Uppsala Conflict Data Program (UCDP) and combining it with health data from the Demographic and Health Survey (DHS) data in Nigeria. We quantify the impact of armed conflict on current contraceptive use and demonstrate how different measurement and data choices impact the point estimate of the relationship between our exposure and outcome. We find that measurement choices do indeed impact the magnitude and significance of the point estimates of the association between armed conflict and current contraceptive use among women of reproductive age (15-49) in our empirical example (Figure 1). Our findings reinforce the importance of deliberate methodological decision-making and transparency in describing such decisions (including the rationale) so that future research can build reliable and comparable evidence on the impacts of armed conflict on population health. In this project, we recommend concrete strategies – and an empirical worked example – for employing such data for public health research.

Figure 1. Forest plot of models of the association between *binary* armed conflict exposure and current contraceptive use



Note: Dataset_1 = Precision level 1: Aggregated at DHS cluster, Dataset_2 = Precision level 2: Aggregated at DHS cluster, Dataset_3 = Precision level 3: Aggregated at Admin 2 boundary, and Dataset_4 = Precision level 4: Aggregated at Admin 1 boundary

Injuries/Violence

Blast Traumatic Brain Injury and Long-Term DNA Methylation in Select Immune Gene Promoter Regions and Repetitive Elements: A Repeated Measures Case-Control Study Among U.S. Military Service Members Jordan McAdam* Jordan McAdam Jennifer Rusiecki Ann Meyer Zygmunt Galdzicki Celia Byrne Louis French

Background: Blast traumatic brain injury (bTBI) is a major source of morbidity and mortality, including neurological deterioration, among military service members (MSM) deployed to conflict regions. Evidence suggests that TBI may induce an immune response, however few studies evaluated DNA methylation (DNAm) patterns of immune-related genes associated with TBI. We evaluated differences in DNA methylation (DNAm) at various loci on inflammatory response genes measured in uniquely available pre- and post-deployment serum samples from U.S. MSM with and without bTBI.

Methods: We obtained samples from the Department of Defense Serum Repository from 150 bTBI cases (93 mild; 57 moderate/severe) and 50 controls, frequency matched by age, sex (male, female), and race (White, Black, Other). Both cases and controls were <40 years of age at their first deployment to Afghanistan or Iraq. DNAm was quantified via Pyrosequencing for nine inflammatory response genes and two markers of global methylation. We conducted multivariate ANOVA to compare the adjusted mean differences in DNAm from pre- to post-deployment between cases and controls at each locus.

Results: The mean (standard deviation) time between cases' diagnosis and their post-deployment serum was 315.8 (261.1) days. For IL8 gene (CXCL8) loci, the statistically significant differences in DNAm from pre to post-deployment samples were larger among controls than for moderate/severe cases ($p<0.05$). In contrast, for one IL10 gene locus, the statistically significant difference in DNAm from pre to post-deployment samples was larger among moderate/severe cases than controls. No other clear or consistent trends in DNAm were noted for loci of other genes.

Conclusions: These findings suggest differences in DNAm at some loci of IL8 and Il10 genes may be associated with bTBI injury. These results need to be evaluated in other studies that are able to account for treatment and blast exposure training.

Disclaimer: The opinions and assertions expressed herein do not reflect the official policy or position of the Uniformed Services University of the Health Sciences, Henry M. Jackson Foundation for the Advancement of Military Medicine, Inc., or the Department of Defense.

Perinatal & Pediatric

Heat stress and placental abruption: A space–time stratified case-crossover study in Japan
Shuhei Terada* Shuhei Terada Hisaaki Nishimura Naoyuki Miyasaka Takeo Fujiwara

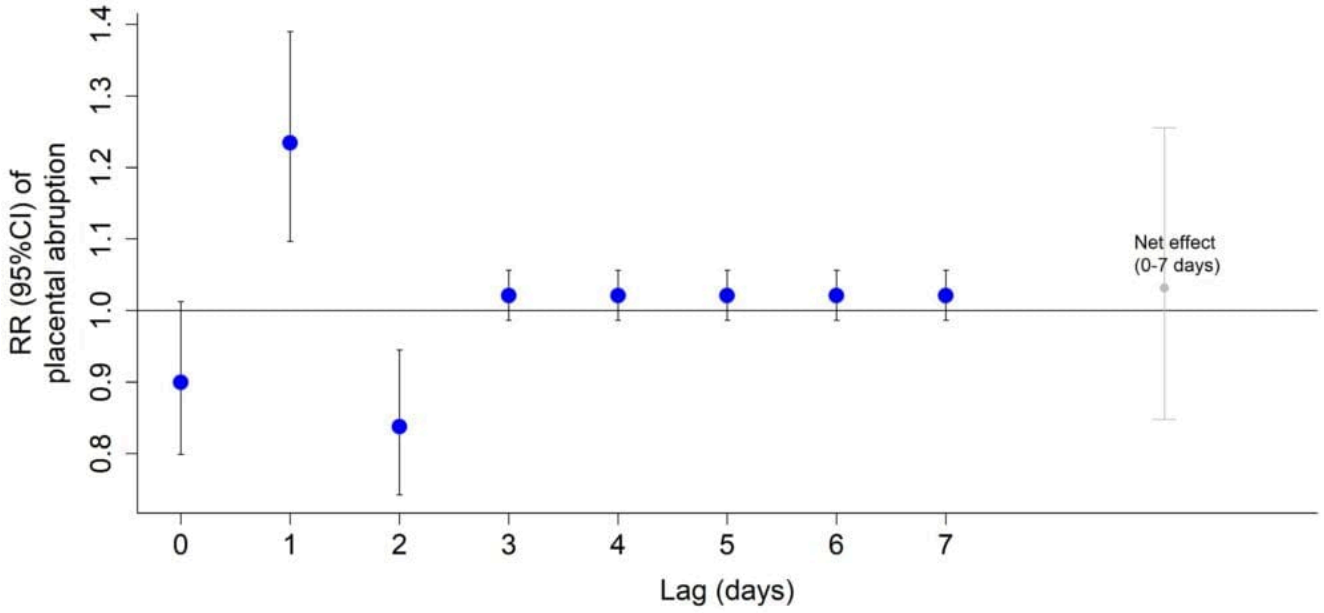
Background: Previous studies have highlighted associations between heat stress during pregnancy and perinatal complications such as preterm birth. However, surprisingly little evidence exists regarding environmental triggers of placental abruptions, despite its significant impact on maternal and fetal mortality and morbidity.

Objective: To examine whether heat stress, measured by WBGT (which incorporates temperature, humidity, wind speed, and solar radiation), is associated with an increased risk of placental abruption within the following 7 days.

Methods: We used a space–time-stratified case-crossover design with data from the Japan Perinatal Registry Network, covering daily placental abruption cases in 11 regions during the warm season (June–September) from 2011 to 2020. Heat stress was defined as daily maximum WBGT exceeding the 95th percentile of regional distributions, with data from 11 observatories across Japan. Associations were assessed using quasi-Poisson regression with distributed lag linear models over a lag period of 0–7 days. Stratified analyses were performed based on gestational week (preterm vs. term pregnancies), hypertensive disorders of pregnancy (HDP), and small for gestational age (SGA).

Results: Among 8,613 cases of placental abruption identified, heat stress was associated with an increased risk of placental abruption on lag 1 (RR: 1.23, 95% CI: 1.11, 1.39). The risk decreased on lag 2 (RR: 0.84, 95% CI: 0.74, 0.95), resulting in negligible cumulative risk over lag 0–7 due to counterbalancing effects. Similar associations were observed in preterm and term pregnancies. Higher risks on lag 1 were observed in women with HDP (RR: 1.57, 95% CI: 1.31, 1.88), and in those with SGA infants (RR: 1.47, 95% CI: 1.26, 1.73).

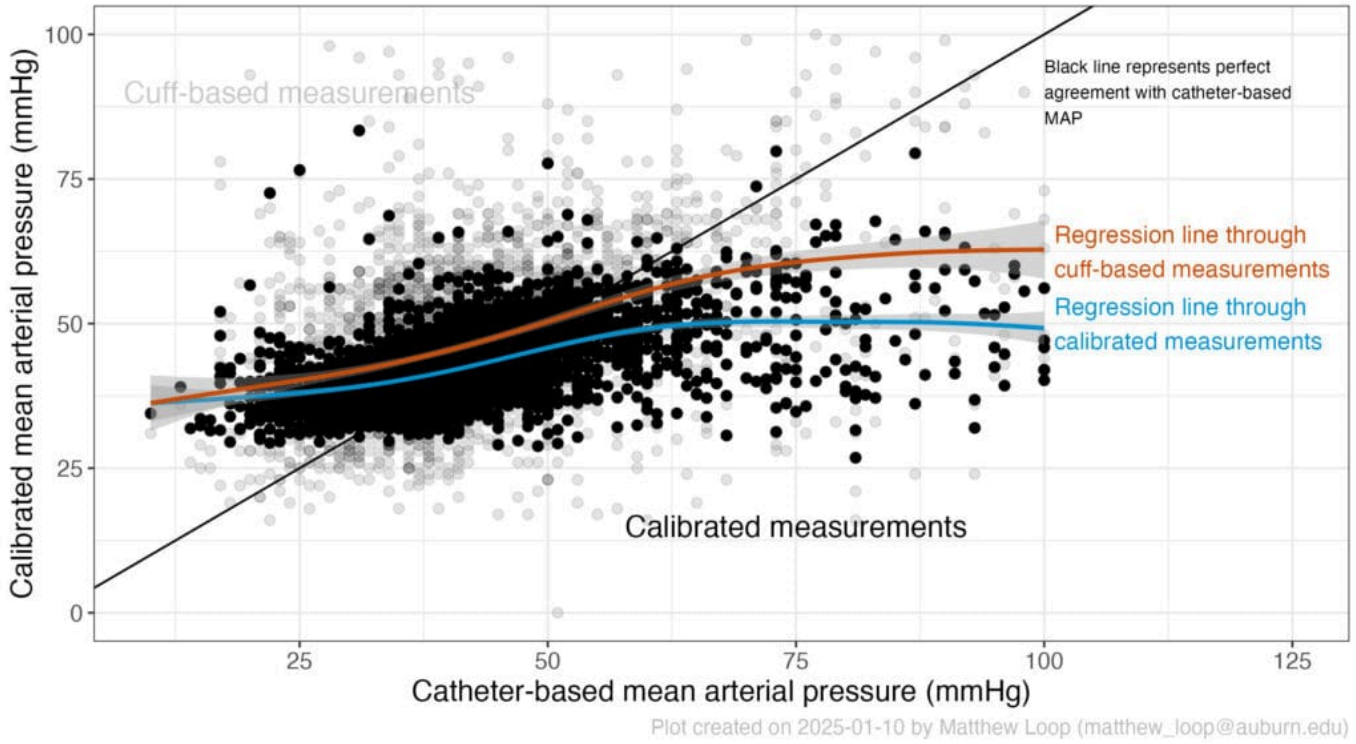
Conclusion: Heat stress during pregnancy was associated with an increased risk of placental abruption the day after exposure, suggesting a short-term displacement effect, particularly in women with HDP or SGA infants.


RR (95%CI) of placental abruption
0.8
0.9
1.0
1.1
1.2
1.3
1.4
0
1
2
3
4
5
6
7
Lag (days)
Net effect
(0-7 days)

Perinatal & Pediatric

Reducing the error in neonatal blood pressure measurements: A calibration study Matthew Loop* Matthew Loop Jieun Park Sarah C Lotspeich Daniel I Feig

Blood pressure is an important vital sign for neonates. Low blood pressures can lead to poor organ perfusion and dangerous intestinal injury, but high blood pressures can also damage the eyes or brain. Despite the potentially life-threatening outcomes of low or high blood pressures, most neonates have their blood pressures measured using an oscillometric cuff, a method known to have large measurement error in routine clinical use. However, a small subset of the sickest neonates have arterial catheters that produce better blood pressure measurements. Some of these neonates also have concurrent cuff-based measurements. Therefore, we conducted a retrospective, EHR-based calibration study of mean arterial pressure (MAP) measurements in a large, academic neonatal intensive care unit. We evaluated linear regression (with and without a spline for cuff-based MAP) and a random forest with 1,000 trees to calibrate the cuff-based MAPs to the catheter-based MAPs, using neonatal and linked maternal covariates. Among 12,966 paired catheter-based and cuff-based MAP measurements across 1,528 neonates, a linear regression model trained on a random 80% subsample: (i) reduced the error of the cuff-based MAPs by 23% from 14.9 mmHg to 11.5 mmHg in the test sample; (ii) produced a calibrated MAP that was closer to the catheter-based MAP than the cuff-based measurement 64% of the time; and (iii) was on average 2.6 mmHg closer to the catheter measurement than the error-prone cuff one. There were also limitations in how well the model calibrated high cuff-based MAP measurements. For catheter-based MAPs above 50 mmHg, the calibration model underestimated these MAPs. (See Figure 1.) Future work will evaluate a broader range of supervised learning methods, identify potentially missing variables that can help improve the underestimation at high MAPs, and transport the calibration model to a population with only cuff-based MAPs available, a population of high clinical importance.



Perinatal & Pediatric

Association between severe maternal morbidity and cerebral palsy in children: A population-based birth cohort study Asma M. Ahmed* Asma Ahmed Bénédicte Driollet Emmalin Buajitti Jennifer A. Hutcheon Laura Rosella Seungmi Yang

Background

Severe maternal morbidity (SMM) has been linked to perinatal complications, but the evidence on associations with children's neurodevelopmental disorders is unclear. We assessed associations between SMM and cerebral palsy (CP) in children.

Methods

A longitudinal cohort study of all live births in Ontario, Canada, between 2003 and 2019 followed up through 2020. SMM was identified from inpatient or emergency department diagnoses during the index pregnancy or postpartum (20 weeks gestation to 42 days postpartum) based on validated algorithms, and CP was defined as a single inpatient or 2 or more outpatient diagnoses at least two weeks apart between birth and the end of follow-up (age 1-17 years). We estimated crude and adjusted associations using Poisson regression models.

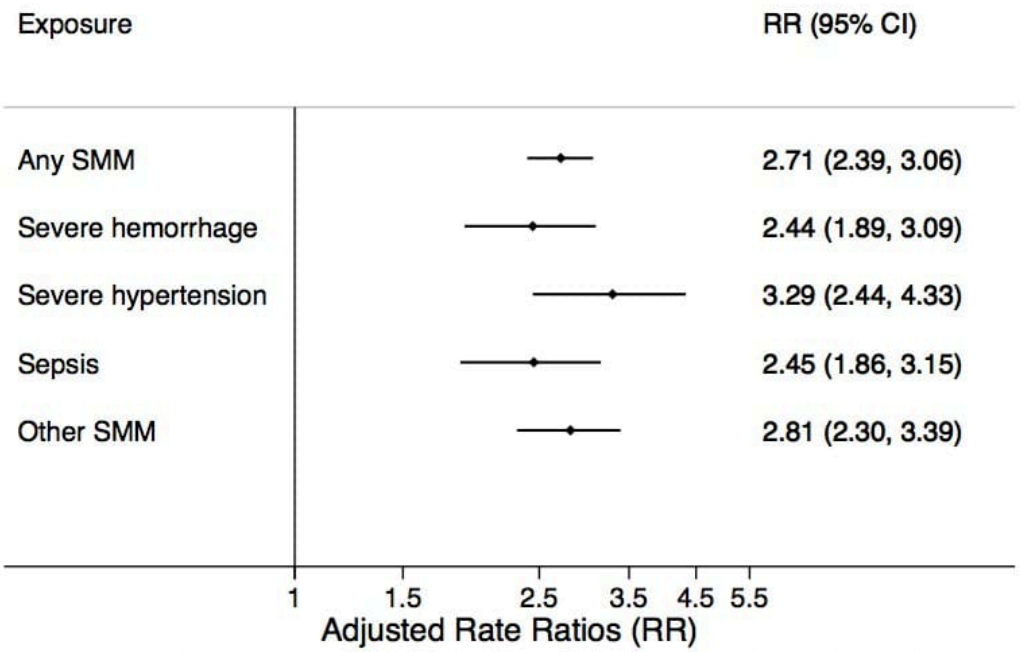
Results

Of 2,136,816 children included, 41,396 (2%) were exposed to SMM. In a median follow-up period of 9.5 years (IQR 5.2-13.7), 5,352 children were diagnosed with CP ((272 CP cases (0.7%) exposed to SMM). The average annual CP incidence was 7.5 per 10,000 child-years in those exposed to SMM and 2.5 per 10,000 in the unexposed. Children of mothers with SMM had an increased risk of CP (RR: 2.71 (95% CI: (2.39-3.06), adjusted for maternal sociodemographic and clinical factors). All SMM subtypes were associated with increased risks of CP, with the strongest associations observed for severe pre-eclampsia, HELLP syndrome, and eclampsia (RR: 3.29 (2.44-4.33), followed by other SMM subtypes (RR: 2.81 (2.30-3.39)) (**Figure**).

Conclusion

In this population-based study of over 2 million births, severe maternal morbidity was associated with increased risk of cerebral palsy. This risk was observed across major severe morbidity subtypes, including hypertensive disorders, hemorrhage, and sepsis. These findings highlight the potential benefits of optimizing maternal health and may support the need for early monitoring of children exposed to these adverse maternal events to detect early signs of cerebral palsy.

Associations of severe maternal morbidity (SMM) and subtypes with cerebral palsy in children



Adjusted for maternal age, parity, pre-pregnancy comorbidities, receiving Ontario drug benefit, immigration status, rurality, area-based deprivation and ethnic diversity, neigborhood income, child's sex, and birth year

Perinatal & Pediatric

Validation of ICD-10 diagnosis codes for antepartum iron-deficiency anemia Anna Booman* Anna Booman Sara Siadat Brian Bateman Irogue Igbinosa Elliott Main Deirdre J. Lyell Cecilia Leggett Stephanie Leonard

Iron deficiency anemia during pregnancy increases risk of adverse perinatal health outcomes, with stark racial disparities: prevalence is more than twice as high in Black compared with White pregnant individuals. Modern epidemiologic research largely relies on International Classification of Diseases, Clinical Modification, 10th Revision (ICD-10) diagnosis codes to identify individuals with antepartum anemia, yet their validity remains unknown. Our objective was to assess the validity of ICD-10 codes for antepartum anemia compared with the diagnostic gold standard of hemoglobin or hematocrit measurements. We used commercial insurance claims data from the Merative™ MarketScan® Research Database for pregnancies during 2018-2022. Those with hereditary anemia (e.g., sickle cell) were excluded. Antepartum anemia was defined using clinically recommended hemoglobin and hematocrit thresholds (<11.0 g/dL and <33% in the first and third and <10.5 g/dL and <32% in the second trimester, respectively). We calculated Cohen's kappa, sensitivity, specificity, positive predictive value, and negative predictive value of the ICD-10 codes. Among 70,752 pregnancies, 30.2% had antepartum anemia based on hemoglobin and hematocrit values and 12.0% had at least one ICD-10 diagnosis code indicating antepartum anemia. Cohen's kappa between anemia identified through laboratory values and ICD-10 codes was 0.205 (95% confidence interval [CI]: 0.196, 0.215). Sensitivity of the ICD-10 codes was 0.238 (95% CI: 0.233, 0.244); specificity was 0.932 (95% CI: 0.929, 0.934); positive predictive value was 0.602 (95% CI: 0.591, 0.612); and negative predictive value was 0.739 (95% CI: 0.735, 0.742). These findings suggest low sensitivity, but high specificity, of ICD-10 diagnosis codes for antepartum anemia. Researchers should be aware of the limitations of relying solely on ICD-10 codes for antepartum anemia and consider conducting bias analyses when hemoglobin and hematocrit measurements are unavailable.

Perinatal & Pediatric

The association between sleeping time and onset of puberty: An application of the parametric G-method Changwoo Han* Changwoo Han

Globally, the onset of puberty is occurring earlier, and early onset of puberty is associated with children's mental health and health outcomes in adulthood. Therefore, identifying modifiable risk factors that can influence puberty onset is an important research priority. This study investigated how sleep duration affects the onset of puberty, represented by menarche in girls and first nocturnal emission in boys.

Data were obtained from the Korea Children and Youth Panel Survey 2010, tracking fourth-grade elementary school students for six years. A total of 915 boys and 806 girls were included in the analysis. The parametric g-formula was applied to estimate the probability of experiencing menarche and first nocturnal emission according to sleep duration. The analytical model was adjusted for the child's age, parental education level, residential area, stress levels, physical activity, height, weight, and household income.

Results showed that shorter sleep duration was associated with earlier onset of menarche and first nocturnal emission. Without any intervention, the cumulative proportions of boys and girls experiencing first nocturnal emission and menarche by the 7th grade were 16% and 58%, respectively. When sleep was restricted to 5 hours, the cumulative proportions increased to 23% (95% CI: 12–39) for nocturnal ejaculation and 70% (95% CI: 59–79) for menarche. In contrast, when sleep was extended to 9 hours, the proportions were 15% (95% CI: 13–18) and 55% (95% CI: 50–60), respectively. Compared to the non-intervention group, the risk of first nocturnal emission in the 5-hour sleep group was 1.45 (95% CI: 0.75–2.37), and the risk of menarche was 1.21 (95% CI: 1.03–1.39). In the 9-hour sleep group, the risk was 0.95 (95% CI: 0.88–1.01) for nocturnal emission and 0.95 (95% CI: 0.92–0.99) for menarche.

This study suggests that the timing of puberty onset may be modifiable based on children's sleep duration.

Big Data/Machine Learning/AI

Digital Solutions for Loneliness: Exploring Heterogeneous Effects of Virtual Communication Using Machine Learning DAISUKE KATO* DAISUKE KATO Ichiro Kawachi Atsushi Nakagomi Katsunori Kondo Koichiro Shiba

Background:

Loneliness among older adults negatively affects health and quality of life, increasing risks of depression, cognitive decline, and mortality. Evidence suggests loneliness's impact varies by demographic and socioeconomic (SES) factors. This study examined whether internet-based virtual communication reduces loneliness and explored potential group differences.

Methods:

Data were analyzed from the Japan Gerontological Evaluation Study (JAGES) using 2019 and 2022 surveys. Participants included 4,807 adults aged 65+ who were independent in daily activities (ADL). The primary exposure was virtual communication (e.g., email, Zoom) between 2021 and 2022, and the outcome was loneliness, measured by the UCLA Loneliness Scale. Covariates included demographic and health factors from 2019, such as age, sex, marital status, baseline health, and in-person interaction frequency.

The average treatment effect (ATE) of virtual communication on loneliness was estimated using Targeted Maximum Likelihood Estimation (TMLE). Causal Forest analysis assessed variations across demographic and SES factors.

Results:

Of 4,807 participants, 2,152 engaged in virtual communication, and 2,655 did not. Virtual communication was associated with reduced loneliness scores (ATE: -0.120, 95% CI: -0.213, -0.026). Causal forest analysis showed 86.3% of participants using virtual communication showed improved loneliness scores. Significant heterogeneity was observed ($p = 0.006$). The Best Linear Predictor estimate was -0.12 (SE = 0.05, $p = 0.012$), suggesting factors like age and social activity levels influenced effects. The mean forest effect (-0.08, $p < 0.001$) supported the overall association, while the differential forest effect (0.12, $p < 0.001$) highlighted group differences.

Conclusion:

Virtual communication is associated with reduced loneliness in older adults, with variations across groups. These findings underscore the potential of digital technologies to address loneliness in aging societies.

Big Data/Machine Learning/AI

Using machine learning to identify novel predictors of Down syndrome Alzheimer dementia

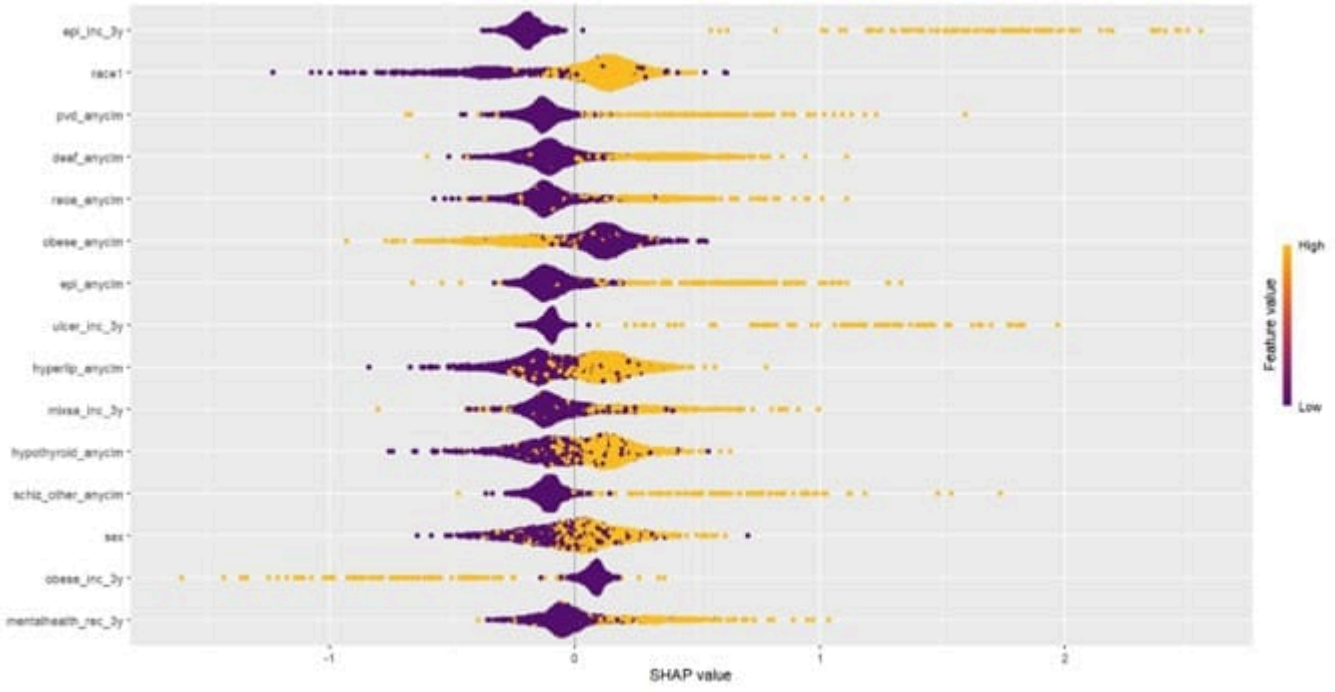
Salina Tewolde* Salina Tewolde Anthony Joseph Rosellini Amy Michals Brian Skotko Juan Fortea Jennifer Weuve Marcia Pescador Jimenez Yorghos Tripodis Eric Rubenstein

Background: Down syndrome Alzheimer Dementia (DSAD) is the leading cause of mortality for people with Down syndrome (DS), with a majority experiencing DSAD during their lifetime. In the general population, several conditions are associated with Alzheimer dementia; people with Down syndrome are at high risk for these conditions. Our goal was to use machine learning models to identify predictors of incident DSAD.

Methods: Data were from a cohort of >130,000 Medicaid- and Medicare-enrolled adults with DS in the US from 2011-2019. We identified DSAD through established Alzheimer dementia algorithms. We r We explored 60 co-occurring conditions a priori selected by a team of clinical experts, determined their onset in relation to the index date, ae. We trained an extreme gradient boosting model to predict incident DSAD in 80% of the observations and tested model performance in the 20% hold-out sample.

Results: Our sample included 128,231 adults, of whom 46% developed DSAD. I. Based on the machine learning model, top predictors of incident DSAD included: epilepsy three years before index date; Black race, and ever having a claim for Peripheral vascular disease, or deafness. Model discrimination was good AUC = 0.82, [0.81-0.83]

Conclusion: Unique DSAD predictors include conditions associated with AD dementia and those common in DS. Identifying them can enable earlier diagnosis through DSAD risk scores from claims data.



Big Data/Machine Learning/AI

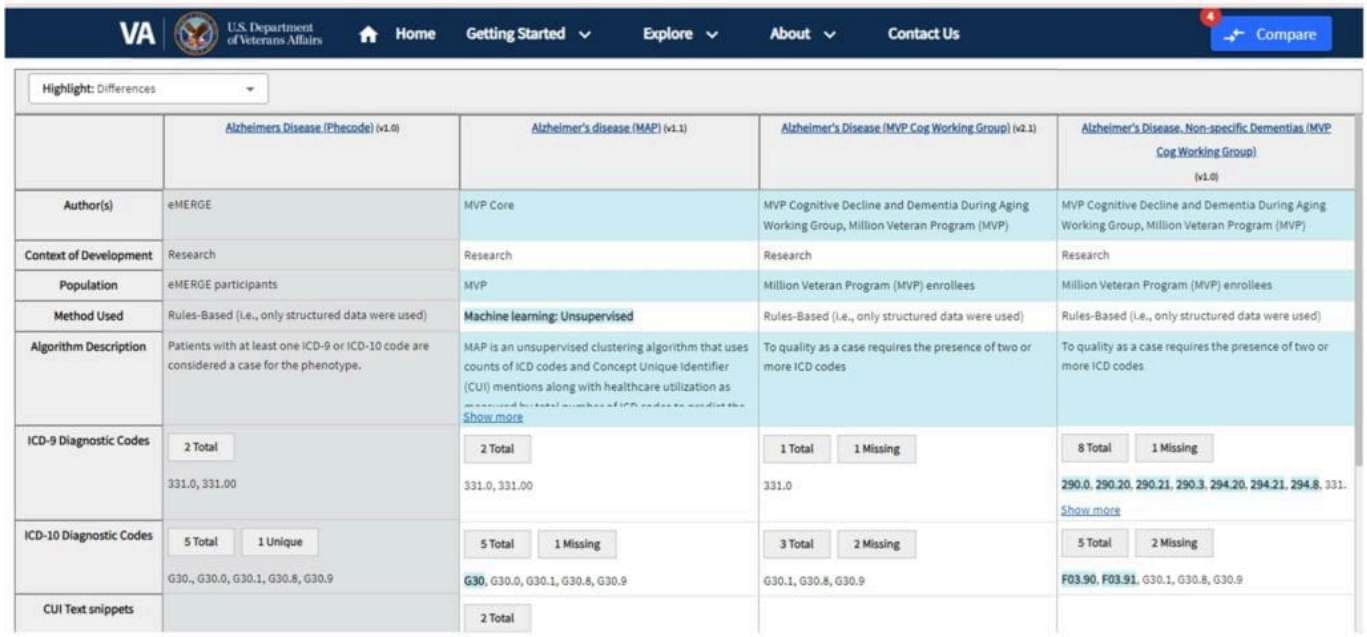
Utilizing CIPHER to identify and compare Alzheimer's Disease Phenotypes: Streamlining EHR-Based Phenotype Discovery and Application Ashley Galloway* Ashley Galloway Vidisha Tanukonda Connor Melley Monika Maripuri Yuk-Lam Ho Jacqueline P. Honerlaw Kelly Cho

Alzheimer's Disease (AD) is one of the most prevalent neurodegenerative disorders, and leading cause of dementia in the United States (US). Due to its complex pathophysiology and symptomatology, significant challenges exist in accurately identifying individuals with AD. This is further complicated by variations in electronic health record (EHR) systems and documentation. These challenges often lead to inconsistency in definitions and barriers to scientific progress. The Centralized Interactive Phenomics Resource (CIPHER) phenotype library provides solutions to these challenges by allowing for comparison of up to seven different phenotypes, while ensuring each definition contains enough information for replication.

We utilized CIPHER's phenotype comparison tool to evaluate and select four computable AD definitions: three rules-based definitions using ICD codes and one algorithm utilizing ICD codes and text strings. Details regarding these phenotypes can be found on CIPHER by navigating to phenomics.va.ornl.gov and searching for the full phenotype names shown in Figure1A. All four algorithms were applied to data from the US Department of Veterans Affairs and validated against 100 gold-standard labels derived from clinician chart review. Performance metrics were calculated for each definition and deposited into CIPHER to promote interoperability and reuse (Figure1B).

Due to variation in project goals and resources, some users may prefer a definition that maximizes sensitivity, while a probabilistic definition may be more suitable for others. CIPHER provides an opportunity to enhance scientific knowledge by streamlining algorithm evaluation. By enabling users to report validation in multiple datasets, CIPHER also facilitates interoperability of definitions. This collective approach can also expedite understanding of multifactorial diseases such as AD for which limitations in diagnosis, detection, and treatment exist.

1A: Phenotype comparison tool, evaluating four computable phenotype definitions



	Alzheimers Disease (Phecode) (v1.0)	Alzheimer's disease (MAP) (v1.1)	Alzheimer's Disease (MVP Cog Working Group) (v2.1)	Alzheimer's Disease, Non-specific Dementias (MVP Cog Working Group) (v1.0)
Author(s)	eMERGE	MVP Core	MVP Cognitive Decline and Dementia During Aging Working Group, Million Veteran Program (MVP)	MVP Cognitive Decline and Dementia During Aging Working Group, Million Veteran Program (MVP)
Context of Development	Research	Research	Research	Research
Population	eMERGE participants	MVP	Million Veteran Program (MVP) enrollees	Million Veteran Program (MVP) enrollees
Method Used	Rules-Based (i.e., only structured data were used)	Machine learning: Unsupervised	Rules-Based (i.e., only structured data were used)	Rules-Based (i.e., only structured data were used)
Algorithm Description	Patients with at least one ICD-9 or ICD-10 code are considered a case for the phenotype.	MAP is an unsupervised clustering algorithm that uses counts of ICD codes and Concept Unique Identifier (CUI) mentions along with healthcare utilization as Show more	To quality as a case requires the presence of two or more ICD codes	To quality as a case requires the presence of two or more ICD codes
ICD-9 Diagnostic Codes	2 Total 331.0, 331.00	2 Total 331.0, 331.00	1 Total 1 Missing 331.0	8 Total 1 Missing 290.0, 290.20, 290.21, 290.3, 294.20, 294.21, 294.8, 331. Show more
ICD-10 Diagnostic Codes	5 Total 1 Unique G30., G30.0, G30.1, G30.8, G30.9	5 Total 1 Missing G30, G30.0, G30.1, G30.8, G30.9	3 Total 2 Missing G30.1, G30.8, G30.9	5 Total 2 Missing F03.90, F03.91, G30.1, G30.8, G30.9
CUI Text snippets		2 Total		

1B: Validation and performance metrics from CIPHER's phenotype library for each definition, respectively

Validation

Validated

Yes

Description of Validation

A total of 100 patient charts were reviewed by 3 clinical adjudicators to create gold standard labels. Labels were subsequently used to validate the Phecode within the MVP_23.1 cohort.

Performance Metric	Value	Value	Value	Value
Sensitivity	0.70	0.35	0.70	0.63
Positive Predictive Value (PPV)	0.8	0.83	0.91	0.83
Negative Predictive Value (NPV)	0.91	1.0	1.0	0.87
Specificity	0.94	1.0	1.0	0.95
Area Under the ROC Curve (AUC)				
Kappa				

Big Data/Machine Learning/AI

Importance of Incorporating Imaging Data into Machine Learning Algorithms for Predicting Post-Stroke Cognitive Decline: Results from the EMMA study Vinivius de Camargo* Vinícius de Camargo Carine Savalli Alessandra Baccaro Isabela M Benseñor Paulo A Lotufo Yuan-Pang Wang Alessandra C Goulart Alexandre Chiavegatto Filho

After a stroke, patients may experience long-term cognitive decline. Predicting cognitive decline in the early stages can help delay its progression. This study aimed to predict cognitive decline one year after a stroke, in patients from a Brazilian community-based cohort (EMMA study). To assess the cognitive status at baseline and after one year, we used the Modified Telephone Interview for Cognitive Status (TICS-M), validated in Brazilian Portuguese, and the outcome was defined as a decrease of at least 10% in TICS-M from baseline. The machine learning algorithm XGBoost was trained with variables collected at baseline, including demographics, comorbidities, clinical, laboratory variables. Also, neuroimaging variables captured by 3 tesla magnetic resonance (thickness, area and intracranial volume (ICV) in the right and left hemisphere) 1-3 months after stroke (subacute phase). After hyperparameter tuning, we evaluated the predictive performance of the model in a repeated 5-fold cross-validation, using the area under the receiver operating characteristic curve (AUROC). The contribution of variables to outcome prediction was assessed using SHAP (Shapley Additive exPlanations) values. A total of 66 patients with a neuroimaging evaluation were included in this analysis. Results indicated robust performance in predicting the decrease of at least 10% in TICS-M score after one year (AUC=0.78, SD=0.16). Imaging exam variables were assessed with greater importance through SHAP, with emphasis on ICV and average thickness of the right hemisphere. These variables were more relevant to model discriminate patients and predict cognitive decline after a stroke. According to our results, variables obtained in image exams can be the key to predict the long-term cognitive decline after a stroke. Future studies should incorporate more detailed information about image exams.

Aging

Heterogeneous Treatment Effects of Contact with Friends on Dementia in a Nationally Representative Dataset Nicola Churchill* Nicola Churchill Roch Nianogo

Background: There are at least 6.9 million Americans living with Alzheimer's disease and this number is expected to rise to about 13.8 million by 2060. Interacting with friends in mid-life can lower the likelihood of developing dementia later in life and improve cognitive performance. We intend to estimate heterogenous treatment effect from friendship social support defined as contact with friends on the risk of dementia using causal forest analysis in the Health and Retirement Study.

Methods: We estimated heterogenous treatment effects for each individual conditional on covariates. To do so, we used a causal forest approach, a type of random forest modeling that is generalized to produce predicted unit-level conditional average treatment effects. The subgroup average treatment effect for the overall population and stratified by race/ethnicity was obtained using inverse and additional weighting for doubly robust estimates.

Results: There was a 3.2% (95% CI: -0.053, -0.011) decrease in dementia cases among those who have contact with friends equal to or more than every few months versus those who had less. After stratifying by race/ethnicity, Whites had a 3.1% decrease (95% CI: -0.053, -0.009), Hispanics had an 8.4% decrease (95% CI: -0.157, -0.012), and Blacks reported no effect (7.9%, 95% CI: -0.016, 0.173).

Conclusion: Having contact with friends every few months or more frequently can have a protective effect on dementia risk. However, when stratified by race it was found the people who identified as Black no longer had a significant effect but both White and Hispanic individuals had maintained fewer dementia cases due to higher contact with friends.

Aging

The Bidirectional Relationship Between Depression and Inflammation and Their Roles in Midlife Cognitive Outcomes: The CHAMACOS Maternal Cognition Study 2022-2024 Thirsten J. Stockton* Thirsten Stockton Lucia Calderon Kelsey MacCuish Katherine Kogut Kara E. Rudolph Nicholas T. Williams Norma Morga José Camacho Lizari Garcia Yesli Perez-Rocha Maria Rodriguez Monica Romero Aaron McDowell-Sánchez Marcella Warner Weihong Guo Julianna Deardorff Nina Holland Brenda Eskenazi Jaqueline M. Torres

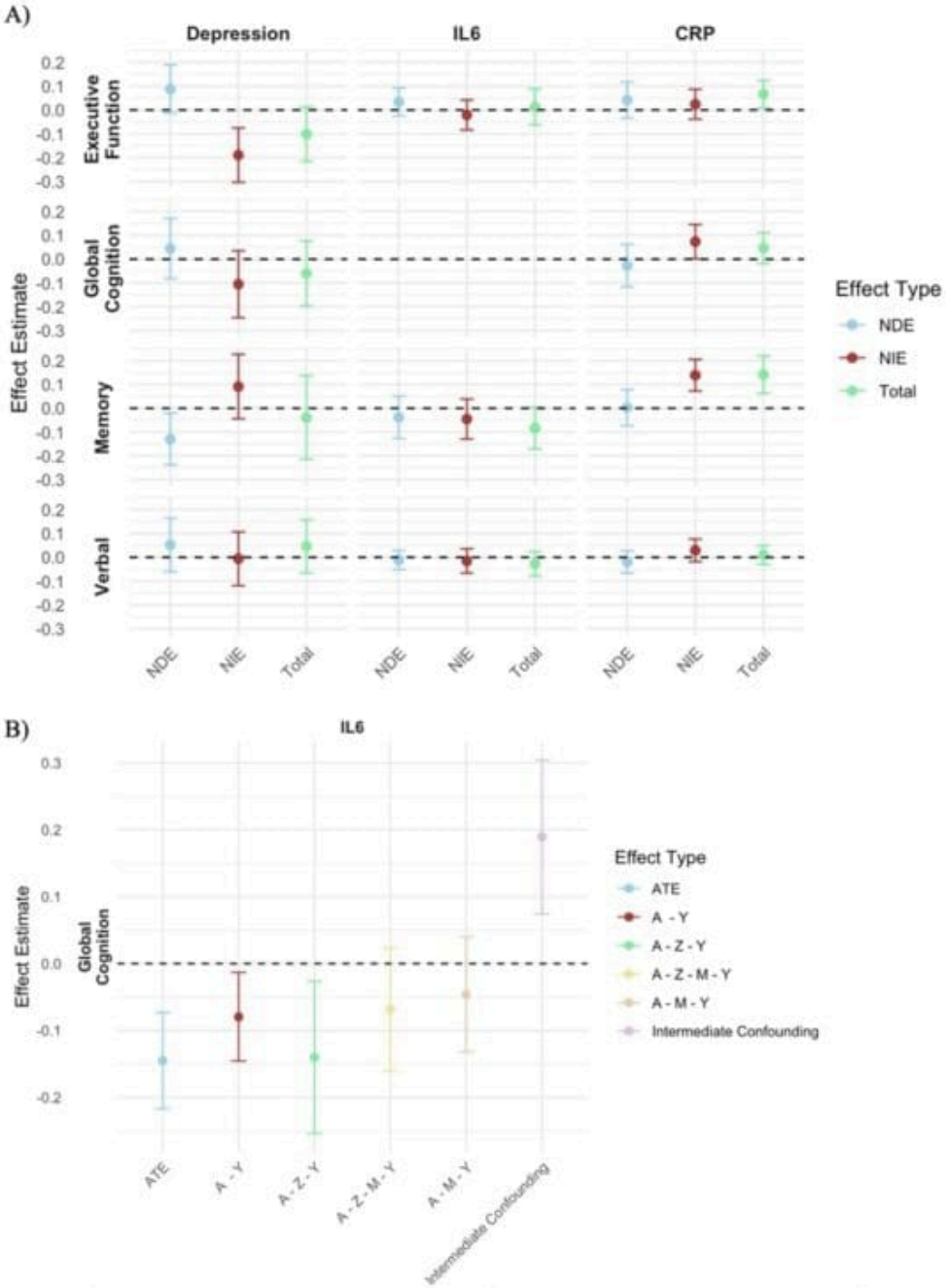
Background: Depression and inflammation share a bidirectional relationship, both being shown to influence cognition over the life course. We evaluated whether inflammation mediates the relationship between depression and cognition and, conversely, whether depression mediates the relationship between inflammatory markers and cognition in a cohort often excluded from cognitive aging research.

Methods: We used data from the CHAMACOS Maternal Cognition Study (2022-2024), which included 483 midlife Latina women from an underserved agricultural region. We measured elevated past-week depressive symptoms, log interleukin-6 (IL-6), log c-reactive protein (CRP), principal component-derived global and domain-specific cognitive scores, and socio-demographic covariates. We estimated both path-specific effects (to quantify the significance of intermediate confounding) and natural effects using a unified machine-learning approach with cross-validation. If significant intermediate confounding was observed, only path-specific effects were reported.

Results: Total and natural (in)direct effects of depressive symptoms on global cognition via inflammation were null. However, for executive function, there was a significant indirect effect via inflammation, while depression directly affected memory. (Fig 1, Panel A). Total and direct effects were null for CRP and global cognition, while indirect effects via depressive symptoms were unexpectedly protective. Significant intermediate confounding was found when estimating whether depressive symptoms mediated the relationship between IL-6 and global cognition (Fig 1, Panel B). Path-specific estimates provided limited evidence of mediation via depressive symptoms and supported a direct relationship between IL-6 and global cognition, alongside other pathways.

Conclusion: Findings highlight a complex interplay between depression, inflammation, and cognition in midlife and the need for careful evaluation of assumptions for mediation analyses.

Figure 1. Effects of depression, IL-6 and CRP on cognitive scores. Depression mediated by both IL-6 and CRP, IL-6 and CRP mediated by depression. Path-specific effects for IL-6 -> Depression -> Global Cognition reported in Panel B. CHAMACOS Maternal Cognition Study, Salinas Valley, CA, 2022-2024.



Abbreviations: NDE, natural direct effect, NIE, natural indirect effect, ATE, average treatment effect, A, treatment, Y, outcome, M, mediator, Z, intermediate confounder. Note: When inflammatory markers were considered the treatment and elevated depressive symptoms was the candidate mediator, we modeled a modified treatment policy increasing CRP/IL-6 by 25%. Conversely, when depression was considered the treatment, a potential outcomes model where everyone received the treatment was compared to one where everyone did not. Intermediate confounders included sleep quality, sleep duration, and, in some cases, CRP. Baseline covariates included nativity/age of migration, BMI, education, marital status, occupational status, age, chronic disease, menopause, and waist circumference.

COVID-19 Pandemic

Outcomes and multimorbidity among children with neurologic and neurodevelopmental disorders hospitalized for COVID-19: The Canadian Immunization Monitoring Program Active (IMPACT) Daniel Farrar* Daniel Farrar Ryan Huang Elizabeth Donner Julie Bettinger Aaron Campigotto Costanza di Chiara Olivier Drouin Joanne Embree Scott Halperin Tajdin Jadavji Kescha Kazmi Charlotte Moore Hepburn Jesse Papenburg Rupeena Purewal Manish Sadarangani Laura Sauvé Karina Top Fatima Kakkar Shaun Morris

Introduction: Children with chronic neurologic and neurodevelopmental (ND) disorders are vulnerable to severe respiratory viral infection. We described comorbidity patterns among children with neurologic or ND disorders hospitalized for COVID-19, and identified neurologic diagnoses associated with severe COVID-19.

Methods: We conducted a national surveillance study at 13 paediatric hospitals in Canada, via the Canadian Paediatric Surveillance Program (April 2020–May 2021) and Canadian Immunization Monitoring Program, ACTive (June 2021–December 2022). Eligible cases were <17 years old and hospitalized for acute COVID-19. Comorbid conditions were categorized using the Medical Dictionary for Regulatory Activities. Severe COVID-19 was defined as intensive care, ventilatory, or hemodynamic support, organ system complications, or death. We conducted network analysis to describe co-occurrence of comorbid conditions, and multivariable robust Poisson regression to estimate the risk of severe COVID-19 by neurologic subgroup.

Results: Among 3218 cases hospitalized for COVID-19, 636 (19.8%) had chronic neurologic or ND disorders. Among these children, most (n=504/636) had ≥2 comorbidities with clustering between cerebral palsy, cortical visual impairment, developmental delay, epilepsy, non-neurologic musculoskeletal disorders, and/or parenteral nutrition (Figure). Most neurologic diagnoses were associated with higher risk of severe COVID-19 – epilepsy was most strongly associated (aRR 2.08, 95% CI 1.56–2.77). There was a dose response where additional neurologic diagnoses further increased risk (e.g., aRR 1.50 [95% CI 1.22–1.84] for 1 vs. 0 neurologic diagnoses; aRR 2.87 [95% CI 2.26–3.66] for ≥4 vs. 0 neurologic diagnoses).

Discussion: Children with neurologic or ND disorders frequently had multiple comorbidities. Those with neurologic multimorbidity had greatest risk of severe COVID-19, and may benefit most from immunization initiatives and early clinical intervention.

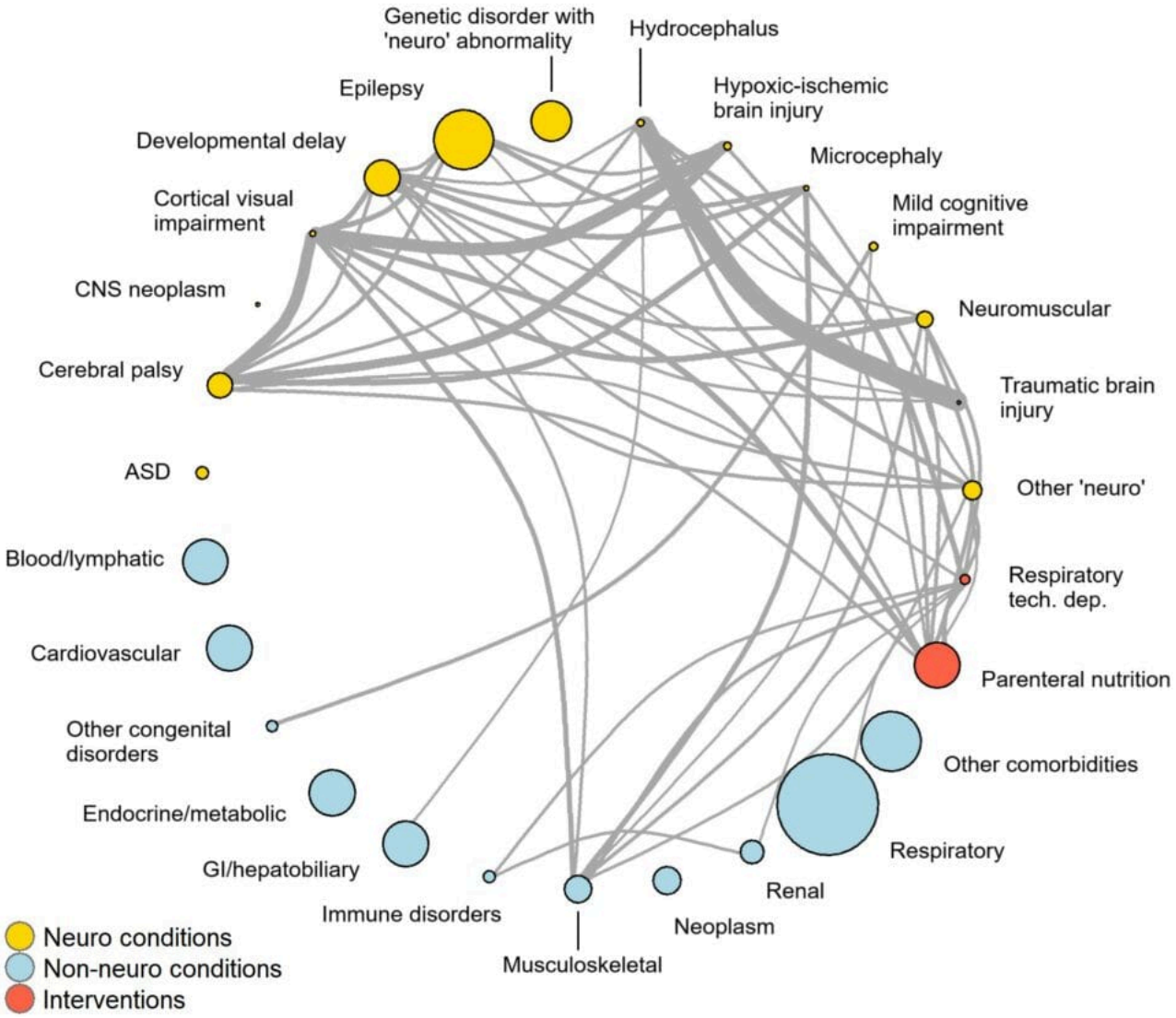


Figure. Co-occurrence network of chronic comorbid conditions among all patients hospitalized with COVID-19 at IMPACT network hospitals.

ASD=Autism spectrum disorder; CNS=Central nervous system; GI=Gastrointestinal; tech. dep.=Technology dependence. The co-occurrence network was generated using the igraph package in R. Nodes (circles) are weighted by the frequency of patients with each comorbid condition, and the comorbid condition categories included are mutually exclusive. We show the 50 strongest associations (edges) between all co-occurring comorbid condition categories reported for at least five patients. Edges (lines/links) are weighted by the observed-to-expected ratio (also known as relative risk).

COVID-19 Pandemic

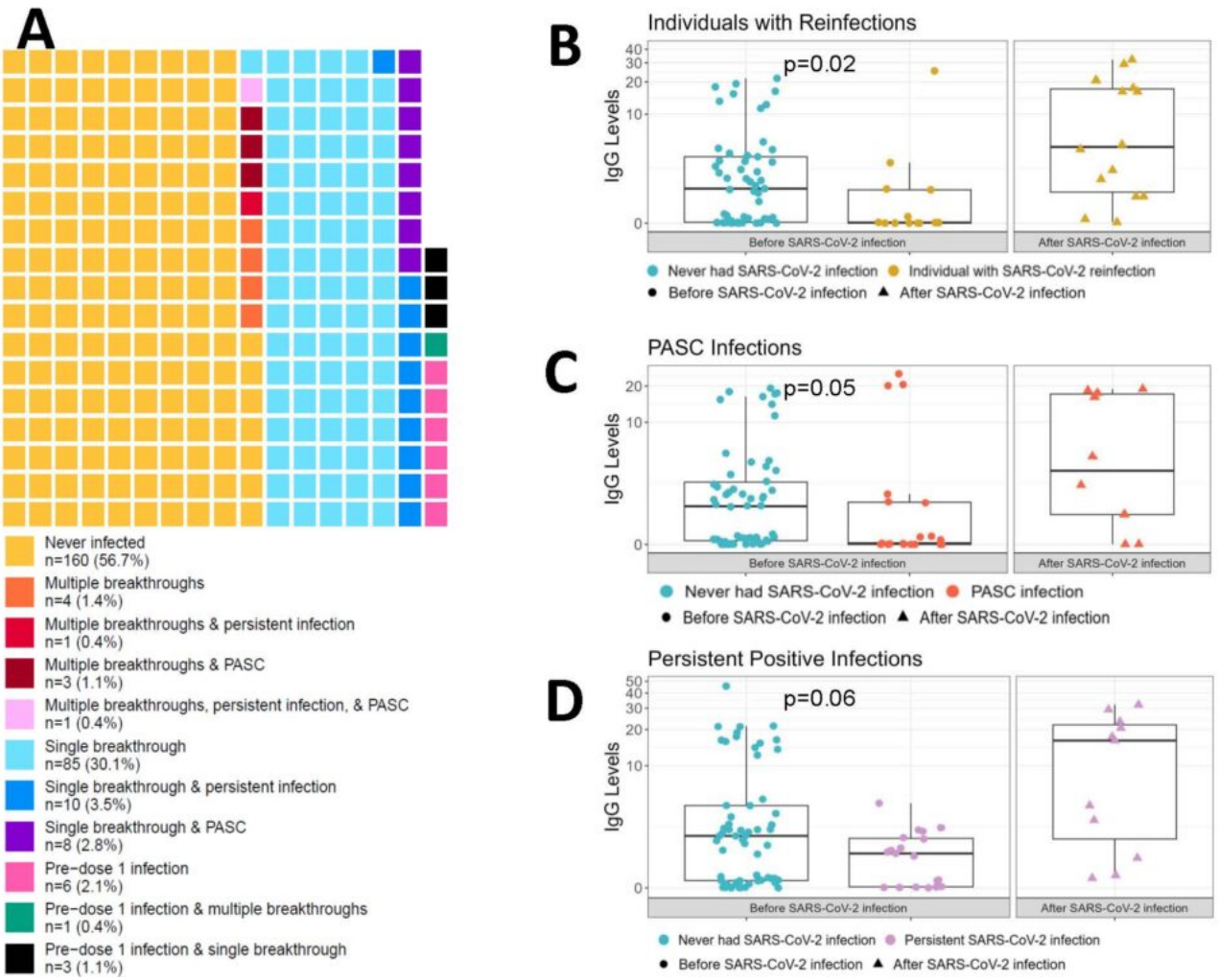
Breakthrough SARS-CoV-2 Outcomes in Immune-Disordered People During the Omicron Era: A Prospective Cohort Study Fausto Andres Bustos Carrillo* Fausto Bustos Carrillo Mackenzie Zendt Viviane Callier Maureen DeGrange Anita Ginigeme Lurline Wu Bevin Manuelpillai Ana Ortega-Villa Emily E Ricotta

Background: Immune-deficient/disordered people (IDP) experience less robust immune responses to COVID-19 vaccinations than immunocompetent individuals, elevating their risk of SARS-CoV-2 infection and its adverse outcomes. Little is known about Omicron breakthrough infections in IDP. In this large prospective cohort study, we describe the rate and characteristics of Omicron breakthrough infections among IDP and healthy volunteers (HV); the occurrence of persistent infections, reinfections, post-acute sequelae of COVID-19 (PASC); and attitudes/behaviors regarding infection prevention.

Methods: We followed 219 IDP and 63 HV throughout the US from April 2021 (peak of Alpha variant) through July 2023 (when Omicron XBB was dominant) and characterized immune responses to COVID-19 vaccination. We quantified anti-spike IgG titers one-, six-, and twelve-months post-vaccination and collected bi-weekly saliva samples. Participants completed standardized surveys on COVID-19 symptoms and preventative attitudes/behaviors.

Results: There were 88 initial breakthrough infections among IDP (incidence rate 23.7/100 person-years) and 28 among HV (27.3/100 person-years). Incidence was 12-fold higher during than before the Omicron era. COVID-19 symptoms were generally mild. Anti-spike IgG titer one-month after the most recent vaccination pre-infection was not associated with breakthrough in either traditional analyses or an emulated trial. HV and IDP frequently practiced infection-limiting behaviors, but IDP were more likely to continue such behaviors after vaccination. IDP experienced persistent infections, PASC, and reinfections more commonly than HV.

Conclusions: Breakthrough rates in IDP were similar to HV despite experiencing less robust immune responses to vaccination. Nevertheless, IDP experienced a slightly higher frequency of symptoms, hospitalizations, infection persistence, PASC, and reinfections than HV.


A
Never infected
n=160 (56.7%)
Multiple breakthroughs
n=4 (1.4%)
Multiple breakthroughs & persistent infection
n=1 (0.4%)
Multiple breakthroughs & PASC
n=3 (1.1%)
Multiple breakthroughs, persistent infection, & PASC
n=1 (0.4%)
Single breakthrough
n=85 (30.1%)
Single breakthrough & persistent infection
n=10 (3.5%)
Single breakthrough & PASC
n=8 (2.8%)
Pre−dose 1 infection
n=6 (2.1%)
Pre−dose 1 infection & multiple breakthroughs
n=1 (0.4%)
Pre−dose 1 infection & single breakthrough
n=3 (1.1%)
B
Individuals with Reinfections
p=0.02
IgG Levels
Before SARS-CoV-2 infection
After SARS-CoV-2 infection
Never had SARS-CoV-2 infection
Individual with SARS-CoV-2 reinfection
Before SARS-CoV-2 infection
After SARS-CoV-2 infection
C
PASC Infections
p=0.05
IgG Levels
Before SARS-CoV-2 infection
After SARS-CoV-2 infection
Never had SARS-CoV-2 infection
PASC infection
Before SARS-CoV-2 infection
After SARS-CoV-2 infection
D
Persistent Positive Infections
p=0.06
IgG Levels
Before SARS-CoV-2 infection
After SARS-CoV-2 infection
Never had SARS-CoV-2 infection
Persistent SARS-CoV-2 infection
Before SARS-CoV-2 infection
After SARS-CoV-2 infection

COVID-19 Pandemic

Adverse Childhood Experiences (ACEs) and COVID-19 severity: a multinational study Mary M Barker* Mary Barker Yue Wang Kadri Kõiv Nora P Skjerdingstad Omid V Ebrahimi Helga Ask Kelli Lehto Thor Aspelund Fang Fang Unnur A Valdimarsdóttir

Aims: Exposure to adverse childhood experiences (ACEs) has been shown to be associated with COVID-19-related-hospitalization and -mortality. In this multinational study we aimed to investigate the associations between ACEs and both self-reported acute COVID-19 severity and long COVID, across four Nordic countries.

Method: Currently, data from the Omtanke2020 study (N=2,043) in Sweden and the Stress-And-Gene-Analysis (SAGA) cohort (N=12,345) in Iceland have been analyzed. ACE exposure was measured using modified versions of the Life Stressor Checklist-Revised and the Adverse Childhood Experiences International Questionnaire (ACE-IQ) in Sweden and Iceland, respectively. All included participants had been previously infected with COVID-19. Severe acute COVID-19 was defined as participants being bedridden due to COVID-19 for ≥7 days, while long COVID was defined as symptoms of COVID-19 lasting ≥3 months. Associations were explored using multivariable modified Poisson regression models in both cohorts, and regression-based causal mediation analysis in the SAGA cohort.

Results: Exposure to ≥1 ACE was associated with a higher prevalence of severe acute COVID-19 in both the Omtanke2020 (prevalence ratio [PR]: 1.42, 95% CI: 1.08-1.87) and SAGA cohorts. (PR: 1.73, 95% CI: 1.42-2.12). Similarly, participants exposed to ≥1 ACE had a higher prevalence of long COVID in both cohorts (Omtanke2020 – PR: 1.51, 95% CI: 1.15-1.99; SAGA – PR: 1.73, 95% CI: 1.46-2.05). Mediation analysis showed that >35% of the associations between ACEs and severe acute COVID-19/long COVID were explained by socioeconomic status, lifestyle, and/or pre-pandemic psychiatric or physical diagnoses.

Conclusions: Our results highlight the role of ACEs in both acute and long-term COVID-19-related outcomes. Next, we will conduct the analysis in three further Nordic cohorts: the Estonian Biobank, MoBa (Norway) and CIPA (Norway), and use meta-analyses to pool all cohort-specific results.

COVID-19 Pandemic

Trajectories of post-traumatic stress disorder symptoms (2003-04 to 2020-21) and risk of long COVID in the World Trade Center Health Registry Julia Sisti* Julia Sisti Samuel Janette Janna

Objective: The etiology of long COVID is not well-understood; however pre-existing mental health conditions have been identified as risk factors. We examined associations between history of post-traumatic stress disorder symptoms (PTSS) and subsequent long COVID among individuals exposed to the World Trade Center disaster.

Methods: Over five waves of follow-up in the World Trade Center Health Registry (2003-04 to 2020-21), we used group-based trajectory modeling to identify five PTSS trajectories (resilient, low-stable, remitted, delayed onset, and chronic-high). Among enrollees who responded to five wave surveys, completed two COVID-19 focused surveys (2021-22 and 2022-23), and reported ever having a COVID-19 infection (N=5,363), we used modified Poisson regression to estimate adjusted RRs and 95% CI for associations of PTSS trajectories with self-report of long COVID symptoms (any vs. none).

Results: In 2022-23, 41% of enrollees reported experiencing any long COVID symptoms. In models adjusted for sociodemographic characteristics and self-reported diagnosed physical health conditions and depression, associations with long COVID were observed for all trajectories compared to the resilient trajectory, which was characterized by very low PTSS at all points. RRs were similar among the three trajectory groups characterized by a high lifetime prevalence (>90%) of probable PTSD (RRremitted=1.82, 95% CI=1.63, 2.03; RRdelayed =1.86, 95% CI=1.67, 2.06; RRchronic=1.80, 95% CI=1.59, 2.03). Risk of long COVID was also elevated among individuals in the low-stable trajectory group, who had a lower lifetime prevalence of probable PTSD (18%) (RR=1.46, 95% CI=1.35, 1.58).

Conclusion: Risk of long COVID is elevated among individuals with a history of elevated PTSS, including among those whose symptoms have improved. Populations at high risk of PTSD, including those exposed to traumatic events, may benefit from targeted screening to identify those with long COVID.

COVID-19 Pandemic

Acute symptoms and return of pre-Covid19 health among vaccinated adults with a SARS-CoV2 infection between 2022-2024 Katie R. Mollan* Katie Mollan Ning Zhang Jessica R. Keys Danyu Lin Becky Straub David Wohl William Fischer

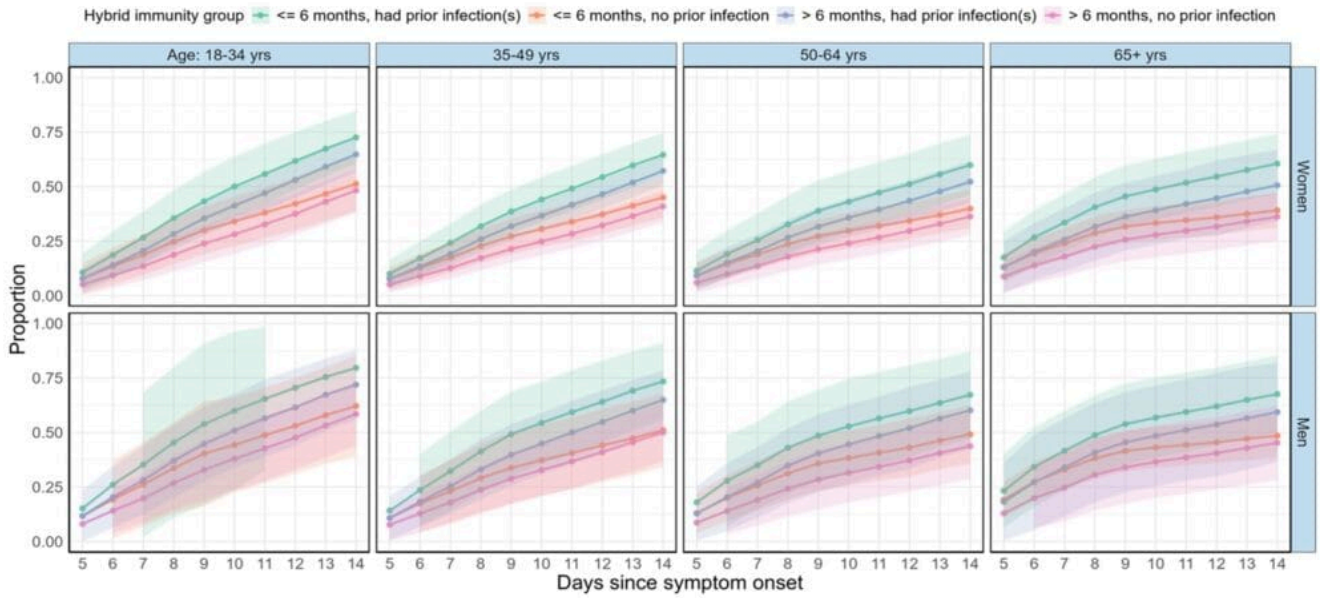
Background: Acute Covid19 symptom experiences and predictors of rapid return to health among non-hospitalized adults remain of great interest. We investigated host and disease-associated predictors of return to pre-Covid19 health.

Methods: The VISION study is a prospective observational cohort of adults in North Carolina who tested SARS-CoV2 positive ≤7 days before online study enrollment (accrual period: Oct 2022-Mar 2024). This analysis includes adults who enrolled 0-7 days after symptom onset and were previously vaccinated; unvaccinated adults were excluded due to sample size limitations. Self-reported Covid19 symptoms and return of pre-Covid19 health were collected daily for 14 days. We estimated the probability of experiencing pre-Covid19 health at days 5-14 after symptom onset using a logistic regression model fit with generalized estimating equations; days since symptom onset was fit via 9 indicators. In our model, we accounted for age (restricted cubic spline), biological sex, race-ethnicity, comorbidities, body mass index, vaccine recency (≤6 vs. >6 months ago), prior infection (0, 1+), and oral SARS-CoV2 medication use.

Results: 2,545 vaccinated adults were eligible for analysis. At baseline, median (IQR) age was 47 (36, 62) years, 74% were women, 43% had prior infection(s), and 58% were vaccinated more than 6 months ago. Within 5 days of symptom onset, 52% started nirmatrelvir-ritonavir or molnupiravir. Return to pre-Covid19 health was reported by 19.6% (95% CI: 18.1-21.1%) at day 7 and 45.1% (43.1-47.0%) at day 14 after symptom onset. Key predictors of pre-Covid19 health during the acute period included days since symptom onset, age, sex, prior infection, and vaccine recency (Figure).

Conclusions: Most vaccinated adults had not returned to pre-Covid19 health at 14 days after Covid19 symptom onset. During the acute phase of Covid19, those with hybrid immunity (i.e., both vaccination and prior infection) were more likely to have return of pre-Covid19 health.

Figure: Return to pre-Covid19 health by age, sex, and hybrid immunity status



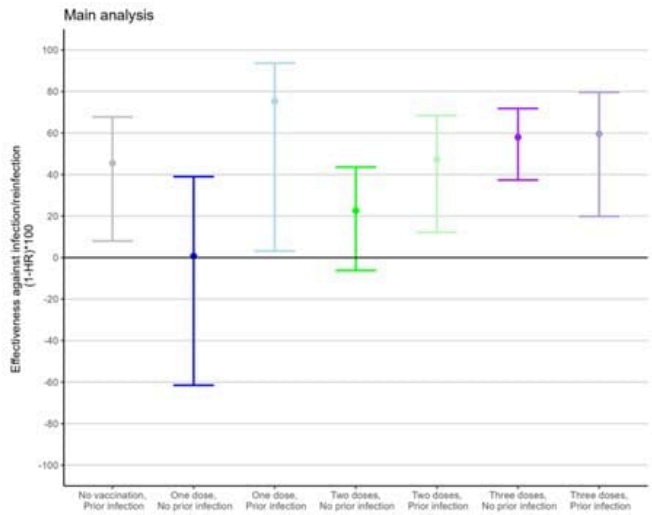
Legend: Estimated probability of return to pre-Covid19 health is displayed over days since symptom onset by baseline hybrid immunity status (4 lines: vaccinated ≤6mo ago and had prior infection (green), vaccinated within ≤6mo and no prior infection (orange), vaccinated >6mo ago and had prior infection (blue-grey), vaccinated >6mo ago and no prior infection (pink)). The results are paneled by age and biological sex, and averaged over the other features in our multivariable repeated-measures model.

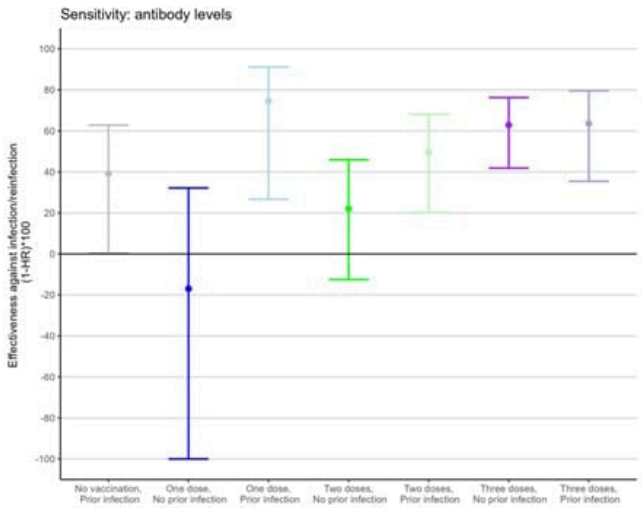
COVID-19 Pandemic

Relative immune protection from combinations of prior infection and vaccination on incident SARS-CoV-2 infection/reinfection: a prospective cohort study comparing self-reported and antibody-based indicators of prior infection, February 2021 to January 2023

Ashley Judge* Ashley Judge Erika Beidelman David Allison Stephanie Dickenson Lilian Golzarri Arroyo Anna Macagno Jon Macy Kevin C. Maki Molly Rosenberg Christina Ludema

Both natural infection and vaccination provide immune protection from future SARS-CoV-2 infections. Better understanding the relative immunity conferred from acquired and vaccine-induced immunity in combination will be helpful in building a stronger evidence base for policy decisions. We assessed the relative effectiveness of combinations of vaccination and prior infection on risk of SARS-CoV-2 infection/reinfection with correction for possible exposure misclassification of prior infection by comparing prior infection operationalized as 1) documented prior infection and 2) documented prior infection and nucleocapsid receptor-binding antibody indication of prior infection. We used extended cox regression with robust standard errors to estimate the association between time-varying number of vaccine doses and time invariant prior infection on risk of infection/re-infection among a prospective cohort of US adults between February 2021 to January 2023, accounting for censoring with inverse probability of censoring weights. N=1905 adults contributed 398,126 person-days of observation. Relative to the unvaccinated with no prior infection, those with documented prior infections had a relative efficacy of 45.5% (95% CI: 8.0-67.7%) against infection/reinfection. For those with three vaccine doses and no prior infection, the relative efficacy of 58.0% (37.3%-71.8%). Similar relative efficacy estimates were observed after correction for prior infection status in the nearly 17% of those without documentation of prior infection who had nucleocapsid antibody levels as high or higher than levels beyond the first quartile of documented cases. Three vaccine doses without prior infection provided substantial protection against infection/reinfection as did naturally acquired immunity without vaccination in a cohort of adults primarily infected/reinfected during the Omicron variant. Correcting for prior infection reporting error did not impact results.





Women’s Health

Association of Historical Redlining with Gestational Diabetes Mellitus: The Mediating Role of Body Mass Index and Area Deprivation Index Wajeeha Umer* Wajeeha Umer Yi Sun Anqi Jiao Karen D. Lincoln Mengyi Li Chantal C. Avila Vicki Y. Chiu Jeff M. Slezak David A. Sacks John Molitor Tarik Benmarhnia Jiu-Chiuan Chen Darios Getahun

Objective

We investigated the association between historic redlining and risk of gestational diabetes (GDM), and if this relationship is mediated by maternal obesity and area-level deprivation.

Research design and methods

This retrospective study included 86,834 singleton pregnancies from Kaiser Permanente Southern California’s (KPSC) health records (2008–2018). Redlining was assessed using digitized Home Owners’ Loan Corporation (HOLC) maps, with patient’s residential addresses geocoded and assigned HOLC grades (A,B,C,D) based on their geographic location within HOLC-graded zones. For GDM cases, exposure was assigned based on address at diagnosis date; for non-cases, it was assigned based on address during the 24th–28th gestational week. Health records were combined with area deprivation index (ADI) from 2011–2015 census data. Mixed-effect logistic regression models assessed associations between redlining and GDM, with mediation by BMI and ADI evaluated using inverse odds ratio weighting. Models were adjusted for maternal age, education, race and ethnicity, neighborhood level income, and smoking status.

Results

Among the 10,134 (11.67%) GDM cases, we found increased risk of GDM in B (“Still desirable,” adjusted odds ratio [aOR] 1.20, 95% confidence interval [CI] 0.99-1.44), C (“Definitely declining,” aOR 1.22, 95% CI 1.02-1.47), and D (“Hazardous, i.e., redlined,” aOR 1.30, 95% CI 1.08-1.57) graded neighborhoods compared to the “Best” graded zone. Pre-pregnancy BMI and ADI mediated 44.2%, and 64.5% of the increased GDM risk among mothers in redlined areas.

Conclusions

Historic redlining is associated with an increased risk of GDM, mediated by maternal obesity and neighborhood deprivation. Future research is needed to explore the complex pathways linking redlining to pregnancy outcomes.

Social

Unraveling residential segregation and its association with fecundability Sharonda M. Lovett* Sharonda M. Lovett Lauren A. Wise Andrea S. Richardson Erin J. Campbell Yvette C. Cozier Collette N. Ncube Amelia K. Wesselink Mary D. Willis

Introduction: Residential segregation (a proxy for structural racism) is a known determinant of health disparities that has been associated with adverse pregnancy outcomes. However, no study has investigated its association with fecundability, the per-cycle probability of conception.

Methods: We analyzed data from 10,438 U.S. female participants aged 21-45 years enrolled in Pregnancy Study Online (2013-2022), an internet-based preconception cohort study. We ascertained data (including full residential addresses) at baseline, and during follow-up for up to 12 months or until conception. Using baseline residential addresses, we calculated residential segregation based on the Index of Concentration at the Extremes (ICE), which was constructed from American Community Survey 5-year estimates. ICE ranges from -1 (“disadvantaged”) to 1 (“privileged”). We operationalized ICE metrics at the census tract level: economic segregation (ICEincome: ≥$100k vs. <$25k), racial segregation (ICEwhite/black: non-Hispanic White vs. non-Hispanic Black), and racialized economic segregation (ICEincome + white/black: non-Hispanic White ≥$100k vs. non-Hispanic Black <$25k). We used proportional probabilities regression to estimate fecundability ratios (FRs) and 95% confidence intervals (CIs), adjusting for age, calendar year of enrollment, and geographic region of residence.

Results: We observed a monotonic inverse association for increasing quintiles of ICEincome and ICEincome + white/black with fecundability, but less evidence of associations with ICEwhite/black. For instance, relative to ICEincome + white/black quintile 5 (“privileged”), FRs for quintiles 4, 3, 2, and 1 (“disadvantaged”) were 0.92 (95% CI: 0.86-0.99), 0.84 (95% CI: 0.78-0.90), 0.84 (95% CI: 0.78-0.90), and 0.79 (95% CI: 0.73-0.86), respectively.

Conclusion: Living in the most disadvantaged neighborhoods with respect to racialized economic segregation was associated with a moderate decrease in fecundability.

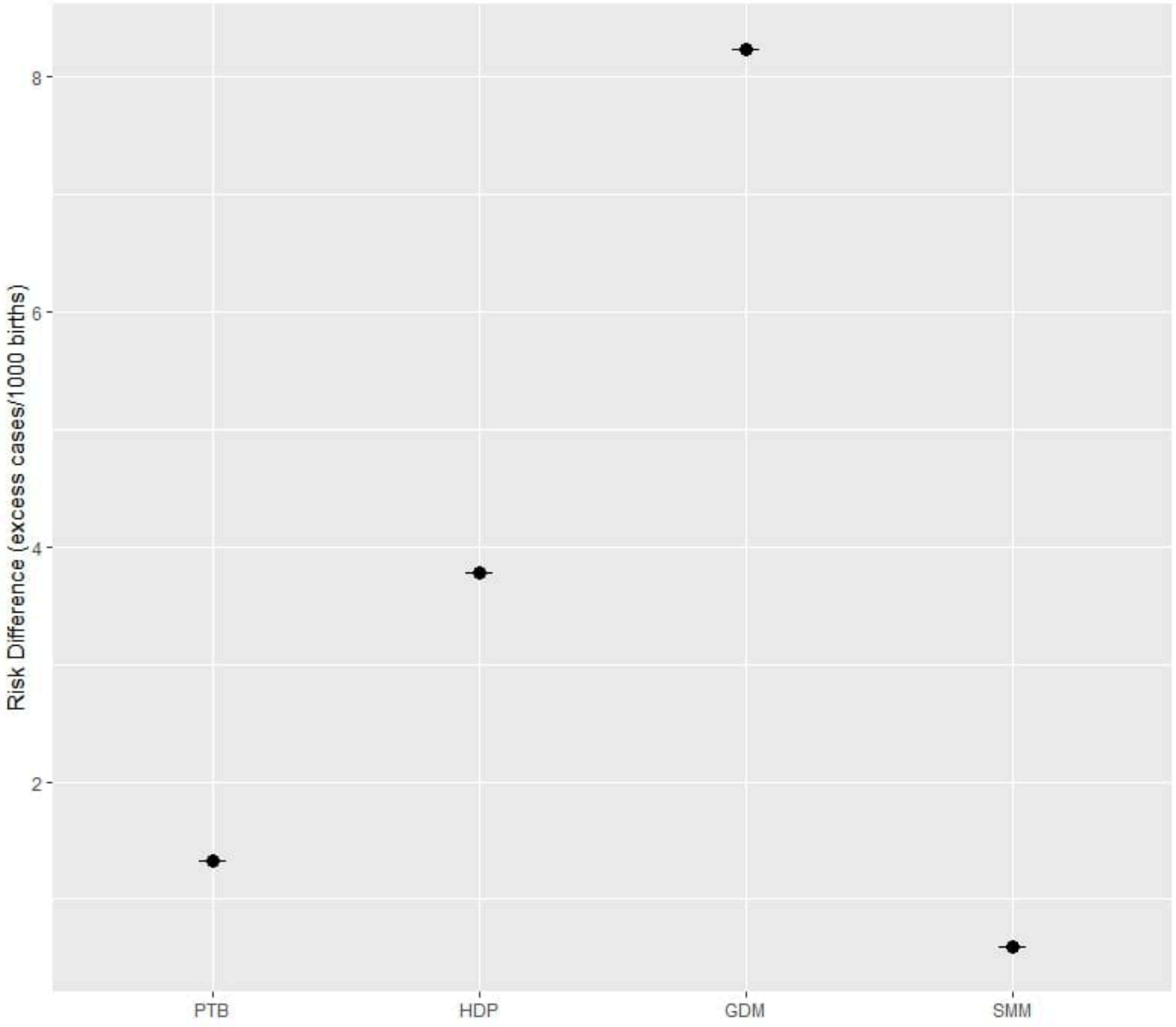
Injuries/Violence

Exposure to Chronic Community Violence and Perinatal Outcomes in California (2007-2018) Shelley Jung* Shelley Jung Caitlin Chan Dana Goin Emily F Liu Kara E Rudolph Kristen Marchi William Dow Paula Braveman Mahasin Mujahid Jennifer Ahern

Community violence is a persistent problem in the US, but its impacts on health in the broader community are not well understood. To better understand community-level determinants of perinatal health, we estimated the association of chronic community violence with perinatal outcomes in California using a strong design to mitigate between community confounding.

We combined neighborhood violence data (rate of deaths/injuries per ZIP Code) with hospital records on singleton live births in California from 2007-2018. We estimated propensity scores to identify neighborhoods with similar characteristics (income, poverty, race/ethnicity), but differing levels of community violence, limiting analyses to areas of common support. We estimated excess risk of perinatal outcomes that include preterm birth (PTB), hypertensive disorders of pregnancy (HDP), gestational diabetes mellitus (GDM), and severe maternal morbidity (SMM) in individuals exposed to high neighborhood violence (≥75th percentile of the 12-month average [Y/N]) during pregnancy. We applied targeted maximum likelihood estimation to estimate risk differences (RD) adjusted for individual- and community-level confounders.

Across 5,067,437 pregnancies (83% of all births), exposure to high community violence was associated with elevated risk of PTB (RD[95% confidence interval (CI)]=1.3 excess cases/1000 births[1.3,1.3]), HDP (RD[95% CI]=3.8 excess cases/1000 births[3.8,3.8]), GDM (RD[95% CI]=8.2 excess cases/1000 births[8.2,8.2]), and SMM (RD[95% CI]=0.6 excess cases/1000 births[0.6,0.6]). We found that exposure to community violence during pregnancy was associated with increased risk of multiple adverse perinatal outcomes, using a design that maximizes the comparability of the exposed and unexposed groups on measured community and individual characteristics. Increased understanding of this relationship has the potential to provide alternative points of intervention to decrease rates of these adverse perinatal outcomes.


Risk Difference (excess cases/1000 births)
8
6
4
2
PTB
HDP
GDM
SMM

COVID-19 Pandemic

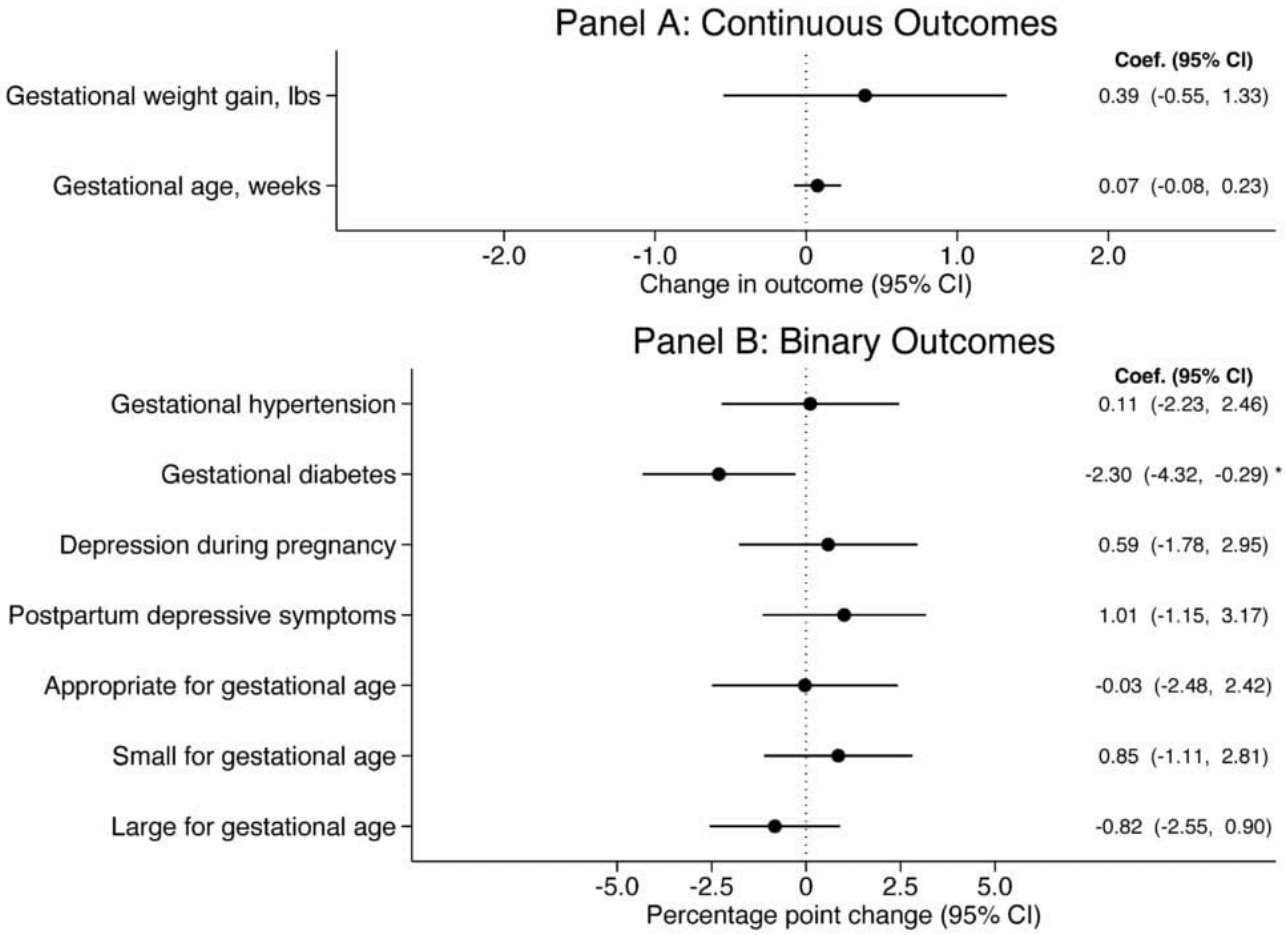
The association between increased SNAP benefits during the COVID-19 pandemic and perinatal health: a quasi-experimental study Daniel Collin* Daniel Collin Kaitlyn Jackson Taylor Robinson Rita Hamad

Background: The COVID-19 pandemic created health and economic hardships for many families. Several existing safety net programs were modified to mitigate these hardships. One such program, the Supplemental Nutrition Assistance Program (SNAP), underwent several modifications, including a 15% increase in monthly benefits in January 2021. These modifications have been linked with improved food and financial security and mental health. However, there is limited research on the impact of the SNAP modifications on the health of pregnant individuals and infants. The goal of this study was to examine the impact of the 15% SNAP benefit increase on perinatal health among SNAP-eligible individuals.

Methods: We used data from the 2019-2021 Pregnancy Risk Assessment Monitoring System (N = 27,736) and a difference-in-differences study design to examine the effect of the SNAP benefit increase. We compared eligible and non-eligible individuals before and after the 15% benefit increase. Parent outcomes included gestational hypertension, gestational diabetes, depressing during pregnancy, postpartum depressive symptoms, and gestational weight gain. Infant outcomes included gestational age and whether the infant's birthweight was appropriate, small, or large for gestational age.

Results: The SNAP benefit increase was associated with decreased gestational diabetes risk (-2.3 percentage points, 95% CI: -4.32, -0.29) among eligible compared to non-eligible individuals. There was no association for other outcomes. Findings were robust to alternative model specifications.

Conclusions: Findings show that pandemic-era enhancements to SNAP led to improvements in gestational diabetes, perhaps due to increased food and financial security. Impacts on other outcomes may have been limited by co-occurring economic hardship or the limited size of the SNAP expansions.


Panel A: Continuous Outcomes
Coef. (95% CI)
Gestational weight gain, lbs
0.39 (-0.55, 1.33)
Gestational age, weeks
0.07 (-0.08, 0.23)
-2.0
-1.0
0
1.0
2.0
Change in outcome (95% CI)
Panel B: Binary Outcomes
Coef. (95% CI)
Gestational hypertension
0.11 (-2.23, 2.46)
Gestational diabetes
-2.30 (-4.32, -0.29) *
Depression during pregnancy
0.59 (-1.78, 2.95)
Postpartum depressive symptoms
1.01 (-1.15, 3.17)
Appropriate for gestational age
-0.03 (-2.48, 2.42)
Small for gestational age
0.85 (-1.11, 2.81)
Large for gestational age
-0.82 (-2.55, 0.90)
-5.0
-2.5
0
2.5
5.0
Percentage point change (95% CI)

Diabetes

The molecular pathways of type 2 diabetes using proteomics, metabolic, and anthropometric profile in cross ancestry biobanks – insights on drug target discovery Junxi Liu* Junxi Liu Zhengming Chen Joanna Howson

Background

Large-scaled plasma proteomic together with genetics provides opportunities to improve understanding of type 2 diabetes (T2D) aetiology, identify biomarkers, and reveal mechanisms. The protein-level discovery is ideal for drug discovery in a precise, individual, and controlled manner.

Methods

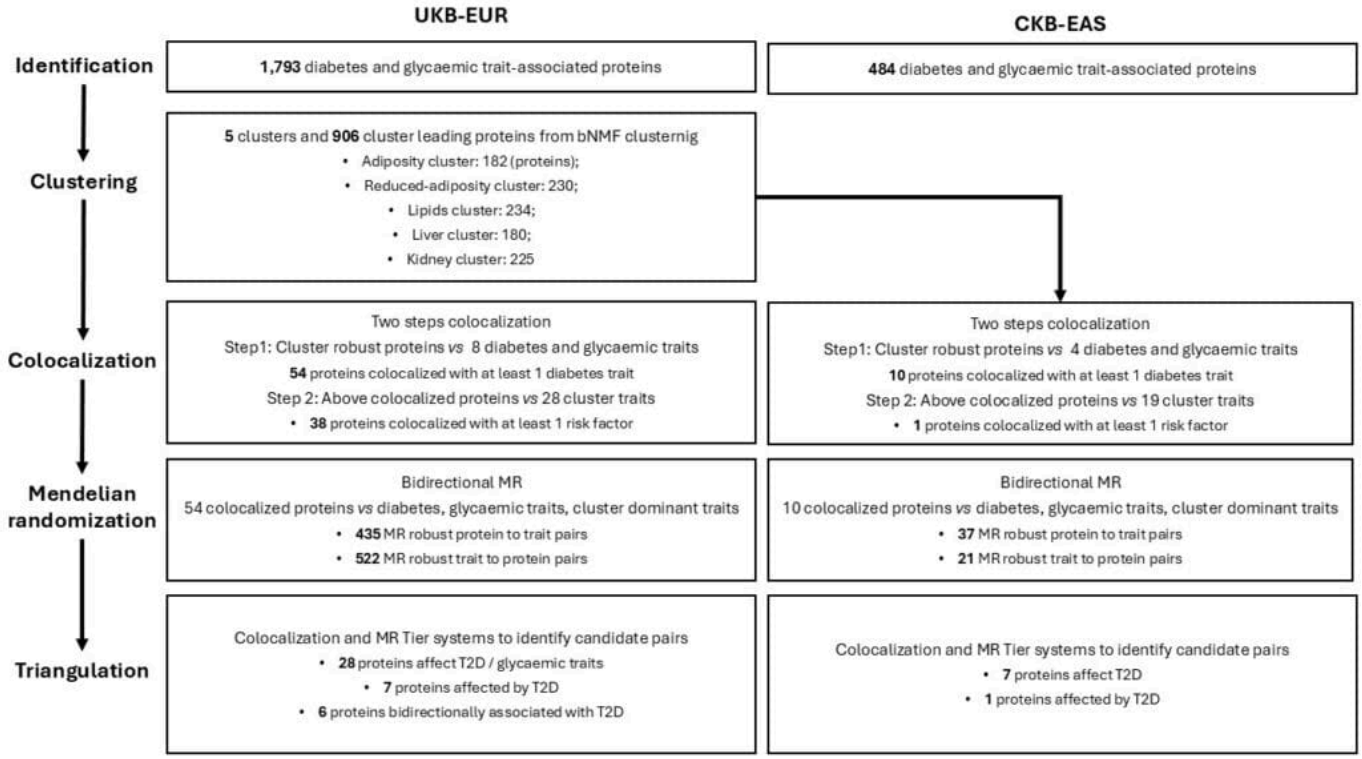
We identified proteins associated with diabetes and glycaemic traits with observational designs in UK Biobank (UKB-EUR). The Bayesian non-negative matrix factorisation (bNMF) was applied to cluster the above-obtained proteins incorporating their phenotypic associations with metabolic and anthropometric profiles. For clusters' leading proteins, colocalization and Mendelian randomization (MR) methods were to investigate tri-variate relationships (i.e., protein – metabolic/anthropometric traits – diabetes traits). We performed the same analyses using China Kadoorie Biobank (CKB-EAS) to investigate the shared findings.

Results

1,793 proteins were observationally associated with diabetes and/or glycaemic traits. bNMF suggested five clusters (Adiposity, Reduced-adiposity, Lipids, Liver, Kidney) and 906 cluster-leading proteins (i.e., top 10% in ranking). The genetic evidence indicated effects of NCR3LG1, RTBDN, and TSPAN8 on T2D as well as T2D on FGFBP3 in both UKB-EUR and CKB-EAS. Effects of CD34, SCT, and KCTD5 on T2D were likely UKB-EUR specific; the effects of PLA2G15 and ENTR1 on T2D were likely CKB-EAS specific. We also revealed candidate proteins linking T2D via adiposity, liver, and kidney traits.

Conclusion

This study provided insights of multiple candidate proteins on T2D treatments. The protein–cluster trait associations revealed different T2D aetiology as well as linking diabetes comorbidities. There were agreements across ancestry though with heterogeneity. Further epidemiological and biological (in vitro and in vivo) validations are required.


UKB-EUR
CKB-EAS
Identification
1,793 diabetes and glycaemic trait-associated proteins
484 diabetes and glycaemic trait-associated proteins
Clustering
5 clusters and 906 cluster leading proteins from bNMF clusternig
• Adiposity cluster: 182 (proteins);
• Reduced-adiposity cluster: 230;
• Lipids cluster: 234;
• Liver cluster: 180;
• Kidney cluster: 225
Colocalization
Two steps colocalization
Step1: Cluster robust proteins vs 8 diabetes and glycaemic traits
54 proteins colocalized with at least 1 diabetes trait
Step 2: Above colocalized proteins vs 28 cluster traits
• 38 proteins colocalized with at least 1 risk factor
Two steps colocalization
Step1: Cluster robust proteins vs 4 diabetes and glycaemic traits
10 proteins colocalized with at least 1 diabetes trait
Step 2: Above colocalized proteins vs 19 cluster traits
• 1 proteins colocalized with at least 1 risk factor
Mendelian randomization
Bidirectional MR
54 colocalized proteins vs diabetes, glycaemic traits, cluster dominant traits
• 435 MR robust protein to trait pairs
• 522 MR robust trait to protein pairs
Bidirectional MR
10 colocalized proteins vs diabetes, glycaemic traits, cluster dominant traits
• 37 MR robust protein to trait pairs
• 21 MR robust trait to protein pairs
Triangulation
Colocalization and MR Tier systems to identify candidate pairs
• 28 proteins affect T2D / glycaemic traits
• 7 proteins affected by T2D
• 6 proteins bidirectionally associated with T2D
Colocalization and MR Tier systems to identify candidate pairs
• 7 proteins affect T2D
• 1 proteins affected by T2D

Diabetes

Prevalence of Metabolic Syndrome in Latin America: A Systematic Review and Meta-Analysis of Observational Studies Laura Alejandra Parra Gomez* Jennifer Paola Puerta Rojas Laura Alejandra Parra Gomez Alberto Javier Vásquez Cadena Maria Angelica Escalante Remolina Alvaro Jose Lora Mantilla Paul Anthony Camacho Lopez Silvia Juliana Villabona Florez

Background: Metabolic Syndrome (MS) is a cardiometabolic condition characterized by cardiovascular risk factors, including dysglycemia, dyslipidemia and central obesity. MS is prevalent in Latin America, contributing significantly to the regions cardiovascular burden. However, precise prevalence data remain scarce.

Objective: To provide a comprehensive review of the prevalence of MS among adults in Latin American countries.

Methods: A systematic review and meta-analysis of observational studies were conducted following the 2020-JBI recommendations and the PRISMA checklist. Included studies were cross-sectional, cohort, and surveys, reporting MS prevalence in the general population of Latin American. Exclusions included studies on special populations, in minors or pregnant women. Study quality was assessed using STROBE guidelines. Meta-analysis used a random-effects model with logit transformations, and Restricted Maximum Likelihood to estimate heterogeneity. Subgroup and sensitivity analyses were performed, and publication bias was assessed using funnel plots and Egger’s test.

Results: 90 studies evaluated MS prevalence using six diagnostic criteria, with an overall prevalence of 40% (95% CI: 32–72). Mexico had the highest prevalence (61%), followed by Ecuador (50%). Factors influencing prevalence included male sex, older age, diagnostic criteria, and urban location. IDF 2006 and JIS 2009 were the most accurate criteria. High heterogeneity reflected the diverse context of Latin America. No publication bias was detected.

Conclusions: MS prevalence has risen, specifically in urbanized areas, females and older adults. Primary care preventive strategies are crucial to reduce its burden. IDF 2006 and JIS 2009 are preferred for their accuracy and concordance.

Key words: Metabolic syndrome, prevalence, systematic review, systematic review and meta-analysis, meta-analysis, metanalysis, Latin America.

Diabetes

Per- and Polyfluoroalkyl Substance and Glycemia-Related Outcomes in Project Viva: A Causal Inference Approach Katlyn McGraw* Katlyn McGraw Arce Domingo-Relloso Linda Valeri Zilan Chai Feng Yan Eva Siegel Jorge Chavarro Marie-France Hivert Emily Oken Pi-I D. Lin Emma V. Preston Jordan Arvayo Burdeau2 Kathryn Tomsho Briana J.K. Stephenson Tamarra James-Todd Ami Zota

Objective: Exposure to per- and polyfluoroalkyl substances (PFAS) can adversely impact glycemic outcomes. Because some PFAS have significantly decreased over the last 20 years, we aimed to investigate whether an earlier decrease in PFAS exposure, during pregnancy, would improve later in life glycemic outcomes.

Methods: Project Viva, an eastern Massachusetts-based pre-birth cohort, enrolled pregnant individuals in 1999-2002. Among 442 participants, we measured plasma concentrations of six PFAS in 1) 1st trimester of pregnancy and 2) ~17-20 years post-pregnancy (i.e., midlife, 2017-2021) using HPLC-MS. Using the g-formula and g-formula extension of the Bayesian Kernel Machine Regression (GBKMR), we used a simulated intervention to estimate the association with glycemic outcomes (HbA1c, 2-hour postprandial oral glucose tolerance test – OGTT, fasting glucose, and HOMA-IR) when pregnancy PFAS were lowered to the 75th percentile of those measured at midlife, compared to the observed median pregnancy PFAS levels, accounting for time-varying confounding. We evaluated interventions for individual PFAS and joint PFAS using the g-formula and for the PFAS mixture using GBKMR to account for any multicollinearity. Models were adjusted for baseline age, race, education, income, pre-pregnancy BMI, smoking status, and time-varying confounders menopause, parity, and breastfeeding duration.

Results: Participants were of median age 33y at enrollment, primarily White (74%), and highly educated (77% ≥bachelor's). Median levels of all PFAS decreased substantially from pregnancy to midlife, except for PFDA, with intraclass correlation values ranging from 23% for PFOS to 64% for PFDA. When pregnancy levels were decreased to the 75th percentile of observed midlife PFAS levels, there was a -24.2 (-25.3, -23.1), -9.09 (-10.4, -7.87), and -1.25 (-2.43, -0.13) mg/dL decrease in midlife postprandial OGTT for PFOS, PFOA, PFHxS, and MEFOSAA, respectively. Additionally, there was a -0.45 (-0.50, -0.40), -0.28 (-0.33, -0.23), and -0.05 (-0.09, -0.00) decrease in midlife HOMA-IR for PFOS, PFOA, and PFHxS, respectively. There were no significant decreases in outcomes when assessing the joint effect of decreased PFAS at pregnancy for the g-formula or GBKMR.

Conclusion: Earlier reductions in certain PFAS may improve glycemic outcomes. Actions to reduce PFAS now are more impactful long-term.

Diabetes

Validation of an Algorithm Based on Electronic Health Record Data to Identify Participants of All of Us With Type 1 Diabetes Mellitus Anna M Pederson* Anna M Pederson Scott C Zimmerman Peter Buto Jingxuan Wang Kendra D. Sims Audrey R. Murchland Mabeline Velez M. Maria Glymour Alana T Brennan Jennifer Weuve

Introduction: Diabetes mellitus (DM) is a leading risk factor for morbidity and mortality, but diagnostic algorithms for distinguishing DM subtypes in large observational, electronic health records (EHR) based cohorts are insufficiently validated. We aimed to develop an algorithm to distinguish individuals with type 1 DM (T1DM) from type 2 DM (T2DM) using EHR subcohorts with additional information on diabetes type.

Methods: We extracted data on participants in the All of Us Research Program (AoU) (N = 341,209) with an EHR record of diabetes who also: completed a self-reported diabetes questionnaire (n=12,464), had a C-peptide laboratory measurement (n=596), or had an islet-specific autoantibody (ISA) measurement (n=393). Three “gold standards” were used to identify T1DM: (1) self-reports via survey (T1DM vs T2DM); (2) C-peptide levels (T1DM: ≤ 0.20 nmol/L vs T2DM: ≥ 0.40 nmol/L); and (3) ISA positivity (T1DM: antibody > 0). We identified all EHR encounters for T1DM or T2DM and determined the optimal number of T1DM encounters to maximize sensitivity and specificity of classifying participants as T1DM versus T2DM.

Results: Among self-reported diabetes, C-peptide, and ISA laboratory measures, we identified, respectively: 1,525, 110, and 182 T1DM cases; and 10,939, 486, and 211 T2DM cases. Among A0U participants with diabetes, sensitivity and specificity were optimized at the following thresholds for EHR encounters: (1) ≥1 encounter for self-reported T1DM (sensitivity=0.63; specificity=0.89); (2) ≥4 encounters for C-peptide-defined T1DM (sensitivity=0.75; specificity=0.80); and (3) ≥5 encounters for ISA-defined T1DM (sensitivity=0.57; specificity=0.72).

Conclusion: We present a validated algorithm for identifying T1DM among diabetics in AoU. Our algorithm demonstrates good, but not perfect sensitivity and only modest specificity. Future work should quantify the direction and magnitude of bias to studies in which both DM subtypes are exposures or outcomes.

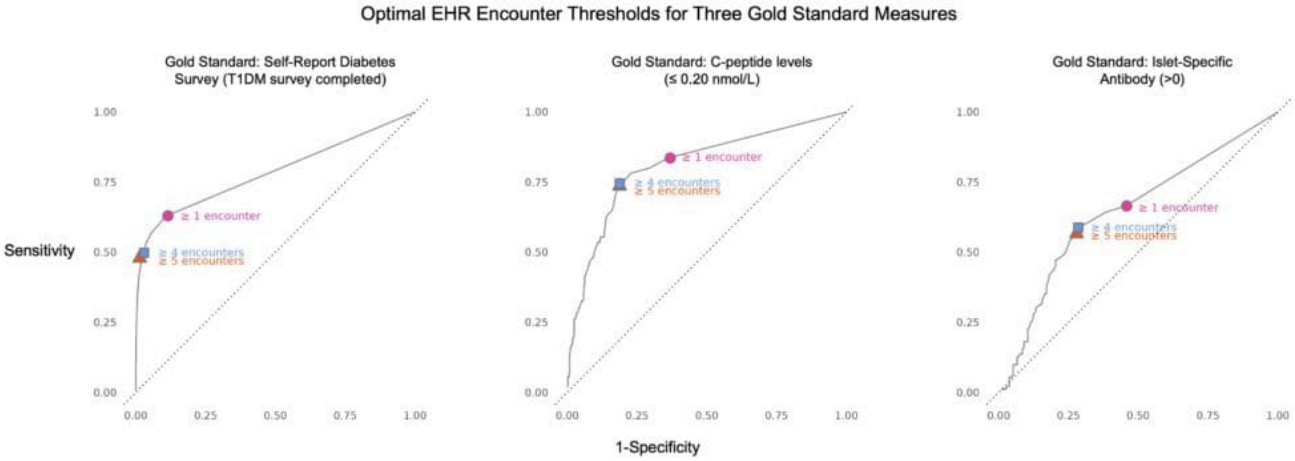


Figure. Sensitivity and specificity of type 1 diabetes classification of 200 thresholds of EHR encounters for diabetes, among All of Us participants with diabetes. Each plot corresponds to the accuracy of given EHR encounter thresholds in predicting type 1 diabetes as defined by (1) self-report, (2) C-peptide levels, and (3) islet-specific antibodies (ISA). The sensitivity and specificity of ≥1 EHR encounter were: (1) self-reported diabetes: sensitivity = 0.63; specificity = 0.89; (2) C-Peptide levels: sensitivity = 0.84; specificity = 0.64; and (3) ISA: sensitivity = 0.66; specificity = 0.55. The sensitivity and specificity of ≥4 EHR encounters were: (1) self-reported diabetes: sensitivity = 0.50; specificity = 0.97; (2) C-Peptide levels: sensitivity = 0.75; specificity = 0.80; and (3) ISA: sensitivity = 0.59; specificity = 0.72. The sensitivity and specificity of ≥5 EHR encounters were: (1) self-reported diabetes: sensitivity = 0.48; specificity = 0.98; (2) C-peptide levels: sensitivity = 0.74; specificity = 0.82; and (3) ISA: sensitivity = 0.57; specificity = 0.72.

Diabetes

Housing insecurity is associated with uncontrolled diabetes among veterans in Veterans Health Administration (VHA) Simin Hua* Simin Hua Rania Kanchi Earle Chambers Giselle Routhier Lorna Thorpe Jay Pendse

Background

Housing insecurity is known to impact health. However, electronic health record systems often lack systematic measures of housing insecurity to identify the health-related conditions of patients with such social needs on a large scale. This study applied a housing insecurity measure using multiple VHA data sources to understand the relationship between housing insecurity and early diabetes management among U.S. veterans.

Method

A total of 833,366 veterans in VHA with newly-diagnosed type 2 diabetes during 2008-2018 were included. Housing status around the time of diabetes diagnosis (+/- 6 months) was classified as (1) housing insecure but not homeless, (2) homeless, or (3) potentially stably housed, based on multiple sources: ICD-9/10 codes, administrative codes, screening questionnaire responses, and use of housing assistance services. We used mixed effect models to obtain odds ratios of reaching target A1c levels (<8%) and of uncontrolled diabetes (A1c>9%) for up to 5 years post-diagnosis, adjusting for demographics, geographic location, comorbidity index, and frequency of clinical visits.

Results

Approximately 2% were documented as experiencing housing insecurity only while 4.6% of veterans were documented as experiencing homelessness around their diabetes diagnosis. During follow-up, veterans experiencing homelessness were less likely to achieve A1c<8% [OR=0.70 (95% CI 0.67-0.73)]. Veterans experiencing homelessness [OR 1.56 (1.50-1.62)] and housing insecurity [OR 1.14 (1.07-1.21)] were more likely to have uncontrolled diabetes compared to stably housed veterans. Associations were stronger in veterans 65+ years old than those under 65, and among Hispanic veterans than Non-Hispanic White veterans.

Conclusion

Housing insecurity and homelessness are associated with worse diabetes control among veterans in VHA. Targeted efforts should be directed to older veterans and non-White veterans to mitigate adverse impact of homelessness on diabetes management.

Diabetes

The association between loneliness and the risk of diabetes mellites in Japanese middle-aged and older adults: a population-based prospective cohort study Yuki Arakawa* Yuki Arakawa Atsushi Goto Miho Hara Kosuke Inoue Izumi Nakayama Kozo Tanno Nobuyuki Takanashi Kazumasa Yamagishi Isao Muraki Nobufumi Yasuda Isao Saito Tadahiro Kato Kazuhiko Arima Ayuko Takatani Hikaru Ihira Rieko Kanehara Taiki Yamaji Motoki Iwasaki Manami Inoue Shoichiro Tsugane Norie Sawada

Background: Diabetes prevention is an important public health issue, and discovering its social determinants of diabetes is crucial. Though several studies have explored the association between loneliness and diabetes risk, large population-based cohort studies linked with outpatient clinical data remain scarce.

Methods: From 114,054 Japanese aged 40-75 years old recruited between 2009 and 2017 in the Japan Public Health Center-based Prospective Study for the Next Generation (JPHC-NEXT), 61,356 individuals who had registered claim data without self-reported diabetes at study participation were analyzed. We used loneliness as an exposure variable assessed by a direct question asking about feelings of loneliness in a baseline questionnaire. Diabetes occurrence was derived from the claim data defined by a validated algorithm using ICD-10 codes starting from “E11-14” and diabetes drug prescriptions. The follow-up duration was until the end of available claim data or 2022 March. We evaluated the association between loneliness and diabetes risk using a Cox proportional hazard model with covariates adjustment. Subgroup analyses by sociodemographic characteristics were also conducted.

Findings: The mean age was 61.1 (SD: 8.8) and females were 54.6%, of whom 2471 (4%) reported high loneliness. Participants with high loneliness tended to live alone, be unmarried, have a depression history, and not be engaged in social participation. During a mean follow-up time of 7.2 years, 3958 new cases of diabetes were identified. Compared to the participants with low loneliness, those with high loneliness had a higher risk of diabetes (HR: 1.21 [95%CI: 1.03, 1.41]). The association was largely consistent across sociodemographic characteristics (p-values for heterogeneity > 0.10).

Conclusions: We identified an association between loneliness and an increased risk of diabetes among Japanese adults, underscoring the importance of recognizing loneliness as a risk factor for diabetes.

Cancer

Estimating breast cancer recurrence in a population-based registry in Georgia, US

Chrystelle Kiang* Chrystelle Kiang Micah Streiff Rebecca Nash Deirdre Cronin-Fenton Anke Huels Kevin C. Ward Timothy L. Lash

Although the descriptive epidemiology of primary breast cancer is well characterized in the US, breast cancer recurrence rates have not been measured at the population level. The number of breast cancer survivors is growing, so a clearer understanding of the descriptive epidemiology of recurrence is a pressing need**.**

We estimated recurrence rates in the Cancer Recurrence and Information Surveillance Program cohort in the Georgia Cancer Registry. We included 25,103 female patients with stage I-III breast cancer diagnosed between 2013 to 2017 who completed primary treatment and had no evidence of disease at least one year after diagnosis, with follow up through 2019. We used missing date methods to impute the outcome of breast cancer recurrence based on an internal validation substudy and further informed by combinations of certain records in the registry (e.g., pathology reports, imaging claims), prognostic variables (e.g., stage), and missing data indicators (e.g., insurance coverage). We pooled HRs across 1000 imputed datasets, adjusted for age, stage, grade, subtype, race and ethnicity, marital status, and urban/rural county at diagnosis.

There were 1,610 patients with a validated outcome (75% with breast cancer recurrence) and we imputed the outcome for the remaining 23,493 patients. The overall incidence of recurrence was ~10% for up to 5 years of follow up. The hazard of recurrence increased as stage and grade increased, but there was no notable difference by tumor subtype. Compared to those aged 55–64 at diagnosis, the HR (95% CI) for ages 35–44 was 1.17 (0.73, 1.87) and 1.05 (0.71, 1.53) for ages 45–54. Compared to Non-Hispanic (NH) White patients, the HR (95% CI) for Hispanic patients was 1.55 (0.89, 2.69), 1.32 (0.56, 3.12) for NH Asian and Pacific Islander patients, and 0.94 (0.73, 1.22) for NH Black patients.

For the first time, we report on the descriptive epidemiology of breast cancer recurrence for up to 5 years in a population-based registry.

Cancer

Social risks and mortality among Black cancer survivors: results from the Detroit Research on Cancer Survivors (ROCS) cohort Theresa A. Hastert* Theresa Hastert Julie J. Ruterbusch Nora Akcasu Ann G. Schwartz

Background: Social risks, or adverse factors associated with poor health, are increasingly considered important predictors of cancer outcomes. This study estimates associations between social risks and mortality among Black cancer survivors.

Methods: We utilized data from 4,069 participants in the Detroit Research on Cancer Survivors cohort. Black adults were invited to participate if they were ages 20-79 at diagnosis with breast, colorectal, lung, or prostate cancer since 1/1/13; or with endometrial cancer (ages 20-79) or any other cancer (ages 20-49) since 1/1/16. Cases were identified through a population-based cancer registry. Patient-reported social risks, including food insecurity, utility shut-offs, housing instability, inability to get medical care due to cost or lack of transportation, and perceptions of neighborhood safety were assessed at ROCS enrollment. Cox proportional hazards models estimated associations between social risks and 10-year all-cause mortality using months since diagnosis as the time scale. All models adjusted for age. Fully adjusted models include income, insurance, site, stage, and treatments received.

Results: At ROCS enrollment, 37% of participants reported any social risks. In age-adjusted models, any social risk was associated with 38% higher mortality (95% CI: 1.21-1.58). Food insecurity (HR: 1.41, 95% CI: 1.18-1.69), housing instability (HR: 1.42, 95% CI: 1.17-1.73), forgoing care due to lack of transportation (HR: 1.79, 95% CI: 1.49-2.15), feeling unsafe in the home neighborhood (HR: 1.25, 95% CI: 1.00-1.55), and utility shut-offs (HR: 1.38, 95% CI: 1.10-1.72) were each associated with higher mortality. Associations attenuated in fully adjusted models, but forgoing care due to lack of transportation remained associated with 31% (95% CI: 1.07, 1.61) higher mortality risk.

Conclusions: Social risks, particularly lack of transportation to care, reflect potentially modifiable risk factors for mortality among Black cancer survivors.

Cancer

The Association Between Metal and Metalloids and Bladder Cancer Risk in the New England Bladder Cancer Study Maria E. Kamenetsky* Maria Kamenetsky Stella Koutros Margaret Karagas Molly Schwenn Alison Johnson Debra T. Silverman Alexander P. Keil

Trace elements, including essential/nonessential metal and metalloids (“metals”), are of interest in the etiology of cancer due to their carcinogenic properties and potential protective properties of essential metals. The combined mixture effect of multiple co-occurring metals on bladder cancer (BC) is not well understood. While previous studies have explored associations between individual metals and BC, there has been limited work in exploring the overall mixture effect of these metals, or by essential or nonessential groupings. We leveraged the New England Bladder Cancer Study (NEBCS), a population-based case-control study, to estimate associations between a mixture of 12 metals and bladder cancer. Toenail clipping samples were obtained from 1213 cases and 1418 controls at time of the interview and analyzed for 7 essential and 5 nonessential metals (Fig 1). Using a novel Bayesian implementation of quantile g-computation, we assessed associations between bladder cancer risk and the overall metals mixture, as well the partial effect associations of essential and nonessentials metals. After adjustment for covariates and factors used for frequency matching (i.e., age, gender, state), we estimated an inverse association between bladder cancer and the overall mixture of metals (odds ratio (OR): 0.76, 95% confidence interval (CI): 0.62-0.92) using standard quantile g-computation. When considered separately, there was limited, but similar evidence of association for essential (OR: 0.85, 95% CI: 0.66-1.08) and nonessential (OR: 0.89, 95% CI: 0.73-1.10) metals. Results were relatively unchanged after omitting adjustment for common sources of metals exposure (diet, occupation). ORs from the Bayesian approach under weak priors were similar. Our findings suggest an overall reduction in risk associated with trace elements on bladder cancer risk in the US general population of Northern New England.

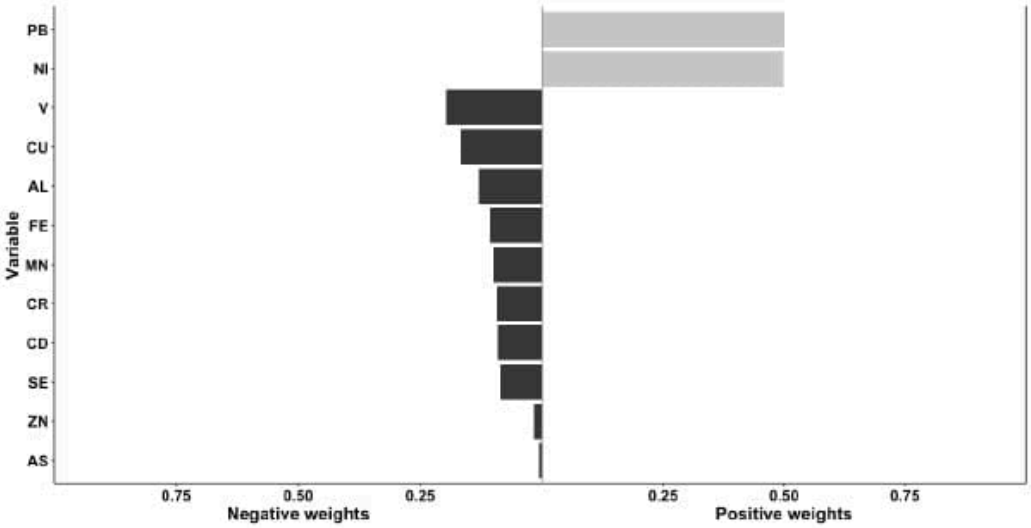


Figure 1: Weights of each metal from standard quantile g-computation regression. Adjusted for sex, age, state, diet, body mass index (BMI), smoking status, high risk occupation status, and average daily total trihalomethanes intake from residence and workplace. PB (lead), NI (nickel), V (vanadium), CU (copper), AL (aluminum), FE (iron), MN (manganese), CR (chromium), CD (cadmium), SE (selenium), ZN (zinc), AS (arsenic).

Cancer

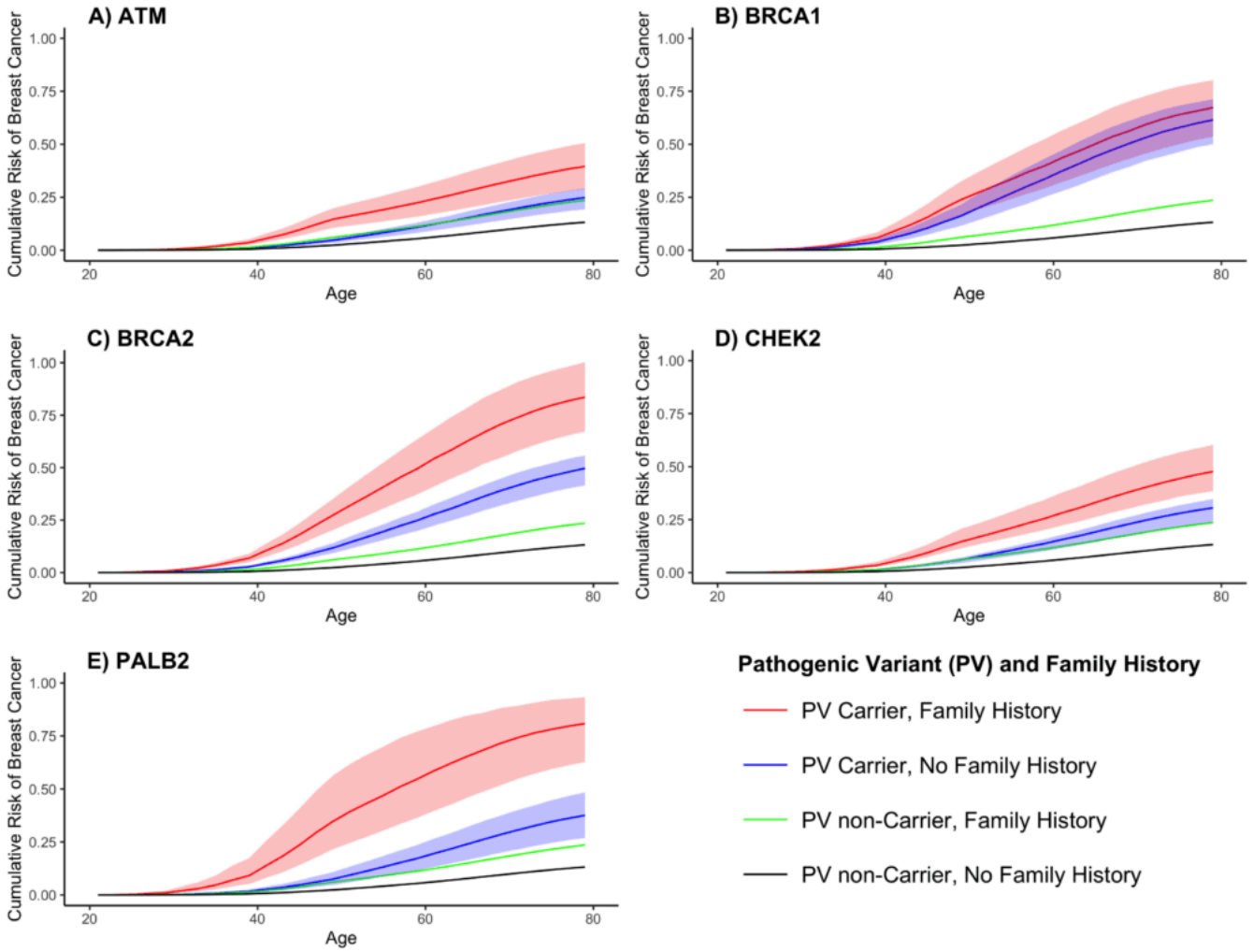
Cumulative risk of breast cancer in the US population, considering pathogenic variants, family history, and established epidemiologic risk factors Katie O'Brien* Katie O'Brien Dale Sandler Alexander Keil

Background Certain variants of BRCA1, BRCA2, and other genes can greatly increase individuals' breast cancer risk. Understanding personal risk may help women make decisions about preventive care, but few studies have investigated the role of these pathogenic variants (PVs) in the general population or in the context of family history and other established risk factors.

Methods We estimated breast cancer odds ratios for PVs of 7 genes in the Cancer Risk Estimates Related to Susceptibility (CARRIERS) consortium (n=67,692, including 33,841 cases). We then combined PV data with nationwide incidence and mortality statistics to estimate conditional cumulative risks of breast cancer, standardized to the U.S. population. Additional models also incorporated population-based data and relative risk estimates for established epidemiologic risk factors.

Results PVs in ATM, BRCA1, BRCA2, CHEK2, and PALB2 were strongly associated with breast cancer, with estimates for BRCA1 and PALB2 PVs demonstrating evidence of heterogeneity by family history. The estimated cumulative risks of breast cancer incidence by age 50 ranged from 2.4% (95% confidence interval [CI]: 2.4-2.4) in women with no PVs and no family history to 35.5% (CI: 21.6-55.1) in PALB2 PV carriers with a family history. Among those breast cancer-free at age 50, the risk of breast cancer by age 80 ranged from 11.1 % (CI: 11.0-11.2) in non-carriers with no family history to 70.5% (CI: 52.8-83.5) for PALB2 carriers with a family history. PV-specific cumulative risk estimates varied across subgroups defined by race/ethnicity and established breast cancer risk factors.

Discussion We present population-based estimates of cumulative breast cancer risk for established PVs for those with and without a family history, overall and for specific subgroups. Such estimates may be useful for prevention and medical decision-making among known PV carriers.


A) ATM
B) BRCA1
C) BRCA2
D) CHEK2
E) PALB2
Cumulative Risk of Breast Cancer
1.00
0.75
0.50
0.25
0.00
20
40
60
80
Age
Pathogenic Variant (PV) and Family History
PV Carrier, Family History
PV Carrier, No Family History
PV non-Carrier, Family History
PV non-Carrier, No Family History

Cancer

Implementation of Biospecimen Collection in the NCI Connect for Cancer Prevention Study

Stephanie Weinstein* Stephanie Weinstein Erin Schwartz Kathleen Wyatt Michelle Brotzman Norma Diaz-Mayoral Amanda Black Hannah Yang Paul Albert Laura Beane-Freeman Amy Berrington Jonas De Almeida Jonine Figueroa Montserrat Garcia-Closas Nicole Gerlanc Gretchen Gierach Rena R. Jones Peter Kraft Charles Matthews Habib Ahsan Brisa Aschebrook-Kilfoy Chun-Hung Chan Robert T. Greenlee Stacey Honda Ben Rybicki A. Blythe Ryerson Katherine Sanchez Mark Schmidt Kevin Sykes Larissa White Jeanette Ziegenfuss Stephen Chanock Mia M. Gaudet Christian Abnet Nicolas Wentzensen

Introduction

The Connect for Cancer Prevention Study is a new prospective cohort aiming to recruit 200,000 participants from 10 integrated healthcare systems across the US. At baseline, participants complete online surveys and donate biospecimens. Intended to be a resource for the wider research community, Connect will focus on studies of cancer etiology, risk prediction, and early detection.

Methods

Blood (SST, K2-EDTA, Li-Hep), urine, and mouthwash are collected at baseline in dedicated study research centers or using clinical phlebotomy labs combined with mailed home mouthwash kits. In addition to the baseline survey modules, participants are asked to complete surveys regarding factors specific to the time of sample collection. Biospecimens are shipped from across the US (CO, GA, HI, IL, MI, MN, ND, OR, SD, TX, WI) in temperature-controlled coolers to a central NCI lab in Maryland for processing and long-term storage. Process metrics to ascertain biospecimen quality include sample completeness, needle-to-receipt time, and specimen deviations. Biospecimen survey completion is also monitored.

Results

As of January 2025, 68% of 55,943 Connect participants (ranging from 56% to 80% across sites) donated any biospecimens, with baseline collections still ongoing. Among collections, 42% were from research centers and 58% from clinical labs, with complete collections (all expected blood, urine, and mouthwash) from 96% and 99%, respectively. Over 80% of biospecimens were received at NCI within 2 days of collection and 97% were received within 4 days. The return of home-collected mouthwash samples was 76%. Among all biospecimens collected, 87% had no protocol or sample deviations. Over 90% of participants submitted the biospecimen survey.

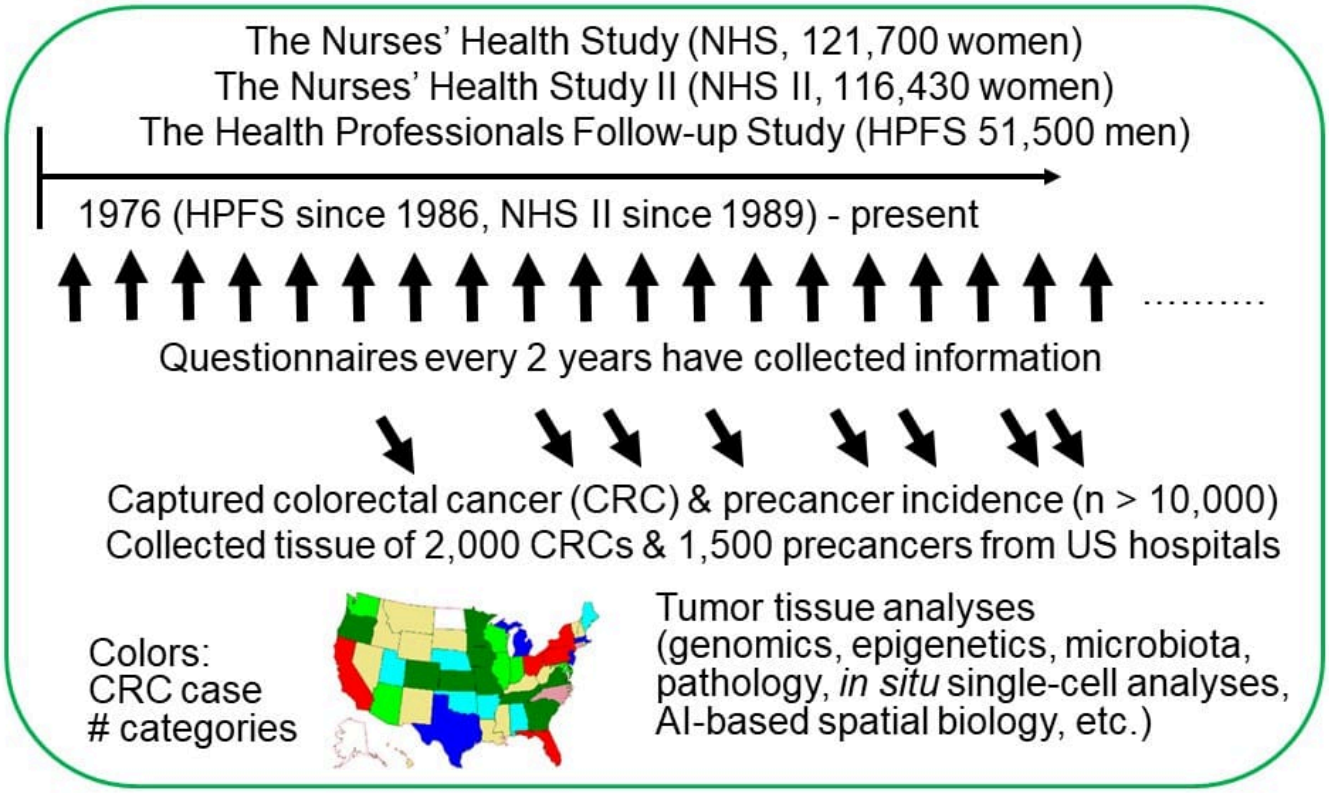
Conclusion

We successfully implemented a robust and efficient biospecimen collection at multiple sites that complements our survey data collection. In the future, Connect data and biospecimens will be available to the research community.

Study Design

Unique Values of the Prospective Cohort Incident-Tumor Biobank Method for Transdisciplinary Cancer Epidemiology Shuji Ogino* Shuji Ogino Tomotaka Ugai

The prospective cohort incident-tumor biobank method (PCIBM) is an unconventional design/method that utilizes a tissue biobank of incident cancer/precancer cases that have occurred in a prospective cohort study. Any prospective cohort study that has accumulated long-term exposure data and given rise to incident tumor cases with available tissues allows research using this method. PCIBM's advantages over tumor tissue-based case-control studies include: 1) the availability of long-term exposure data before cancer diagnosis; 2) less recall bias in past exposures; 3) no differential recall bias in prediagnosis exposures between cancer vs. cancer-free participants; and 4) less patient selection bias. We illustrate the PCIBM, using the Nurses' Health Study (NHS), NHS II, and Health Professionals Follow-up Study, which enrolled over 280,000 participants to follow for decades and assess long-term exposure statuses through biennial questionnaires and tumor development. These studies collected tissue specimens of various cancers that had occurred in the cohort participants. For example, we depict colorectal cancer (CRC)/precancer research using the PCIBM on the cohorts (**Figure 1**). It enabled numerous discoveries of novel etiological links between exposures and CRC incidence plus tumor phenotypes, including one between long-term aspirin use and decreased incidence of PTGS2 protein-positive CRC. For 17 years (as of 2024), no other prospective study has re-tested any of those etiological links. The PCIBM has also enabled the seamless integration of tumor microbiology and immunology into epidemiology. As long-term risk factor exposure appeared to play an important role in early-onset cancer etiology, incident tumor biobanks will contribute to research on the early-onset cancer epidemic. AI-based computational methods will upgrade the PCIBM for worldwide incident tumor biobanks to further improve our understanding of cancer biology/etiology and advance biomedical health sciences.



"The prospective cohort incident-tumor biobank method (PCIBM)" is a research method to utilize the entirety of a prospective cohort study with an incident tumor biobank. The above scheme is an example of the PCIBM using the three prospective cohort studies.

F1

Women’s Health

Temporal trends in age at menarche among women in the United States from 1999 to 2018

Claire Cook* Claire Cook Hilary Brown Sonia Grandi Hailey Banack

Background: Early age at menarche (first menstrual period) is associated with an increased risk of cardiometabolic disease across the lifespan. Age at menarche may therefore represent a sentinel indicator for future chronic disease burden. The aim of this study is to describe the temporal trends in age at menarche from 1999 to 2018 using a nationally representative sample in the United States.

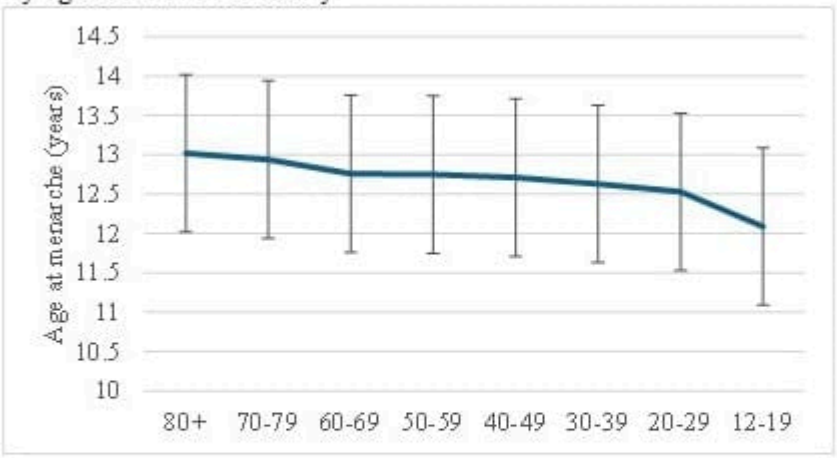
Methods: National Health and Nutrition Examination Survey (NHANES) data collected between 1999 and 2018 were used for this study. The study population included self-identified female participants who completed a retrospective Reproductive Health Questionnaire. Estimates of mean, standard deviation and median and interquartile range for age at menarche described in the total sample and according to age (at the time of the survey), period (NHANES data collection cycle), and cohort (birth cohort defined in 10-year intervals).

Results: Overall, mean age at menarche was 12.64y (± 1.68) among 31,138 women who completed the NHANES survey between 1999 and 2018. Mean age at menarche was highest in women over the age of 80 at the time of survey (13.02y ± 1.69) compared to 12.09y ± 1.03 in women 12-19y. Age at menarche decreased from 12.69y (± 1.65) in 1999-2001 to 12.56y (± 1.71) in 2017-2018. It also decreased by birth cohort, from 13.30y (± 1.69) among participants born in 1910-1919 to 11.79y (± 1.19) among participants born in 2000-2009 (Figure 1). Similar trends in age at menarche were seen based on birth cohort by period and age by period.

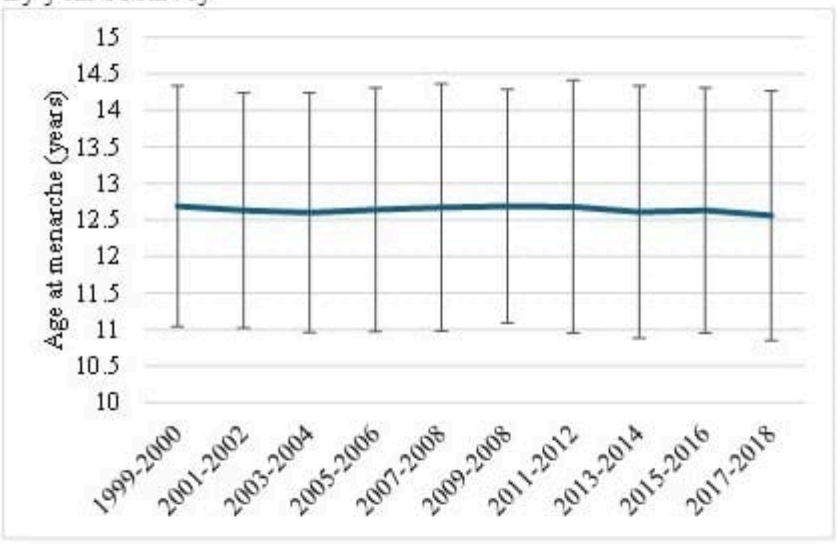
Conclusions: This study provides contemporary estimates on trends in age at menarche, highlighting decreasing temporal trends according to age, period, and birth cohort. These findings underscore the need for future research on the effect of age at menarche on women’s health outcomes across the lifecourse.

Figure 1. Mean age at menarche among all female NHANES participants between 1999 and 2018 (n=31,138)

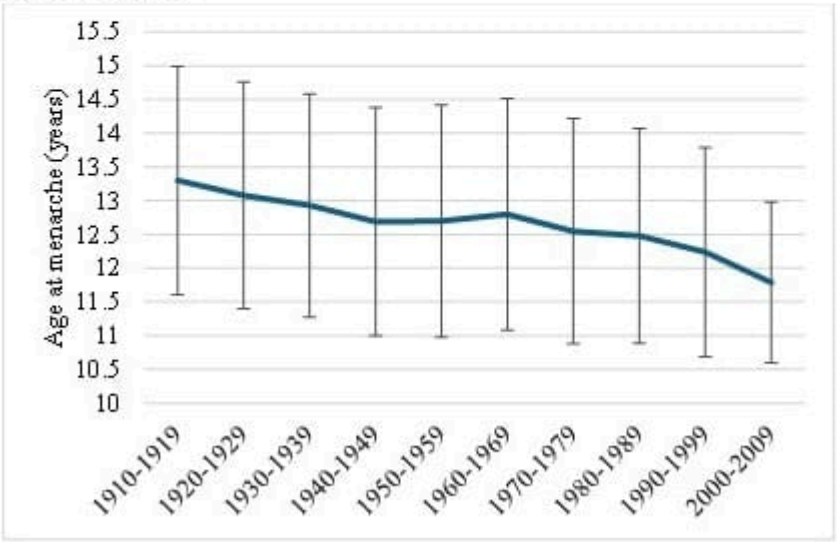
a. By age at the time of survey



b. By year of survey



c. By birth cohort



Women’s Health

Premenstrual symptom patterns and risk factors: a cross-sectional study of college-aged women Margaret Kucia* Margaret Kucia Ariel Scalise Aparna Tiwari Gloria DiFulvio Lynnette Sievert Tara Mandalaywala Donghao Lu Elizabeth Bertone-Johnson

Premenstrual symptoms impact over 75% of reproductive-age women and include physical, emotional, cognitive, and behavioral symptoms that occur cyclically during the luteal phase of the menstrual cycle. Approximately 13% of women miss work or school due to symptoms, and nearly 50% of women have visited a healthcare provider for menstruation concerns. Our study sought to identify latent patterns of premenstrual symptoms and to determine whether associations with risk factors varied between patterns. Our population included n=569 women aged 18–30 yrs who completed a revised version of the Calendar of Premenstrual Experiences (2022-23). Participants also provided information on body mass index, physical and mental health history, and childhood trauma. Mean age of participants was 20.3 (SD 1.7), and 67.1% self-identified as white, 5.8% as Black, 18.5% as Asian/Asian American, and 5.1% as another race. Latina ethnicity was self-reported by 8.0%. Using factor analysis we identified three distinct symptom patterns: 1) anxious, Cronbach α=0.80, symptoms with highest factor loadings (> 0.50) = dizziness, palpitations, anxiety, insomnia, confusion, and forgetfulness; 2) labile mood, Cronbach α=0.88, symptoms >0.50 = irritability, hypersensitivity, mood swings, crying easily, angry outbursts, and depression, and 3) somatic, Cronbach α=0.72, symptoms >0.50 = abdominal bloating, cramping, and back pain. Patterns were consistent with those identified in previous studies, suggesting stability across populations. Our study continues with multivariable modeling to compare how childhood trauma, body mass index, substance use, age at menarche, and hormonal birth control are associated with each of the three patterns. This analysis provides further evidence for the existence of distinct subtypes of premenstrual symptomatology. Our work will contribute to better understanding the complex etiology of symptoms, identifying risk factors, and developing tailored mitigation strategies.

Women's Health

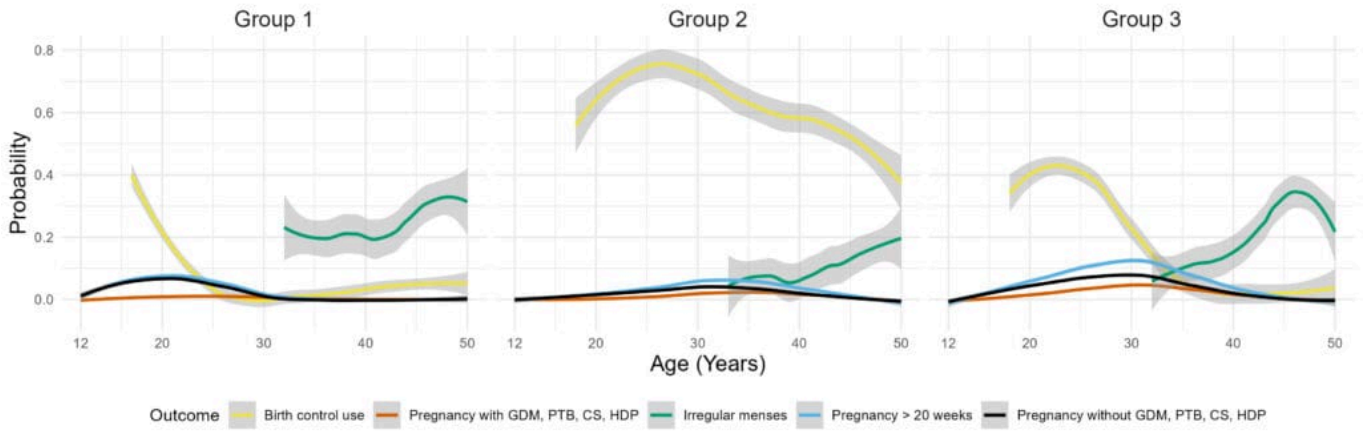
Reproductive trajectories from menarche to menopause: identifying patterns and differences by childhood maltreatment. Kaitlyn K Stanhope* Kaitlyn Stanhope Audrey Gaskins Erica P Gunderson Catherine Kim Cora Lewis

Objective: Few studies to date have considered holistic methods to capture the reproductive life course, largely relying on single indicators. By identifying unique trajectories of reproductive events over the reproductive years we can improve the understanding of how early life experiences impact reproductive outcomes. The goal was to identify unique trajectories of reproductive events across the life course and to explore whether socioeconomic position in early life (parental educational attainment) or childhood maltreatment determine trajectory membership.

Methods: We used data from the Coronary Artery Risk Development in Young Adults (CARDIA) study on all female-bodied participants (n = 2800). We included self-reported reproductive events (complicated pregnancies (with a hypertensive disorder of pregnancy, preterm birth, cesarean delivery, and/or gestational diabetes), uncomplicated pregnancies, irregular menses, and birth control use) and coded each for each year of the reproductive life course (individual determined from reported date of menarche to menopause or loss-to-follow-up). We fit group-based trajectory models and used model fit to identify optimal trajectories. We determine associations with self-reported childhood physical or emotional maltreatment using polytomous logistic regression models controlling for baseline age, parental educational attainment, and race as potential confounders.

Results: We identified three unique trajectories of reproductive events (1: (n = 1,161); 2: (n=498); 3: (n = 1,128)). Group 1 had the youngest age at first pregnancy (mean 19.8, (standard deviation 4.7), 2: 29.29, (6.3), 3: 26.72, (6.2)) Any reported childhood maltreatment was associated with membership in group 1 (adjusted odds ratio: 1.49, 95% confidence interval (1.15, 1.93) versus group 2. Trajectories were similar by baseline obesity status.

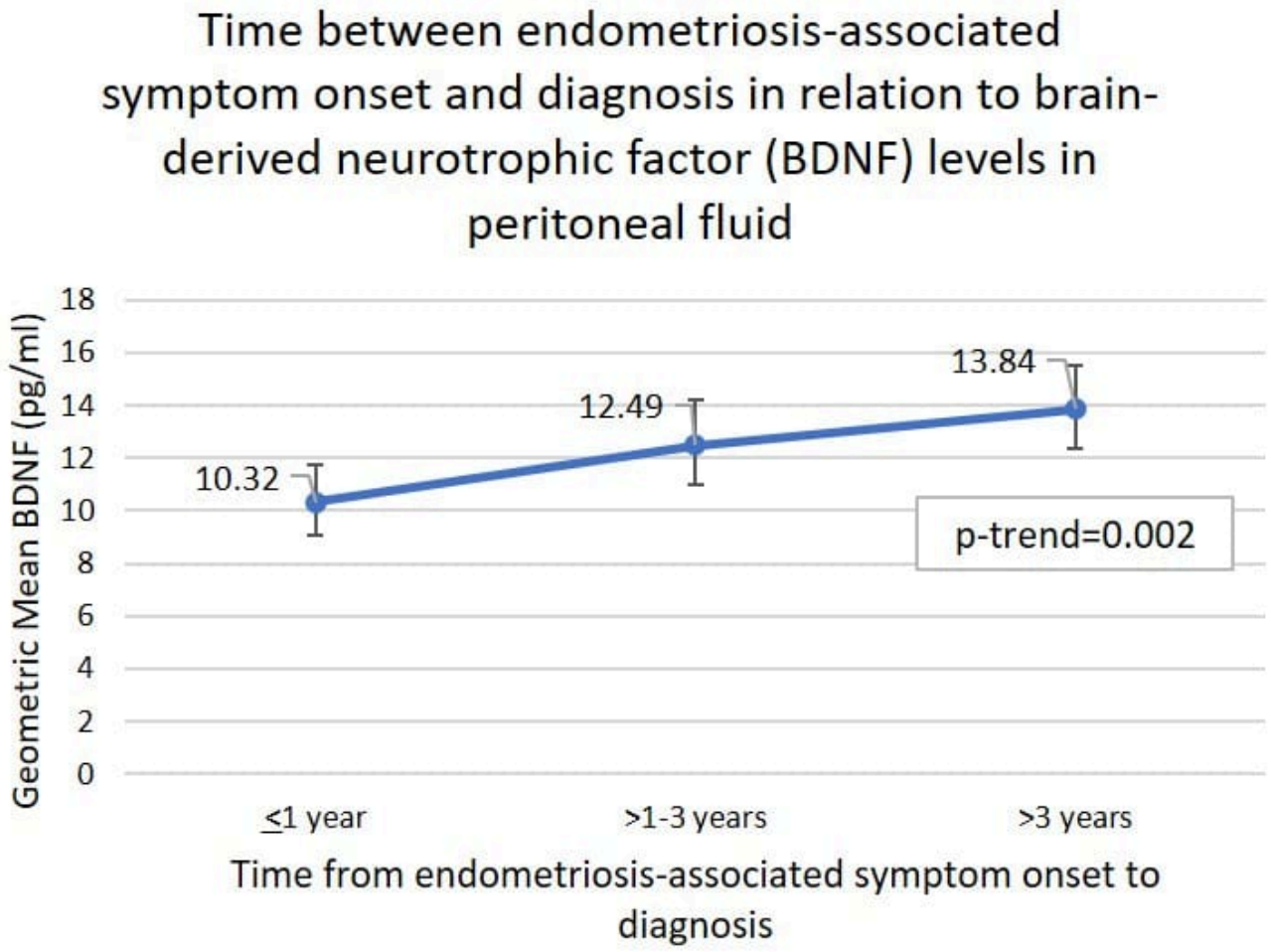
Conclusion: Childhood maltreatment is associated with a pattern of earlier childbearing.



Women’s Health

Peritoneal fluid brain-derived neurotrophic factor and endometriosis characteristics, symptoms and comorbidities Amy Shafrir* Amy Shafrir Ashley Laliberte Allison F. Vitonis Kathryn L. Terry Christine B. Sieberg Stacey A. Missmer

One-third of people with endometriosis experience persistent chronic pelvic pain, potentially via nociplastic pain – a process of increased sensitivity of the central nervous system (i.e., central sensitization [CS]). Brain-derived neurotrophic factor (BDNF) is a marker of CS development, but no research has assessed localized BDNF levels and pain symptoms among people with endometriosis. Using BDNF levels measured in peritoneal fluid (PF) and self-report questionnaires, we investigated the association of endometriosis characteristics, symptoms, and comorbidities with localized BDNF levels among 290 surgically-diagnosed endometriosis participants from the Women’s Health Study: from Adolescence to Adulthood (A2A) cohort. BDNF was measured using an enzyme-linked immunosorbent assay and natural-log transformed. Linear regression was used to calculate geometric means (GM) with 95% CI of BDNF for each endometriosis characteristic adjusting for age, physical activity, body mass index, physician-diagnosed depression, and hormone and anti-depressant use. At surgery, median age was 17 years (interquartile range:15-20y) and 97% had rASRM stage I/II endometriosis. BDNF levels were higher with greater time between endometriosis-associated symptom onset and diagnosis (GM for <1 year:10.32 [CI:9.09-11.73] pg/ml vs. GM for >3 years:13.84 [CI:12.37-15.49] pg/ml; p-trend=0.002). Participants with physician-diagnosed migraines had higher BDNF levels (GM:14.78 [CI:12.86-17.00] pg/ml) compared to those without migraines (GM:11.53 [CI:10.62-12.53] pg/ml; p=0.004). No significant associations were observed between BDNF levels and current pelvic pain type or severity. These results suggest that BDNF levels in the peritoneal cavity may increase with longer duration of undiagnosed endometriosis but may not be associated with endometriosis-associated pain experience – particularly among those with pain types and severity that warranted surgical intervention.


Time between endometriosis-associated symptom onset and diagnosis in relation to brain-derived neurotrophic factor (BDNF) levels in peritoneal fluid
Geometric Mean BDNF (pg/ml)
18
16
14
12
10
8
6
4
2
0
10.32
12.49
13.84
p-trend=0.002
≤1 year
>1-3 years
>3 years
Time from endometriosis-associated symptom onset to diagnosis

Women's Health

Symptomatic Uterine Fibroids at an Academic Urban Safety Net Hospital Kendra Lujan*
Kendra Lujan Julia C. Bond Ezinnem Ugoji Nyia L. Noel

Key Words: gynecology, healthcare utilization, fibroids, anemia

Introduction

We aimed to identify and characterize factors associated with repeat emergency department (ED) visits for symptomatic uterine leiomyomas (fibroids). Understanding factors associated with repeat ED visits can inform future clinical decision-making and interventions to improve patient care and reduce overall healthcare burden.

Methods

We performed a retrospective chart review of individuals aged 18-89 years presenting to the ED for uterine fibroids between June 2014 and February 2020. ED visits were identified by primary ICD-10 diagnosis, and the presence of pre-identified fibroid-related symptoms. We used generalized linear models to estimate prevalence ratios (PR) and 95% confidence intervals (CI) for the association between patient and visit characteristics at initial ED visit and repeat ED visit prevalence.

Results

A total of 873 participants contributed 1036 ED visits. The mean encounter age was 48.5 (SD +/- 8.8) years. Most participants were Black or African American (76.5%), English-speaking (63.5%), and publicly insured (61.3%). Subjects were grouped number of ED visits: 1 (n = 750) and >1 visit (n = 123, 14%) Anemia diagnosis and iron transfusion therapy at the initial ED visit were positively associated with a repeat visit (PR 2.58, 95% CI 1.65, 4.27; PR 2.92, 95% CI 1.72, 4.40). Neither receiving an outpatient gynecology referral at initial visit, nor seeing a gynecologist for follow up within 2 weeks of initial visit, were appreciably associated with the prevalence of a repeat visit.

Discussion

Our analysis revealed that anemia status and the need for blood transfusion during an initial ED visit for fibroid was the strongest predictor of a repeat ED visit for fibroids. Providers should be aware of anemia as a particularly salient feature for patients presenting with uterine fibroids to the ED.

Women’s Health

Per- and Polyfluoroalkyl Substances and Vasomotor Symptoms among Midlife Women: A Cross-sectional Analysis in the Study of Women’s Health Across the Nation Jiaxin Wu* Jiaxin Wu Wenzhiyuan Zhang Xin Wang Carrie A Karvonen-Gutierrez Zhenke Wu Bhramar Mukherjee Siobán D. Harlow Ellen B. Gold John F Randolph Sung Kyun Park

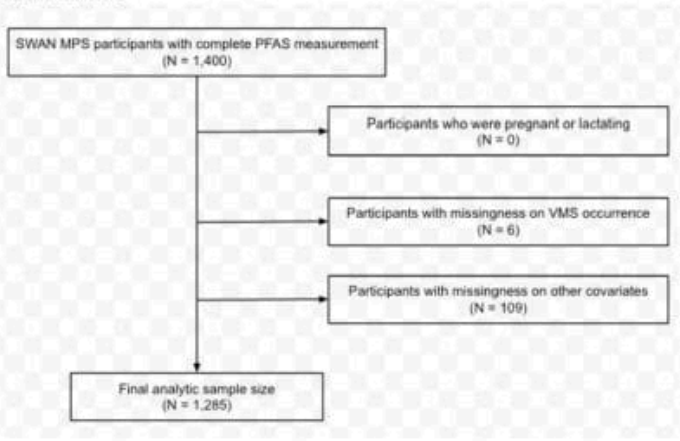
Vasomotor symptoms (VMS), ie, hot flashes and night sweats, are reported by most women during the menopause transition. Per- and polyfluoroalkyl substances (PFAS) have been associated with disrupted sex hormone levels and earlier menopause, but associations between PFAS and VMS are unexplored. This study aimed to assess associations between PFAS and prevalent VMS in midlife women.

We included 1,285 women aged 45-56 years from the Study of Women’s Health Across the Nation (SWAN) at Visit 3 in 1999-2000. VMS was defined as any VMS reported in the previous two weeks. Serum concentrations of seven PFAS with high detection rates (>96%) were included: linear perfluorooctanoate (n-PFOA), linear perfluoroctane sulfonate (n-PFOS), sum of branched isomers of PFOS (Sm-PFOS), perfluorononanoate (PFNA), perfluorohexane sulfonate (PFHxS), 2-(N-methyl-perfluorooctane sulfonamido) acetate (MeFOSAA), and 2-(N-methyl-perfluorooctane sulfonamido) acetate (EtFOSAA). Total PFOS were computed as the sum of n-PFOA and Sm-PFOS. Logistic regressions computed odd ratios (ORs) and 95% confidence intervals (95% CIs) for associations at this visit. PFAS mixture effects were evaluated using quantile g-computation.

After adjusting for age, race/ethnicity, site, education, body mass index, physical activity, smoking, environmental tobacco smoke exposure, menopausal status, prior anxiety, and symptom sensitivity score at Visit 1, ORs (95% CIs) for each doubling of PFAS exposure were 1.20 (1.03, 1.40) for n_PFOA, 1.20 (1.04, 1.39) for n_PFOS, 1.11 (0.98, 1.26) for Sm_PFOS, 1.19 (1.03, 1.38) for total PFOS, 1.20 (1.04, 1.38) for PFNA, 1.12 (1.003, 1.25) for PFHxS, 1.16 (1.02, 1.32) for MeFOSAA, and 1.05 (0.95, 1.15) for EtFOSAA. A mixture of 7 PFAS had an OR of 1.38 (1.08, 1.75) for each tertile increase.

These study results suggest that some PFAS and their mixtures may increase the odds of VMS in midlife women. Further longitudinal studies are needed to examine if PFAS exposure predicts incident VMS.

Flow Chart



Logistic regression results (N = 1,285)

PFAS	Tertiles of original PFAS concentrations			*p*-value for trend	Per doubling increase OR (95% CI)	*p*-value
	Tertile 1 OR (95% CI)	Tertile 2 OR (95% CI)	Tertile 3 OR (95% CI)			
n_PFOA						
Median (IQR), ng/mL	2.4 (1.9, 2.9)	4.1 (3.8, 4.5)	6.8 (5.9, 8.9)			
Model 1	Ref	1.11 (0.83, 1.49)	**1.50 (1.12, 2.02)**	**0.016**	**1.27 (1.10, 1.47)**	**0.001**
Model 2	Ref	1.12 (0.84, 1.51)	**1.46 (1.07, 2.00)**	**0.038**	**1.25 (1.06, 1.45)**	**0.003**
Model 3	Ref	1.04 (0.77, 1.40)	1.36 (0.99, 1.86)	0.081	**1.21 (1.04, 1.41)**	**0.013**
Model 4	Ref	1.01 (0.74, 1.37)	1.32 (0.96, 1.81)	0.089	**1.20 (1.03, 1.40)**	**0.020**
n_PFOS						
Median (IQR), ng/mL	10.5 (8.5, 12.3)	17.4 (15.7, 19.2)	29.8 (24.8, 38.8)			
Model 1	Ref	1.14 (0.87, 1.51)	**1.49 (1.12, 1.99)**	0.058	**1.26 (1.10, 1.45)**	**0.001**
Model 2	Ref	1.07 (0.81, 1.42)	**1.41 (1.05, 1.88)**	0.135	**1.22 (1.06, 1.41)**	**0.006**
Model 3	Ref	1.04 (0.78, 1.38)	1.32 (0.98, 1.78)	0.203	**1.20 (1.04, 1.39)**	**0.015**
Model 4	Ref	1.06 (0.79, 1.41)	1.31 (0.97, 1.77)	0.156	**1.20 (1.04, 1.39)**	**0.015**
Sm_PFOS						
Median (IQR), ng/mL	3.9 (3.0, 4.7)	7.4 (6.4, 8.3)	13.4 (11.2, 17.8)			
Model 1	Ref	1.16 (0.88, 1.54)	**1.37 (1.02, 1.83)**	**0.040**	**1.17 (1.04, 1.32)**	**0.008**
Model 2	Ref	1.15 (0.86, 1.54)	1.30 (0.97, 1.76)	0.094	**1.15 (1.01, 1.30)**	**0.029**
Model 3	Ref	1.12 (0.83, 1.50)	1.20 (0.88, 1.64)	0.201	1.11 (0.98, 1.26)	0.096
Model 4	Ref	1.10 (0.82, 1.48)	1.20 (0.88, 1.63)	0.138	1.11 (0.98, 1.26)	0.099
Total PFOS						
Median (IQR), ng/mL	14.7 (11.9, 17.6)	24.7 (22.2, 27.9)	43.0 (35.8, 55.4)			
Model 1	Ref	1.22 (0.93, 1.61)	**1.55 (1.17, 2.07)**	**0.045**	**1.26 (1.10, 1.45)**	**0.001**
Model 2	Ref	1.16 (0.87, 1.54)	**1.45 (1.08, 1.95)**	0.110	**1.22 (1.06, 1.41)**	**0.006**
Model 3	Ref	1.12 (0.84, 1.49)	**1.36 (1.004, 1.83)**	0.187	**1.19 (1.03, 1.38)**	**0.017**
Model 4	Ref	1.12 (0.84, 1.50)	1.35 (0.99, 1.82)	0.137	**1.19 (1.03, 1.38)**	**0.018**
PFNA						
Median (IQR), ng/mL	0.3 (0.3, 0.4)	0.6 (0.5, 0.6)	0.9 (0.8, 1.1)			
Model 1	Ref	0.97 (0.73, 1.28)	**1.57 (1.17, 2.10)**	**0.023**	**1.23 (1.06, 1.41)**	**0.002**
Model 2	Ref	0.97 (0.73, 1.29)	**1.53 (1.15, 2.06)**	**0.045**	**1.22 (1.06, 1.40)**	**0.005**
Model 3	Ref	0.95 (0.71, 1.27)	**1.48 (1.08, 1.97)**	0.081	**1.19 (1.04, 1.37)**	**0.014**
Model 4	Ref	0.94 (0.70, 1.27)	**1.47 (1.09, 1.99)**	0.071	**1.20 (1.04, 1.38)**	**0.012**
PFHxS						
Median (IQR), ng/mL	0.8 (0.6, 1.0)	1.5 (1.3, 1.7)	3.2 (2.4, 5.0)			
Model 1	Ref	1.08 (0.82, 1.43)	**1.36 (1.01, 1.81)**	0.360	**1.11 (1.005, 1.23)**	**0.041**
Model 2	Ref	1.08 (0.82, 1.44)	**1.36 (1.01, 1.82)**	0.352	**1.12 (1.01, 1.24)**	**0.040**
Model 3	Ref	1.04 (0.78, 1.39)	1.29 (0.96, 1.75)	0.372	1.10 (0.99, 1.23)	0.070
Model 4	Ref	0.98 (0.73, 1.32)	1.30 (0.96, 1.77)	0.236	**1.12 (1.003, 1.25)**	**0.044**
MeFOSAA						
Median (IQR), ng/mL	0.8 (0.6, 0.9)	1.5 (1.3, 1.7)	2.8 (2.3, 3.7)			
Model 1	Ref	1.05 (0.79, 1.41)	**1.35 (1.003, 1.83)**	**0.002**	**1.21 (1.06, 1.37)**	**0.002**
Model 2	Ref	1.03 (0.77, 1.39)	1.26 (0.93, 1.71)	**0.011**	**1.15 (1.04, 1.33)**	**0.009**
Model 3	Ref	1.03 (0.76, 1.39)	1.25 (0.92, 1.71)	**0.019**	**1.17 (1.03, 1.32)**	**0.015**
Model 4	Ref	0.99 (0.73, 1.34)	1.26 (0.92, 1.72)	**0.020**	**1.16 (1.02, 1.32)**	**0.021**
EtFOSAA						
Median (IQR), ng/mL	0.5 (0.4, 0.7)	1.2 (1.0, 1.4)	3.0 (2.2, 4.4)			
Model 1	Ref	1.16 (0.87, 1.55)	1.29 (0.96, 1.73)	0.773	1.07 (0.98, 1.17)	0.156
Model 2	Ref	1.14 (0.85, 1.52)	1.24 (0.92, 1.68)	0.789	1.06 (0.97, 1.16)	0.232
Model 3	Ref	1.17 (0.87, 1.58)	1.22 (0.90, 1.65)	0.639	1.05 (0.96, 1.15)	0.307
Model 4	Ref	1.14 (0.85, 1.54)	1.19 (0.88, 1.62)	0.613	1.05 (0.95, 1.15)	0.343

Model 1 was adjusted for age, race, and site.
Model 2: Model 1 + education, BMI, physical activity, smoking status, and passive smoking.
Model 3: Model 2 + menopausal status.
Model 4: Model 3 + prior anxiety and symptom sensitivity score
*** Results in bold are statistically significant at alpha = 0.05 level.**

Infectious Disease

A comparison of respiratory virus shedding patterns in a prospective longitudinal state-wide cohort Sarah Bassiouni* Sarah Bassiouni Dolapo Raheemat Raji Amy Callear Rachel Truscon Emileigh Johnson Arnold Monto Emily Martin

Background: Viral shedding has important implications for isolation and infection prevention guidelines. Our objective was to compare shedding of three respiratory viruses (RespV) among individuals in a community-based cohort over two consecutive RespV seasons.

Methods: Community Vaccine Effectiveness against Asymptomatic and Symptomatic SARS-CoV-2 Infection in Michigan is a prospective longitudinal cohort study that evaluates SARS-CoV-2 and other respiratory viruses year-round using weekly nasal swabs. Data was collected for RespV seasons 7/2022-6/2023 and 7/2023-6/2024. If participants met the case definition, they were considered symptomatic and collected an additional swab at onset; all specimens were PCR tested to determine RespV status. For this analysis, cessation of viral shedding was defined as the total duration of RespV positive swab results with two sequential negatives (RespV+/-/-).

Results: Results were analyzed from 25860 unique nasal swabs collected from 917 participants. Of those, 597 had specimens that were RespV+/-, with 95 positive for respiratory syncytial virus (RSV), 88 for SARS-CoV-2, and 45 for influenza. For participants who had specimens +/-/-, the median days to viral shedding cessation was: 7.0 (min=1, max=90) for RSV, 7.0 (min=3, max=41), and 7.0 (min=1, max=54) for influenza. Median RT-PCR cycle threshold values were comparable for all three respiratory viruses (RSV: 30.45, SARS-CoV-2: 31.4, and influenza: 31.00). A Bayesian analysis for interval censoring (using a semiparametric method under a proportional hazards model) is also in progress.

Conclusions: These findings reveal that, within this study population, time to viral shedding cessation was similar for all three RespV compared in this time frame. Median length of RespV shedding provides sufficient time for other household members to be exposed, thus disrupting patterns of RespV shedding within households can have major public health and infection prevention implications.

Figure 1. Defining viral shedding and cessation

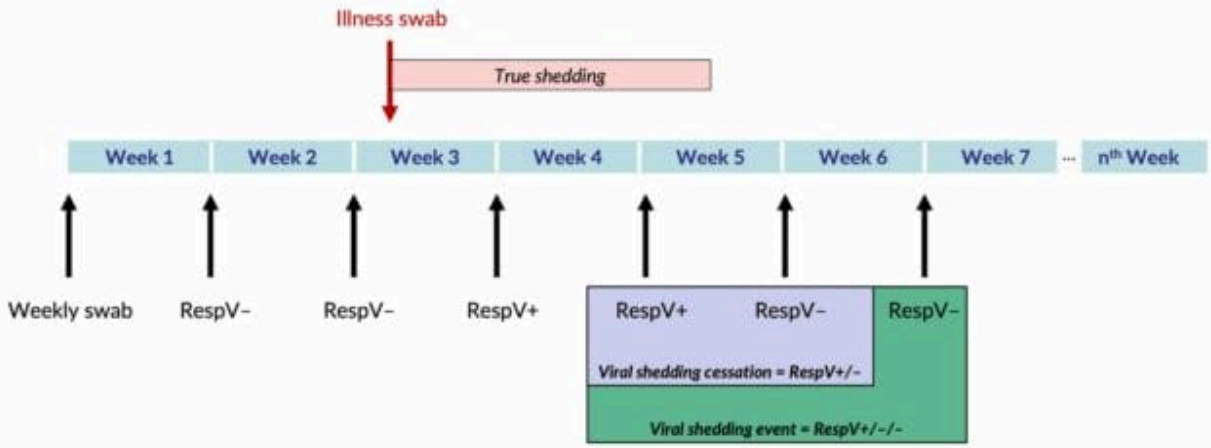


Figure 2. Box and whisker plot comparing time to cessation of viral shedding for RSV, SARS-CoV-2, and influenza

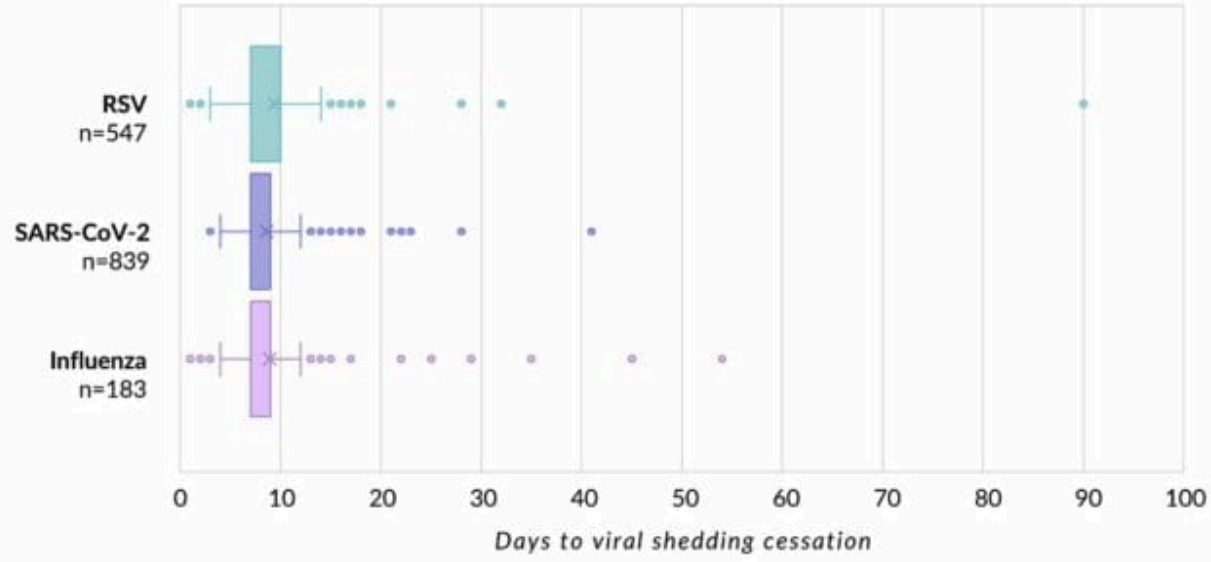
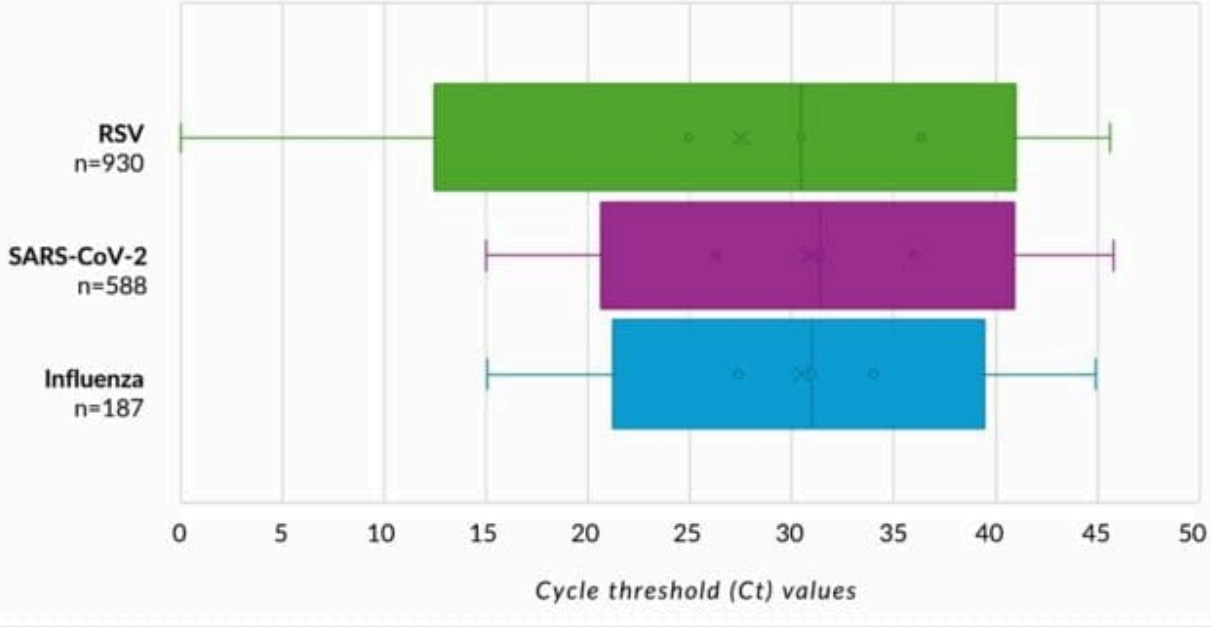


Figure 3. Box and whisker plot comparing cycle threshold (Ct) values for positive nasal samples of RSV, SARS-CoV-2, and influenza



Infectious Disease

Conflation of prediction and causality in observational cohort studies of HIV and drug-resistant tuberculosis Matthew L. Romo* Matthew Romo Lucia Barcellini Molly F. Franke Palwasha Y. Khan

Observational data can answer both predictive and etiologic research questions; however, the model-building approach and interpretation of results differ based on the research goal (i.e., prediction versus causal inference). Conflation occurs when aspects of the methodology and/or interpretation that are unique to prediction or etiology are combined or confused, potentially leading to biased estimates and erroneous conclusions. Drug-resistant (DR) tuberculosis (TB) remains a major global public health threat, and living with HIV might be a predictor and/or cause of worse treatment outcomes. We conducted a rapid review using MEDLINE (2018–2023) to identify cohort studies among people with DR-TB that considered HIV status an exposure of interest and reported on TB treatment outcomes. Using signaling questions related to elements of predictive and etiologic studies, two reviewers assessed four domains of each article: (i) research question, (ii) statistical approach, (iii) presentation of results, and (iv) discussion and interpretation of results. An article was classified as conflated if any one of the domains was conflated (i.e., containing both etiologic and predictive elements) or at least two domains had discordant classifications (e.g., predictive research question domain with etiologic interpretation of results). Of 177 unique articles from our search, 40 articles met the inclusion criteria and were included in the review. Research questions were classified as unclear for 17 (43%) articles. When considering the four domains, 31 (78%) articles had evidence of conflation. The most common types of conflation were recommending or proposing interventions to modify exposures in a predictive study and having a causal interpretation of predictors. Conflation between prediction and etiology was common in the HIV and DR-TB literature highlighting the importance of increasing awareness about it and its potential consequences, and ways to avoid it.

Infectious Disease

Varying Malaria Rapid Diagnostic Test Accuracy by Regional Transmission Level and Demographics in Mainland Tanzania Danielle Wiener* Danielle Wiener Zachary R. Popkin-Hall Misago D. Seth Rashid A. Madebe Rule Budodo Dativa Pereus Catherine Bakari Sijenunu Aaron Daniel Mbwambo Abdallah Lusasi Stella Kajange Samwel Lazaro Ntuli Kapologwe Celine I. Mandara Jeffrey A. Bailey Jonathan J. Juliano Timothy P. Sheahan Deus Ishengoma

A cornerstone of malaria control is accurate diagnosis and rapid treatment, which predominantly relies on point-of-care effective malaria rapid diagnostic tests (RDTs). This is of particular importance in Tanzania, where overall cases remain high, but where transmission intensity can vary from very low to very high depending on the district/region. Thus, it is important to quantify the accuracy of these tests across different transmission settings and by different demographic groups. Clarifying how RDT results differ from qPCR results, and the nature of additional variance in sensitivity and specificity by test manufacturer, will be useful for reducing outcome misclassification when studying malaria prevalence and optimizing their routine use. We compared 3 national standard histidine rich protein 2 (HRP2) based RDTs (Care Start, First Response, and SD Bioline), and a research RDT based on detection of lactate dehydrogenase (Rapigen) to qPCR. Data were collected in a nation-wide survey in 2021 covering 10 of the 26 regions in Mainland Tanzania from the four strata of high, moderate, low and very low transmission intensities. We found differences by age, gender and regional transmission rate of malaria. The research RDT had overall low performance, with the lowest sensitivity across the 4 designated transmission strata (very low: 0.66, low: 0.82, moderate: 0.82, high: 0.68) and across most demographic subgroups (range: 0.70-0.82). Additionally, negative predictive value was low for all tests in moderate to high transmission regions (range: 0.52-0.78). These results offer pertinent information on test accuracy and reliability, compare a new RDT to current national standard RDTs in Tanzania, and decrease outcome misclassification for malaria prevalence estimates.

Table 2.2. Results of Sensitivity and Specificity Analyses of mRDTs compared to qPCR Stratified by Malaria Transmission Levels in Geographical Districts, Tanzania 2021(?)

mRDT Test Type	Sensitivity	Specificity	Positive Predictive Value (PPV)*	Negative Predictive Value (NPV)*
Very Low				
Care Start**	0.783	0.986	0.947	0.932
First Response	0.635	0.916	0.777	0.844
SD Bioline	0.866	0.931	0.933	0.861
Rapigen	0.655	0.987	0.968	0.831
Low				
Care Start	0.933	0.920	0.976	0.793
First Response	0.893	0.826	0.893	0.826
SD Bioline	0.871	0.897	0.951	0.753
Rapigen	0.816	0.968	0.977	0.754
Moderate				
Care Start	0.907	0.667	0.936	0.571
First Response	0.931	0.863	0.959	0.786
SD Bioline	0.841	0.883	0.948	0.688
Rapigen	0.823	0.913	0.967	0.624
High				
Care Start**	0.725	0.833	0.905	0.577
First Response	0.901	0.763	0.894	0.777
SD Bioline	0.906	0.741	0.932	0.667
Rapigen	0.681	0.950	0.974	0.524

*For these analyses, the prevelance of the usage of mRDT tests compared to qPCR in the sample population is inherent to the calculation. For a population with differening levels of mRDT test administration, the PPV and NPV will be different.

**These strata had small sample sizes (Very Low Care Start: n = 93, 1 false positive, 5 false negatives; High Care Start: n = 58; 3 false positive, 11 false negatives).

Infectious Disease

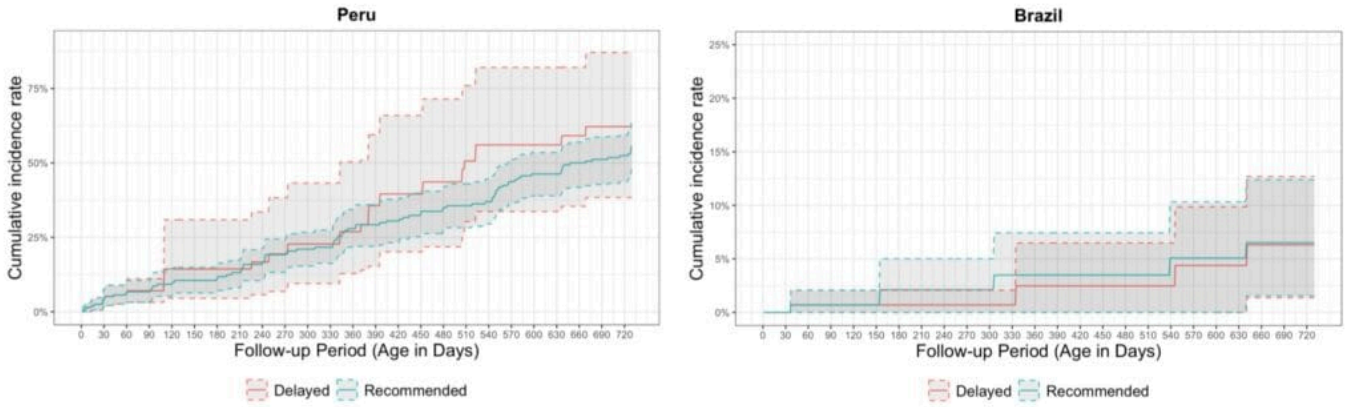
Comparative Effectiveness of Recommended vs. Delayed Dosing Schedules for Rotavirus Vaccines: Target Trial Emulation Shae Gantt* Shae Gantt Toshiaki Komura Elizabeth Rogawski McQuade Kayoko Shioda

Background: Live oral rotavirus vaccines are less effective in low- and middle-income countries (LMICs) compared to high-income countries when following the same dosing schedule. We hypothesized that altering dose timing may improve immune protection in LMICs.

Methods: We emulated a target trial with clone-censor weighting to compare the effectiveness of the recommended two-dose rotavirus vaccine schedule with a delayed schedule in preventing rotavirus infection among children under two in Peru and Brazil. Secondary data from the Malnutrition and Enteric Disease Study (MAL-ED) multisite birth cohort (2009-2014) were analyzed. The recommended schedule administers the first dose at 38-65 days and the second dose at 66-168 days after birth, with at least four weeks between doses. The delayed schedule administers the first dose at 66-104 days and the second dose at 105-240 days after birth, also with at least four weeks between doses. Children were followed until the earliest of rotavirus infection, protocol nonadherence, or their second birthday. Cox proportional hazards models estimated inverse probability of censoring weights, adjusted for birth weight, birth height, and duration of exclusive breastfeeding.

Results: We included 145 children in Brazil and 191 in Peru in the clone-censor weight analysis. Under the recommended schedule, the weighted cumulative risk of rotavirus infection at two years was 0.07 (95% confidence interval CI: 0.02-0.12) in Brazil and 0.55 (95% CI: 0.48-0.64) in Peru. For the delayed schedule, the weighted cumulative risk was 0.06 (95% CI: 0.01-0.13) in Brazil and 0.62 (95% CI: 0.38-0.87) in Peru. The risks did not differ significantly between schedules in both countries.

Discussion: We found no difference in the effectiveness of rotavirus vaccines between the recommended and delayed dosing schedules in these settings.



Infectious Disease

Using spatial and genomic analyses to investigate Mycobacterium tuberculosis transmission in a large city in Taiwan Yu Lan* Yu Lan Chieh-Yin Wu Benjamin Sobkowiak Joshua L. Warren Ted Cohen Hsien-Ho Lin

Background: The estimated incidence of tuberculosis (TB) in Taiwan has declined by an average of 6% a year since 2016 and was at 28 cases/100,000 individuals in 2022. In the setting of declining disease and increasing concentration in old age groups, a better understanding of where and amongst whom transmission of Mycobacterium tuberculosis (Mtb) is occurring can help inform elimination strategies.

Design: We aimed to sequence Mtb isolates from culture-positive cases in Kaohsiung between 2018-2022. Laboratory and epidemiological data were available from routinely collected records.

Methods: Mtb isolates were grouped into putative transmission clusters based on a standard single nucleotide polymorphism distance threshold of 12. Investigation of spatial foci of transmission was done using a non-parametric distance-based approach. Analysis of factors associated with membership in a transmission pair was done using a hierarchical Bayesian regression model.

Results: Among 4,064 culture-positive cases of TB during the study period, whole genome sequencing data was available for 3,379 cases. We found 217 genomic transmission networks comprising 796 cases, while 11 networks included at least 10 cases. We detected statistically significant spatial foci in 9 large networks. Pairwise analysis revealed that younger ages, smaller age differences, and shorter spatial distance between two patients were associated with greater odds of two patients being in the same network. For every two-year decrease in the sum of ages of two patients, the odds of being in the same network increased by 12% (95%CI: 10%-14%); for every two-year decrease in age difference between two patients, the odds increased by 5% (3%-7%); and for every 5km decrease in spatial distance between two patients, the odds increased by 24% (16%-30%).

Conclusion: Integrating spatial and genomic analysis provide evidence of local Mtb transmission and reveal factors associated with being a member of a transmission pair, including younger total age, more similar age, and smaller distance for the pair.

Causal Inference

The transportability of the causal effect of an infectious disease intervention to a target population Christopher Boyer* Christopher Boyer Juan Gago

Infectious disease outbreaks are dynamic events characterized by repeated and often rapid shifts in infection patterns, population immunity, host behaviors, and antigenic evolution. This changing landscape makes it challenging to monitor the effectiveness of interventions to reduce or modify the course of disease, as new circumstances require continual re-estimation of their impact. However, direct re-estimation, through additional trials or observational studies, may be impractical as these studies may be hard to justify (in the case of controlled trials) or they may take too long and incur additional risk of bias (in the case of observational studies). In this case, a possible research goal is to "transport" the causal effect estimated in an initial trial to the new setting.

Recent methodological developments for analyses that extend –generalize or transport– inferences from a trial to a target population aim to accomplish this goal through techniques that standardize the data distribution observed in the trial to the covariate distribution in the target population, assuming that all relevant effect modifiers are measured. However, infectious disease outbreaks introduce additional complexities that often violate the core identifiability assumptions that motivate these techniques, even when all effect modifiers have been accounted for. Specifically, the transmission of an infectious disease between individuals introduces the possibility of interference, whereby an intervention affecting one individual's risk of infection also affects the risk of their contacts. Furthermore, due to the dynamic nature of an outbreak, the structure and degree of post-baseline exposure are likely to vary between the trial and the target population.

In this study, we examine the transportability of infectious disease interventions from a source to target population and discuss the conditions under which relevant causal effect estimands are identifiable using existing approaches. We also propose alternative strategies based on transporting so-called per exposure effects, i.e. effects under hypothetical interventions on exposure. We derive estimators and illustrate our methods via an agent-based simulation of an outbreak in a source and target population.

Health Disparities

Intersectional Dynamics of Physical and Mental Health Inequalities Across the Life Course: A Longitudinal MAIHDA Analysis of the United Kingdom Household Longitudinal Study

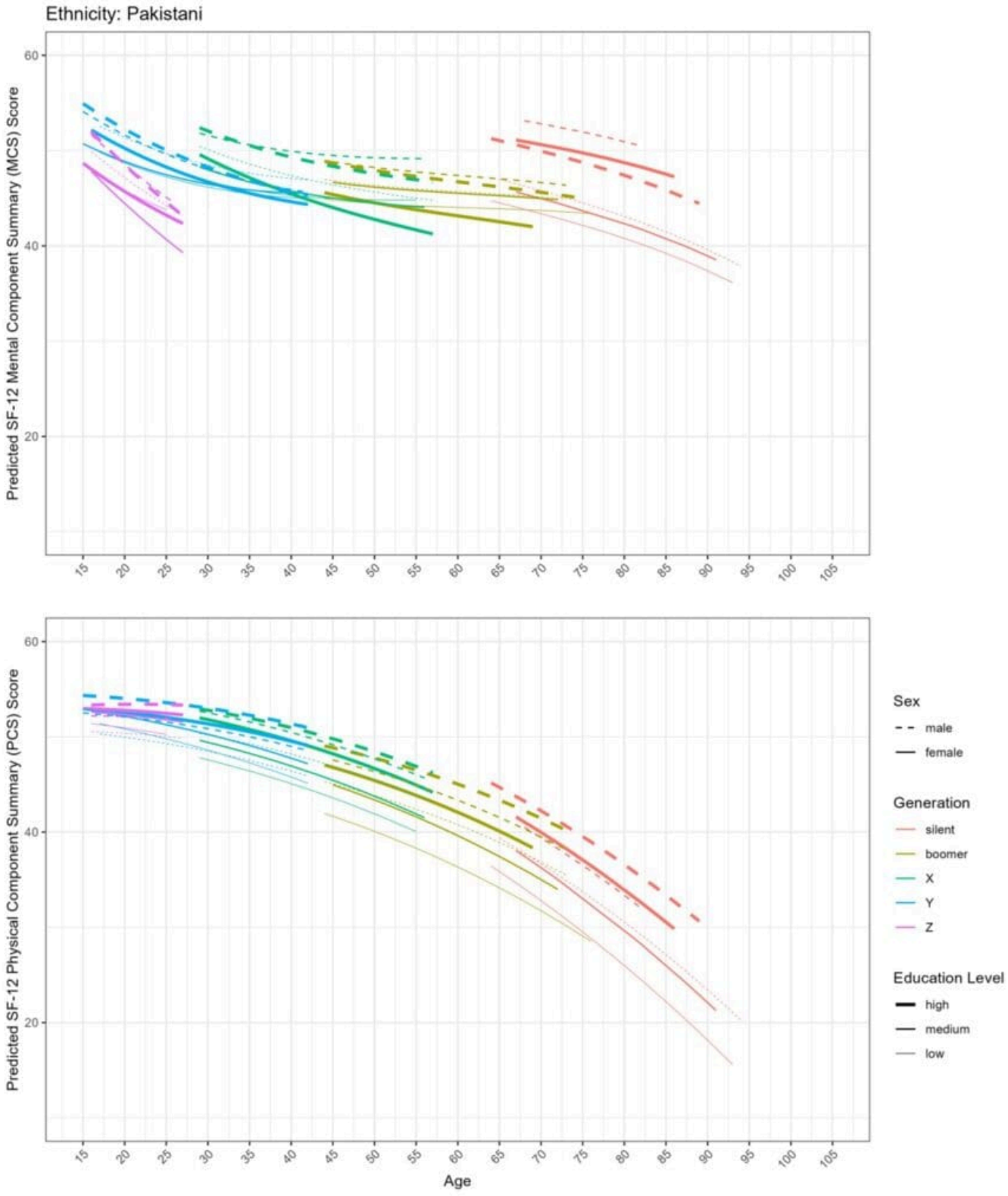
Daniel Holman* Daniel Holman Andrew Bell Helena Mendes Constante Mark Green Aneta Piekut Matthew Bennett

The existence of physical and mental health inequalities in the UK according to socioeconomic position, gender and ethnicity is well-established. Increasingly, scholars are applying intersectionality to understand how these axes of inequality layer and interact. However, very little is known about intersectional trajectories across the life course, and how this varies for those in different generational cohorts.

This study applies a highly novel longitudinal MAIHDA (Multilevel Analysis of Heterogeneity and Discriminatory Accuracy) approach to understand intersectional dynamics in physical (SF-12 PCS) and mental (SF12-MCS) health inequalities. MAIHDA nests individuals within their intersectional strata to estimate how much variability in an outcome is attributable to intersectional subgroups, and to assess the nature and extent of intersectional inequalities. The analysis uses data from people aged 15-103 in the United Kingdom Household Longitudinal Study (n=78,991) from 2009-2022. Intersectional variables are ethnicity (10 categories), gender (2 categories), education (3 categories) and generation (5 categories), resulting in 330 intersectional groups.

The findings suggest that mental health shows clear generational effects, whereas physical health is mainly driven by age. Physical health varies more between than within people over time, showing significant intersectional inequalities. Mental health is more volatile within individuals over time, and intersectional inequalities are minimal. Low education women typically experienced the worse health trajectories, and for mental health, this was particularly the case for generation Z. Pakistani and Bangladeshi ethic groups had the worst physical and mental health.

The results suggest a complex picture of mental and physical health over the life course, which can provide valuable information for interventions and policies to target and tailor approaches to address the nuances of health inequalities.


Ethnicity: Pakistani
Predicted SF-12 Mental Component Summary (MCS) Score
Predicted SF-12 Physical Component Summary (PCS) Score
60
40
20
15
20
25
30
35
40
45
50
55
60
65
70
75
80
85
90
95
100
105
Age
Sex
male
female
Generation
silent
boomer
X
Y
Z
Education Level
high
medium
low

Health Disparities

Climate-Related Shocks Associated with Depression and Anxiety in Bangladesh: Exploring Geographical and Socioeconomic Inequalities JUWEL RANA* JUWEL RANA Arnab Dey Khandaker Jafor Ahmed

Climate change–related extreme weather events have significant implications for mental health, yet evidence of their impact in disaster-prone Bangladesh remains limited. This study examines the associations between climate-related shocks and depression and anxiety among reproductive-age women and explores geographic and socioeconomic disparities in these relationships. A retrospective cohort was constructed using the 2022 Bangladesh Demographic and Health Survey (BDHS). Data on annual floods and storms (2017–2022) were obtained from the DMT global dataset. Each participant was assigned a total number of events they experienced (based on district of residence) during 2020–May 2022. The district was also assigned the INFORM Risk Index for floods in Bangladesh. Depression and anxiety were measured using the Patient Health Questionnaire-9 (PHQ-9) and Generalized Anxiety Disorder-7 (GAD-7) scales, respectively. Multivariable Generalized Estimating Equations with an exchangeable covariance structure were applied to estimate the risk of depression and anxiety associated with extreme weather events. Regional and socioeconomic disparities were assessed using the Cochrane Q-test statistic. A total of 19,012 women (aged 15–49) were included. The national weighted prevalence of depression was 20.0%, while anxiety stood at 5.2%. Exposure to flooding within three years preceding the survey increased the risk of both depression (1.21 [1.09–1.34], $p<0.047$) and anxiety (1.08 [1.00–1.17], $p=0.045$). High flood-prone districts were linked to elevated risks of these conditions. Significant geographic and socioeconomic disparities were observed in the flood–mental health relationship. Special attention should be given to the most affected districts and vulnerable groups to effectively mitigate the associated health risks.

Social

Deaths, medical transfers, and infirmary visits among incarcerated people in Pennsylvania state prisons following extreme ambient temperatures Jaquelyn Jahn* Jaquelyn Jahn Claudia Anderson Jessica T. Simes Leah H Schinasi Michael Leung Josiah Kephart Bruce Western

Objectives: To examine excess deaths, medical transfers, and infirmary visits associated with extreme hot and cold temperatures in Pennsylvania state prisons and evaluate subgroup heterogeneity.

Methods: Using administrative data on people incarcerated in Pennsylvania state prisons (2000-2023) and outdoor temperature data for each prison facility, we estimated risk associated with the hottest and coldest 1% of the temperature distribution using distributed lag time series models.

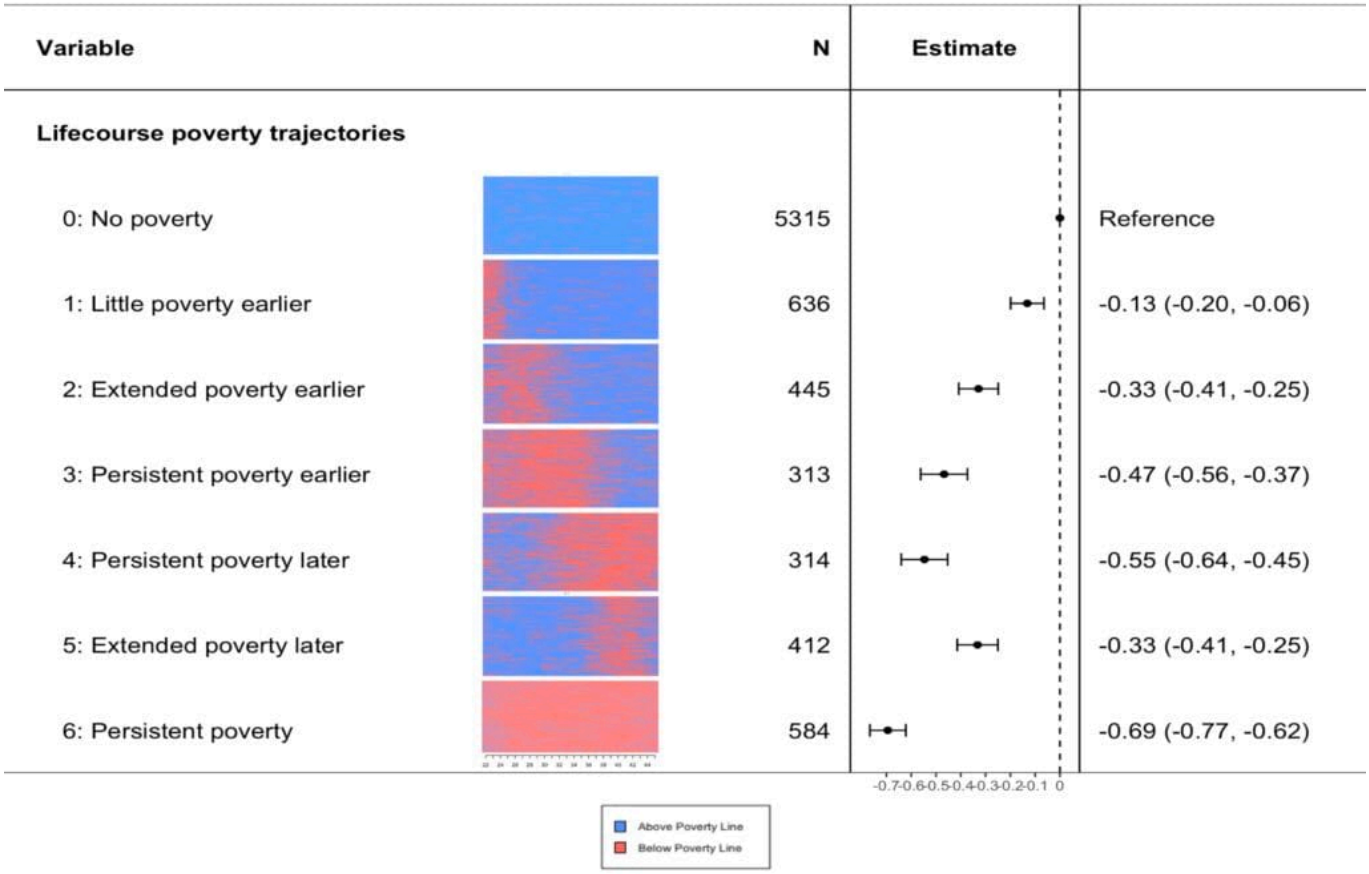
Results: We observed an increased risk of all-cause mortality (RR 1.36, 95% CI: 1.01, 1.84), and infirmary visits (RR 1.08, 95% CI: 1.01, 1.15) associated with extreme heat exposure compared to a reference temperature of 20 degrees C. There was limited evidence of increased risk associated with extreme cold exposure, except among adults aged 55+ for whom we observed a rise in medical transfers (RR: 1.26, 95% CI: 1.00, 1.58).

Conclusions: Our findings contribute to the growing research on the adverse health implications of extreme hot and cold temperature exposure for incarcerated populations. As climate change continues to amplify temperature extremes, particularly in the frequency, duration, and severity of heatwaves, policy action including decarceration is urgently needed to protect the health of incarcerated populations.

Health Disparities

Duration of life-course poverty impacts cognitive performance: an NLSY79 sequence analysis Mia Navarro* Mia Navarro Lucia Pacca Jillian Hebert Anusha Vable

Measures of experienced disadvantage, such as poverty status and SES, are known correlates of cognitive decline and other adverse outcomes. We estimate associations of poverty persistence, including differences in poverty timing and duration, as a potential determinant of midlife cognitive performance. We used data from the National Longitudinal Survey of Youth 1979 (NLSY79, N=8019). We quantified differences between individual level poverty trajectories from ages 20 – 45 using sequence analysis and grouped similar trajectories using cluster analysis. We created a composite measure of cognitive performance using measures of immediate and delayed word recall, serial 7 subtractions and backwards counting. We performed multivariate linear regression analyses to assess the association between lifecourse poverty trajectories and cognitive performance around age 50 and adjusted for race, sex, and birthplace. We imputed missing covariate and outcome values using Multiple Imputation by Chained Equations. There were seven lifecourse poverty trajectories represented in the NLSY data that varied by amount of time in poverty (duration) and poverty timing (Figure 1): no poverty; little poverty earlier; extended poverty earlier; persistent poverty earlier; persistent poverty later; extended poverty later; persistent poverty. Compared to no poverty, those who experienced poverty had lower cognitive performance (b for little poverty = -0.13, 95% CI: -0.20, -0.06), and longer duration of poverty was associated with lower cognitive performance (b for persistent poverty = -0.69, 95% CI: -0.77, -0.62). We found little evidence that timing of poverty was associated with differential cognitive performance. Longer poverty duration was associated with poorer cognitive performance among middle age adults, but there was little evidence that timing of poverty earlier or later in the lifecourse mattered for cognitive performance.



Structural

State-level LGBTQ-related policy trajectories (2015-2022) and health and healthcare access outcomes (2023) in the United States: A sequence and cluster analysis approach

Dougie Zubizarreta* Dougie Zubizarreta Ariel L. Beccia Anusha M. Vable Allegra R. Gordon S. Bryn Austin

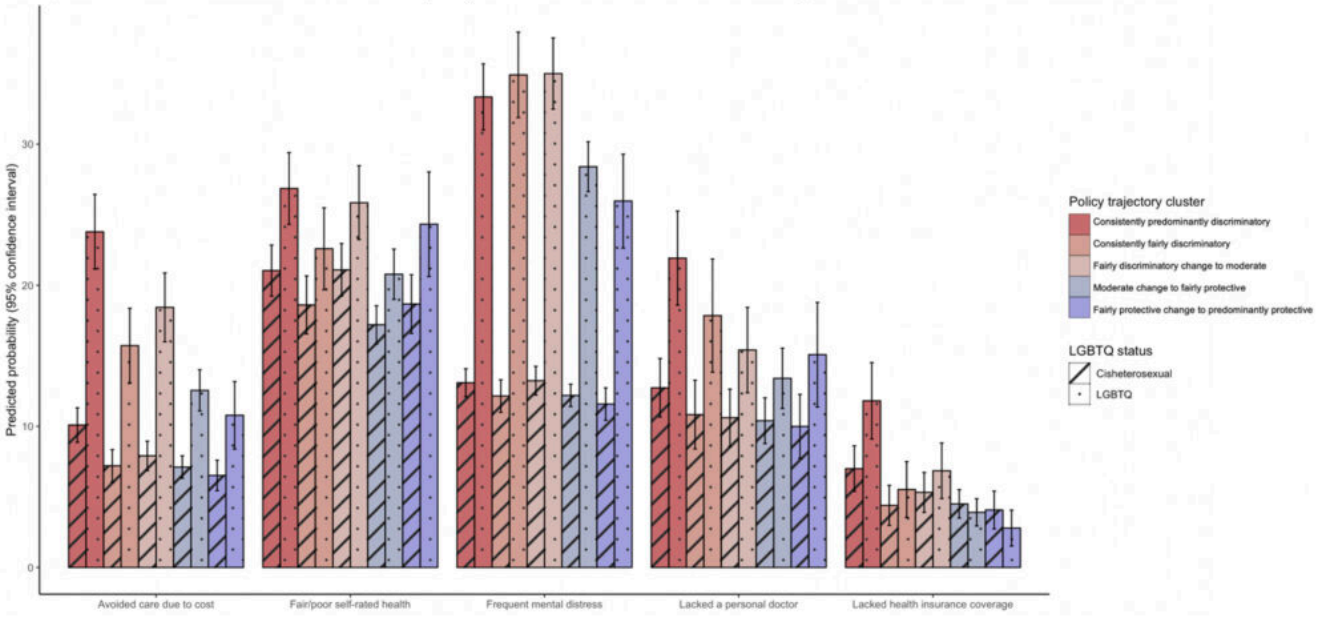
Background: Discriminatory policies are a root cause of LGBTQ health inequities. Over the past decade, there has been a cascade of legislative attacks targeting LGBTQ people's rights, yet limited research has characterized state-level LGBTQ-related policy trajectories over time and examined their implications for population health.

Methods: Using LGBTQ-related policy data from the Movement Advancement Project, we constructed state-level policy trajectories for 2015-2022. We conducted a sequence analysis to quantify differences between policy trajectories and cluster analysis to group similar trajectories. We fit survey-weighted multilevel logistic models to estimate associations between policy trajectory clusters and individual-level health and healthcare access outcomes using data from the 2023 Behavioral Risk Factor Surveillance System. Predicted probabilities for each health outcome by policy trajectory cluster and LGBTQ status (LGBTQ, cisheterosexual (CH)) were obtained via marginal standardization.

Results: From 37 unique trajectories, we identified 5 trajectory clusters: "consistently predominantly discriminatory (C1)", "consistently fairly discriminatory", "fairly discriminatory change to moderate", "moderate change to fairly protective," and "fairly protective change to predominantly protective (C5)." For most outcomes, health was worse in states with consistently discriminatory policies compared to states with increasingly protective policies, with disproportionate impacts for LGBTQ adults. We observed inequities between LGBTQ and CH adults within policy trajectories, and inequities within LGBTQ status groups across trajectories. For example, predicted probabilities of avoiding care due to cost ranged from 24% in C1 states to 11% in C5 states among LGBTQ adults, and from 10% in C1 states to 7% in C5 states among CH adults.

Conclusions: Findings underscore the need to abolish harmful policies and enact protective policies to mitigate health inequities.

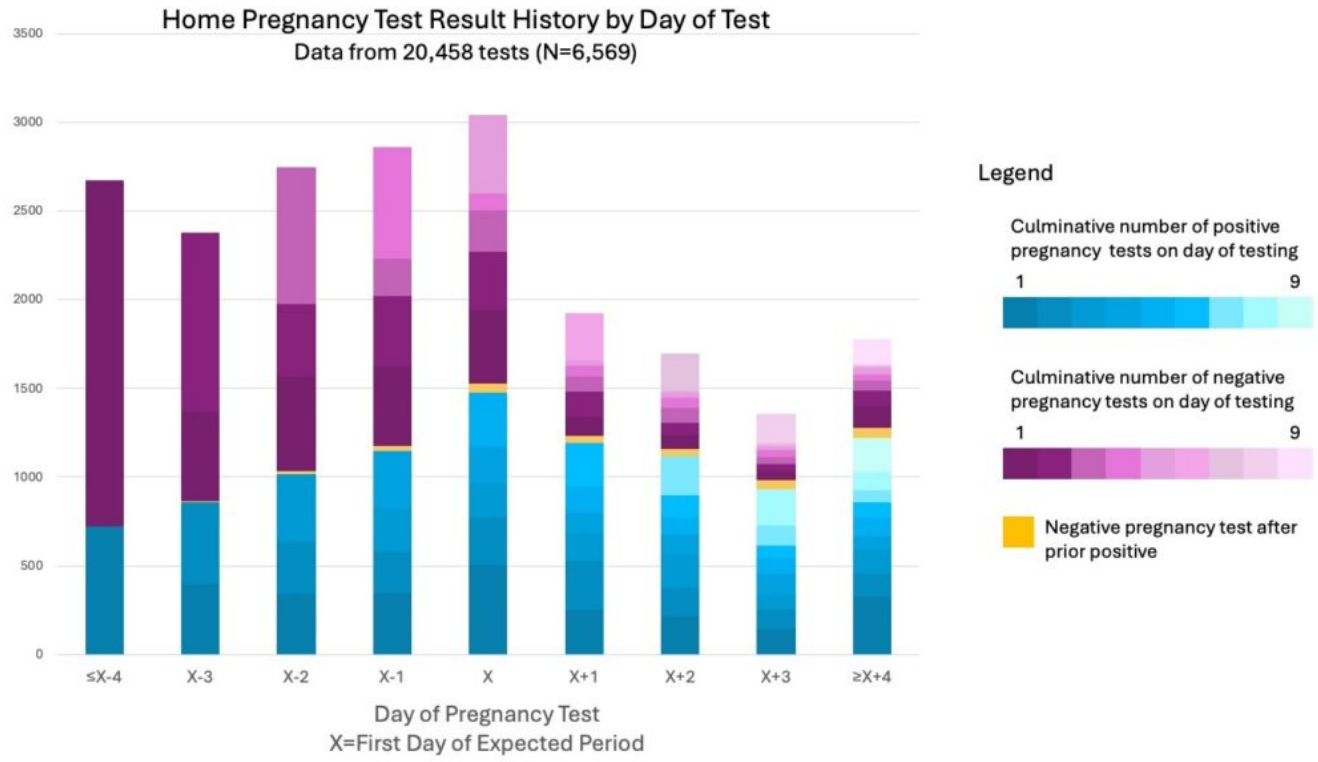
Figure 1. Predicted probabilities of health and healthcare access outcomes (2023, Behavioral Risk Factor Surveillance System) by state-level LGBTQ-related policy trajectory cluster (2015-2022, Movement Advancement Project) and LGBTQ status among U.S. adults



Reproductive

Pregnancy Testing Behavior in a Prospective Cohort of North American Pregnancy Planners Alexandra Sundermann* Alexandra Sundermann Anne Marie Jukic Kenneth Rothman Lauren Wise

Home pregnancy testing is linked to timing of pregnancy detection and, subsequently, lifestyle modifications and eligibility for study entry in cohorts of pregnancy health. Yet, little is known about the timing and frequency of home pregnancy testing among individuals who are trying to conceive. In PRESTO (Pregnancy Study Online), a prospective cohort study of North American preconception pregnancy planners (2018-2024), participants reported day-specific information about whether they tested for pregnancy and the result of each test from four days before the day of expected menstruation through four days after. We analyzed data from the first cycle after enrollment, which included 20,458 individual tests across 6,569 unique participants. The median number of home pregnancy tests used was two (inter-quartile range [IQR]: 1, 4); 9% of participants reported testing every day within the queried range. Forty percent of participants reported testing more than four days before their expected period, whereas 26% waited to test until the day of their expected period or later. Almost half of participants had at least one positive pregnancy test (49%, n=3,241) and 60% of participants with a positive result repeated testing at least once (median number of positive tests: 2; IQR: 1, 4). We observed a range of pregnancy testing intensity, with some participants testing only once and others testing every day, even after a positive test (Figure). Participants with a history of miscarriage were more likely to be early, frequent testers compared with their counterparts (risk ratio adjusted for maternal age and parity 1.26, 95% confidence interval 1.14, 1.39). Young maternal age and increasing parity were also associated with earlier initiation of testing and more frequent testing. A deeper understanding of real-world home pregnancy test behaviors will inform quantitative assessment of biases related to timing of study entry in early pregnancy cohorts.



Reproductive

Validation of Administrative Healthcare Records for Women with Infertility Rachel Myrer* Rachel Myrer Leslie V. Farland Anna Pollack Joseph Stanford Matthew Peterson Christy Porucznik Karen Schliep

Background: Infertility affects approximately 12.1% of women and 9.4% of men in the U.S. Administrative healthcare records offer a cost-effective means to study infertility in large populations over time. However, the validity of these records to identify infertility cases remains underexplored, particularly in the U.S. where insurance coverage for fertility treatments is limited.

Objective: Validate infertility diagnoses in administrative healthcare records using self-reported time to pregnancy (TTP) as the primary reference method.

Methods: We utilized data from the Endometriosis, Natural History, Diagnosis, and Outcomes (ENDO) study (2007–2009), focusing on participants from the Utah site linked to the Utah Population Database (UPDB). The primary reference method (gold standard) for infertility was defined as having a self-reported TTP of 12 months or more. Women were infertile in the test method if they had an ICD-9 infertility diagnosis prior to or within one month of starting the ENDO study. Diagnostic accuracy was assessed using sensitivity, specificity, positive predictive value, negative predictive value, and Cohen’s kappa.

Results: The study included 505 women. The test method (UPDB) showed 77.0% agreement with the primary reference method (TTP). Sensitivity was low (15.5%), but specificity was high (98.1%). Positive predictive value was 74.0% and negative predictive value was 77.2%. Cohen’s kappa indicated slight agreement (k=0.18, CI 0.10-0.26).

Conclusions: Diagnostic codes in administrative records exhibit high specificity but low sensitivity for identifying infertility. This suggests that while these codes are reliable for confirming non-infertility, they miss many true infertility cases. Future research should address sociodemographic disparities in infertility diagnoses and incorporate additional data sources such as prescriptions, procedures, male partner records, and clinical notes to improve sensitivity and reduce false negatives.

Diagnostic accuracy measures among individuals participating in the Endometriosis, Natural History, Diagnosis, and Outcomes (ENDO) study (July 2007 – August 2009) Utah site (n=505).

Statistics	Test[1] vs. ENDO TTP (primary reference)[2]	Test[1] vs. ENDO Treatment (secondary reference)[3]
% Agreement	N = 389, 77.0%	N = 411, 81.4%
Sensitivity	15.5	19.2
Specificity	98.1	98.4
PPV	74.0	77.7
NPV	77.2	81.5
Cohen's k	0.18 (0.10, 0.26)	0.24 (0.14, 0.33)

PPV, positive predictive value; NPV, negative predictive value

[1]Test method: Utah Population Database Linked Healthcare Facility ICD-9 records (inpatient, ambulatory surgery, or emergency department).

[2]Primary reference method: Self-reported via ENDO baseline questionnaire that they tried longer than 12 months to get pregnant.

[3]Secondary reference method: Self-reported via ENDO baseline questionnaire that they had sought treatment for infertility.

Environment/Climate Change

Impact of exposure to air pollution mixtures on sperm epigenetic age Carrie Nobles* Carrie Nobles Timothy Canty Pauline Mendola Lindsey M Russo Kaniz Rabeya Karen C Schliep Akanksha Singh Allison M Ring Rachael Hemmert Neil J Perkins C Matthew Peterson Erica B Johnstone J Richard Pilsner

Introduction: While air pollution is associated with decrements in semen quality, underlying mechanisms and impacts on fertility remain less understood. Air pollution-induced redox stress may disrupt the blood-testes barrier similar to aging, leading to changes in sperm DNA methylation associated with poorer semen quality and longer time to pregnancy.

Methods: We evaluated air pollution and sperm epigenetic age (SEA), the acceleration or deceleration of age-related changes in sperm DNA methylation, among 1220 men in the FAZST Trial (2013-2018) from Utah, residing predominately along the Wasatch Front. Residential exposure to nitrogen dioxide (NO2), ozone (O3), sulfur dioxide (SO2), and fine particulate matter (PM2.5) and its constituents was estimated by the Community Multiscale Air Quality Model fused with monitor data and averaged across susceptible windows of spermatogenesis. Single- and multipollutant models and mixture models (quantile-based g-computation) adjusted for participant characteristics. Secondary analyses adjusted for season and temperature.

Results: We observed accelerated SEA with higher O3, higher NO2, and lower SO2 (e.g. MD 0.292 [95% CI 0.030, 0.553], MD 0.192 [95% CI -0.049, 0.434], and MD -0.052 [95% CI -0.118, 0.015] years per IQR in multipollutant models during mitosis, respectively), with no clear associations for total PM2.5. In mixture models breaking down PM2.5 constituents, the air pollution mixture was associated with accelerated SEA (e.g. MD 0.211 [95% CI 0.003, 0.420] years per quantile increase during meiosis), with O3, NO2, sulfates, and nitrates contributing most strongly to positive weights (e.g. 32.8%, 30.8%, 19.6%, and 15.2%, respectively, during meiosis). Findings were similar adjusting for season and temperature.

Discussion: Exposure to air pollution during cell division stages of spermatogenesis along the Wasatch Front was associated with accelerated SEA, with NO2 and its secondary pollutants the strongest contributors.

Reproductive

Ambient air pollution mixtures and fecundability in a preconception time-to-pregnancy cohort Michelle R. Klawans* Michelle Klawans Kathryn S. Konrad Ian D. Buller Johanna R. Jahnke Alexander P. Keil D. Robert McConnaughey Anne Z. Steiner Anne Marie Z. Jukic

Background: While previous studies have found associations between air pollution and fertility, none have used exposure mixtures models. This study aimed to assess the effect of ambient air pollution mixtures on fecundability. **Methods:** Time to Conceive participants were females aged 30-44 living in central North Carolina attempting to conceive and had no known history of infertility. Ambient concentrations of particulate matter less than 10 microns in diameter (PM10) or 2.5 microns (PM2.5), ozone (O3), carbon monoxide (CO), nitric oxide (NO), nitrogen dioxide (NO2), and sulfur dioxide (SO2) obtained from the U.S. Environmental Protection Agency were linked to geocoded residential addresses at enrollment. Five exposure windows were assessed: spermatogenesis, early follicle development, follicular and luteal phases of the menstrual cycle, and implantation. For each window and pollutant, we calculated average and single-day peak concentrations. Time to conception was the number of menstrual cycles from enrollment until a positive urinary home pregnancy test. We used quantile g-computation to estimate the association of a simultaneous quantile increase of all pollutant concentrations in an exposure window with the probability of conception, adjusting for attempt cycle number, season, age, BMI, education, parity, race/ethnicity, occupation, smoking, and alcohol use, and partner age, race/ethnicity, and smoking. **Results:** Participants (N=924) contributed 3,671 cycles, of which 626 were conception cycles. During early follicle development, a quantile increase in all pollutant concentrations at once was associated with a fecundability odds ratio of 1.185 (95% confidence interval: 1.004-1.398). No associations were observed for other exposure windows or peak pollutant concentrations in any exposure window. **Conclusions:** In areas of relatively low pollutant levels**,** exposure to ambient air pollutant mixtures does not appear to negatively impact the probability of conceiving.

Reproductive

Preconception dietary patterns in association with live birth and early pregnancy loss: a couples-based approach Kyle Busse* Kyle Busse Stefanie Hinkle Bhaavna Peri Derartu Ahmed Enrique Schisterman Ellen Caniglia Naria Sealy James Mills Erica Johnstone Pauline Mendola Ginny Ryan Matthew Peterson Jim Hotaling Leah Lipsky Sunni Mumford

Infertility affects 1 in 6 U.S. couples. In up to 30% of cases, the cause is unexplained. There is evidence that diet may play a role. Our objective was to estimate associations of live birth and early pregnancy loss (<20 weeks' gestation) with preconception diet patterns of female and male partners seeking fertility treatment.

Data came from 2370 male participants and female partners in the Folic Acid and Zinc Supplementation Trial. Scores for 4 diet patterns were estimated at baseline, during preconception. These included 2 diet quality indices (Healthy Eating Index-2015 [HEI] and Mediterranean Diet) and 2 fertility-specific patterns (Pro-Fertility and Fertility Diet) associated with greater female fertility in previous studies. Log-binomial models estimated crude and adjusted RRs per 1 SD increase in diet pattern score, separately for each partner and combined (sum of partners' scores). In pregnancy loss models, inverse probability weights accounted for selecting on pregnant couples (n=1054). RRs were also estimated by infertility diagnosis (any vs. none) and median time trying to conceive (<19.5 vs. ≥19.5 months). Multiple imputation was used for missingness.

Of 2370 couples, 821 had a live birth and 287 had an early pregnancy loss. For females, males, and combined, a 1 SD higher score for HEI and Mediterranean Diet was suggestive of greater likelihood of live birth (**Figure**). For female partners, a 1 SD higher score for the Fertility Diet pattern was also suggestive of greater likelihood of live birth. HEI score was positively associated with the likelihood of live birth among females without an infertility diagnosis (adjusted RR=1.07 [95% CI 1.01-1.15]) and among females trying to conceive for <19.5 months (adjusted RR=1.08 [1.00-1.16]). No associations were observed for early pregnancy loss.

For couples seeking fertility treatment, higher diet quality may increase the likelihood of a live birth.

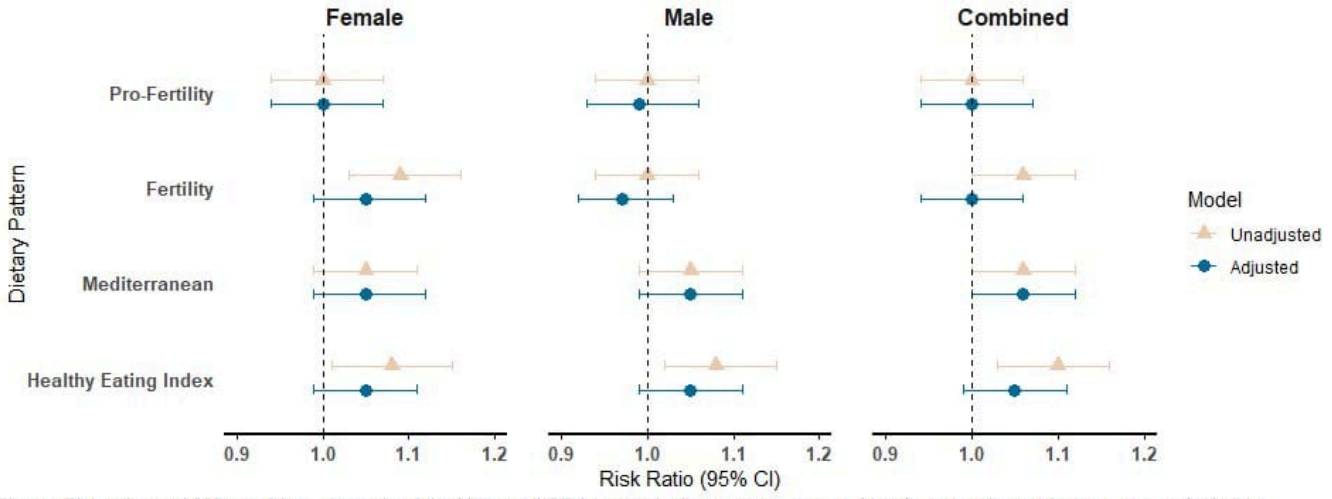


Figure. Risk ratios and 95% confidence intervals of live birth per 1-SD increase in dietary pattern score. Models were adjusted for age, race and ethnicity, physical activity, smoking, education, months trying to conceive, parity, infertility diagnosis, and treatment group. All models except those for Healthy Eating Index were additionally adjusted for total energy intake.

Methods/Statistics

Resurrecting complete-case analysis: A defense Maya Mathur* Maya Mathur Ilya Shpitser Tyler VanderWeele

Complete-case analysis (CCA) is often criticized on the belief that CCA is only valid if data are missing-completely-at-random (MCAR). Influential papers have thus recommended abandoning CCA in favor of methods that make a weaker missing-at-random (MAR) assumption. We argue for a different view: that CCA with principled covariate adjustment provides a valuable complement to MAR-based methods, such as multiple imputation. When estimating treatment effects, appropriate covariate control can, for some causal structures, eliminate bias in CCA. This can be true even when data are missing-not-at-random (MNAR) and when MAR-based methods are biased. We describe principles for choosing adjustment covariates for CCA, and we characterize the causal structures for which covariate adjustment does, or does not, eliminate bias. Even when CCA is biased, principled covariate adjustment will often reduce the bias of CCA, and this method will sometimes be less biased than MAR-based methods. When multiple imputation is used under a MAR assumption, adjusted CCA thus still constitutes an important sensitivity analysis. When conducted with the same attention to covariate control that epidemiologists already afford to confounding, adjusted CCA belongs in the suite of reasonable methods for missing data. There is thus good justification for resurrecting CCA as a principled method.

Study Design

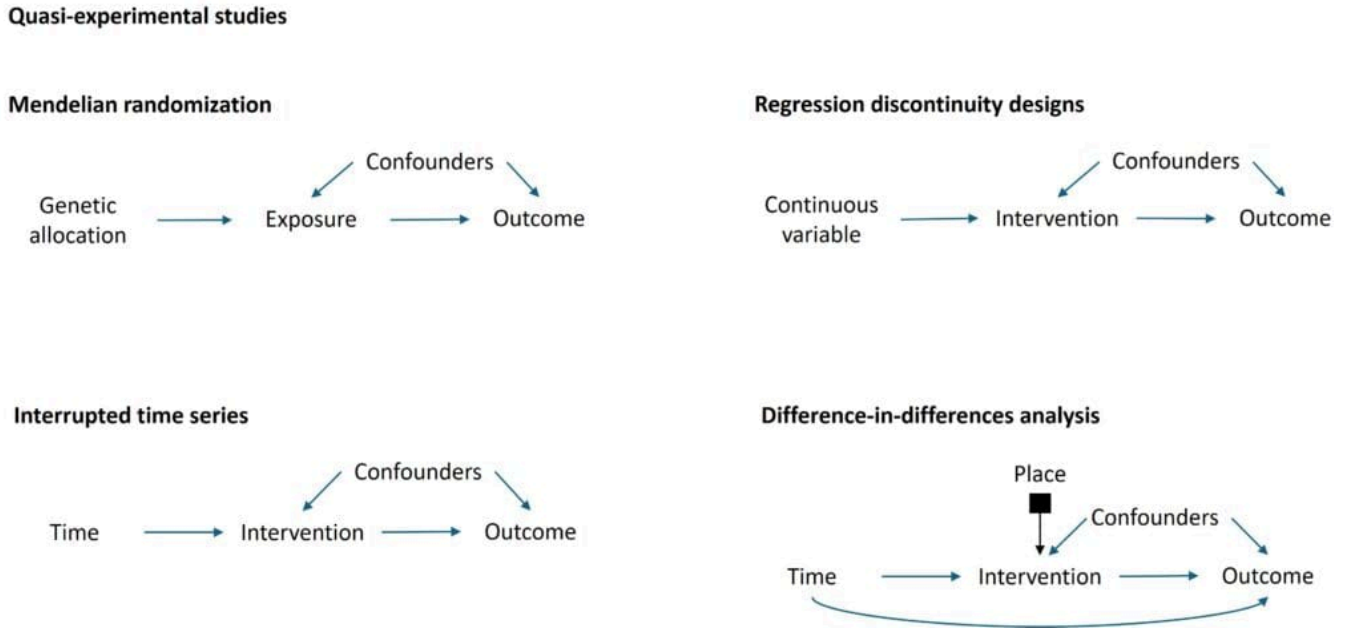
Causal diagrams of epidemiological study designs conceptualized as instrumental variable analyses Guoyi Yang* Guoyi Yang Abigail Ada Rath Heidi Jones C Mary Schooling

Background: Most observational studies evaluate causation using confounder-control methods. Directed acyclic graphs (DAGs) are useful in depicting causal structures and have been increasingly used to identify confounders in observational studies. However, the structures of alternative study designs that do not rely on confounder adjustment have not been explained systematically.

Methods: We propose that epidemiological study designs that do not rely on confounder adjustment can be conceptualized as instrumental variable (IV) analyses. We use DAGs to illustrate the causal structures of randomized controlled trials, quasi-experimental studies, including Mendelian randomization, regression discontinuity designs, and interrupted time series, self-controlled case series, and ecological studies. We use a selection diagram for difference-in-differences analysis.

Results: We argue that these seemly heterogenous study designs share a common causal structure as IV analysis. Specifically, IVs are random allocation in randomized controlled trials, genetic allocation in Mendelian randomization, a continuous variable in regression discontinuity designs, time in interrupted time series and self-controlled case series, place in ecological studies, and the interaction between time and place in difference-in-differences analysis. We further explain how IV assumptions are applied to these study designs and provide solutions to address biases due to violation of IV assumptions.

Conclusions: Conceptualizing different epidemiological study designs as IV analyses provides a unified approach to understanding their causal structures and recognizing threats to study validity.



Causal Inference

Confounding in DiD: formal definition and variable selection strategies Daniela Rodrigues*
Daniela Rodrigues Laura Hatfield

Confounding represents the key challenge to causal inference for non-experimental studies. Over the years, significant efforts have been made to define confounding and develop confounding variable selection strategies in cross-sectional studies. However, in the context of difference-in-differences (DiD), the definition of confounding has not been formalized. In addition, there is a lack of guidance on which confounding variables make the assumption of conditional parallel trends most plausible. In this work, we use causal diagrams to formalize the definition of confounding in DiD and propose strategies to aid in the selection of confounding variables in this context. We apply these developments to the study of the effect of Comprehensive Primary Care Plus on healthcare equity.

Methods/Statistics

Which policy works and where? Estimation and inference for state level treatment effects using difference-in-differences Nichole Austin* Nichole Austin Sunny Karim Matt Webb Erin Strumpf

New difference-in-differences (DID) estimators have been developed to estimate treatment effects in the context of staggered policy adoption. Most estimate the average treatment effect on the treated (ATT) at the treatment timing group (g) and year (t) level, or the ATT(g,t). However, this overlooks heterogeneity within groups: for example, in an analysis of state-level abortion bans, policies implemented at the same time may vary in terms of travel restrictions or gestational age thresholds. Accordingly, researchers may be interested in treatment effects at the state level which map more directly to policy characteristics.

We demonstrate how to estimate state-by-year level treatment effects (ATT(s,t) terms) using two new DiD estimators: unpooled DID (UN-DID) and intersection DID (DID-INT). We propose methods for cluster robust inference for ATT, ATT(g,t) and ATT(s,t) terms using these estimators. The cluster jackknife and randomization inference are of broader interest, as they are valid in settings where the standard cluster robust variance estimator is not. We used Monte Carlo simulation to compare traditional DID to UN-DID/ DID-INT with and without cluster robust estimation.

The new methods recover the true ATT(s,t) values. First, all over-time differences are calculated by state. Within-state differences for controls are then aggregated. Comparing this difference with a single treated state’s difference yields an ATT(s,t). Conversely, if it is compared to the aggregated treated differences by timing group (g), we estimate an ATT(g,t). Our new estimators are unbiased and correctly sized in most settings (e.g., when the number of clusters is sufficient).

In policy evaluation, the parameter of interest is often the ATT(s,t), but the ATT(g,t) is typically reported. We introduce methods to estimate the ATT(s,t). Both estimates are important in understanding the impact of policy shifts that are heterogeneous in terms of policy timing and characteristics.

Causal Inference

Causal survival analysis in the presence of unmeasured confounding for a competing event

Emma McGee* Emma McGee Mathieu Chalouni Daniela K. Van Santen Sara Lodi Miguel A. Hernán

Prior work characterizing causal effects in the presence of competing events has relied on the assumption of no unmeasured confounding for the competing event. This assumption is often violated in real-world analyses (e.g., if treatment is prioritized based on unmeasured factors to individuals more or less likely to experience a competing event, like death). We examined the magnitude of bias for different estimands in the presence of unmeasured confounding for a competing event via a simulation study.

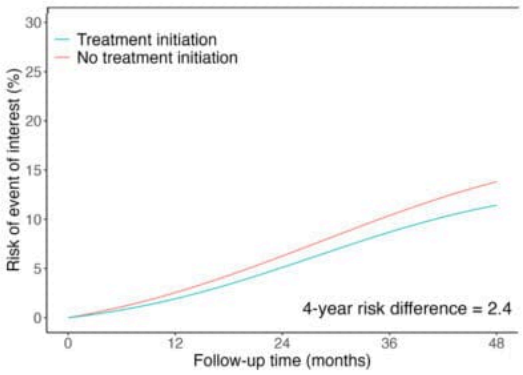
We simulated 500,000 individuals under a null effect of a binary baseline treatment. We estimated the total effect, controlled direct effect, and separable direct effect for a time-to-event outcome and, for comparison, the total effect for a competing event. We varied the strength of unmeasured confounding for the competing event, risk of the competing event, and strength of an unmeasured common cause of the competing event and outcome. Bias was defined as the difference between the estimated 4-year risk difference and risk ratio vs. the null.

All estimands were biased. Bias increased as the strength of unmeasured confounding for the competing event, risk of the competing event, and strength of the unmeasured common cause of the competing event and outcome increased. For example, when bias for the competing event was -8.4 percentage points [-0.35 on the risk ratio scale], bias for the total, controlled direct, and separable direct effects was 0.6 [0.04], 0.4 [0.03], and 0.2 [0.01], respectively. When bias for the competing event was -15.2 [-0.63], bias for the total, controlled direct, and separable direct effects was 2.4 [0.20], 2.1 [0.18], and 1.6 [0.18].

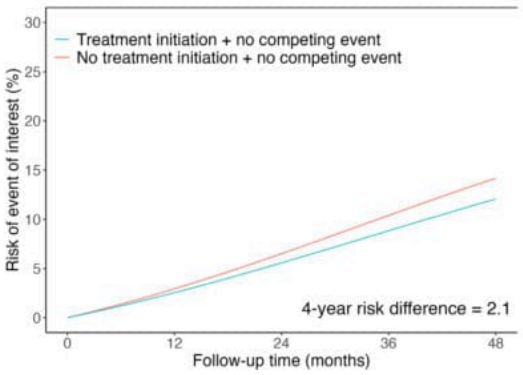
Unmeasured confounding for a competing event leads to biased estimates for the outcome of interest. The magnitude of bias may be modest unless bias for the competing event is strong. Researchers should consider the potential strength of unmeasured confounding for a competing event and conduct sensitivity analyses.

Figure 1. Risk curves and risk differences for different causal estimands under strong simulated unmeasured confounding for the competing event and a strong unmeasured common cause of the competing event and outcome.

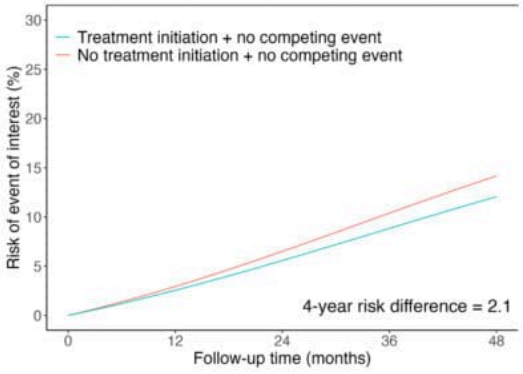
a) Total effect on the outcome



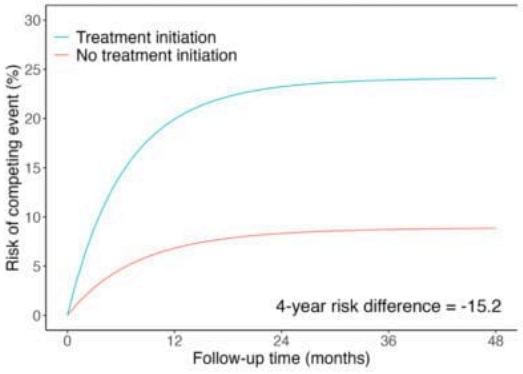
b) Controlled direct effect on the outcome



c) Separable direct effect on the outcome



d) Total effect on the competing event



Methods/Statistics

Extending Intersectional Methods to Population Health Research Victoria Fisher* Victoria Fisher Kiana Ramos Nicole Alkhouri Nadia N. Abuelezam

Background: Intersectionality theory has been used to describe the interconnectedness of identities within social, institutional, and structural systems of power. Recently introduced methods aim to produce better intersectional analyses (beyond multiple interactive terms), including multilevel analysis of individual heterogeneity and discriminatory accuracy (MAIHDA). MAIHDA relies on categorical strata as both fixed and random effects but has been met with concerns of collinearity and issues with interpretation. We propose an extension of MAIHDA to population-level infectious disease data, which allows for the use of continuous fixed effects to address potential collinearity.

Methods: Concerns about MAIHDA come from the reduction in random effects variance after the strata are added to the model as fixed effects. We propose using continuous measures as fixed effects that correspond to the categorical strata. This allows for greater within-group variation and the possible application to population-level research. We apply our proposed methods to U.S. county-level COVID-19 mortality data (CDC Wonder) via three multilevel models: random effects only, with continuous fixed effects, and with the strata as fixed effects (3044 counties were included in our analysis).

Results: The results from our three models suggest that using continuous count fixed effects provided the best fit. Continuous fixed effects reduced variance accounted for by the strata from 19% (null model) to 14%, while categorical fixed effects reduced the variance accounted for to 1.2%, suggesting that the use of categorical fixed effects may be sufficient for modeling the data on their own, but would not capture the interactive effects integral to intersectional analyses.

Conclusions: We illustrate the use of a novel application of MAIHDA methods in a population-level analysis, where strata were created from continuous variables. This method may be beneficial when individual-level data is not accessible.

Aging

Heterogeneity in the Association Between Retirement and Cognitive Function Koryu Sato*
Koryu Sato Haruko Noguchi Kosuke Inoue

Background

Developed countries are increasingly raising their state pension age, a policy change that may affect cognitive health through delayed retirement. However, the impact of retirement on cognitive function likely varies among individuals and countries. This study investigates the heterogeneous association between retirement and cognitive function.

Methods

We analyzed harmonized data from three longitudinal studies: the Health and Retirement Study, the English Longitudinal Study on Ageing, and the Survey of Health, Ageing and Retirement in Europe. The dataset encompassed three waves across 19 counties from 2014 to 2019. This study included 12 811 individuals who worked in the first wave, from whom each survey collected covariate information. We assessed retirement status among participants aged 50–80 years in the second wave and measured cognitive function using word recall tests in the third wave. The analysis employed instrumental variable causal forests estimation, utilizing state pension age as an instrument for retirement.

Results

Among 7432 individuals with retirement propensity scores between 0.1 and 0.9, 2165 (29.1%) retired during the second wave. Analysis revealed that retirees recalled 1.348 more words than workers on average. The association between retirement and cognitive function showed significant heterogeneity. Greater cognitive benefits were observed among women, individuals with higher socioeconomic status, those with robust pre-retirement health, and those who engaged in physical activity before retirement. Projections suggest that increasing the state pension age from 65 to 66 will result in higher financial burdens for dementia care in England compared to the United States.

Conclusions

The observed heterogeneity in retirement’s effects on cognitive function suggests policymakers should consider incorporating early retirement options into the pension system, allowing individuals to make retirement decisions based on their circumstances.

Aging

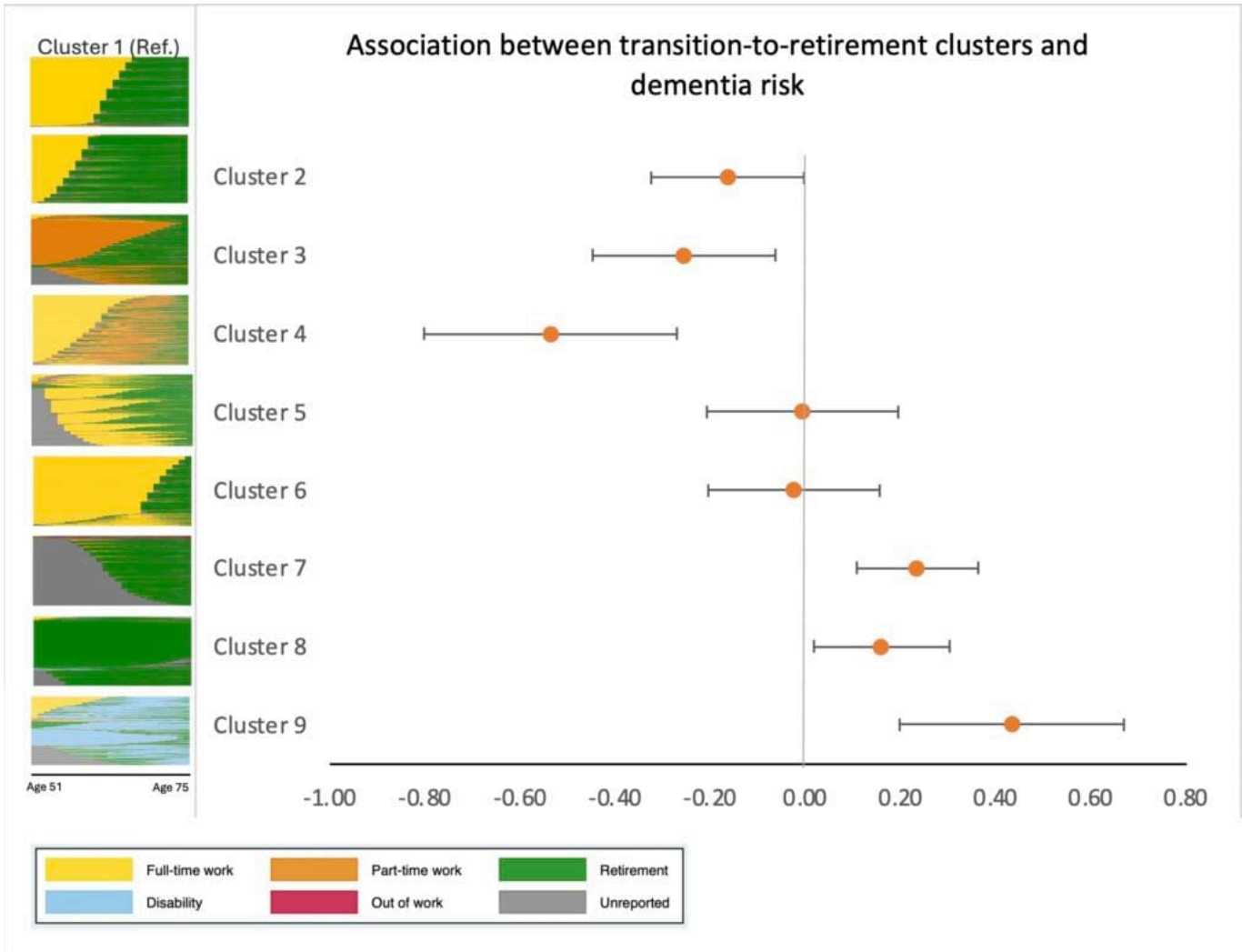
Retirement paths and dementia risk: an application of sequence analysis Lucia Pacca* Lucia Pacca Anusha M. Vable Amal Harrati

There is a relationship between retirement and cognition, however questions remain regarding the transition to retirement including retirement timing, transitions to part-time work before retirement, s and associations with subsequent cognition.

We used data from N=10,831 Health and Retirement Study (HRS) participants. Using self-reported employment information, we classified each year between ages 51-75 into one of six mutually exclusive categories: working part-time, working full-time, retired, disabled, out of the labor force or unreported. We used sequence analysis to quantitatively compare individual transition-to-retirement trajectories, and hierarchical agglomerative clustering to group similar trajectories. Our outcome was a dementia probability score from age 76 onwards. We used generalized estimating equations to estimate the association between employment trajectories and dementia adjusting for age, gender, race and ethnicity, education and wave of outcome measurement.

We identified 9 transition-to-retirement clusters (Figure 1). Compared to typical retirement (cluster 1, reference, characterized by full-time work followed by retirement between age 60-65), we found that retiring 5-10 earlier after full-time work (cluster 2) was associated with lower dementia risk (b:-0.16, CI: -0.32, 0.0). Retiring at any time after part-time work (Cluster 3) was associated with lower dementia risk compared to the reference group (b:-0.26; CI: -0.45, -0.06), and transitioning from full-time to part-time work before retiring around age 70 (Cluster 4) was associated with the lowest dementia risk (b:-0.54, CI:-0.80, -0.27). By contrast, retiring with unreported prior employment (Cluster 7), retiring around age 50 or earlier (Cluster 8) and retiring before or after a period of disability (Cluster 9) were associated with higher dementia risk.

Results suggest that timing of retirement, part-time employment and periods of disability or unreported work are differentially associated with later-life dementia risk. Transitioning to part-time work before retirement was associated with the lowest dementia risk, suggesting combining a better work-life balance with the cognitive and social stimulation offered by employment may be particularly beneficial for cognition.


Cluster 1 (Ref.)
Association between transition-to-retirement clusters and dementia risk
Cluster 2
Cluster 3
Cluster 4
Cluster 5
Cluster 6
Cluster 7
Cluster 8
Cluster 9
Age 51
Age 75
-1.00
-0.80
-0.60
-0.40
-0.20
0.00
0.20
0.40
0.60
0.80
Full-time work
Part-time work
Retirement
Disability
Out of work
Unreported

Aging

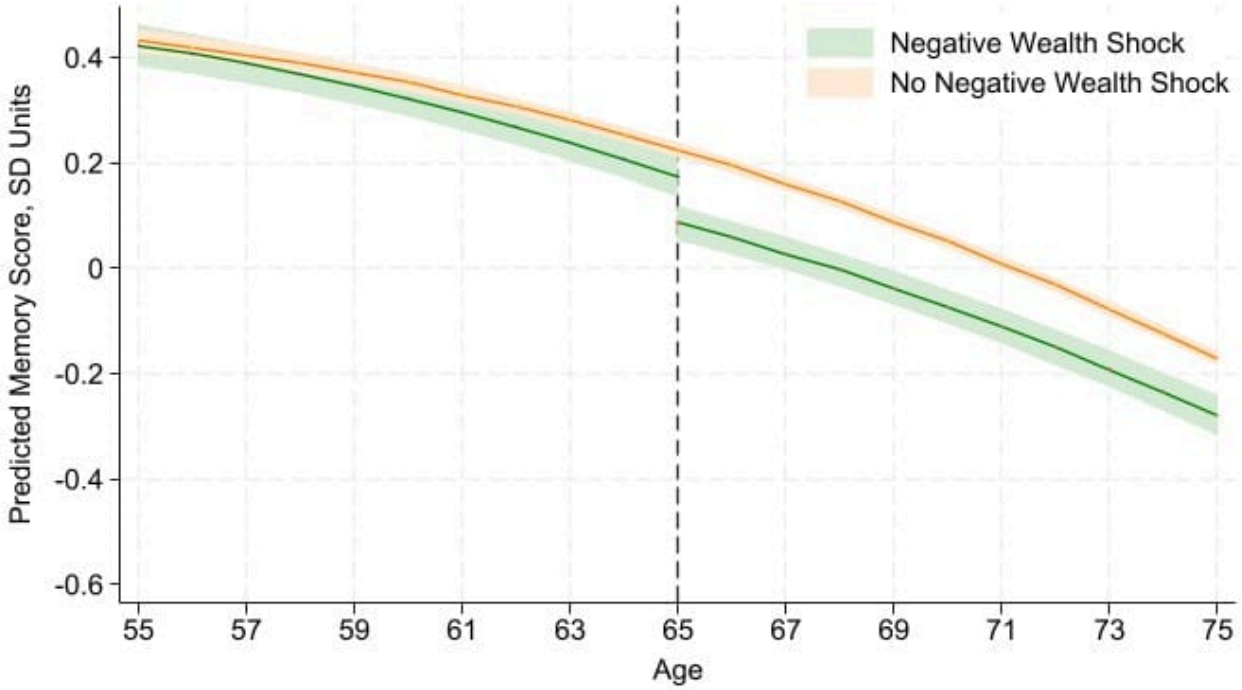
Memory Trajectories Before and After a Negative Wealth Shock, the United States Health and Retirement Study, 1998-2020 Tsai-Chin Cho* Tsai-Chin Cho Ashly C. Westrick Sara D. Adar HwaJung Choi Kenneth M. Langa Lindsay C. Kobayashi

Background: Negative wealth shocks are sudden wealth losses that may contribute to worse cognitive health and may result from advanced financial planning after the onset of dementia symptoms. To investigate the bidirectional relationships between negative wealth shocks and cognitive aging outcomes, we examined the acute change in memory function immediately after a negative wealth shock (vs. no shock) in mid-to-later life, as well as the long-term memory aging before and after a negative wealth shock in comparison to memory aging in the absence of the shock.

Methods: The sample population included participants aged ≥55 from the US Health and Retirement Study survey in 1998 (baseline) and all their follow-up interviews until 2018. The study outcome was an imputed composite memory function z-score (in SD units), which captured both self and proxy memory assessments. A negative wealth shock was defined as a loss of ≥75% in equivalized household total net worth between biennial survey interviews. We employed multivariable-adjusted mixed-effect linear models with segmented time effects to examine differences in memory aging slopes before and after a negative wealth shock.

Results: There are 3,197 participants (26,233 participant-year observations) with the experience of a negative wealth shock and 8,932 participants (66,956 observations) without. An acute drop of 0.17 SD units (95% CI: -0.19, -0.15) in memory function immediately following a negative wealth shock. Comparing those who did vs. did not experience a negative wealth shock, the difference in the memory aging slope before a negative wealth shock was nearly null, while the memory aging slope was 0.13 SD units (95% CI: -0.17, -0.09) steeper per decade after the shock. Figure 1 visualizes the predicted slopes of memory decline according to the experience of a negative wealth shock.

Discussion: This study provides evidence of the detrimental cognitive health effects of negative wealth shocks in later adulthood, which may inform the design of interventions and means of supporting healthy cognitive aging.


Negative Wealth Shock
No Negative Wealth Shock
Predicted Memory Score, SD Units
0.4
0.2
0
-0.2
-0.4
-0.6
55
57
59
61
63
65
67
69
71
73
75
Age

Aging

COVID-Related Healthcare Disruptions and Subsequent Impacts on Chronic Disease Management among Older Adults with Multiple Chronic Conditions Receiving Care in the New York City Safety-Net Healthcare System Sarah Conderino* Sarah Conderino John A. Dodson Yuchen Meng Rania Kanchi Jasmin Divers Samrachana Adhikari Saul Blecker Rajesh Vedanthan Nichola Davis Stan Kogan Karyn Singer Hannah Jackson Andrew Wallach Theodore Long Mark G. Weiner Lorna E. Thorpe

Background: The COVID-19 pandemic had a significant impact on healthcare delivery. Older adults with multimorbidities were particularly vulnerable to disruptions in care for the management of their chronic conditions. Our goal was to characterize healthcare disruptions and effects on disease management among older adults with multimorbidities who were patients of NYC Health + Hospitals, the largest safety-net system in the country.

Methods: The study population included NYC residents aged 50 or older with multimorbidities who had at least one ambulatory visit in the 6 months before COVID-19 pandemic onset (3/6/2020). We descriptively identified independent predictors of disruption in care during the first 7 months of the pandemic and estimated the effect of disruption in care on blood pressure control, HbA1c and low-density lipoprotein cholesterol (LDL) using difference-in-differences models. Inverse probability weighting was used to improve exchangeability between those with disruption in care vs. those with some care.

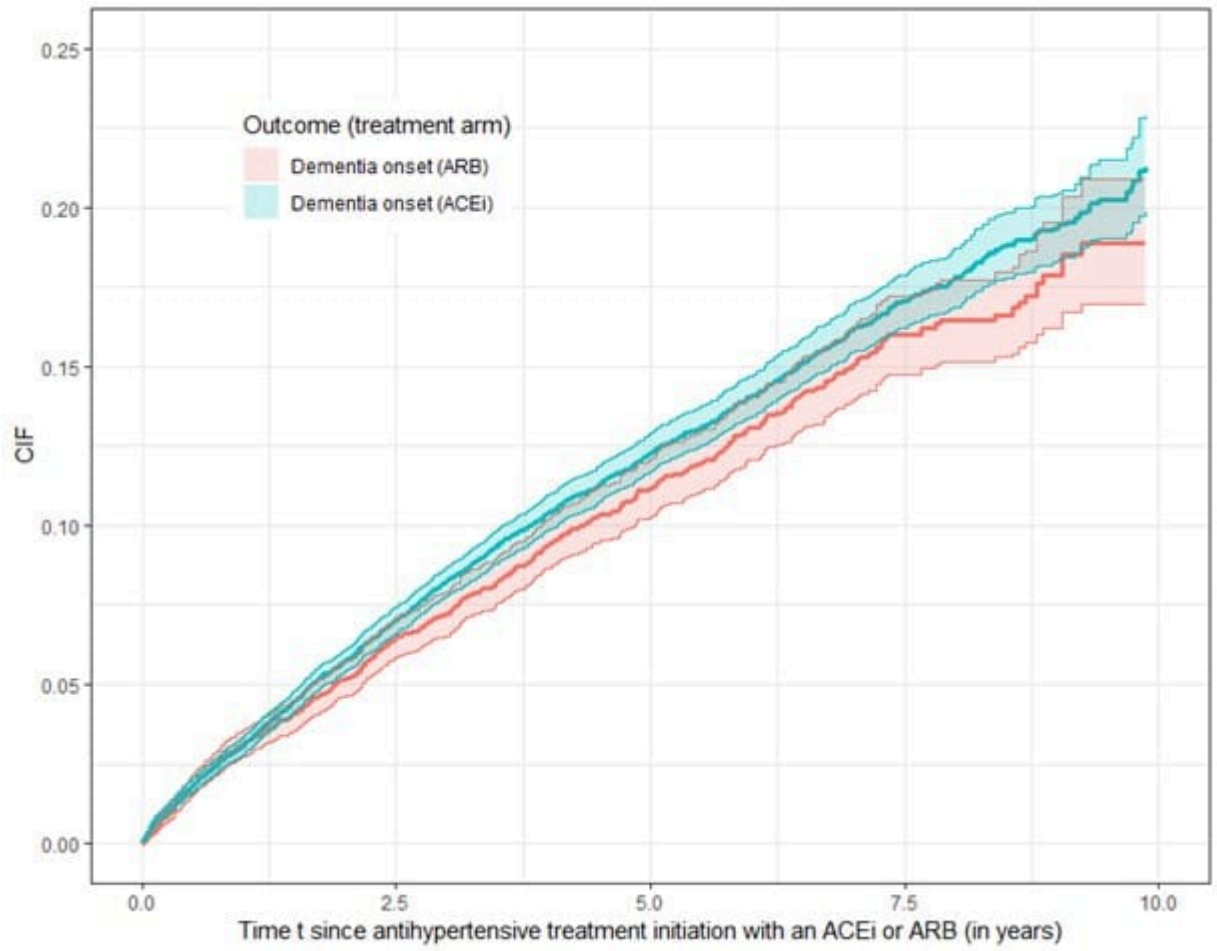
Results: A total of 90,718 older adult patients with multimorbidities were seen within the 6 months prior to the COVID-19 pandemic, 17.9% of whom received no care during the first 7 months of the pandemic. Poor baseline health status, low pre-pandemic healthcare utilization and older age were independent predictors of disruption in care. Compared to those who received care, the total disruption group had a 2.7% greater decrease in blood pressure control (67.4% to 59.0% vs. 69.5% to 63.8%). Disruption did not have a significant impact on mean HbA1c or LDL levels.

Conclusions: Total disruption in care was associated with declines in blood pressure control that, while clinically modest, would have an impact on cardiovascular outcomes at the population level. Implementation of telehealth may have mitigated impacts of the pandemic on care disruption and subsequent disease biomarkers. Targeted outreach during future crises is needed to improve access to care.

Aging

Comparative effectiveness of ACE inhibitors and angiotensin receptor blockers for preventing dementia: a target trial emulation using US electronic health records Marie-Laure Charpignon* Marie Laure Charpignon

Alzheimer’s disease, the most common type of dementia, affects 6.7 million Americans and costs $345B annually. Since disease-modifying therapies are limited, repurposing FDA-approved drugs may offer an alternative, expedited path to preventing dementia. Hypertension is a major risk factor for dementia onset. However, prior observational studies contrasting antihypertensive drug classes (Angiotensin Converting Enzyme inhibitors: ACEI, Angiotensin Receptor Blockers: ARB, and Calcium Channel Blockers: CCB), provided mixed results. We hypothesize that ACEI have an off-target pathogenic mechanism. To test this assumption, we emulate a target trial comparing patients initiating ACEI vs ARB using electronic health records from the US Research Patient Data Registry. We perform intention-to-treat analyses among 25,507 patients aged 50 and over, applying Inverse Propensity score of Treatment Weighting to balance the two treatment arms and accounting for the competing risk of death. In a cause-specific Cox Proportional Hazards (PH) model, the hazard of dementia onset was higher in ACEI vs ARB initiators (HR=1.10 [95% CI: 1.01-1.21]). Findings were robust to outcome model structures (i.e., Cox PH vs nonparametric) and generalized to patients with no hypertension diagnosis at initiation but receiving such drugs for another indication (e.g., heart failure). Ongoing work includes evaluating differential effects by brain penetrance, discovering subgroups of responders, and assessing the mediating role of blood pressure (BP) control with ACEI vs ARB. Future research will incorporate longitudinal markers (e.g., BP, HbA1c, LDL) in time-to-event models and consider stroke incidence or recurrence under ACEI vs ARB initiation as a mediator.


Outcome (treatment arm)
Dementia onset (ARB)
Dementia onset (ACEi)
CIF
0.25
0.20
0.15
0.10
0.05
0.00
0.0
2.5
5.0
7.5
10.0
Time t since antihypertensive treatment initiation with an ACEi or ARB (in years)

Aging

Antidepressant initiation, quitting, and continued use in a nationally representative cohort of older adults Maria Springall De Pablo* Maria Springall De Pablo Diane S Lauderdale

Antidepressants (AD) are widely prescribed. There are several drug classes, and their effectiveness and side effects vary for individuals. Benzodiazepines are deemed inappropriate for older adults. Using a nationally representative longitudinal study of older adults, the National Social Life, Health and Aging Project (NSHAP), we present a descriptive analysis of AD use among 4,907 older adults, measured in 2015/16 (W3) and again in 2022/23 (W4), and sociodemographic associations of patterns of longitudinal use. W3 data were collected by interviewers examining medications in the home, but W4 was multimodal due to the pandemic. Sociodemographics include age, gender, race/ethnicity, education, assets (logged), and social isolation (marital status and frequency of group participation). 18% in W3 and 22% in W4 were AD users. In W3, 43% of AD prescriptions were for selective serotonin reuptake inhibitors (SSRI), 13% for serotonin-norepinephrine reuptake inhibitors (SNRI), and 13% for benzodiazepines. Distribution in W4 was similar. Logistic multinomial models compared correlates of sustained, quitting and initiating AD users to consistent nonusers. Among 2,728 participants in both waves, significant RRRs for female compared to male were 2.6 (95% CI 1.9, 3.5), 4.0 (95% CI 1.9, 8.5) and 1.7 (95% CI 1.1, 2.6) for sustained, quitting and initiating use, respectively. Black and Hispanic participants had much lower RRRs for sustained use, with similar results for initiation. In addition, greater log household assets were significantly associated with lower RRR (0.85; 95% CI 0.79, 0.81). Education and marital status were not associated with any of the use patterns. Greater frequency of volunteering and religious service attendance were associated with less risk of quitting AD use. Older adults are still being prescribed benzodiazepines despite guidelines. While wealth was protective, social participation appears to maintain rather than decrease AD use over time.

Environment/Climate Change

Disparities in experiencing multiple types of climate-related natural disasters and race-based obstacles to preparedness services in the U.S., 2023 Heather D'Angelo* Heather D'Angelo Abigail

Racial/ethnic minority populations are often vulnerable to the effects of climate-related natural disasters (CRND). Experiencing multiple types of CRND could compound existing health disparities, especially if systemic racism creates obstacles to disaster preparedness. We examine whether racial/ethnic minority populations experience: 1) multiple types of CRND; and 2) race-based obstacles to preparedness services.

Using the 2023 FEMA National Household Survey (n=7,604), associations between race/ethnicity and experiencing CRNDs (i.e. extreme heat, drought, flood, hurricane, tornado, typhoon, and/or wildfire) was examined with negative binomial regression(range 0 to 7). Logistic regression examined associations between race/ethnicity and experiencing race-based obstacles to disaster preparedness services (yes/no). Models were weighted and adjusted for age, sex, rurality, income, and education.

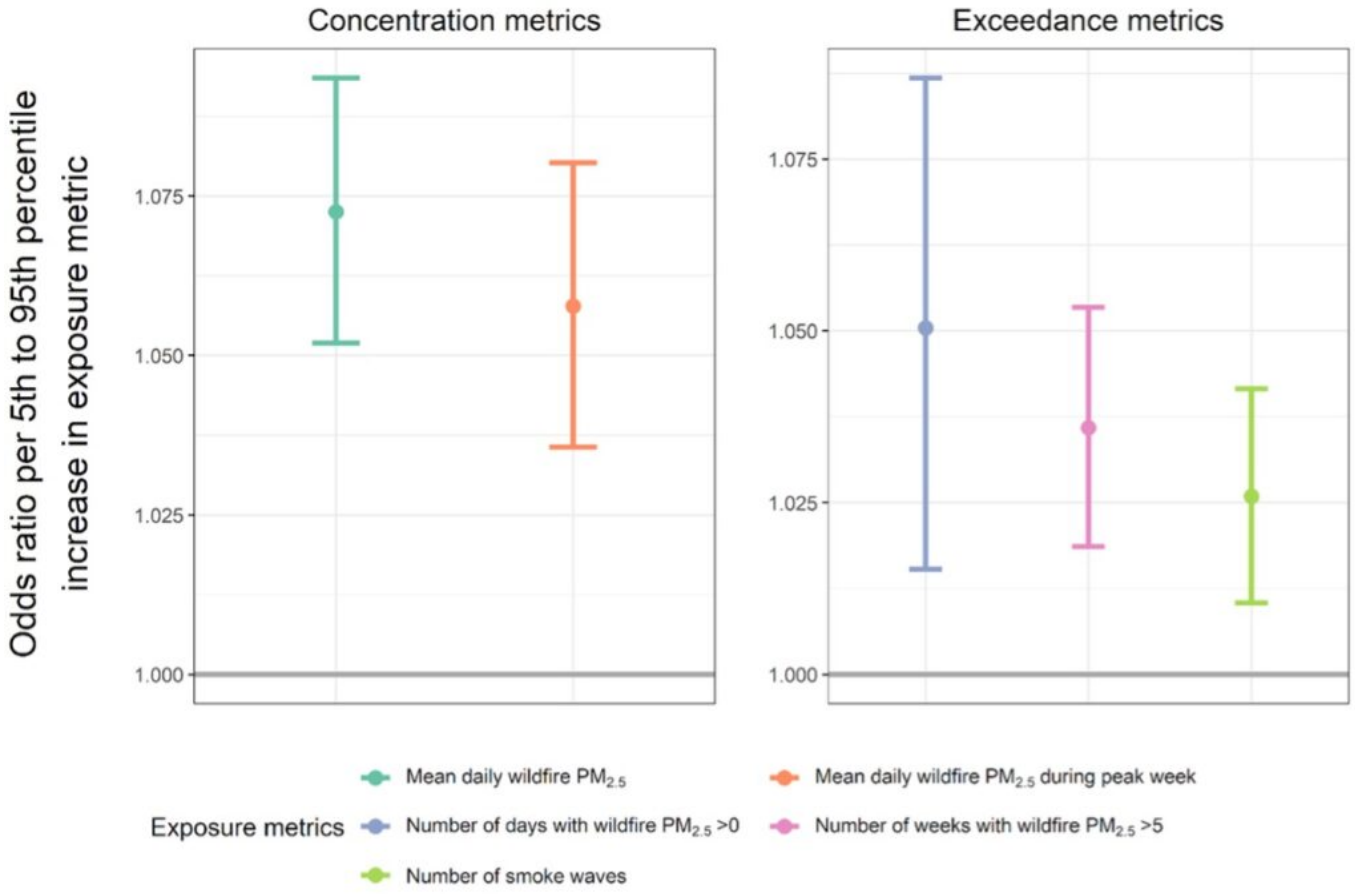
Experiencing ≥ 2 types of CRND was reported by 16.3% of U.S. adults, 22.7% of American Indian/Alaska Native, 19.0% of Black, and 18.0% of Hispanic adults. American Indian/Alaska Native adults experienced more types of CRND (IRR 1.33 [95%CI 1.04,1.69]) compared with White adults. American Indian/Alaska Native (OR 2.32 [95%CI 1.61, 3.34]), Black (OR 2.18, [95% CI 1.71, 2.78]) and Hispanic adults (OR 1.14, [95% CI 1.12, 1.71]) had greater odds of experiencing race-based obstacles to preparedness services vs. White adults.

In this national survey, American Indian/Alaska Natives experienced multiple types of CRND, and obstacles to preparedness services based on race were experienced by American Indian/Alaska Native, Black and Hispanic adults. Race-based barriers may exacerbate the impact of disasters on vulnerable populations, and further compound existing health disparities.

Environment/Climate Change

Long-term exposure to wildfire smoke and mortality: differences in effects by exposure metric and vulnerable populations Lara Schwarz* Lara Schwarz Chen Chen Timothy B. Frankland Sara Y. Tartof Gina S. Lee Yuqian M. Gu Elizabeth Rose Mayeda David González Tarik Benmarhnia Joan A. Casey

Wildfire smoke was once a rare event but has become a repeated exposure globally. Evidence to demonstrate the acute health effects of wildfire particulate matter (PM2.5) is growing, yet little is known about its long-term effects. Using a cohort of Kaiser Permanente Southern California (KPSC) members aged ≥60, we estimate the association between three-year exposure to five different census tract-level wildfire smoke metrics (mean daily wildfire-specific PM2.5, mean daily wildfire-specific PM2.5 during the peak wildfire week, number of days with daily wildfire-specific PM2.5 above zero, number of weeks with average wildfire-specific PM2.5 above five, and number of smoke wave days) and all-cause mortality, and evaluate differences by individual and community-level socio-demographics. We apply a discrete-time approach with a pooled logistic regression, adjusting for age, sex, race and ethnicity, marital status, smoking status, calendar year, requiring an interpreter and census tract-level poverty and population density. Of the 1,250,083 KPSC members aged ≥60 included in the study population, 53% were women, and most identified as non-Hispanic White (49%) or Hispanic (26%). When comparing those highly exposed (95th percentile) to those minimally exposed (5th percentile), we find an increased odds of mortality for those highly exposed across all five wildfire smoke metrics. Results suggest that mean daily wildfire PM2.5 may be the most harmful smoke metric [odds ratio (OR): 1.073, 95% CI: 1.052, 1.093]. Those aged 60 to 65, those who identified in the Black or Other race or ethnic group or those who lived in a census tract with higher poverty appear to be more vulnerable to the long-term effects of smoke. Understanding what long-term wildfire smoke exposure is most harmful and what populations are most at risk will help us understand biological mechanisms and inform effective adaptation strategies to limit exposure and protect population health and health equity.


Concentration metrics
Exceedance metrics
Odds ratio per 5th to 95th percentile increase in exposure metric
1.075
1.050
1.025
1.000
Exposure metrics
Mean daily wildfire PM2.5
Number of days with wildfire PM2.5 >0
Number of smoke waves
Mean daily wildfire PM2.5 during peak week
Number of weeks with wildfire PM2.5 >5

Environment/Climate Change

Effectiveness of heat alert warning systems to reduce psychiatric emergency services utilization during heat waves in Boston, MA: a difference-in-differences analysis Flannery Black-Ingersoll* Flannery Black-Ingersoll Mary D. Willis Stephanie T. Grady Kaylin Vrkljan Alison Duncan Kate Burrows Rachel Oblath Amruta Nori-Sarma

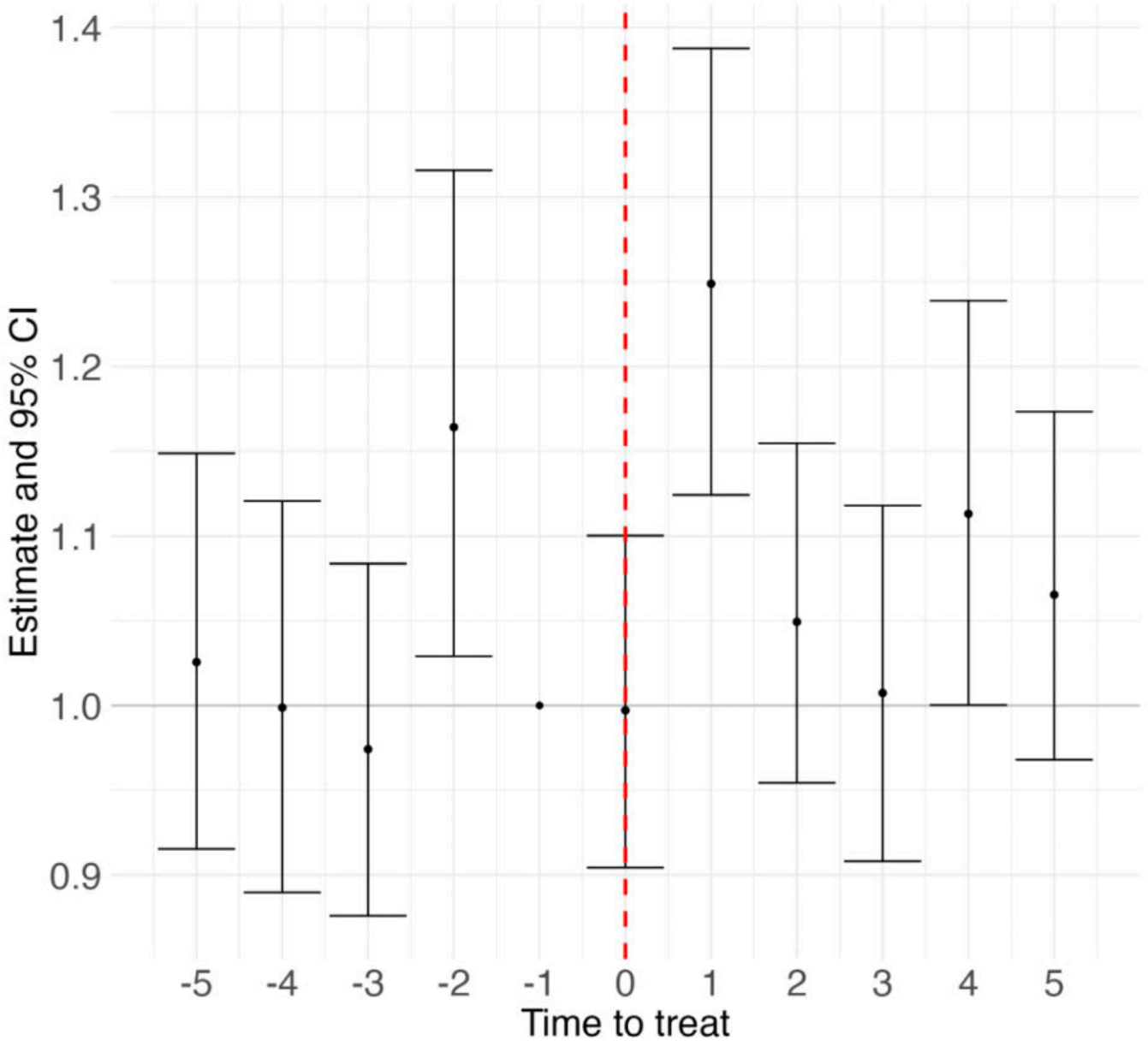
Background: Climate change is increasing the frequency, intensity, and duration of extreme heat events, and emerging research shows that extreme heat events increase the risk of adverse mental health outcomes. To date, research on physical health has found limited effectiveness of heat alert systems (i.e., public health interventions to warn and educate populations ahead of high heat events) and the effectiveness in vulnerable low-income populations has been challenging to assess. Additionally, potential protective effects of heat alerts for mental health outcomes have not been examined.

Methods: Using a quasi-experimental study design, we implemented a difference-in-differences analysis to examine associations between extreme heat and psychiatric emergency services (PES) use before and following the 2016 implementation of Boston's city-wide heat warning system. We calculated daily total PES encounters for 2012-2019 using the Boston Emergency Services Team (BEST) electronic health records, a program run by a safety net hospital designed to serve vulnerable uninsured and publicly insured persons. Using the National Weather Service temperature data, we flagged each day for extreme heat (i.e., maximum temperature). We estimated risk ratios and 95% CIs using Poisson regression, adjusting for temporal variation.

Results: We identified 154,913 encounters within the BEST program (19.4% unhoused, 62.6% nonwhite, 84.7% publicly insured). Contrary to our hypothesis, extreme heat events occurring after the implementation of the heat warning system were associated with increased PES use among BEST patients compared with events occurring prior to the heat warning system implementation (RR=1.04, 95% CI: 0.99, 1.10).

Discussion: Our preliminary findings show that the implementation of a heat warning system does not appear to yield the expected reductions in the direction or magnitude of association between extreme heat and PES use in this highly vulnerable study population.

Figure 1. Event study plot of the association between extreme heat events and psychiatric emergency services use over the years before (-5 to -2) and after (1 to 5) implementation of the heat warning system by the city of Boston, MA, with the implementation year (2016, time to treat = 0) indicated in red and the reference year (2015, time to treat = -1) indicated with the null effect estimate of 1.0.



Environment/Climate Change

Mediated impacts of China's clean heating policy on blood pressure by indoor air pollution and indoor temperature Talia Sternbach* Talia Sternbach Xiaoying Li Xiang Zhang Ellison Carter Brian Robinson Chris Barrington-Leigh Wenlu Yuan Collin Brehmer Kaibing Xue Kennedy Hirst Shu Tao Yuanxun Zhang Guofeng Shen Jill Baumgartner Sam Harper

The Clean Heating Policy (CHP) was implemented in 2016 to transition millions of homes in northern China from coal- to electric-based heating and improve air quality. Household heating interventions may improve health, including blood pressure (BP), through improved indoor temperature and reduced air pollution (PM2.5), but can also drive behavioral, environmental, and health-related changes that may affect the assumed health benefits. Understanding the mechanisms of these interventions is thus important to maximize health benefits. We leveraged the natural experiment created by the CHP's staggered rollout across villages in rural Beijing and applied causal mediation analysis to understand how much of the CHP's impact on BP may be mediated through temperature and PM2.5.

We enrolled 1,438 participants >40y from 50 villages not yet treated with the CHP in winter 2018-19. In the next 3 winters, 20 villages were treated. We visited homes each winter to measure BP, administer questionnaires, and place indoor temperature and PM2.5 sensors. Mediators were the indoor temperature measured in the 5-min before BP in all homes and the winter average indoor PM2.5 measured in 25% of homes. We estimated the CHP's total effect on BP using a difference-in-differences design, then controlled for each mediator separately, and both together, in additional models to estimate the controlled direct effects (CDE).

The CHP reduced systolic BP by 1.4 mmHg (95%CI: -3.3, 0.5) and diastolic BP by 1.6 mmHg (95%CI: -2.9, -0.3). Holding indoor temperature and PM2.5 at their baseline means (14˚C and 71 µg/m3, respectively), the CDEs for systolic and diastolic BP in the multiple mediation analysis were 0.3 mmHg (95%CI: -1.9, 2.5) and -0.6 mmHg (95%CI: -2.1, 0.9), respectively. Our analysis shows that CHP-driven improvements to indoor temperature and PM2.5 contributed to modest reductions in BP. These results provide insight into how the CHP affected BP and may inform future clean heating policies.

Causal Inference

Design-based weighted regression estimators for conditional spillover effects Fei Fang* Fei Fang Edoardo Airoldi Laura Forastiere

In a clustered interference setting, with networks collected within clusters and no interference between clusters, we introduce a general causal estimand for conditional spillover effects, offering flexible ways of integrating unit-to-unit spillover effects. In particular, we define spillover effects from the treatment received by one neighbor, averaged over the distribution of the cluster treatment, and conditional on the characteristics of the treated unit. Such definition enables to access the heterogeneity of a unit's spillover effect on their neighbors with respect to the unit's characteristics. Two weighted regression-based estimators are proposed: i) at the individual level, taking neighbors' averages either in the outcomes or in the treatments within weights; and ii) at the dyadic level, where the outcome of one unit is regressed on the treatment of each neighbor. When covariates driving the heterogeneity are categorical, we prove the equivalence of the two regression-based estimators to the non-parametric Hajek estimator. For continuous covariates, we demonstrate that both estimators consistently estimate the proposed estimands. Under a design-based perspective, we derive HAC variance estimators and establish the central limit theorem. Simulations are conducted to compare the performance of our estimators. Finally, we apply our methods to a randomized experiment conducted in Honduras to evaluate the spillover effect of a behavioral intervention.

Causal Inference

Contrasting Natural Effects and Separable Effects: Insights into Mediation Analysis Etsuji Suzuki* Etsuji Suzuki Tomohiro Shinozaki Eiji Yamamoto

As has been well appreciated in the causal mediation literature, the total effect can be decomposed into the natural direct effect and the natural indirect effect in the counterfactual framework. If certain assumptions about confounding are met, we can use the so-called mediation formula to identify these effects under the nonparametric structural equation models with independent errors (NPSEM-IE). However, the natural effects have been criticized because they are cross-world quantities, and the so-called cross-world independence assumption cannot be empirically verified. Furthermore, interventions on the mediator may sometimes be challenging even to conceive. As an alternative approach, separable effects were more recently proposed and applied in mediation analysis, often under the finest fully randomized causally interpretable structured tree graph (FFRCISTG) models. In this approach, the exposure is assumed to be separated into two (or more) components, one having a direct effect only on the mediator and the other one having a direct effect only on the outcome. Furthermore, each separable component can in principle be intervened on separately, and the total effect can be decomposed into the separable direct effect and the separable indirect effect. The separable effects are not defined as cross-world quantities and are claimed to be identifiable under assumptions that are, in principle, testable, thereby addressing some of the challenges associated with natural effects. In this presentation, we contrast natural effects and separable effects under the NPSEM-IE, thus highlighting their similarities and differences. Additionally, we illustrate these two approaches graphically by using causal directed acyclic graphs, incorporating potential outcomes determined by the NPSEM-IE. By examining their required properties/assumptions and sufficient conditions for identification, we aim to provide deeper insights into mediation analysis.

Causal Inference

Toward a Clearer Definition of Per-protocol Estimand When Emulating a Target Trial
Haidong Lu* Haidong Lu

The adherence-adjusted per-protocol effect, which represents the effect of adhering to the treatment protocol, has received increasing attention among both trialists and observationalists employing observational data to emulate hypothetical target trials, as this estimand is considered more patient-centered compared to the intention-to-treat effect (i.e., the effect of the assigned treatment, regardless of adherence status). However, the definition of the per-protocol effect remains ambiguous, especially in observational studies designed to emulate a target trial. To enhance clarity in defining this estimand, we propose the following guidelines: 1) Distinguish the causal adherence-adjusted per-protocol effect from the non-causal per-protocol difference; 2) Utilize the ICH E9 (R1) addendum to provide a more precise definition of the per-protocol estimand, which is often mistakenly equated with the as-treated effect; 3) Clarify the feasibility of identifying or approximating treatment assignment in observational settings; 4) Establish a comprehensive study protocol that explicitly defines protocol deviations (e.g., including specifying those allowable deviations) before initiating a target trial emulation. Implementing these suggestions will sharpen the definition of the per-protocol estimand and improve transparency in reporting studies.

Causal Inference

Generalized Simple Graphical Rules for Assessing and Addressing Selection Bias Haidong Lu* Haidong Lu Yichi Zhang

Selection bias is a major obstacle toward valid causal inference in epidemiology. Over the past decade, several simple graphical rules based on causal diagrams have been proposed as the sufficient identification conditions for addressing selection bias and recovering causal effects. However, these simple graphical rules are usually coupled with specific identification strategies and estimators. In this work, we show two important cases of selection bias that cannot be addressed by these existing simple rules and their estimators: one case where selection is a descendant of a collider of the treatment and the outcome, and the other case where selection is affected by the mediator. To address selection bias in these two cases, we construct identification formulas by the g-computation and the inverse probability weighting (IPW) methods based on single-world intervention graphs (SWIGs). They are generalized to recover the average treatment effect by adjusting for post-treatment upstream causes of selection. We propose two IPW estimators and their variance estimators to recover the average treatment effect in the presence of selection bias in these two cases. We conduct simulation studies to verify the performance of the estimators when the traditional crude selected-sample analysis returns erroneous contradictory conclusions to the truth.

Causal Inference

The effect of SARS-CoV-2 rapid antigen self-test use on healthcare seeking behaviour at primary care level: implications for COVID-19 vaccine effectiveness estimates in test-negative design studies. Cheyenne van Hagen* Cheyenne van Hagen Eric R.A. Vos Charlotte Lanièce Delaunay Hester E. de Melker Esther Kissling Mirjam J. Knol

Widespread diagnostic (self-)testing for SARS-CoV-2 may lead to selection bias in test-negative case-control designs (TND) for COVID-19 vaccine effectiveness (CVE) at primary care level by compromising blinding of patients and general practitioners (GP). We investigated whether self-testing among those with an acute respiratory infection (ARI) is associated with healthcare seeking behavior at primary care level in the general Dutch population.

We pooled questionnaire data from three study rounds (June 2022, November 2022 & April 2023) of the nationwide PIENTER Corona cohort study. Among participants aged 18-91 years, we selected the first self-reported ARI episode, defined as cough, sore throat, dyspnea and/or coryza, since March 2022. We performed log-binomial regression analyses adjusted for age, sex and education level to assess associations (Figure 1, orange arrows) between COVID-19 vaccination, SARS-CoV-2 self-testing and GP consultation, and between GP consultation and self-test result overall and stratified by vaccination status.

Among 3,152 participants with an ARI episode, vaccinated participants more often took a self-test (adjusted RR [95% CI]: 1.07 [1.04–1.11]) or consulted a GP (1.57 [1.21–2.09]) than those unvaccinated (Figure 1). Self-test result was overall not associated with GP consultation (0.86 [0.69–1.08]). Stratification by vaccination status showed that vaccinated individuals were less likely to consult the GP after a positive self-test (0.62 [0.49–0.79]), while those unvaccinated were more likely to (2.00 [1.08–3.51]).

In this Dutch population-based cohort, GP consulting was differential by self-test result and vaccination status between May 2022 and March 2023, indicating a potential for selection bias in TND CVE estimates due to self-tests. Our findings suggest that this may cause an overestimation of CVE. More research in various settings and larger study populations is needed to further explore and quantify this bias.

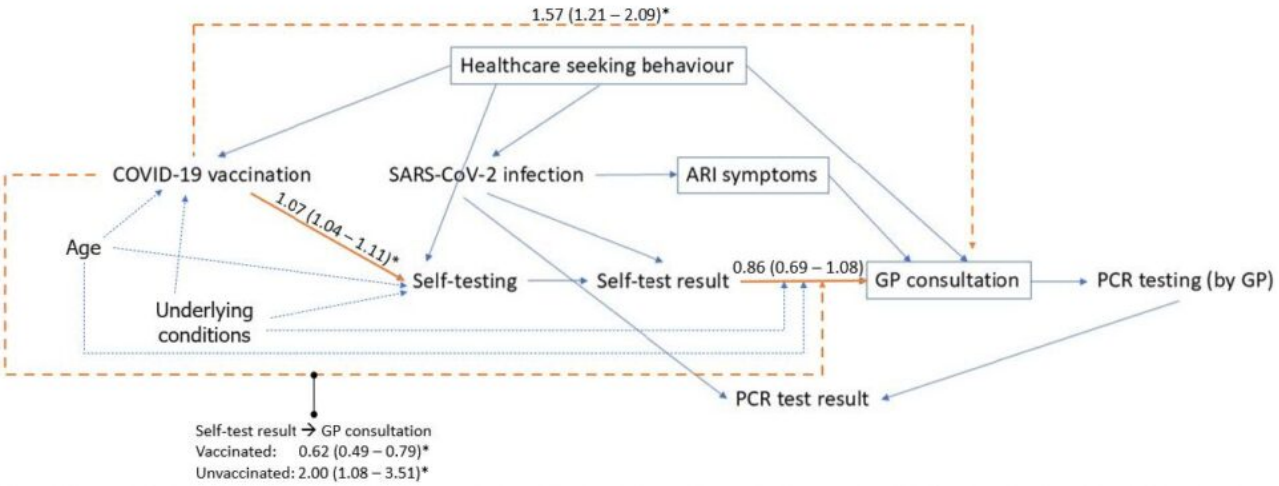


Figure 1: Directed Acyclic Graph (DAG) showing the two potential routes to biased CVE estimates (ceduced from Laniéce Delaunay et al, SSRN, 2024). Firstly, if COVID-19 vaccination is directly associated with self-testing and the self-test result is associated with GP consultation, there is an open backdoor path between COVID-19 vaccination and SARS-CoV-2 infection in a TND study (COVID-19 vaccination → Self-testing → Self-test result ← SARS-CoV-2 infection) as a result of selecting on GP consultation, a descendent of the collider self-test result. Secondly, if COVID-19 vaccination is associated with GP consultation, there is an open backdoor path from COVID-19 vaccination → [GP consultation] ← Self-test result ← SARS-CoV-2 infection in which COVID-19 vaccination might act as an effect modifier of the association between self-test result and GP consultation. Adjusted risk ratios of relevant associations (orange arrows) between COVID-19 vaccination and GP consultation, COVID-19 vaccination and SARS-CoV-2 self-testing and SARS-CoV-2 self-test result and GP consultation (overall and stratified by COVID-19 vaccination status) are presented.

Health Disparities

The Roles of Healthy Start Service Provision on Perinatal Outcomes among Healthy Start Participants, South Carolina, 2011-2019 Jihong Liu* Jihong Liu Xingpei Zhao Rokonuzzaman S.M. Ishan Suthar Curisa Tucker Kimberly Alston

Healthy Start (HS) Programs are federally funded, community-based initiatives designed to reduce disparities in perinatal outcomes in communities where infant mortality rates were 1.5 to 2 times higher than the national average. However, few studies have evaluated the effectiveness of direct HS service delivery in improving perinatal outcomes.

This cohort study included 2,142 mother-newborn dyads who were served by the Midlands HS Program from 2011 to 2019 in South Carolina. The birth certificates were linked with program data, restricted to singleton births with a birthweight of ≥500 grams. HS staff recorded all services provided via home visits, office visits, phone calls, or mailings, including access to perinatal care, health education, screening and referral for depression, parenting, and father involvement etc. Participants were grouped as receiving low (0-1), modest (2-4), and high (≥5) service groups based on the total number of services received during pregnancy.

HS participants were 25.3 years old (±5.6), 59.0% African Americans, 33.3% White, 7.7% other races, 55.2% with a high school education or less, and 74.5% on Medicaid. HS participants received a mean of 4.5 services (±6.0), with 43.4% of participants receiving modest services and 24.4% high levels of services. After adjusting for maternal age, race, education, Medicaid, prepregnancy BMI, parity, and adverse pregnancy histories, compared to low levels of services, both modest and high levels of HS services were associated with lower risks of prenatal smoking (ORHigh: 0.73, 95% CI 0.50-1.08; ORModest: 0.70, 0.50-0.97), gestational hypertension (ORHigh: 0.58, 0.37-0.89; ORModest: 0.67, 0.47-0.97), low birthweight (ORHigh: 0.61, 0.41-0.91; ORModest: 0.73, 0.52-1.02), and primary cesarean delivery (ORHigh: 0.95, 0.70-1.28; ORModest: 0.70, 0.53-0.92). Receiving ≥2 breastfeeding-related services was associated with higher odds of initiating breastfeeding (OR: 1.38, 1.07-1.80) compared to those not receiving breastfeeding services.

The results demonstrated that HS services provided by community health workers and social workers have potential to improve perinatal outcomes in underserved communities, suggesting that HS programs could play a significant role in reverse rising trends in maternal morbidity and infant mortality in the US.

Health Disparities

Association between county-level aggregate anti-Black implicit bias and Black youth suicides in the US Parvati Singh* Parvati Singh

Persistent exposure to racism may increase risk factors for suicide among Black populations, and particularly among Black youth. Structural racism shapes societal attitudes and policies, which, in turn, may contribute to the development of implicit biases against minority groups, corresponding with a vicious feedback loop of social priming and bias reinforcement. Aggregate-level implicit anti-Black bias may thus represent one aspect of structural racism that permeates multiple systems and processes, placing Black populations at a continuous disadvantage. Whereas individual-level implicit bias reflects personal attitudes and prejudices, aggregate-level implicit anti-Black bias may offer a more comprehensive measure of structural racism and anti-Black discriminatory attitudes. We examined whether and to what extent, county-level aggregate implicit anti-Black bias scores (exposure) correspond with suicides among Black youth populations (outcome) in the US. We used longitudinal county-level data on aggregate implicit anti-Black bias (retrieved from the Project Implicit database) and suicide deaths among Black youth aged <25 years across all US counties (from CDC's Restricted Use mortality database) over an 18 year period spanning 2002 to 2019 and examined within-county variations in the patterning of Black youth suicide mortality in relation to aggregate scores of implicit anti-Black bias. County-level two-way fixed effects Poisson regression analyses controlled for several socio-structural factors (e.g. poverty, income, health insurance) that may confound the relation between the exposure and outcome. Analytic results indicate 1.6 additional suicides among Black youth per unit increase in within-county aggregate implicit bias scores ($p < 0.001$). Our national, ecological study may contribute to current knowledge by providing the first large-scale evaluation of the association between aggregate implicit anti-Black bias scores and suicides among Black youth populations.

Health Disparities

A Population-Based Retrospective Cohort Study on Colorectal Cancer Survival in Kentucky

Jemal Gishe* Jemal Gishe Francis Pleban Mohamed Kanu Elizabeth Brown Meng-Han Tsai

Background: Colorectal cancer (CRC) mortality in Kentucky exceeds the national average, with some recent studies indicating an increase of up to 29.6%. Non-Hispanic Blacks (NHBs) and rural residents are disproportionately affected, experiencing higher CRC incidence and poorer survival outcomes. This study aims to identify factors contributing to the elevated CRC mortality in Kentucky.

Methods: This retrospective cohort study analyzed Surveillance, Epidemiology, and End Results (SEER) data from 2000 to 2021, including 42,963 eligible CRC patients from Kentucky. Demographic characteristics, diagnostic outcomes, and treatment modalities were examined. Kaplan-Meier and Cox regression model were used.

Results: Among patients, the highest proportion of distant CRC diagnoses was observed in NHBs (17.8%), while the lowest was in non-Hispanic Others (NHOs) (11.9%) ($P<0.01$). NHB patients also had the highest CRC mortality rate (42.7%) compared to NHOs (22.9%) ($P<0.01$). Unadjusted survival time was shortest for NHBs (70.6 months) and longest for NHOs (81.3 months) ($P<0.01$). Cox regression analysis (all P-values<0.01) revealed that counties not adjacent to metropolitan areas had a 13% higher mortality risk than large metropolitan areas, HR=1.13 CI(1.09, 1.18). NHBs had an 18% higher CRC mortality risk compared to non-Hispanic Whites, HR=1.18 CI(1.11, 1.26). Patients diagnosed with regional or distant stages had 165% (HR=2.65 CI 2.51, 2.80) and 853% (HR=9.53 CI 8.99, 10.10) higher mortality risks, respectively, compared to those with localized disease. Additionally, patients not recommended or refused surgery had a 233% higher mortality risk, HR=3.33 CI(3.18, 3.48).

Conclusion: This study identifies key factors influencing CRC mortality in Kentucky, such as being NHB, rural residency, late-stage diagnosis, and lack of surgical options. These findings highlight the need for targeted public health strategies and policy changes to address CRC-related health disparities in Kentucky.

Health Disparities

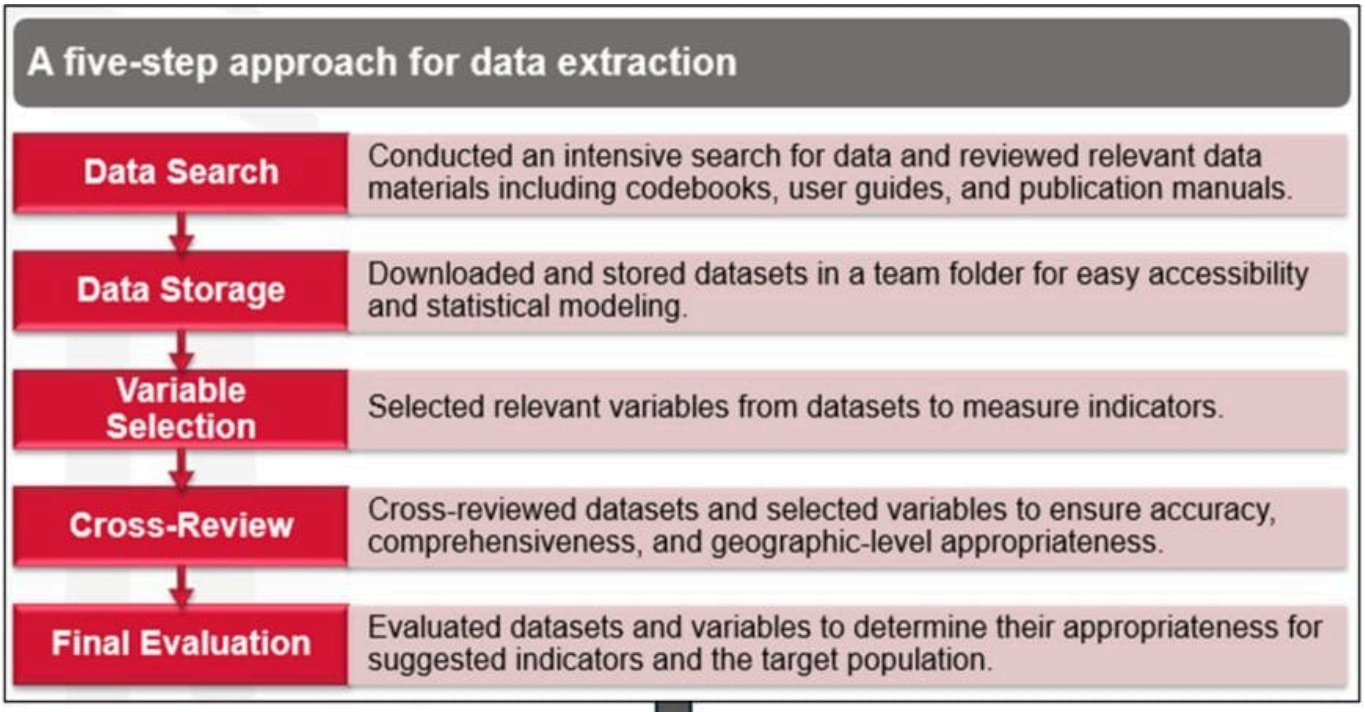
Developing an Index to Measure Structural Racism: Methodological Challenges and Considerations Yu-Hua Fu* Christopher Amissah Alisha A. Crump Yu-Hua Fu Sheela Khadka Jennifer Contreras Salene M. W. Jones Bryce B. Reeve Ester Villalonga Olives

Introduction: Access to valid and reliable measures of structural racism is essential for addressing health inequities. We developed an ecological-level index to assess structural racism among Black and Hispanic populations in the U.S.

Methods: We adapted the National Institute on Minority Health and Health Disparities framework to guide the development of the index. A content development team comprising social epidemiologists (N=4), an expert panel of health inequality researchers (N=5), community members (N=3), and economic inequality specialists (N=2) participated in a modified Delphi process alongside psychometricians (N=2) to build consensus on selecting key indicators of structural racism. Once consensus was reached, we followed a five-step approach to extract geographic-level data from existing databases to measure the proposed indicators. In this process, we encountered several challenges that needed to be resolved (Fig. 1).

Results: We categorized the challenges into two types: 1) **Data challenges** included barriers related to data availability and completeness at county or ZIP-code levels. Some datasets had inadequate descriptions and inconsistent reporting frequencies. Adapting data to fit our needs was also challenging, as many did not capture the granularity required to meaningfully assess structural racism such as racial disparities in access to business loans and mortgages; 2) **Statistical challenges** involved complexities in integrating diverse datasets, each with its unique methodologies, formats, and scales. Efforts to overcome these challenges focused on standardizing data across sources to ensure consistency, carefully addressing missing data to avoid bias, and resolving variability in indicator measurement.

Conclusion: Addressing these challenges was crucial for creating a reliable index of structural racism. Future research should use advanced data integration techniques and AI to enhance data processing, address missing data, and ensure consistency.



Data extraction and statistical challenges

Challenges	Description	Resolutions
Data Extraction Challenges		
Limited Geographic Data	Misalignment between structural racism indicators and available dataset aggregation levels (e.g., state-level vs. county level).	Used proxies and supplemental sources to approximate ecological-level granularity when county or ZIP code data were unavailable.
Reporting Frequency	Temporal mismatches in data reporting complicated analysis.	Developed aggregation methods to align temporal data.
Data Adaptability	Publicly available datasets often lacked variables relevant to structural racism.	Explored alternative sources and adapted broad indicators to approximate variables of interest.
Limited Access to Data	Some datasets required permissions, training, or purchase (e.g., AHA, HCUP).	Navigated access protocols for restricted datasets and utilized publicly available data.
Inadequate Data Description	Vague dataset descriptions hindered indicator identification.	Reviewed data documentations and supplementary literature for a better understanding.
Limited Use of AI Tools	AI tools provided broad but sometimes irrelevant dataset suggestions, requiring manual validation.	Used AI-generated suggestions as starting points, followed by manual evaluation, quality checks, and alignment with research goals.
Statistical Challenges		
Integration Challenges	Variations in geographic granularity (e.g., state- vs. county-level) and geographic context (e.g., urban vs. rural).	Standardized geographic units using consistent metrics and applied psychometric analyses to evaluate robustness of integrated measures.
Methodological Differences	Divergent methodologies, definitions, and sampling techniques across datasets complicated synthesis.	Harmonized race classifications, measurement scales, and definitions, and adjusted for biases using statistical methods.
Data Missingness	Missing data due to nonresponse, incomplete records, or systemic collection issues posed a risk of bias.	Applied multiple imputation techniques, triangulated data from multiple sources, and validated imputed results.
Variations in Data Quality	Disparities in data reliability and completeness across sources complicated cross-comparisons.	Prioritized similar data sources to minimize variability and interpreted measures cautiously.
Measurement Variability	Differences in operational definitions and coding schemes complicated data synthesis.	Aggregated granular data when needed while maintaining interpretative caution.

Health Disparities

Mammography Screening and Risk Factor Prevalence by Sexual Identity: A Comparison of Two National Surveys Hanwen Zhang* Hanwen Zhang Brittany M. Charlton Phillip W. Schnarrs Amy Trentham-Dietz Felicitas Kuehne Uwe Siebert Navkiran K. Shokar Michael P. Pignone Jennifer C. Spencer

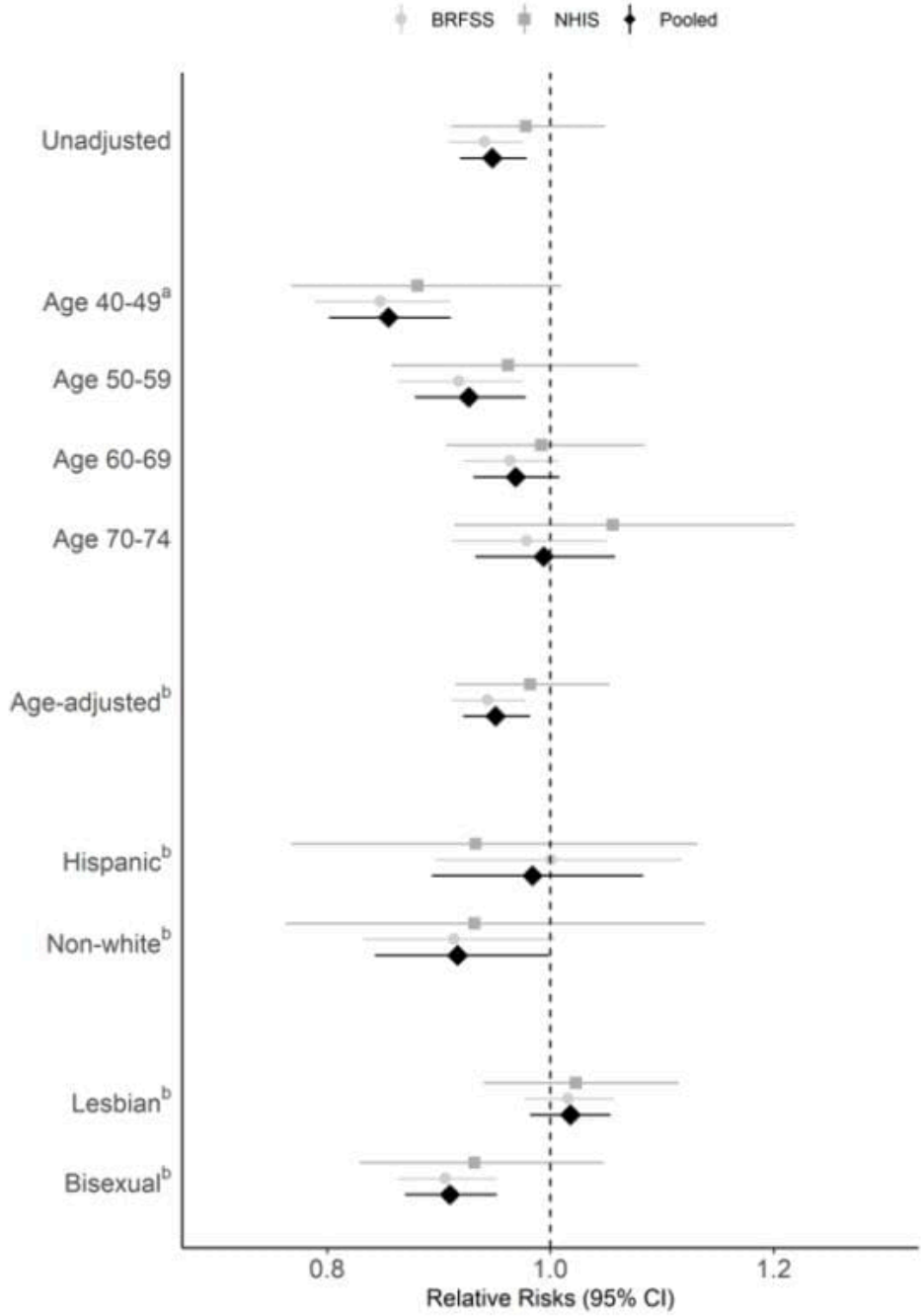
Background: Emerging research suggests lesbian, gay, bisexual, and queer (LGBQ) women face barriers to breast cancer screening, yet few studies have quantified disparities in mammography screening, healthcare access, and lifestyle-related breast cancer risk factors between LGBQ and straight women across multiple national surveys.

Methods: We analyzed data from the 2018, 2019, and 2021 National Health Interview Survey (NHIS), as well as the 2018, 2020, and 2022 Behavioral Risk Factor Surveillance Survey (BRFSS). We used Poisson regression to estimate relative risks (RR) of biennial mammography for women identifying as lesbian/gay or bisexual/queer versus straight, and we pooled RRs (pRR) with a random effects meta-analysis. We also assessed sexual identity disparities in healthcare access and lifestyle-related breast cancer risk factors with prevalence and 95% CIs. All analyses applied survey weights.

Results: Compared to straight women, LGBQ women reported lower biennial mammography (pRR: 0.95; 95%CI: 0.92-0.98), driven by differences among bisexual/queer women (pRR: 0.91[0.87-0.95]) and those entering screen-eligibility, aged 40–49 (pRR: 0.86[0.80–0.91]) and 50–59 (pRR: 0.93[0.88–0.98]). LGBQ women were more likely than straight women to be uninsured (BRFSS: 8.6% [6.5–11.2] vs. 5.1% [4.8–5.4]) and to experience financial barriers to care (BRFSS: 13.8% [11.6–16.3] vs. 8.9% [8.5–9.2]). Lifestyle-related breast cancer risk factors were more common among LGBQ versus straight women, including current smoking (BRFSS: 19.0% [17.1–21.2] vs. 13.9% [13.6–14.3]).

Conclusions: LGBQ women were more likely than straight peers to be exposed to lifestyle-related breast cancer risk factors, compounded by being screened less often and facing healthcare access barriers. It is crucial to develop and implement targeted interventions for screening and risk reduction that are accessible and effective for LGBQ women, particularly bisexual/queer women and those aging into screen-eligibility.

Figure 1: Relative Risks of Biennial Mammography Screening LGBQ vs. Straight, across 2 National Surveys



Legend:
NHIS - National Health Interview Survey, BRFSS - Behavioral Risk Factor Surveillance Survey. Data from NHIS 2018, 2019, and 2021 (n Straight = 19,198, n Lesbian/gay = 241, n Bisexual/queer = 186); BRFSS 2018, 2020, and 2022 (n Straight = 184,816, n Lesbian/gay = 2,473, n Bisexual/queer = 4,111).
[a] Women aged 40–49 (NHIS: n Straight = 6,207, n LGBQ = 250; BRFSS: n Straight = 45,478, n LGBQ = 2,982) were not included in the unadjusted and age-adjusted estimates.
[b] Age-adjusted estimates that were adjusted for categorical age (50–59, 60–69, and 70–74).

Health Disparities

The role of personality in the association between adverse childhood experiences with chronic conditions Luke Barry* Luke Barry Mina Habib Roch Nianogo

Background

Adverse childhood experiences (ACEs) may contribute to physiological dysregulation and increased morbidity. Modifiable personality traits can influence this relationship. This study examines the association between ACEs and number of chronic conditions over the lifecourse, and the mediating role of personality.

Methods

Data from the 2006 and 2008 US Health and Retirement Study were analyzed. Exposures included any ACEs (before age 18) and specific ACEs (repeating a school year; parental substance use; physical abuse). Mediators were the top quartile (Y/N) of Big Five personality traits (conscientiousness, agreeableness, neuroticism, openness, extraversion). The outcome was the number of chronic conditions. Exclusions included childhood chronic conditions, missing baseline or exposure data (n=9,458). Missing mediator and outcome values were imputed using multiple imputation. Causal mediation analysis with generalized linear regression and 200 bootstrap iterations estimated associations and quantified mediators' roles, adjusting for baseline confounders (age, age-squared, gender, race/ethnicity, childhood health and socioeconomic status, and parental smoking).

Results

Individuals with any ACEs reported 6% more chronic conditions compared to those with no ACEs (IRR = 1.06 [95% CI = 1.03, 1.10]). Physical abuse by a parent was linked to 18% more chronic conditions (IRR = 1.18 [1.11, 1.25]). High neuroticism amplified the ACE-morbidity association (Excess Ratio due to reference interaction [ER-Ref] = 0.02 [0.01, 0.04]), overall explaining 42% of this link. High openness and conscientiousness (ER-Ref for both = -0.01 (-0.03, 0.01) modestly buffered the ACE effect on morbidity but precision was lower.

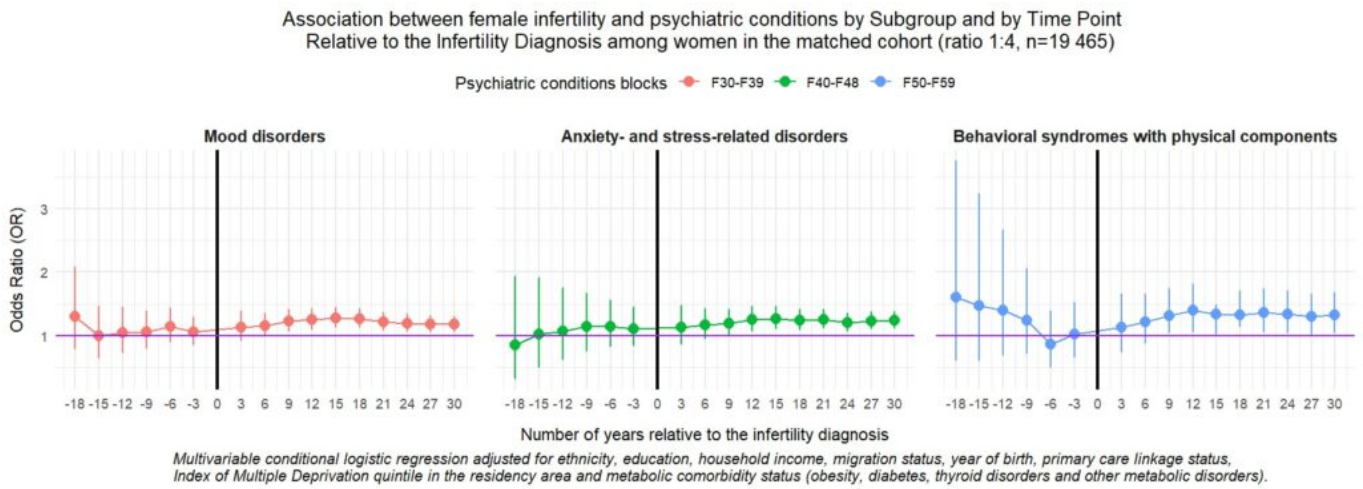
Conclusion

ACEs were associated with higher morbidity, particularly parental physical abuse. High neuroticism exacerbated this link, while openness and conscientiousness offered some protective effects. Interventions targeting neuroticism could mitigate 42% of the ACE-morbidity association.

Women's Health

Infertility and Lifelong psychiatric disorders in Women: A Matched Cohort Study Linda Kahn* khaoula Ben Messaoud Nina Zaks

Research has demonstrated increased rates of anxiety and depression in females, particularly around the time of infertility diagnosis and treatment. Yet, gaps remain in the understanding of the relationships between **female infertility (FI)** and psychiatric health over longer time periods and across a broader range of psychiatric conditions. This study uses a matched-pair design (infertility +ve vs. -ve, ratio 1:4) within the UK Biobank cohort to examine the association between FI and psychiatric conditions by ICD-10 code blocks: mood disorders (F30-F39); anxiety- and stress-related disorders (F40-F48); and behavioral syndromes with physical components (F50-F59). We implemented multivariable conditional logistic regressions adjusted for socio-demographic variables and metabolic comorbidity. All associations were estimated overall and across different time points relative to the first diagnosis of FI (from 18 years prior to 30 years after, in 3-year intervals). We also tested the interactions between infertility diagnosis and (a) miscarriage and (b) live birth on psychiatric outcomes and performed sensitivity analyses parsing the sources of psychiatric outcome and infertility information (self-report, primary care, hospitalization). Findings show that infertility is significantly associated with a higher risk of all three psychiatric diagnosis groups (mood, anxiety- and stress-related, and behavioral disorders) overall and in almost all intervals starting nine years after diagnosis of infertility (Fig 1). We report a different trend in infertile females with an history of miscarriage prior the first FI diagnosis and live birth for all the outcomes. Our results are consistent across sources of psychiatric and infertility information. These findings show for the first time links between FI and psychiatric disorders beyond the care phase, emphasizing the critical need for long-term monitoring of psychiatric conditions in infertile women.



Social

Adverse childhood experiences and lifetime risk of polycystic ovarian syndrome Lauren A. Wise* Lauren A. Wise Krystal E. Kuan Yael I. Nillni Julia C. Bond Andrea S. Kuriyama Nyia Noel Renée Boynton-Jarrett

Background: Adverse childhood experiences (ACEs) have been associated with several health outcomes, but their effects on reproductive disorders such as polycystic ovarian syndrome (PCOS) are not well characterized. ACEs may influence PCOS risk via chronic activation of the hypothalamic-pituitary-adrenal axis, thereby resulting in ovarian dysfunction.

Methods: We assessed the association between ACEs and PCOS risk using data from Pregnancy Study Online (PRESTO), a North American preconception cohort study of female pregnancy planners aged 21-45 years. At baseline, participants completed the 8-item ACE scale from the Behavioral Risk Factor Surveillance System module. We summed across all ACE items to create a score (range: 0 to 8). Participants reported PCOS diagnoses on baseline and follow-up questionnaires. We fit log-binomial regression models to estimate risk ratios (RRs) and 95% CIs, adjusting for age, race, ethnicity, and childhood socioeconomic position.

Results: Among 10,759 participants, 52% reported 1-3 ACEs and 26% reported ≥4 ACEs; 10.7% reported a PCOS diagnosis. RRs for ACE scores of 1-3 and ≥4 (vs. 0) were 1.35 (95% CI: 1.14-1.60) and 1.62 (95% CI: 1.34-1.95), respectively (per 1-ACE increase: RR=1.09, 95% CI: 1.06-1.12). Individual ACE items associated with the largest increase in PCOS risk included: household mental illness (RR=1.49, 95% CI: 1.26-1.77), incarceration of a household member (RR=1.51, 95% CI: 1.13-2.03), parental interpersonal violence (RR=1.66, 95% CI: 1.36-2.07), physical abuse (RR=1.61, 95% CI: 1.32-1.96), emotional abuse (RR=1.55, 95% CI: 1.31-1.84), and sexual abuse (RR=1.73, 95% CI: 1.42-2.21).

Conclusions: In a North American preconception cohort study, greater exposure to ACEs was associated with a higher lifetime risk of PCOS diagnosis.

Table 6. Association between childhood adversity and polycystic ovarian syndrome at baseline in PRESTO, stratified by social support before age 18 (June 2013-November 2024)

	Overall (n=10,759)				High Childhood Social Support[a] (n=8,114)			Low Childhood Social Support[a] (n=2,645)		
	Cases	Total	Crude PR (95% CI)[b]	Adjusted PR (95% CI)[c]	Cases	Total	Adjusted PR (95% CI)[c]	Cases	Total	Adjusted PR (95% CI)[c]
ACE Module										
Cumulative Score										
0	171	2357	1.00 (ref)	1.00 (ref)	148	2126	1.00 (ref)	23	231	1.00 (ref)
1-3	581	5590	1.42 (1.21-1.68)	1.35 (1.14-1.60)	441	4382	1.40 (1.16-1.68)	140	1208	1.04 (0.68-1.58)
≥4	404	2812	1.91 (1.61-2.27)	1.62 (1.34-1.95)	213	1606	1.67 (1.35-2.07)	191	1206	1.18 (0.77-1.81)
Per one unit increase in ACE score			1.12 (1.09-1.14)	1.09 (1.06-1.12)			1.09 (1.06-1.13)			1.05 (0.99-1.10)
Substantive Domains[d]										
Household mental illness	631	5095	1.68 (1.42-1.97)	1.49 (1.26-1.77)	402	3478	1.52 (1.26-1.84)	229	1617	1.14 (0.75-1.74)
Household substance abuse	419	3491	1.64 (1.38-1.95)	1.35 (1.12-1.63)	256	2328	1.40 (1.13-1.73)	163	1163	1.02 (0.66-1.59)
Household incarceration	122	884	1.80 (1.45-2.25)	1.51 (1.13-2.03)	62	528	1.40 (0.99-1.98)	60	356	1.37 (0.74-2.55)
Parental separation or divorce	444	3497	1.72 (1.45-2.04)	1.43 (1.19-1.73)	261	2359	1.36 (1.10-1.69)	183	1138	1.28 (0.83-1.99)
Parental IPV	267	1851	1.94 (1.61-2.33)	1.66 (1.32-2.07)	142	1053	1.69 (1.30-2.21)	125	798	1.23 (0.77-1.97)
Physical abuse	348	2465	1.91 (1.60-2.28)	1.61 (1.32-1.96)	187	1401	1.73 (1.37-2.17)	161	1064	1.10 (0.71-1.70)
Emotional abuse	710	5509	1.75 (1.49-2.06)	1.55 (1.31-1.84)	432	3560	1.59 (1.32-1.93)	278	1949	1.16 (0.77-1.75)
Sexual abuse	318	2090	2.04 (1.71-2.44)	1.73 (1.42-2.12)	167	1242	1.73 (1.37-2.18)	151	848	1.35 (0.87-2.11)
Brief Trauma Questionnaire										
No abuse	630	6709	1.00 (ref)	1.00 (ref)	488	5543	1.00 (ref)	142	1166	1.00 (ref)
Physical abuse only	131	1063	1.30 (1.09-1.55)	1.18 (0.99-1.42)	78	656	1.27 (1.01-1.59)	53	407	0.95 (0.71-1.27)
Sexual abuse only	206	1796	1.20 (1.04-1.39)	1.15 (0.99-1.33)	147	1303	1.21 (1.02-1.44)	59	493	0.93 (0.70-1.24)
Physical and sexual abuse	189	1191	1.65 (1.42-1.91)	1.43 (1.22-1.68)	89	612	1.46 (1.18-1.82)	100	579	1.20 (0.93-1.54)

Note: ACE = adverse childhood experiences; CI = confidence interval; PR = prevalence ratio; IPV = intimate partner violence; PRESTO = Pregnancy Study Online; [a]Defined via an adapted Berkman-Syme Social Network Index (SNI score: ≥6 [high] vs. <6 [low]); [b]Adjusted for age at enrollment; [c]Adjusted for age at enrollment, race and ethnicity, childhood economic resources, and highest parental education; [d]Exposure referent = No adverse childhood experiences.

Global Health

Perinatal depression, maternal engagement, and child social-emotional development in Kenya Anna Larsen* Anna Larsen John Kinuthia Felix Abuna Julia C. Dettinger Lauren Gomez Mary Marwa Nancy Ngumbau Ben Odhiambo Salphine Watoyi Joshua Stern Barbra A. Richardson Grace John-Stewart Jillian Pintye

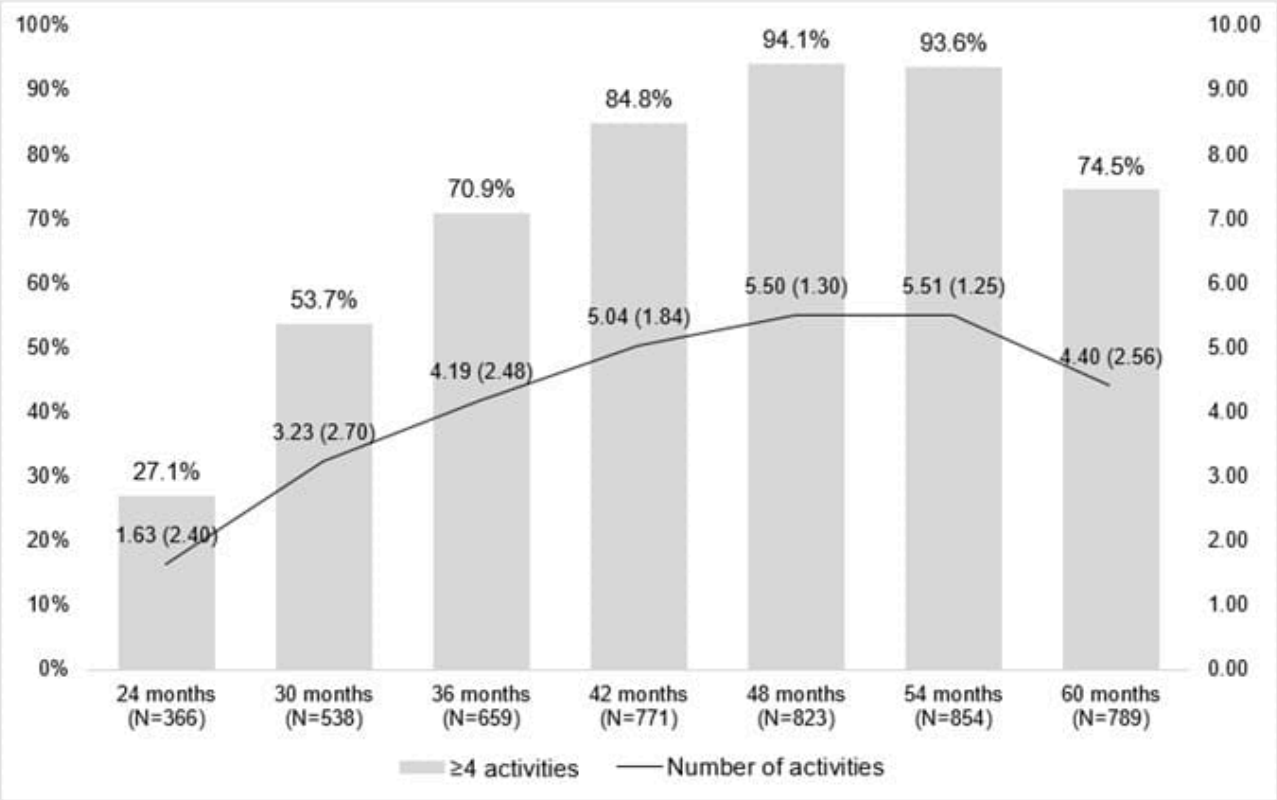
We assessed relationships between perinatal depression, mother-child engagement, and child social-emotional development among Kenyan mother-child pairs.

Mother-child pairs attending maternal-child health services in four sites in Western Kenya were followed from pregnancy through early childhood. Study nurses serially assessed perinatal depression (pregnancy, 6 weeks, and 9 months postpartum with the Center for Epidemiologic Studies Depression scale, CESD-10 scores ≥10), mother-child engagement activities (6-monthly, 24 to 60 months post-delivery with UNICEF Multiple Indicator Cluster Surveys), and child social-emotional delay (6-monthly, 30 to 60 months post-delivery with Ages and Stages Questionnaires). We used generalized estimating equations to identify correlates of low mother-child engagement and social-emotional delay.

Among 884 mothers, median age was 26 years (IQR:22.0-30.3), 92% were married, and 37% had perinatal depression. High mother-child engagement (≥4 activities in prior 3-days) ranged 27%-94% from 24 to 60 months post-delivery. Frequency of child social-emotional delay ranged 4%-27% from 30 to 60 months (higher frequency earlier in childhood). Low mother-child engagement at any point (<4 activities) was more common among women with perinatal depression (aRR:1.2, 95% CI:1.1-1.3) and associated with twice the risk of child social-emotional delay (aRR:2.2, 95% CI: 1.8-2.8). Mothers who reported adverse childhood experiences (ACES) (aRR:1.1, 95% CI:1.0-1.1) and intimate partner violence (IPV) (aRR:1.3, 95% CI:1.1-1.5) interacted less frequently with their children than women not reporting these experiences. Having a mother with more ACES (aβ:0.8, 95% CI:0.03-1.6) and IPV (aβ:4.7, 95% CI:0.9-8.6) increased a child’s risk of poorer social-emotional development.

In this large cohort of Kenyan mother-child pairs, maternal perinatal depression was associated with lower mother-child engagement, which doubled risk of child social-emotional delay.

Figure 1. Mother-child engagement from 24-60 months post-delivery among Kenyan mother-child pairs



*We present mean and standard deviation for number of mother-child engagement activities at each time point

Mental Health

Maternal perinatal cannabis use disorders and the risk of anxiety disorders in offspring: Insights from a longitudinal data-linkage cohort study Abay Woday Tadesse* Abay Woday Tadesse Getinet Ayano Berihun Assefa Dachew Kim Betts Rosa Alati

Abstract
Background: Cannabis use is rising among women of reproductive age, yet research on its impact on childhood anxiety disorders remains limited. This study examines whether maternal cannabis use disorder (CUD) during pregnancy and postpartum periods is associated with a higher risk of anxiety disorders in offspring.

Methods: We used linked health data from New South Wales, Australia, covering live births from 2003 to 2005. ICD-10 coded maternal CUD and child anxiety disorders, including generalized anxiety disorder (GAD), phobic anxiety disorder (PAD), posttraumatic stress disorder (PTSD), and early childhood-onset anxiety disorders (CAD), were extracted from patient records. Generalized linear models (GLMs) with log-binomial regression estimated the risk of anxiety disorders linked to maternal CUD exposure.

Results: After adjusting for covariates, offspring prenatally exposed to maternal CUD had an increased risk of any anxiety disorder [adjusted risk ratio (aRR) = 1.79 (95% CI 1.40, 2.26)]; specifically PTSD [aRR = 2.46 (95% CI 1.78, 3.33)], GAD [aRR = 2.18 (95% CI 1.03, 4.60)], and CADs [aRR = 1.91 (95% CI 1.05, 4.60)], compared to non-exposed offspring. Postnatal CUD exposure was also associated with an increased risk of any anxiety disorder [aRR = 2.02 (95% CI 1.22, 3.14)] and specifically PTSD [aRR = 2.97 (95% CI 1.56, 5.17)]. These associations remained consistent in sensitivity analyses excluding maternal tobacco use disorders.
Conclusion: Both in-utero and postnatal CUD exposures are associated with increased risks of anxiety disorders in offspring. These findings highlight the need for targeted interventions, including perinatal counselling, to reduce anxiety risks in offspring.

Women’s Health

Mental Health and Home Pregnancy Testing Behavior Alexandra Sundermann* Alexandra Sundermann Kenneth J. Rothman Lauren A. Wise

Mental health is integral to pregnancy health, yet little is known about its effect on pregnancy testing behavior among those trying to conceive. In PRESTO (Pregnancy Study Online, 2018–2024), a prospective cohort of individuals planning a pregnancy, participants provided information about mental health and day-specific use of a home pregnancy test, including test results from four days before expected start of menstruation through four days after. We analyzed data from 20,458 pregnancy tests across 6,569 participants. Thirty-two percent of participants reported an anxiety diagnosis and 27% reported a depression diagnosis; 16% of participants reported a diagnosis of both anxiety and depression. Testing was categorized as infrequent (1 test, 34%), moderate (2-3 tests, 35%), or frequent (≥4 tests, 31%). Behavior was further characterized by timing of first test as very early (≥4 days before expected period, 41%), early (1-3 days before expected period, 33%), or expected/late (day of expected period or later, 26%). We use log-binomial regression models to estimate risk ratios and 95% confidence intervals [CI], with adjustment for age, parity, and history of miscarriage. Participants with anxiety were more likely to be very early and frequent testers (adjusted risk ratio [aRR] 1.31, 95% CI 1.20, 1.43). When accounting for a concurrent depression diagnosis, participants with anxiety alone were most likely to be very early and frequent testers (aRR 1.37, 95% CI 1.18, 1.58) compared with participants with anxiety and depression (aRR 1.17, 95% CI 0.99, 1.38) or depression alone (aRR 1.16, 95% CI 0.97 1.41). Higher baseline perceived stress scores were associated with increased pregnancy testing frequency (Figure). Home testing is one of the first modifiable behaviors of pregnancy, and individuals with anxiety tend to test earlier and more frequently than those without.

Predicted frequency of pregnancy testing with perceived stress score modeled using restricted cubic splines; model adjusted for maternal age and parity

Perinatal & Pediatric

Trauma, post-traumatic stress disorder symptoms, and adverse pregnancy outcomes: sexual orientation disparities in a prospective cohort study Michelle W. Tam* Michelle Tam Isa Berzansky Payal Chakraborty Colleen A. Reynolds Kodiak Soled Sarah McKetta Cindy Veldhuis Karestan Koenen Brittany Charlton

Background: Sexual minority (SM) individuals are at heightened risk for trauma exposure and post-traumatic stress disorder (PTSD) symptoms, as well as adverse pregnancy outcomes. Yet, little research has elucidated the link between trauma histories, PTSD symptoms, and adverse pregnancy outcomes in this population.

Methods: The Nurses' Health Study 3 is a longitudinal cohort of nurses born on or after January 1, 1965, living in the US or Canada (N= 27,359 pregnancies from 10,086 participants). We estimated person-level prevalence of traumatic events and PTSD symptoms, and pregnancy-level prevalence of adverse pregnancy outcomes (i.e., gestational diabetes, gestational hypertension, pre-eclampsia, preterm birth, low birthweight, macrosomia) across sexual orientation groups (completely heterosexual, heterosexual with same-sex experience, mostly heterosexual, bisexual, and lesbian/gay). Moderation analyses examining adverse pregnancy outcomes across sexual orientation and PTSD/trauma are forthcoming.

Results: Compared to completely heterosexual individuals, mean age at first traumatic event was younger for all SM groups; completely heterosexual individuals were 18.5 years, heterosexual with same-sex experience (16.1 years), mostly heterosexual (15.8 years), bisexual (13.9 years), and lesbian/gay (12.9 years). All SM groups had a higher prevalence of PTSD symptoms— bisexual (74%), lesbian/gay (71%), mostly heterosexual (67%), heterosexual with same-sex experience (58%)—compared to the completely heterosexual group (55%). Pregnancies to lesbian/gay individuals (36%) had the highest prevalence of any adverse pregnancy outcomes, followed by completely heterosexual (30%), heterosexual with same-sex experience (28%), bisexual (27%), and mostly heterosexual (27%).

Conclusions: Future research should investigate mechanisms underlying sexual orientation-related inequities (e.g., discrimination and minority stress) in traumatic experiences, PTSD, and adverse pregnancy outcomes.

Social

Mechanisms linking adverse childhood experiences to co-occurring mental health and substance use disorder in young adulthood Ethan Ecret* Ethan Ecret Elizabeth Vasquez Allison Appleton Tomoko Udo Muntasir Masum Melissa Tracy

Adverse childhood experiences (ACEs) are linked to poor health outcomes later in life, though the mechanisms connecting ACEs to health outcomes in young adulthood are less understood. This study explores the extent to which behavioral and psychosocial factors mediate the relationship between ACEs and co-occurring mental health and substance use disorders (SUD) in young adulthood. We used data from 3,420 participants in the Avon Longitudinal Study of Parents and Children (ALSPAC). Using semiparametric group-based trajectory modeling, we identified five childhood adversity trajectories from birth through age 12: stable low (57.1%), stable mid (30.2%), increasing from mild to high (6.7%), decreasing from moderate to mid (4.0%), and stable high (2.1%). At age 24, 16.7% of participants met criteria for a mental disorder (e.g., depression, anxiety) only, 11.3% met criteria for alcohol use disorder (AUD) or cannabis use disorder (CUD) only, and 6.4% met criteria for both mental health and substance use disorders. In multinomial logistic regression models, adjusted for socio-demographics and maternal factors, ACEs were associated with mental health and substance use disorders, with participants with stable-high adversity showing the highest odds of mental health disorders only (OR=2.00, 95% CI=1.09-3.67), those with decreasing adversity showing the highest odds of AUD and/or CUD (OR=2.02, 95% CI=1.18-3.45), and those with increasing adversity showing the highest odds of both mental health and substance use disorders (OR=2.31, 95% CI=1.39-3.84), all relative to those with stable low adversity. Substance use, impulsivity, antisocial activities, and internalizing problems in adolescence together explained 7-32% of the estimated effects of ACEs. Early intervention among children with ACEs is critical, but targeting behavioral and psychosocial factors in adolescence may also help reduce progression to co-occurring mental health and substance use problems in young adulthood.

Social

The adverse effects of criminal legal system involvement on mental health in later adulthood among young people in the United States Pui Ying Chan* Pui Ying Chan Zachary Shahn Katarzyna E. Wyka Kristin Turney Heidi E. Jones

Background
Prior studies in the United States have shown an association between criminal legal system (CLS) involvement and poor mental health. However, most studies were cross-sectional or, if longitudinal, did not address bias from treatment-confounder feedback. To address this gap, we applied the parametric g-formula to explore the relationship.

Methods
We used self-reported data on CLS encounters and mental health over the period of 2000-2010 collected among 5,611 persons from the National Longitudinal Study of Youth 1997, who were 15-21 years of age at baseline. We conducted g-computation to estimate the risks of two outcomes in 2010: having mental health symptoms, defined by the Mental Health Inventory 5-item version, and binge drinking. We adjusted for a priori confounders including sociodemographic, family contextual factors, mental health risk factors, and prior CLS involvement. We used chained equations to singly impute missing data and censored participants at first missed interview. We estimated the outcome risks under the natural course and under two interventions, removing arrests and incarcerations ("no CLS involvement") and removing incarcerations only, to estimate the resulting risk differences (RDs).

Results
At the end of the study, 4,424 respondents remained. The estimated end-of-follow-up risk was 9.4% for mental health symptoms and 17.3% for binge drinking under the natural course of CLS involvement with no loss to follow up (which aligned closely with observed estimates). The "no-CLS involvement" intervention was estimated to lower binge drinking risk by 0.7 percentage-points (95% confidence interval [CI]: -1.5, -0.3) but had no effect on the risk for mental health symptoms (RD: -0.3, 95% CI: -0.7, 0.2). The "no incarceration" intervention had no effect on either outcome.

Conclusions
There is evidence that CLS involvement has long-lasting harm to mental health among young people as manifested through binge drinking behaviors in later adulthood.

Social

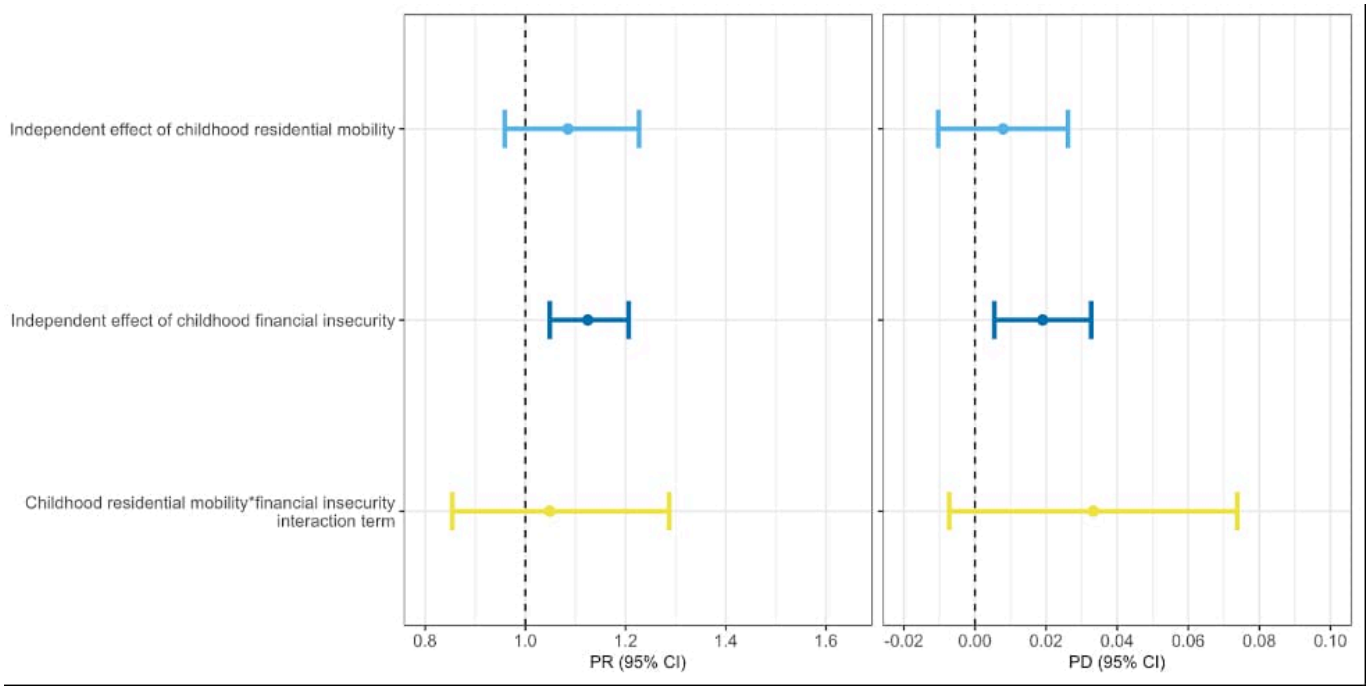
Estimating independent and joint effects of high childhood residential mobility and financial insecurity on mid- and late-life functional difficulty in a national population-based sample Taylor Mobley* Taylor Mobley Kathryn M. Leifheit Onyebuchi A. Arah Elizabeth Rose Mayeda

Introduction: A growing body of evidence suggests high childhood residential mobility and financial insecurity influence health across the lifecourse. No studies have assessed the interaction between these exposures on mid- and late-life ("later-life") health. We aimed to estimate independent and joint effects of high childhood mobility and financial insecurity on later-life functional difficulty in a national population-based sample.

Methods: This study comprised non-Hispanic White, non-Hispanic Black, and Hispanic participants aged 50+ from the Health and Retirement Study with complete exposure and covariate data (n = 9,459). Participants reported childhood mobility and financial wellbeing through age 16 retrospectively. Functional difficulty, which was assessed biennially from 1992-2020, was defined as any endorsement of difficulty with 6 activities of daily living (ADLs) or 5 instrumental ADLs. We used generalized estimating equations to estimate prevalence ratios (PRs) and differences (PDs) for the independent and joint effects of high (4+ moves, 90th percentile) vs. low (<4 moves) childhood mobility and childhood financial insecurity (poor vs. high/average wellbeing) on later-life functional difficulty. We adjusted for age, sex/gender, race and ethnicity, parental education, and US Southern birth.

Results: Estimates suggested high childhood mobility and financial insecurity were independently associated with later-life functional difficulty (PR 1.08, 95% CI: 0.96, 1.23; PR 1.12, 95% CI: 1.05, 1.21, respectively). We found no evidence of interaction between exposures (PR interaction term 1.05, 95% CI: 0.85, 1.29). Estimates on the additive scale were qualitatively similar.

Conclusions: High childhood mobility and childhood financial insecurity were independently associated with later-life functional difficulty, possibly without interaction. Interventions targeting both exposures may reduce the risk of later-life functional difficulty.


Independent effect of childhood residential mobility
Independent effect of childhood financial insecurity
Childhood residential mobility*financial insecurity interaction term
0.8
1.0
1.2
1.4
1.6
PR (95% CI)
-0.02
0.00
0.02
0.04
0.06
0.08
0.10
PD (95% CI)

Social

Unequal burdens of parenthood: Heterogeneity in cardiovascular risk factors among parents Whitney Wells* Whitney Wells Fan Xia Jacqueline M. Torres Rita Hamad Anusha M. Vable

Background: For the 28 million parents of young children in the U.S., the demands of parenthood can increase time pressure and financial stress, prevent health maintenance, and potentially impact health into midlife. Health challenges related to parenthood likely vary by sociodemographic context, but evidence on heterogeneity is limited.

Method: We used the National Health Interview Survey (NHIS) 2000-2018 waves to examine the relationship between parenthood and five self-reported cardiovascular disease risk factors: physical activity, alcohol use, smoking, sleep duration, and body mass index (n=151,765 parents, n=375,220 non-parents). We adjusted for sociodemographic factors, year, and region, and examined effect modification by sociodemographic factors.

Results: Parents (compared to non-parents) had lower odds of being physically active (OR: 0.69; 95% Confidence Interval [CI]: 0.67, 0.71), higher BMI (□: 0.14; 0.08, 0.20), and fewer hours of sleep per night (□: -0.19; -0.21, -0.18). Parents also had lower odds of being a current drinker (OR: 0.78; 95% CI: 0.77, 0.80) or current smoker (OR: 0.81; 95% CI: 0.79, 0.83). We observed heterogeneity across all outcomes by sex, race and ethnicity, income, and relationship status (p-values for interaction <0.05). In stratified results, the most pronounced differences were by sex (women had greater decreases in physical activity but also in drinking, smoking, and BMI) and by partnership status (those unmarried or without cohabitating partners had greater increases in drinking, smoking, and BMI) (Figure 1).

Conclusion: While U.S. parents have lower use of alcohol and smoking, they also have worse physical activity, BMI, and sleep vs non-parents. Parents may feel increased pressure to reduce unhealthy behaviors, but may also face structural challenges in maintaining cardiovascular health, particularly single parents. Family support policies to alleviate time and financial pressures may be crucial in supporting parents' health.

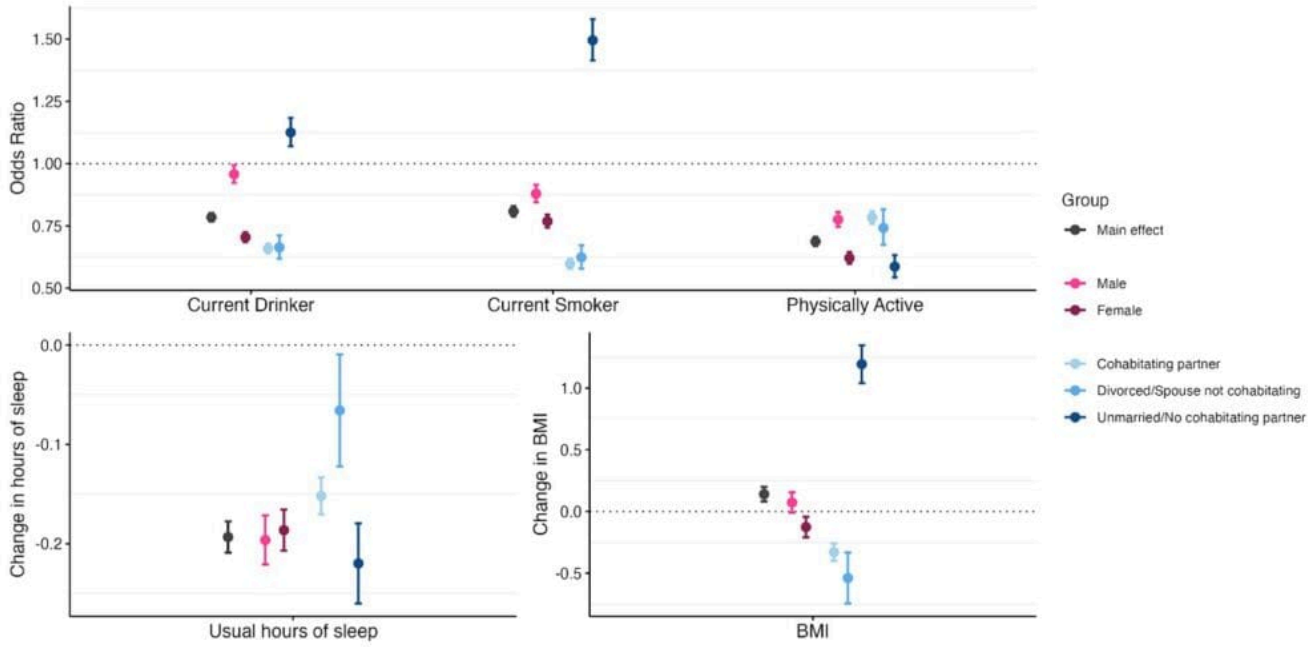


Figure 1. Association between parenthood and cardiovascular risk factors, overall and by sex and partnership status

Social

Heterogeneous association between social isolation and all-cause mortality among Japanese older adults Frances Rom Lunar* Frances Rom Lunar Naoki Kondo Yukiko Honda Atsushi Nakagomi Toshiaki Komura Kosuke Inoue Koichiro Shiba

Background: Social isolation has been linked to higher mortality; however, it remains unknown how this association varies across individuals and which social groups are vulnerable.

Methods: We used data from a nationwide cohort study of nearly 20,000 Japanese older adults with a 9·4-year follow-up period (Japan Gerontological Evaluation Study, 2013–2022), adjusting for 60 pre-baseline covariates. We linked the cohort data to a national insurance database to ascertain 4,299 all-cause deaths. Using a causal machine-learning method, we estimated the heterogeneous association between social isolation and mortality.

Results: Social isolation was more prevalent among those with lower income and educational attainment and associated on average with 65-day shorter survival time (restricted mean survival time [RMST] difference; 95% CI: -106, -24·2). There was evidence of heterogeneity such that social isolation was associated with even shorter survival days in some sub-groups (e.g., -214 days among the bottom quintile of the estimated RMST differences [95% CI: -332, -97·0]). These sub-groups tended to report lower educational attainment and pre-existing health problems. The adverse association of social isolation was particularly strong when lower educational attainment was combined with higher income, especially among women. Our simulation indicated that decreasing the prevalence of social isolation would reduce education- and income-based disparities in survival time.

Implications: Social isolation may be more harmful among those from socially disadvantaged backgrounds, and a combination of some characteristics can synergistically amplify its adverse effects on mortality. Population-level interventions reducing social isolation would not only improve health on average but also mitigate existing health disparities.

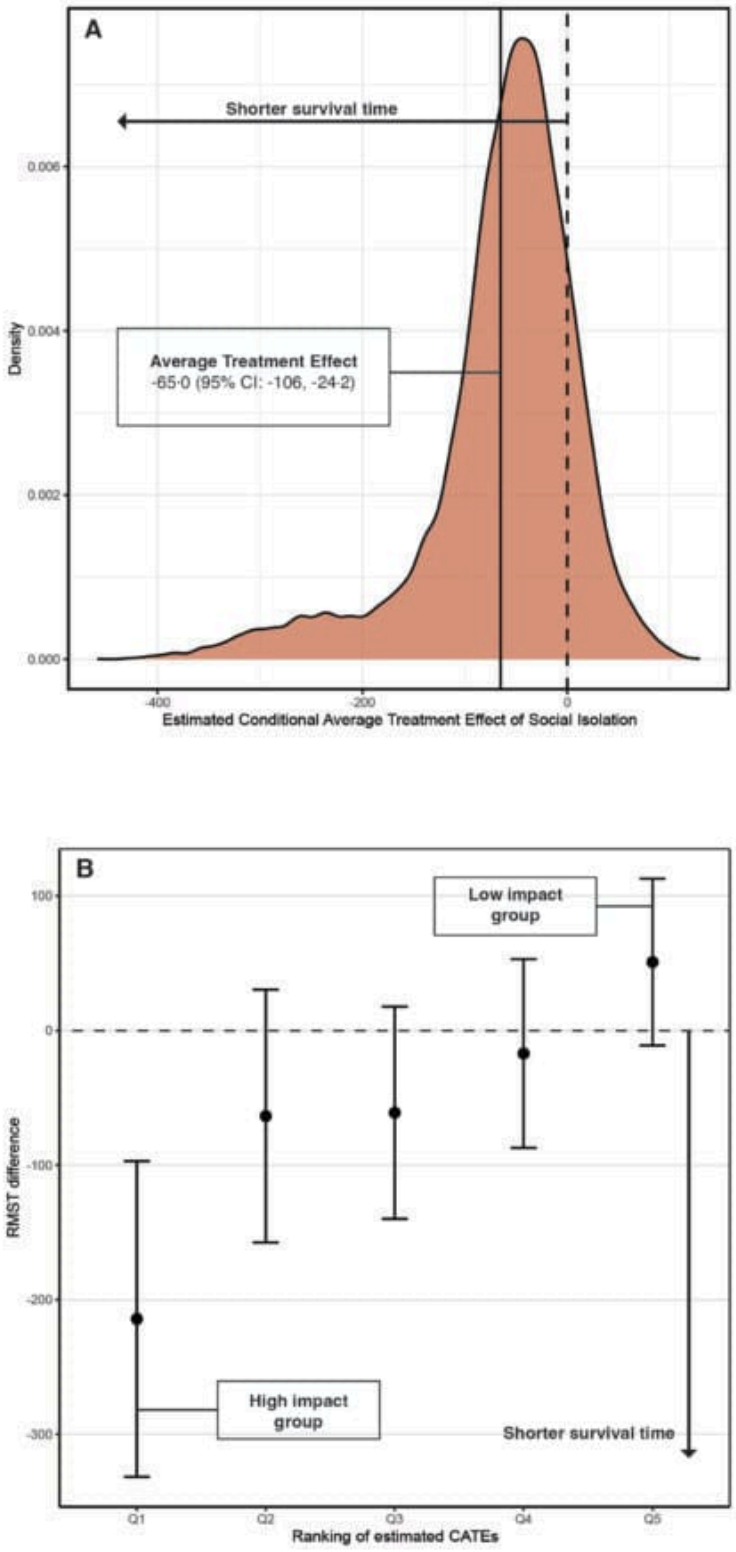


Figure 2. Results from the survival forest analysis: A) Density plot of estimated CATEs, and B) Group average treatment effects using RMST by CATE-based quantiles

CATE: Conditional Average Treatment Effects; RMST: Restricted Mean Survival Time

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Study Design

Is more always better? Implications of the number of cognitive assessments within a limited follow-up time on bias and precision of estimated effects on cognitive change Mary Thoma* Mary Thoma Jingxuan Wang Elizabeth-Rose Mayeda Charles McCulloch Maria Glymour Eleanor Hayes-Larson Jacqueline Torres

Background: Repeated cognitive performance assessments are necessary for dementia research, but longitudinal data collection is costly. Within a set follow-up period, similar estimates of association with cognitive change may be achievable with fewer assessments. We compared the bias and precision of cognitive change estimates (age effect) across models with varying total assessments across 8 years of follow-up.

Methods: Using data from the U.S. Health and Retirement Study among 65-80 year-olds in 2006 (N=7736), we estimated linear mixed models for associations of baseline diabetes, stroke, depression, and neighborhood safety with change in cognitive performance z-scores via interactions between each risk factor and current age. Reference estimates were derived from a model in a random 50% of the cohort with 5 cognitive assessments completed every 2 years over 8 years of follow-up (2006-2014). Comparison estimates were obtained from the other 50% of the cohort using (a) standard linear regression with cross-sectional data (2006); linear mixed models with (b) 2 assessments separated by 8 years (2006, 2014); and (c) 3 assessments each separated by 4 years (2006, 2010, 2014). Bias of estimates was defined as the absolute difference from reference model estimates. Design effects (DEFF) were calculated as the variance from a given estimate relative to the variance of the reference model estimate.

Results: Estimates of the four risk factors using cross-sectional data had substantial bias (mean across risk factors=0.013; SD=0.009) and DEFF (mean across risk factors=3.49; SD=0.32). Using 2 assessments the mean bias was 0.007 (SD=0.004) with DEFF=1.30 (SD=0.07). Using 3 assessments improved results only slightly to a mean bias of 0.005 (SD=0.004) and DEFF of 1.15 (SD=0.06).

Conclusions: When total follow-up time was limited to 8 years, using 2-3 equally spaced assessments resulted in minimal bias and loss of precision compared to using 5 equally spaced assessments.

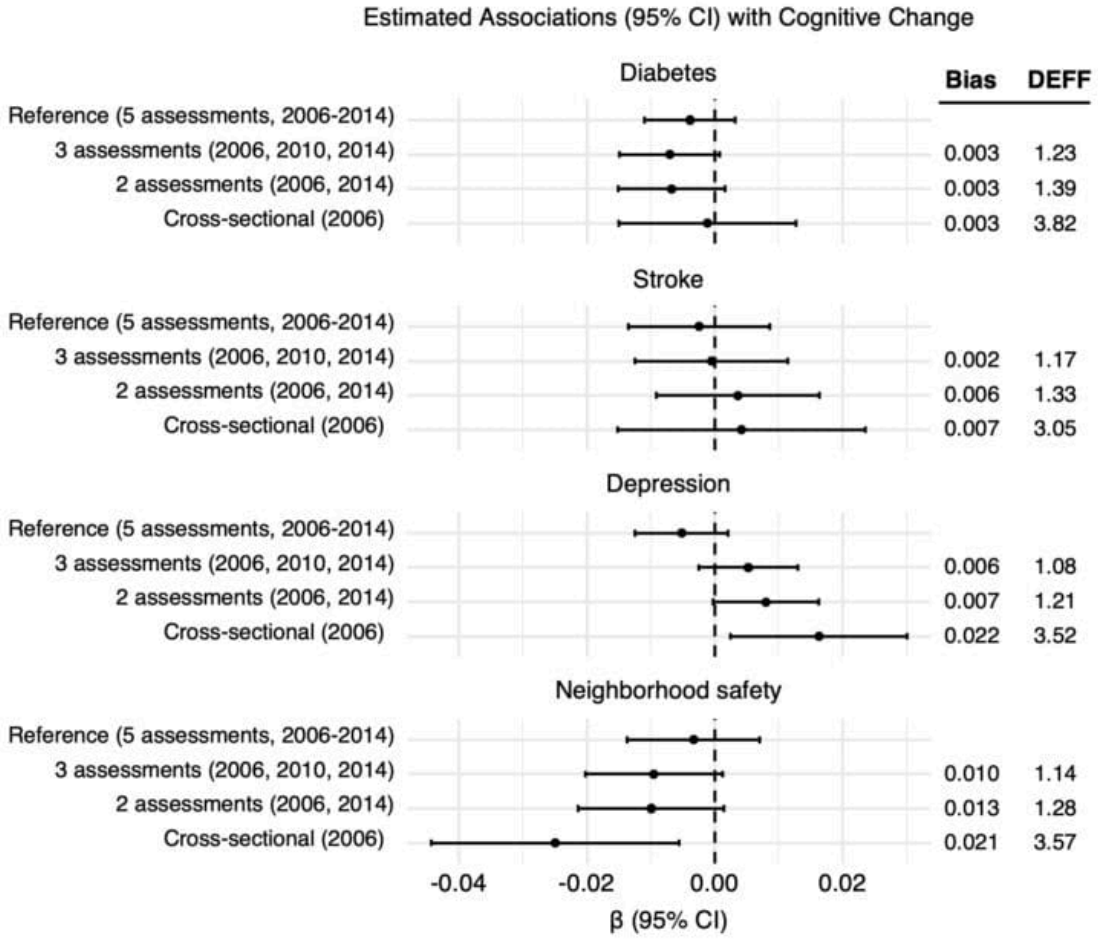


Figure 1. Estimated associations and 95% confidence intervals (CI) between four risk factors and cognitive change among U.S. Health and Retirement Study participants aged 65-80 years old at baseline. Reference estimates were derived from a random 50% subsample (N=3868) using linear mixed effects models with 5 assessments across 8 years of follow-up. Comparative estimates were derived from the remaining 50% of the cohort (N=3868) using standard regression models with cross-sectional data and linear mixed effects models with 2 equally spaced or 3 equally spaced assessments across 8 years of follow-up. Models include measures of sex, race, education, baseline history of diabetes, baseline history of stroke, depressive symptoms, and perceived neighborhood safety, and a mutiplicative interaction term between the risk factor with time-varying age. Bias=absolute difference in estimated association compared to reference estimate. Design effect (DEFF)=variance of estimate relative to variance of reference estimate.

Neurology

Sleep disturbance and neighborhood disadvantage interact to affect cognitive health in older Mexican Americans Yu Yu* Yu Yu Shiwen Li Kimberly Paul Beate Ritz

Background: Both sleep disturbance and neighborhood disadvantage have been separately linked to cognitive impairment. Here, we aim to examine how sleep disturbance and neighborhood disadvantage interact to influence the development of incident dementia or cognitive impairment without dementia (CIND) among older Mexican Americans followed over almost a decade for cognitive decline.

Methods: We used 1,582 Mexican American participants from the Sacramento Area Latino Study on Aging conducted from 1998 to 2007. Sleep disturbance was defined according to five questions such as waking up to urinate during night and having trouble falling asleep at baseline and was converted into a standardized score (z-score). A neighborhood disadvantage index was created via principal component analysis based on percent of population with education below high school, linguistically isolated households, population with income below federal poverty line, population that were unemployed from 2010 American Community Survey. Using Cox proportional hazard models, we estimated the hazard of incident dementia or CIND according to the sleep disturbance score and further investigated whether neighborhood disadvantage modified the association between sleep disturbances and dementia or CIND.

Results: In total, 96 incident dementia and 150 incident dementia/CIND cases were identified during 10-years of follow-up. For each 1 standard error increase in the sleep disturbance score, the hazard of incident dementia increased 24% (HR= 1.24, 95%CI: 1.00, 1.55). The hazard ratio for sleep disturbance related dementia was stronger (HR=1.41, 95% CI: 1.04, 1.91) among those living in the disadvantaged neighborhood areas compared to those living in the advantaged areas.

Conclusion: Our study indicates that sleep disturbances adversely affect cognition in older Mexican Americans and that this effect may be modified by neighborhood disadvantages such that cognitive function in vulnerable populations is most affected.

Neurology

Are Individuals with Diabetes Less Likely to Develop Amyotrophic Lateral Sclerosis? Mario Flores* Mario Flores Éilis O'Reilly Marianna Cortese Alpa Patel Yikyung Park Laurence Kolonel Kjetil Bjornevik Alberto Ascherio

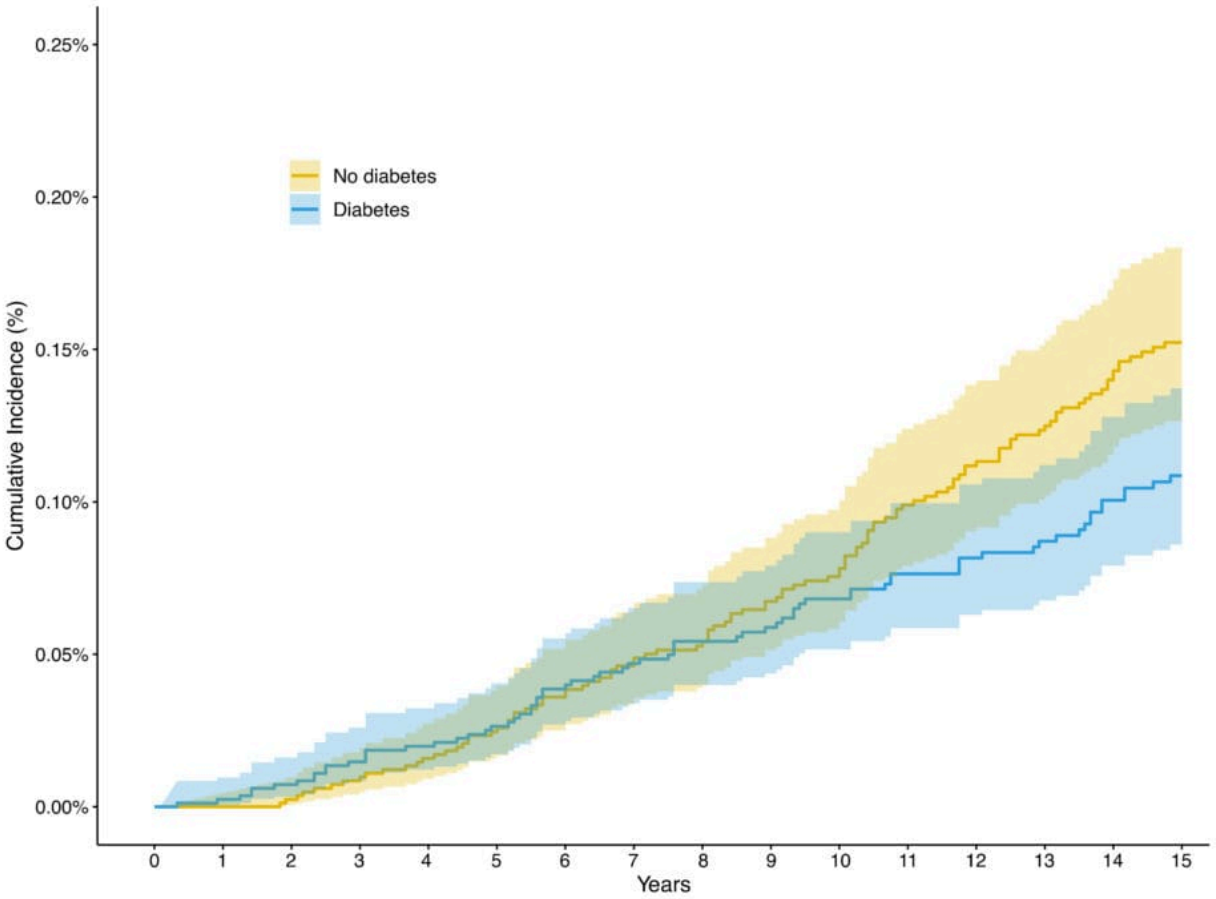
Objective–To examine whether individuals with diabetes have a lower risk of amyotrophic lateral sclerosis (ALS) than those without diabetes.

Background–Although an inverse association between diabetes and ALS has been consistently reported in epidemiological studies, these studies have lacked information on potential confounders such as smoking and physical activity, and have not examined temporal variations in ALS risk.

Methods–We used prospectively collected data of 985,805 individuals from five US cohort studies. Individuals with diabetes at baseline were matched to those without diabetes in a 1:1 ratio according to age, sex, race, cohort, obesity, smoking status, and level of physical activity. We estimated the risk of ALS at 5, 10, and 15 years in those with and without diabetes using the Kaplan-Meier estimator. Risk ratios were obtained by dividing risk estimates. Percentile-based confidence intervals (CI) were calculated using bootstrapping.

Results–This analysis included 84,066 individuals with diabetes at baseline with a mean age of 63 (SD, 6.5) years, who were matched to 84,066 individuals without diabetes; 197 individuals developed ALS during follow-up. Among those with diabetes, the estimated risk of ALS (events/10,000 persons) was 2.6 (95% CI:1.7-4.0) at 5 years, 6.8 (95% CI:5.2-9.0) at 10 years, and 10.9 (95% CI:8.6-13.7) at 15 years. The corresponding risks among those without diabetes were 2.7 (95% CI:1.7-4.1), 7.8 (95% CI:6.1-10.1), and 15.4 (95% CI:12.7-18.3). The risk ratio of ALS comparing individuals with and without diabetes was 0.98 (95% CI:0.35-1.98), 0.87 (95% CI:0.48-1.41), and 0.71 (95% CI:0.46-1.17), at 5, 10, and 15 years, respectively.

Conclusion–Individuals with diabetes appeared to have a lower ALS risk than similar individuals without diabetes; this difference increased over follow-up time but failed to reach statistical significance. The impact of prevalent user bias, competing events, and diabetes treatment will be explored in sensitivity analyses.


0.25%
0.20%
0.15%
0.10%
0.05%
0.00%
Cumulative Incidence (%)
No diabetes
Diabetes
0
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
Years

Neurology

The Effects of Cancer on Alzheimer's Disease and Related Dementia Risk by Type, Stage, and Treatment: The Multiethnic Cohort Study Gina Nam* Gina Nam Unhee Lim Song-Yi Park Yingyan Wu L. Paloma Rojas-Saunero Zuo-Feng Zhang Elizabeth Rose Mayeda

Background: Most research on cancer and subsequent Alzheimer's disease and related dementias (ADRD) has treated cancer as homogeneous. Given cancer heterogeneity, effects on ADRD risk may vary.

Methods: The Multiethnic Cohort Study includes Black, Japanese American, Latino, Native Hawaiian, and White adults aged 45-75 at baseline in 1993. We estimated total and controlled direct effects of incident cancer on ADRD risk (RR) over 26 years (censored by 2019) using inverse probability weighting. We used the Aalen-Johansen estimator to estimate total effects (including paths mediated by death) and the Kaplan-Meier estimator to estimate controlled direct effects (eliminating paths mediated by death). Stratified analyses were conducted by cancer type, stage, and initial treatment.

Results: The study included 104,258 participants (74% non-White; 55% female), with 24,083 incident cancer identified from SEER tumor registries and 23,147 incident ADRD subsequently identified from Medicare claims. The five most common cancers were prostate (24%), breast (17%), colorectal (12%), lung (10%), and non-Hodgkin lymphoma (4.9%). Of the cancer cases, 56% were diagnosed at early stages and 58% received surgery for initial treatment. Total effect RRs for ADRD ranged from 0.19 (95% CI: 0.15-0.28) for lung cancer to 1.02 (0.89-1.06) for breast cancer. Controlled direct effect RRs ranged from 1.09 (0.99-1.21) for endometrium cancer to 1.56 (1.47-1.84) for stomach cancer. For late-stage cancers, total and controlled direct effect RRs for ADRD were 0.42 (0.39-0.46) and 1.29 (1.26-1.41), respectively. Among initial treatments, chemotherapy had the greatest reduction in total effect (RR 0.43; 0.39-0.47), while immunotherapy had the highest controlled direct effect (RR 1.44; 1.18-1.67) compared to other treatments.

Conclusions: Specific cancer characteristics influence the effects of incident cancer on ADRD risk, underscoring the importance of considering cancer heterogeneity in related research.

Environment/Climate Change

Long-term exposure to outdoor ultrafine particles and black carbon and mortality from neurodegenerative outcomes in Canada's two largest cities. Emmanuelle Batisse* Emmanuelle Batisse Marshall LLoyd Christel Renoux Arman Ganji Junshi Xu Marianne Hatzopoulou Jill Baumgartner Scott Weichenthal

Background: In urban areas, transportation and industrial activities emit large quantities of air pollutants such as ultrafine particles (UFP, <0.1 um) and black carbon (BC). Due to their smaller size, UFP can reach vital organs including the central nervous system. Emerging evidence suggests that long-term exposures to UFP may increase the risk of mortality from neurodegenerative diseases, but studies are limited and none accounted for UFP size.

Aim: We evaluated associations between long-term exposures to outdoor UFP and BC and mortality from neurodegenerative outcomes among members of the Canadian Census Health and Environment Cohorts living in Montreal and Toronto.

Methods: We followed 2.1 million adults between 2001 and 2019. Information on vital status and cause of death were from the Canadian Vital Statistics Database and high-resolution exposure data for UFP number concentrations, UFP size, and BC mass concentrations were assigned to residential locations using three-year moving averages. We used Cox proportional hazards models to estimate associations between outdoor UFP/BC and mortality from dementia, Parkinson's disease and amyotrophic lateral sclerosis (ALS), adjusting for sociodemographic confounders and co-pollutants. In future analyses, we will use inverse-probability weighting to estimate the controlled direct effect of UFP/BC under the hypothetical scenario where competing events are eliminated.

Preliminary results: We included over 19 million person-years and 20,000 deaths. UFP were associated with increased neurodegenerative mortality (HR, 95% CI per 10,000 particles/cm³ UFP: 1.112, 1.074–1.152; per 500 ng/m³ BC: 0.993, 0.977–1.008). Further, UFP were linked to dementia mortality (1.149, 1.107-1.192), while BC was associated with mortality from Parkinson's disease (1.051, 1.002-1.103) and ALS (1.028, 0.947-1.116). Our findings suggest that UFP and BC could be modifiable risk factors to target in efforts to reduce neurodegenerative mortality.

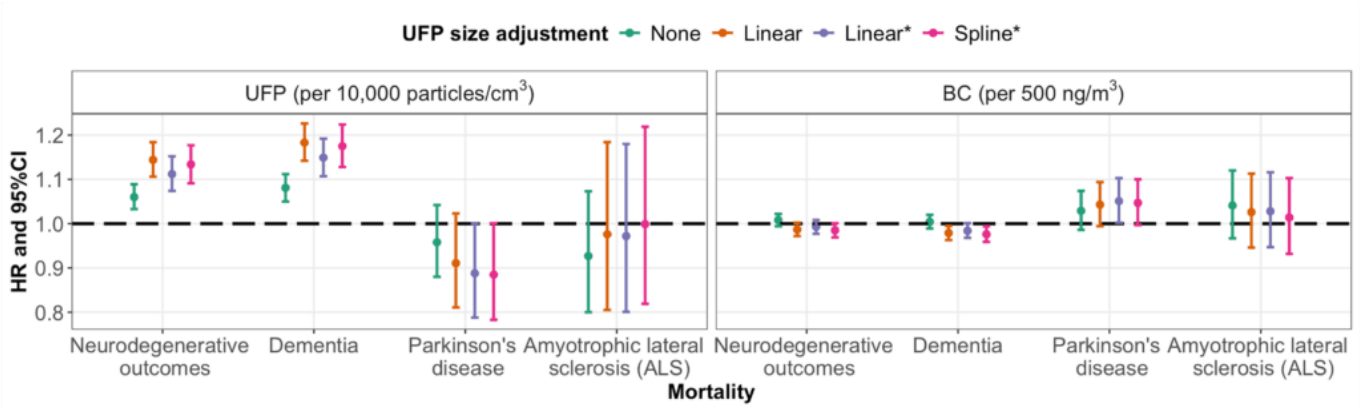


Figure 1: Associations between long-term outdoor exposures to UFP/BC concentrations and mortality from neurodegenerative diseases. Note: *Models also adjusted for $PM_{2.5}$.

LATEBREAKER

Causal Inference

Understanding and depicting survey mode effects using directed acyclic graphs (DAGs)
Georgia Tomova* Georgia Tomova Richard Silverwood Liam Wright

Survey data can be collected in many ways, such as via a face-to-face, video or phone interview, or through self-completion questionnaires on paper, web or mobile app. The medium through which a survey is collected is referred to as its ‘mode’. Although surveys have traditionally employed a single mode, there has been a recent shift towards mixed-mode data collection. While this can help reduce costs and increase participation rates, it can also generate bias in analyses of the resulting data.

The mode of data collection can influence variable measurement. For example, while respondents may give more considered answers when an interviewer is present compared to in an (anonymous) web survey, they may also provide more socially desirable answers. The difference in responses due to differences in measurement is termed a ‘mode effect’. Mode can also be related to selection since people with certain characteristics may be more or less likely to respond via a specific mode. Commonly, differences in both measurement and selection are likely to exist and give rise to different responses between modes. Mode effects can be accounted for in a variety of ways. One of the most common is to condition on survey mode by stratification or covariate adjustment. While this is straightforward to implement, it could, in practice, increase bias.

Directed acyclic graphs (DAGs) offer an intuitive approach to understanding the implications of mode effects. Using DAGs, we explore different scenarios that may exist, such as the presence of mode effects, mode selection, or both. We demonstrate that where mode is related to measurement but not selection, adjustment for mode may improve the accuracy and precision of estimates. However, if the exposure and outcome are causally related to mode selection, adjustment for mode risks introducing collider bias and should be avoided. Finally, we demonstrate how collider bias may also be introduced via an unobserved common cause of mode and the outcome.

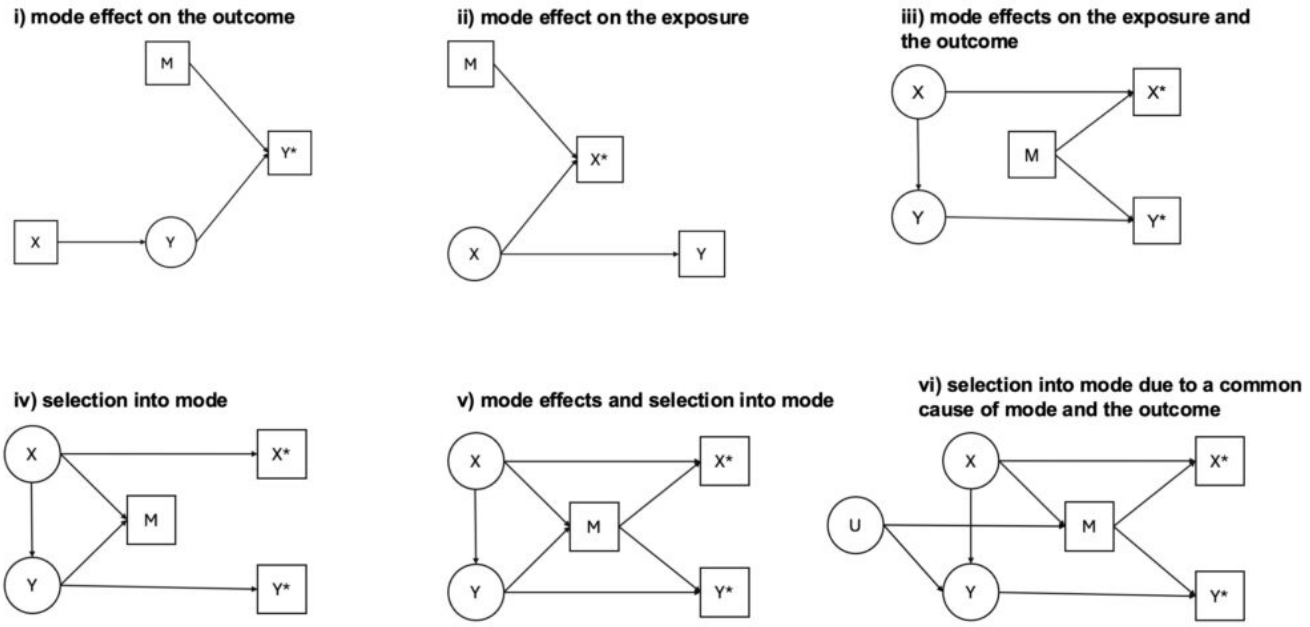


Figure 1. Directed acyclic graphs (DAGs) depicting a variety of settings where mode effects or mode selection may be present in relation to the exposure and/or outcome.
X exposure (latent), **X*** exposure (observed), **Y** outcome (latent), **Y*** outcome (observed), **M** survey mode, **U** unobserved variable

LATEBREAKER

Methods/Statistics

A Simulation Study of the Finite Sample Performance of Per-Protocol Estimators Catherine X. Li* Catherine Li Stephen Cole

Background: Per-protocol analyses of randomized trials can supplement the more commonly estimated intention-to-treat (ITT) effect, especially when there are nontrivial amounts of nonadherence or loss to follow-up. Per-protocol estimators require accounting for selective attrition when analyzing the subset of trial participants that remained adherent and in the study. In the following analyses, we compare the finite sample performance of several per-protocol estimators.

Methods: Data generating mechanisms were constructed with baseline and time-varying covariates, and nonadherence. Simulation scenarios varied the number of trial participants and the proportion of participants that remained adherent in the study, and were iterated 2,000 times. For each simulation, per-protocol estimates were computed using inverse probability of censoring weighting (IPCW), g-computation, and targeted maximum likelihood estimation (TMLE). Nonparametric bootstrap was used for variance estimation.

Results: In our scenarios, estimators that did not appropriately account for selective attrition were biased and bias increased as protocol deviations increased. When 70% of participants were adherent, per-protocol estimators that accounted for bias due to nonadherence were unbiased with relative bias ≤1% when identification assumptions were met (IPCW: 1.0%, g-computation: 1.0%, TMLE: 0.8%). Across scenarios, bias increased as protocol deviations increased. Empirical standard error (ESE) was lowest for g-computation (ESE: 0.026), and was comparable for IPCW and TMLE (ESE: 0.027); this pattern was observed across scenarios. When scenarios were unbiased, confidence interval coverage was appropriate for all estimators.

Conclusions: Per-protocol analyses using methods that appropriately account for bias due to selective attrition should be estimated alongside the ITT when interpreting results from randomized trials where protocol deviations including nonadherence and loss to follow-up are nontrivial.

LATEBREAKER

Methods/Statistics

Choosing negative controls in the presence of competing events Natalia Ortega* Natalia Ortega Valerie Aponte-Ribero

Negative controls can aid the detection of unmeasured confounding in observational studies. To be valid for bias detection, negative controls must satisfy two conditions: they must share the same structure of unmeasured and measured confounders as the exposure-outcome relationship of interest, and they must be independent of the exposure, in case of a negative control outcome (NCO), or independent of the outcome in case of a negative control exposure (NCE). However, in the presence of competing events we need to make additional assumptions for valid negative control selection, especially when interested in direct effects. For NCEs, the expectation of the competing event under the NCE should equal the expectation of the competing event under the exposure of interest. For NCOs, the expectation of the outcome should equal the expectation of the NCO in the survivors. Here, we formalize these additional assumptions for selecting valid negative controls in the presence of competing events when interested in total and direct effects. We exemplify the relevance of satisfying these assumptions in a recently published paper on the direct effect of occupation on Alzheimer's disease and show that ignoring them could provide false certainty in non-causal effect estimates.

LATEBREAKER

Causal Inference

Causal Machine Learning Methods for Estimating Personalised Treatment Effects – Insights on Validity From Two Large Trials Miquel Serra-Burriel* Hongruyu Chen Helena Aebersold Milo Alan Puhan Miquel Serra-Burriel

Causal machine learning (ML) methods hold great promise for advancing precision medicine by estimating personalized treatment effects. However, their reliability remains largely unvalidated in empirical settings. In this study, we assessed the internal and external validity of 17 mainstream causal heterogeneity ML methods—including metalearners, tree-based methods, and deep learning methods—using data from two large randomized controlled trials: the International Stroke Trial (N=19,435) and the Chinese Acute Stroke Trial (N=21,106). Our findings reveal that none of the ML methods reliably validated their performance, neither internal or external, showing significant discrepancies between training and test data on the proposed evaluation metrics. The individualized treatment effects estimated from training data failed to generalize to the test data, even in the absence of distribution shifts. These results raise concerns about the current applicability of causal ML models in precision medicine, and highlight the need for more robust validation techniques to ensure generalizability.

LATEBREAKER

Causal Inference

Implementation of g-computation in practice: a new diagnostic tool to guide outcome model specification Daisy Shepherd* Daisy Shepherd Margarita Moreno-Betancur Stijn Vansteelandt

Causal inference is a central goal of many clinical and public health studies. When using observational data to investigate the causal effect of an exposure on an outcome, an appropriate analytic method is required to minimize confounding bias. G-computation is one such method, which in the point-exposure setting extends outcome regression by allowing exposure-confounder interactions in the outcome model. Consistent estimation with g-computation relies on correct specification of the outcome model, which cannot be empirically verified. It is well understood that variables included in the outcome model should be driven by expert-knowledge, however, there is a lack of formal guidance or tools to aid the selection of parametric specification of the outcome model (e.g., which interaction or non-linear terms to include). This presents a challenge when applying g-computation in practice.

We propose a new diagnostic tool to address this gap, that distinguishes between candidate outcome model specifications based on the expected bias in the resulting g-computation estimator. The expected bias depends not only on the outcome model specification but also on the propensity score, which we estimate flexibly and equally across candidate specifications using SuperLearner. Therefore differences in the resulting statistic depend solely on the outcome model specification.

Using simulations, we investigated the performance of g-computation using our diagnostic tool to select the outcome model specification compared to g-computation using other common approaches, as well as targeted maximum likelihood estimation. The simulation study was based on a real investigation from the Longitudinal Study of Australian Children (LSAC) and considered a range of true outcome generation models and sample sizes, investigating the bias of each method in estimating the average causal effect. We demonstrated implementation of the tool in the LSAC case study with the tool available as an R function.

Cancer

Impact of Time Since Recent Childbirth on Survival in Young Women Diagnosed with Ductal Carcinoma in Situ (DCIS) in the Breast Zhenzhen Zhang* Zhenzhen Zhang Solange Bassale Ken R Smith Emily Guinto Alison Fraser Pepper Schedin

Background: Postpartum breast cancer (PPBC), diagnosed within 5-10 years after childbirth, is associated with increased metastasis, but its impact on mortality among women with Ductal Carcinoma in Situ (DCIS) remains unclear. This study examined the associations between time since recent childbirth and mortality outcomes in young women (≤45 years) diagnosed with DCIS.

Methods: Using the Utah Population Database (UPDB) and SEER Utah Cancer Registry data, we conducted a retrospective cohort study of 597 young women diagnosed with DCIS (stage 0) from 1996 to 2017, with a median follow-up of 12.5 years. Women were classified as nulliparous (n=183) or parous, with parous women grouped by time since recent childbirth and DCIS diagnosis: <5 years (n=87), 5–<10 years (n=131), or ≥10 years (n=196). Cox proportional hazards models assessed associations between time since recent childbirth and mortality, adjusting for diagnosis year, age at diagnosis, tumor stage, and estrogen receptor (ER) status. Published UPDB data on invasive breast cancer (BC) were used to compare frequency with DCIS. Chi-square tests evaluated distributions of BC type (DCIS vs invasive).

Results: Of 597 women, 23 deaths occurred during follow-up, with only 2 BC-related deaths total, both in the <5 year postpartum group. DCIS was less frequent in the <5-year postpartum group (12.4%) compared to nulliparous (17.6%) and 5–<10 years group (17.6%), and invasive BC was more frequent in the <5-year group. ER-negative DCIS was higher in the <5-year group (18%) compared to other groups (7%, 6%, 9%). All-cause mortality for postpartum women diagnosed <10 years after childbirth was comparable to nulliparous women [HR=0.97 (95% CI: 0.33–2.90), P=0.96], with no significant differences for those diagnosed <5 years [HR=2.28 (95% CI: 0.68–7.66), P=0.18] or 5–<10 years [HR=0.40 (95% CI: 0.08–1.98), P=0.26], and for those diagnosed ≥10 years [HR=1.15 (95% CI: 0.40–3.26), P=0.80].

Conclusion: BC-specific mortality was very low during the follow-up, implicating standard care as largely curative. All-cause mortality showed no significant differences by time since recent childbirth. The lower frequency of DCIS and higher ER-negative % in the <5-year postpartum group suggest potential progression of DCIS to invasive carcinoma during the early postpartum period.

Cancer

Breast cancer prevalence among privately insured same-sex female couples in the US

Kodiak RS Soled* Kodiak Soled Isa Berzansky Landon Hughes Tonia Poteat Shail Maingi Alexis Miranda Aimee K Huang Brittany M Charlton

Background: Female individuals with same-sex (SS) partners are more likely than those with different-sex (DS) partners to have breast cancer risk factors, yet little is known about breast cancer prevalence due to prior data limitations.

Methods: We used 2016–2022 data from the Merative MarketScan Research Database, which includes paid insurance claims and healthcare encounter data on enrollees who receive employer-sponsored healthcare. We identified breast cancer cases using International Classification of Disease-10 codes for malignant neoplasms and carcinoma in situ of the breast. Ongoing analyses include weighted and unweighted unadjusted period prevalence rate (PPR) ratios comparing female enrollees with SS vs DS partners. Age-specific comparisons are also underway using the NCI's SEER*Stat software to report age-standardized PPR.

Results: Between 2016–2022, female enrollees with a DS partner totaled 10,501,932 compared to 214,095 with a SS partner. We identified breast cancer cases among 243,587 enrollees with a DS partner and 3,375 enrollees with a SS partner. Overall, we found that the PRR among enrollees with a DS partner was 46% greater than those with a SS partner (PRR: 1.46, $p<0.001$). When stratifying by age, we found the PPR among enrollees with a DS partner compared to a SS partner to be: 1.30 ($p=0.099$) among those <29 years old, 1.42 ($p<0.001$) among those 30 – 49 years old, and 1.20 ($p<0.001$) among those 50 – 69 year olds. Weighted and adjusted results are forthcoming.

Conclusions: Higher breast cancer PPR among enrollees with DF compared to SS partners may be explained by data biases (e.g., private insurance, partnered individuals) as well as survivorship bias among enrollees with SS partners — namely that cancer may be more advanced due to delayed screening and care and consequently not living as long. Improved data collection on cancer staging and sexual orientation is essential to understand if population-level breast cancer inequities persist.

Cancer

Adverse Pregnancy Outcomes and Subsequent Risk of Breast Cancer among Postmenopausal Women Godness BIney* Godness Biney Su Yon Jung Angela M. Malek Michelle J. Naughton Lihong QI Peter Schnatz Cassandra Spracken

Epidemiological evidence suggests that pregnancy offers some level of protection against breast cancer possibly due to changes in hormonal profiles that result in a more differentiated and less susceptible mammary gland, or changes within specific epithelial cell subpopulations. However, the extent to which pregnancy offers protection if it ends in an adverse outcome (e.g., preeclampsia and preterm birth) remains uncertain. This study aimed to examine the association between adverse pregnancy outcomes, including preeclampsia, gestational hypertension, gestational diabetes, preterm birth, low birth weight and high birth, and the subsequent risk of breast cancer. The WHI is a large, multi-racial cohort of postmenopausal women in the US. At baseline, women were first asked to report if they had ever been pregnant. Participants were later asked during follow up to report the outcomes of their pregnancies whether any of their pregnancies resulted in adverse outcomes, including preeclampsia, gestational hypertension, gestational diabetes, preterm birth, low birth weight and high birth weight. Based on the information collected at baseline and follow-up (Extension II), we created an all-adverse pregnancy variable (Yes/No) to collectively assess the relationship with the outcome. Incident breast cancers were all adjudicated and binary in nature (Yes/No). Cox proportional hazard regression models were used to estimate the unadjusted and adjusted hazard ratios (HR) and their 95% confidence intervals (95% CI) for the association between adverse pregnancy outcomes and incident breast cancer. After adjusting for crucial covariates (e.g., age at first birth, family history of breast and ovarian cancer, race/ethnicity, etc.), we found that women with any adverse pregnancy outcomes were at slightly decreased risk of developing breast cancer (HR: 0.92 (95% CI : 0.84 – 0.99)) compared to their counterparts without adverse pregnancy outcomes. Our results indicates that pregnancy regardless of its adverse outcome may still offer some level of protection against breast cancer.

Cancer

Breast cancer reproductive risk factors and gut microbiome in US women: findings from a large epidemiological study Tengteng Wang* Tengteng Wang Curtis Huttenhower Mingyang Song Eric N. Taylor Rulla Tamimi Cheng Peng Eric B. Rimm Walter C. Willett Yang-Yu Liu A. Heather Eliassen

Background: No epidemiological study has systematically examined the association between breast cancer reproductive risk factors and gut microbiome features.

Methods: Participants of this cross-sectional study included 1,982 postmenopausal women from microbiome sub-studies embedded in the Nurses' Health Study II. Reproductive factors and other covariates were measured by questionnaires. We calculated lifetime ovulatory years (LOY) as the difference between age at menopause and age at menarche, subtracting the duration of oral contraceptive use and one year per pregnancy. We collected stool samples and performed shotgun metagenomics sequencing using the 100nt Illumina HiSeq platform. We applied the bioBakery workflow to process the sequencing data and correct batch effects. We performed the a-diversity (using the Shannon index) and the b-diversity analyses (using the Bray-Curtis dissimilarity). We then performed the PERMANOVA test to investigate microbial composition variation according to eight reproductive factors. Multivariable-adjusted generalized linear regressions were used for per-feature analysis.

Results: Our taxonomic and functional profiling resulted in 1,323 species, 2,844 enzymes, and 605 MetaCyc pathways. We observed that microbial a-diversity was statistically significantly higher for women breastfed children ≥6 months (vs. none/shorter duration); however, no differences were observed by other factors. PERMANOVA revealed that breastfeeding (R2 = 0.34%), current postmenopausal hormone (PMH) use (R2 = 0.28%), LOY (R2 = 0.27%), and age at menopause (R2 = 0.26%) were statistically significantly associated with taxonomic variation characterized by beta diversity (all P-values <0.005). In the per-feature analysis, ~90% of the top species belonged to the phylum Bacillota. For example, longer LOY was associated with the abundance of 25 Bacillota-related species and five enzymes related to common housekeeping.

Conclusion: Our study is the first and largest to date to examine the associations between reproductive factors and the gut microbiome. Reproductive factors may contribute to the structural variation of the gut microbiome communities. Factors such as breastfeeding, PMH use, and LOY were associated with multiple β-glucuronidase and short-chain fatty acid-related species and pathways for common housekeeping.

Cancer

Oral contraceptive use and the expression of CD44, CD24, and ALDH1A1 stem cell markers in benign breast tissue Maisey Ratcliffe* Maisey Ratcliffe Yujing J. Heng Brian Sardella Rulla M. Tamimi Lusine Yaghjyan

Purpose: We investigated, for the first time, the association between oral contraceptive (OC) use and the expression of CD44, CD24, and ALDH1A1 stem cell (SC) markers in benign biopsy tissue.

Methods: This study included 731 cancer-free women with biopsy-confirmed benign breast disease (BBD) within the Nurses' Health Study II cohort. Information on OC use was collected in 1989 and then updated biennially. Histologically normal breast tissue cores were used to construct tissue microarrays (TMAs). Immunohistochemistry (IHC) was performed on TMA sections to analyze the expression of SC markers. For each core, the IHC expression was assessed using semi-automated software and reported as the % of positively stained cells for each of the markers out of the total cell count. All expression measures were log-transformed for analysis. Generalized linear regression was used to examine the associations of OCs (use status, total duration, age at first and last use, and time since last use) with each marker's expression (within stroma and epithelium), while adjusting for known breast cancer risk factors and BBD subtype.

Results: In this study of 731 cancer-free women, the average age at the time of biopsy was 44 years (range 27-63), with the majority of participants being premenopausal at the time of biopsy (81%). OC use status at biopsy was positively associated with stromal CD44 expression (current vs. never β=0.75, 95% Confidence Interval [CI] 0.11, 1.39, p-trend=0.02). Age at first use was inversely associated with CD44 expression (in stroma: β= -0.04, 95% CI -0.08, -0.01; in epithelium β=-0.04, 95% CI -0.06, -0.02). No associations were found for CD24 and ALDH1A1. Total duration, age at last use, and time since last use were not associated with the expression of any of the three markers.

Conclusions: Our findings suggest a greater expression of CD44 in stroma of current OC users and a reduced CD44 expression with a later age at first OC use.

Study Design

Evaluating indirect antimicrobial effects via a two-stage randomized trial: a simulation of oral vancomycin vs. metronidazole for C. difficile infection Juan Gago* Juan Gago Christopher Boyer Marc Lipsitch

Antimicrobial treatments are often approved on the basis of efficacy results from individually randomized trials. However, these trials are unable to capture the indirect or “spillover” effects of the treatment of one individual on the outcomes of others. These indirect effects are particularly important in the context of antimicrobial resistance as the treatment of an index patient can affect others’ exposure to resistant pathogens through a variety of mechanisms, even when the direct effects on de novo resistance are rare. We simulate a two-stage randomized trial, informed by a prior study of oral vancomycin for C. difficile infection in the Veterans Affair (VA) Health System, to illustrate how this design can better capture both direct and indirect effects of antimicrobial treatment strategies on vancomycin-resistant Enterococci (VRE) infections.

In the first stage, hospitals (clusters) were assigned a treatment strategy that varied the proportion of vancomycin vs. metronidazole use. In the second stage, individual patients within each cluster were randomized to one of the treatments approved by their hospital’s assigned strategy. By comparing clusters with different proportions of vancomycin use over multiple time points (six months, one year, and two years), we estimated how the varying distribution of therapies influences overall and indirect antimicrobial effects.

This design extends beyond the classic trial approach, which can overlook how antimicrobial treatment strategies might affect the broader hospital environment. While our simulations suggest that direct effects of oral vancomycin on VRE risk may remain minimal, the two-stage design highlights subtle differences in population-level impacts that could emerge over time . By explicitly capturing cluster-level variation, two-stage randomization enables a more comprehensive evaluation of antimicrobial strategies, informing decisions that optimize both individual and population outcomes.

Infectious Disease

IV+Survival with IPDMA data in outbreaks Heather* Heather Hufstedler

Quasi-experimental methods are increasingly utilized in infectious disease research to address confounding and establish causal relationships. While instrumental variable analysis has been combined with survival models in prior work, its application within the context of individual participant data meta-analyses (IPDMAs) remains unexplored.

In this study, we propose a novel methodological framework that integrates IV analysis with survival outcomes in an IPDMA setting. We develop and compare frequentist and Bayesian implementations, exploring their strengths and limitations. A secondary aim is to evaluate the practicality of this approach in low-resource settings, where data collection challenges can further complicate analysis. This application demonstrates the method’s potential in real-world scenarios characterized by incomplete or heterogeneous data, in addition to its inherent challenges. This work is part of ongoing research.

Infectious Disease

Use of the test-negative design to estimate the protective effect of a scalar immune measure: identification and estimation Christopher Boyer* Christopher Boyer Marc Lipsitch Ziyuan Zhang

The relationship between antibody levels (more generally, a scalar measure of immune protection) at the time of exposure to infection (so-called exposure-proximal correlates of protection) and the risk of infection given exposure is of central interest in evaluating the evolution of immune protection conferred by prior infection and/or vaccination. Recently, a modified version of the test-negative study design (TND) has been proposed to assess this relationship. Under this design, those enrolled and tested in a TND also have an antibody titer taken and the odds ratio comparing titer levels among test-positive cases and test-negative controls is taken as an exposure-proximal measure of protection. However, the conditions under which such a study identifies the relationship between immune measurements and protection have not been rigorously defined. Here we propose formal identifiability criteria under which the TND recovers the population level conditional probability of protection given marker value as well as the causal effect of a hypothetical intervention to change marker level. We suggest possible estimation strategies and interrogate their performance using an agent-based simulation. Finally, we discuss other potential uses of collecting antibody titers in TND to better understand vaccine waning.

Infectious Disease

Examining the potential for bias in influenza, COVID-19, and respiratory syncytial virus test-negative vaccine effectiveness designs due to inclusion of vaccine preventable disease controls Margaret K. Doll* Margaret K. Doll Margaret K. Doll Jana L. Hirschtick

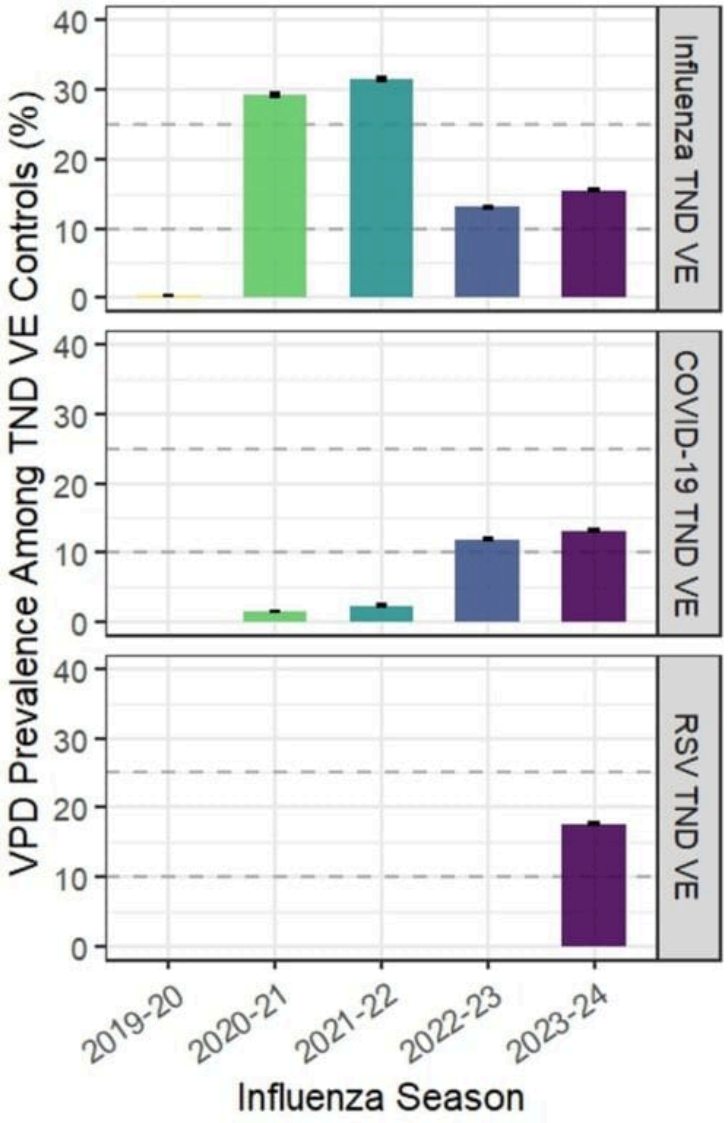
Background: The test-negative case-control design (TND) is used to estimate influenza, COVID-19, and respiratory syncytial virus (RSV) vaccine effectiveness (VE). In these studies, participants with a respiratory illness test positive (cases) or negative (controls) for the disease of interest. Research has shown that bias may arise from inclusion of controls with another vaccine-preventable disease (VPD), since vaccination behaviors across VPDs are associated. If uncontrolled, the magnitude of this bias depends, in part, on the prevalence of VPD controls; therefore, we estimated the prevalence of VPD controls eligible for inclusion in TND VE studies.

Methods: Using 2019-24 data from the largest US Midwestern nonprofit healthcare system, we identified hospitalizations for respiratory illnesses via ICD-10 criteria used in prior TND VE studies. To examine the potential for bias in influenza (2019-24), COVID-19 (2020-24), and RSV (2023-24) TND VE studies, we calculated the prevalence of alternate VPD etiologies among TND control participants. VPDs were identified via ICD-10 codes for Streptococcus pneumoniae, Haemophilus influenzae type B, influenza, SARS-CoV-2, and RSV (2023-24), with the disease of interest excluded. Based on VPD prevalence, we classified the potential for VE bias as no/low (<10%), moderate (10-<25%), or high (≥25%).

Results: Between 2019-24, we identified 796,149 hospitalizations due to respiratory illness. Of these, 188,274 (23.6%) had a VPD etiology. Figure 1 presents VPD prevalence among potential TND VE controls by season and disease of interest. The percentage of VPD controls varied from 0.4% to 31.5%, representing a range of no/low to high potential VE bias.

Conclusions: We demonstrate that VPD controls may represent up to nearly one-third of TND VE controls, depending on season and disease of interest. Researchers should consider whether alternate VPD controls are included in their TND VE studies, and the implications for potential bias.

Figure 1. Estimated seasonal prevalence and 95% confidence intervals of vaccine preventable disease (VPD) etiologies among eligible controls in influenza, COVID-19, and respiratory syncytial virus (RSV) test negative design (TND) vaccine effectiveness (VE) studies[+]. Potential for bias in VE estimates was classified as no/low (<10%), moderate (10-<25%), or high (≥25%).



[+]*Abbreviations*: VPD: vaccine preventable disease; RSV: respiratory syncytial virus; TND: test negative design; VE: vaccine effectiveness.

Infectious Disease

Leveraging seasonal dynamics to identify the strength of disease transmission along multiple environmental pathways: structural identifiability analysis Miwa Watanabe* Miwa Watanabe Kayoko Shioda Matthew Freeman Karen Levy Andrew Brouwer

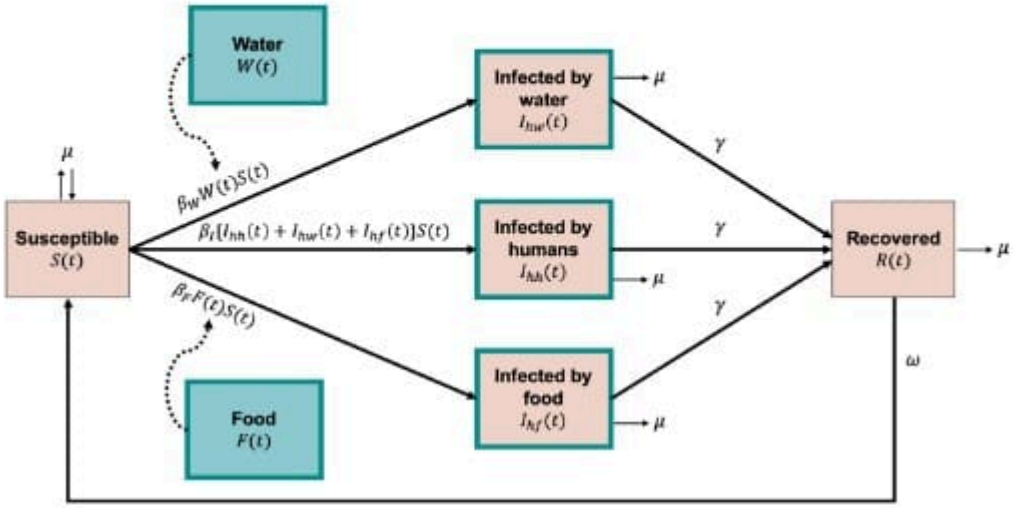
Background: Many pathogens are transmitted via multiple different pathways, so it is important to include a comprehensive set of relevant pathways in infectious disease transmission (IDT) models to understand the contribution of each pathway. Such IDT models can help to compare the impact of potential control strategies targeting specific pathways and to identify the most effective one. However, even if we collect relevant empirical data, it is not clear when IDT models are able to differentiate multiple pathways and estimate their transmission rates.

Methods: To answer this question, we conducted structural identifiability analysis for an IDT model with three transmission pathways: direct person-to-person and two indirect environmental pathways (food-to-person and water-to-person). We ran a series of simulations to understand what kind of conditions are necessary to successfully identify the dominant transmission pathway. We specifically explored the effects of different magnitudes of transmission rates via water and food and the seasonal timing of peak pathogen concentrations in food and water.

Results: The IDT model was able to successfully determine the dominant transmission pathway when the simulated seasonality in water and food contamination was different by three months or six months, even when the difference in the true transmission rates was small. When the simulated contamination in water and food peaked at the same time, the IDT model failed to determine the dominant pathway, regardless of the relative magnitudes of true transmission rates.

Discussion: Our analysis found that the IDT model can be a powerful tool to differentiate the contribution of different pathways to human infection with relevant empirical data on pathogen contamination data from exposure sources. Our findings can help researchers design their future studies and determine the feasibility of a study based on the seasonality in environmental samples if such data are available.

Figure 1. Structure of the infectious disease transmission model with multiple transmission pathways



Definitions of compartments and parameters can be found in the text and tables, but briefly:

- $S(t)$ – the fraction of individuals who are susceptible to infection at time t
- $I_{hh}(t)$ – the fraction of individuals who are infected through person-to-person transmission at time t
- $I_{hw}(t)$ – the fraction of individuals who are infected through water-to-person transmission at time t
- $I_{hf}(t)$ – the fraction of individuals who are infected through food-to-person transmission at time t
- $R(t)$ – the fraction of individuals who have recovered from infection at time t
- $F(t)$ – pathogen concentration in food at time t
- $W(t)$ – pathogen concentration in water at time t
- β_I – rate of transmission through person-to-person
- β_W – rate of transmission from water
- β_F – rate of transmission from food
- μ – birth rate and mortality rate
- γ – rate of recovery
- ω – rate of waning immunity

Health Disparities

Are we missing folxs? Sexual orientation and gender identity measurement in a sample of California high school students Riley Saham* Riley Saham Emma Jackson Ricardo Vera Monroy Jay G. Silverman Sabrina C. Boyce

Sexual and Gender Minority (SGM) youth are at high risk for depression and suicide. However, current measures of sexual and gender identity (SOGI) may be misclassifying youth identifying as SGM, leading to underestimates of this population's size and risk for depression and suicide. There is currently no gold standard for SOGI measures, but emergent research suggests more inclusive (i.e., expanded) SOGI questions could lead to better identification of SGM individuals. This study compares two SOGI measures, standard and expanded, used in the California Healthy Kids Survey (CHKS), a school climate and health survey of California public schools. A census sample of 9th and 11th graders in five school districts in Southern and Central California administered the CHKS core survey and an optional module in the 2021-22 and 2022-23 academic years, containing an experimental expanded SOGI measure along with the standard SOGI measure offered in the core module. This research assessed the two SOGI measures by comparing the individuals identifying as either Gender Minority (GM) or Sexual Minority (SM) solely in the expanded SOGI measure to those who identified as SGM in both measures (GM N = 1,620; SM N = 4,274). Using hierarchical multivariable Poisson regression models clustering on school, we assessed risk for suicide and depression among those who identify as SGM only in the expanded measure, relative to those who identify as SGM in both measures. Preliminary results indicate 558 youth identified as GM and 114 as SM only in the expanded SOGI measure (34.44% of the GM and 7.86% of the SM samples). We hypothesize that those youth are at the same or greater risk for depression and suicide as youth identifying as SGM in both measures (results to be finalized before the conference). These results indicate that more comprehensive gender and sexuality SOGI questions better identify SGM youth, allowing for more accurate identification of the needs of this population.

Social

Causal diagrams for sexual and gender minority health disparities Travis Salway* Vandad Hazrati Noor Bainwait Ashleigh Rich Ace Chan Amit Gupta Christoffer Dharma Ayden Scheim Travis Salway

Social epidemiologists have long deliberated the application of directed acyclic graphs (DAGs) in understanding disparities linked to non-modifiable characteristics, such as gender/sex and race. However, these methodological challenges are less frequently explored within the context of sexual and gender minority (SGM) health research. While SGM identity is intrinsic and self-determined, related constructs like status disclosure and minority stress are dynamic and integral to causal pathways influencing health outcomes.

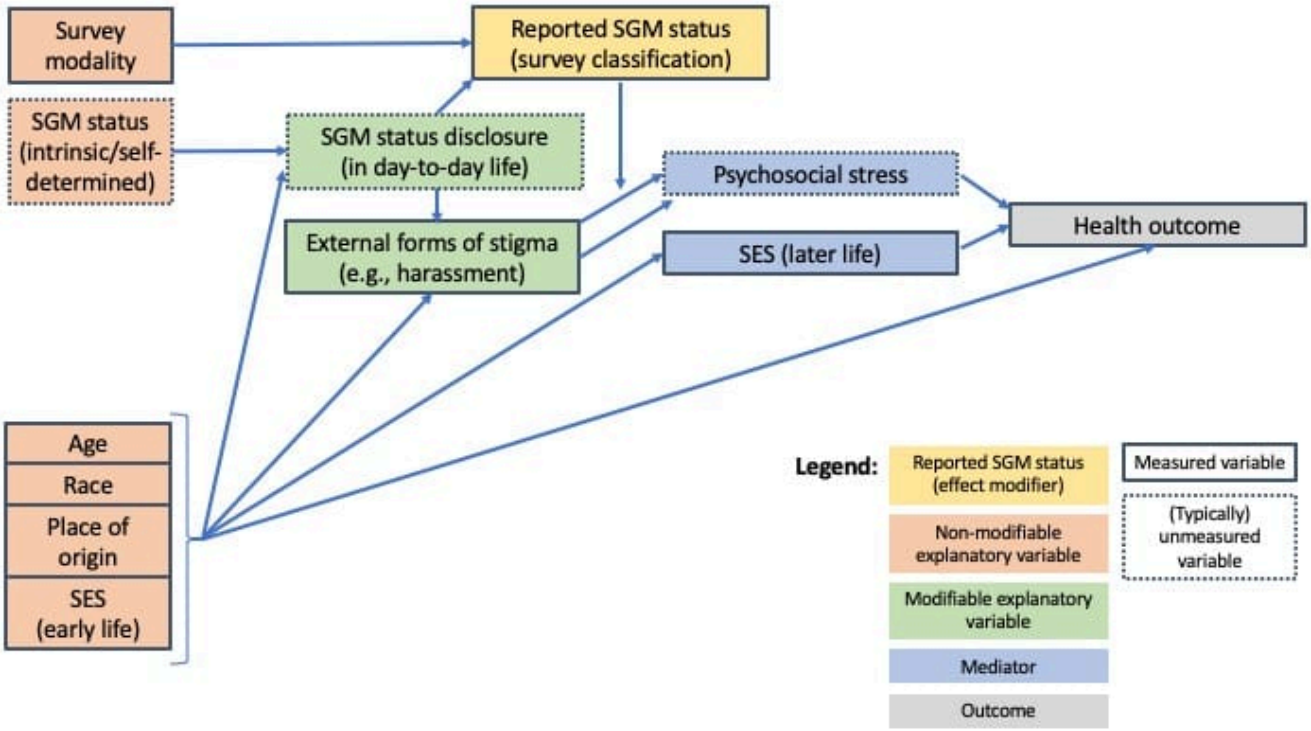
We conducted a scoping review of SGM epidemiological studies indexed in Medline in 2024, resulting in 19 articles that inform our analysis. Drawing on these examples, this talk explores how SGM epidemiologists are adapting DAGs to enhance causal inference in health disparities research. Three key strategies emerge:

1. **Measurement Bias:** SGM status can act as an imperfect proxy for daily disclosure behaviors, influenced by factors like age, race, socioeconomic status, and modality of data collection.

1. **Stigma as Exposure:** External stigma (e.g., harassment or discrimination) can be reframed as modifiable exposure variables. Policies and structural interventions aimed at reducing stigma provide opportunities for addressing disparities, positioning SGM status as a fundamental but not sole causal factor, akin to how racism drives race-related health inequities.

1. **Effect Modification:** Emerging evidence supports the idea that the health effects of generalized stigma vary across SGM subgroups, with certain identities (e.g., bisexual, gay/lesbian) experiencing amplified negative impacts. These variations necessitate subgroup-specific analyses to refine causal interpretations.

Through these examples, we propose actionable solutions for researchers employing DAGs to study SGM health disparities, advocating for greater integration of nuanced data sources and subgroup-specific analyses.


Survey modality
Reported SGM status (survey classification)
SGM status (intrinsic/self-determined)
SGM status disclosure (in day-to-day life)
Psychosocial stress
Health outcome
External forms of stigma (e.g., harassment)
SES (later life)
Age
Race
Place of origin
SES (early life)
Legend:
Reported SGM status (effect modifier)
Non-modifiable explanatory variable
Modifiable explanatory variable
Mediator
Outcome
Measured variable
(Typically) unmeasured variable

Health Disparities

Structural Determinants of Medical Mistrust Among Transgender Women of Color: A Mixed Methods Analysis of the TURNNT Cohort Alexander Furuya* Alexander Furuya Jenesis Merriman Adam Whalen Asa Radix Su Hyun Park Jessica Contreras Roberta Scheinmann Denton Callendar John A. Schneider Krish J. Bhatt Dustin Duncan

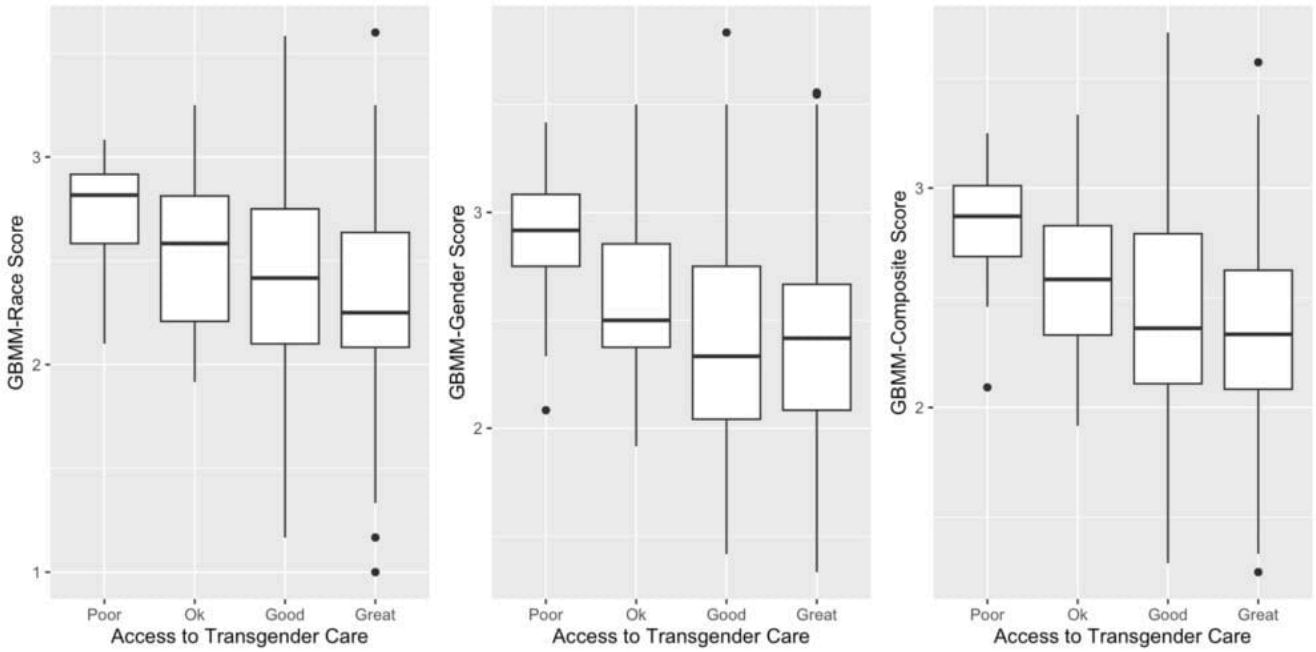
Background: Medical mistrust is associated with lower healthcare utilization among marginalized populations, including transgender women of color. However, medical mistrust as a construct has often placed the onus of blame on the individual or the community, rather than on systems and structures. We investigated whether structural factors, such as medical mistreatment and lack of access to transgender care, were causes of medical mistrust.

Methods: We used mixed methods to triangulate the structural determinants of medical mistrust using survey data from 193 transgender women of color living in New York City. For the quantitative analysis, we conducted t-tests and ANOVA to assess the association between our exposures (medical mistreatment and access to transgender care) and outcome (medical mistrust). We measured medical mistrust using two Group-Based Medical Mistrust (GBMM) scales, one regarding perception of medical mistrust among people of color and one regarding perception of medical mistrust among transgender women. For the qualitative analysis, we coded open-ended survey data from the participants regarding their trust towards medical institutions.

Results: We found those who had experienced discrimination in healthcare had higher levels of medical mistrust measured using both GBMM scores. Additionally, those who rated poorer access to transgender care had higher levels of medical mistrust. The open-ended survey questions corroborated these results, with many participants stating that their negative experiences with the healthcare system caused them to have distrust in medical institutions.

Conclusion: Among transgender women of color, intersecting systems of power within the healthcare setting caused these individuals to have medical mistrust. Addressing medical mistrust should not be targeted at the individual level, but rather at the structural level.

Figure 3. Boxplot of Group-Based Medical Mistrust Scores by Transgender Care Access Rating.



Health Disparities

Perceived access to gender-affirming health care and everyday discrimination among transgender women of color in New York: The TURNNT Cohort Study Adam M. Whalen* Adam Whalen Alex Furuya Jessica Contreras Roberta Scheinmann Kim Watson Su Hyun Park John Schneider Cristina Herrera Sahnah Lim Chau Trinh-Shevrin Krish Bhatt Asa Radix Dustin Duncan

Background: Transgender people experience widespread discrimination. Access to gender-affirming health care may allow trans women to blend more easily into public life (i.e., “pass”) and avoid discrimination or harassment from others. We explored the relationship between perceived access to gender-affirming care and everyday discrimination among transgender women of color in New York.

Methods: We included 271 transgender women of color at baseline and 191 after 6 months of follow-up. Our exposure of perceived access to gender-affirming healthcare was dichotomized as full access (all needs met) and incomplete access. Discrimination was measured using the Everyday Discrimination Score, categorized as any experience of discrimination within the previous 6 months. We performed multivariable robust Poisson regression to obtain prevalence ratios (PRs) for the association between gender-affirming care access and discrimination, both at baseline and longitudinally. We adjusted for potential confounders including age, income, education, HIV status, race/ethnicity, and housing stability.

Results: At both visits most participants had access to health care, though only a third noted that all their gender-affirming care needs were being met. Almost 70% reported discrimination at baseline, and 56% reported discrimination at 6 months. At baseline, trans women with incomplete access to gender-affirming care were 9% more likely to report discrimination compared to those with full access, after adjustment (PR=1.09, 95%CI: 1.02-1.17). Baseline access to care was not associated with discrimination after 6 months of follow-up.

Conclusions: Access to gender-affirming health care is slightly protective against discrimination for transgender women of color, though this relationship does not hold over time. Gender-affirming care access should be protected and expanded, in addition to identifying other mechanisms for reducing transphobic discrimination.

Health Disparities

Sexual Orientation Disparities in Pregnancy Loss: Mediation by Chronic Hypertension

Colleen A Reynolds* Colleen Reynolds Payal Chakraborty Isa Berzansky Brittany M. Charlton

Background: Emerging research suggests pregnancies among sexual minorities (e.g., heterosexual with same-sex experience, mostly heterosexual, bisexual, or lesbian individuals) are more likely to end in pregnancy loss (i.e., miscarriage or stillbirth) than among heterosexuals. Chronic hypertension is associated with increased risk of pregnancy loss, but no research has assessed whether hypertension mediates these disparities.

Methods: We pooled data from two cohorts, the Growing up Today Study and Nurses' Health Study 3. Because of likely post-exposure confounding, we estimated interventional mediated effects (interventional pure natural direct effect [iPNDE] and total natural indirect effect [iTNIE]). Baseline confounders included demographics, and post-baseline confounders included marital status, socioeconomic status, health behaviors, chronic health conditions, and medically assisted reproduction.

Results: Among 14,178 pregnancies to completely heterosexual individuals (reference group), the prevalence of chronic hypertension was 6%, and 22% of pregnancies ended in a loss. Among 3,141 pregnancies to heterosexuals with same-sex experience/mostly heterosexuals, hypertension prevalence was 9%, and 25% ended in loss. Among 416 pregnancies to bisexuals/lesbians, hypertension prevalence was 8%, and 34% ended in loss. In complete case analyses, we found no evidence that chronic hypertension mediates disparities in pregnancy loss for heterosexuals with same-sex experience/mostly heterosexuals (iPNDE: 1.13; 95%CI: 0.93–1.37; iTNIE: 1.00; 95%CI: 0.98–1.03) or bisexuals/lesbians (iPNDE: 3.67; 95%CI: 2.14–5.73; iTNIE: 1.00; 95%CI: 0.93, 1.09). Multiple imputation and subgroup analyses are ongoing.

Conclusions: Future research must identify proximal pathways of pregnancy loss disparities to guide policy and clinical practice interventions among sexual minorities.

Health Disparities

Sexual orientation disparities in unintended pregnancies and pregnancy outcomes Payal Chakraborty* Payal Chakraborty Payal Chakraborty Corinne H. Rocca Colleen A. Reynolds Kodiak R.S. Soled Sarah McKetta Natalia Linos Ange-Marie Hancock Danielle Bessett Sebastien Haneuse Brittany M. Charlton

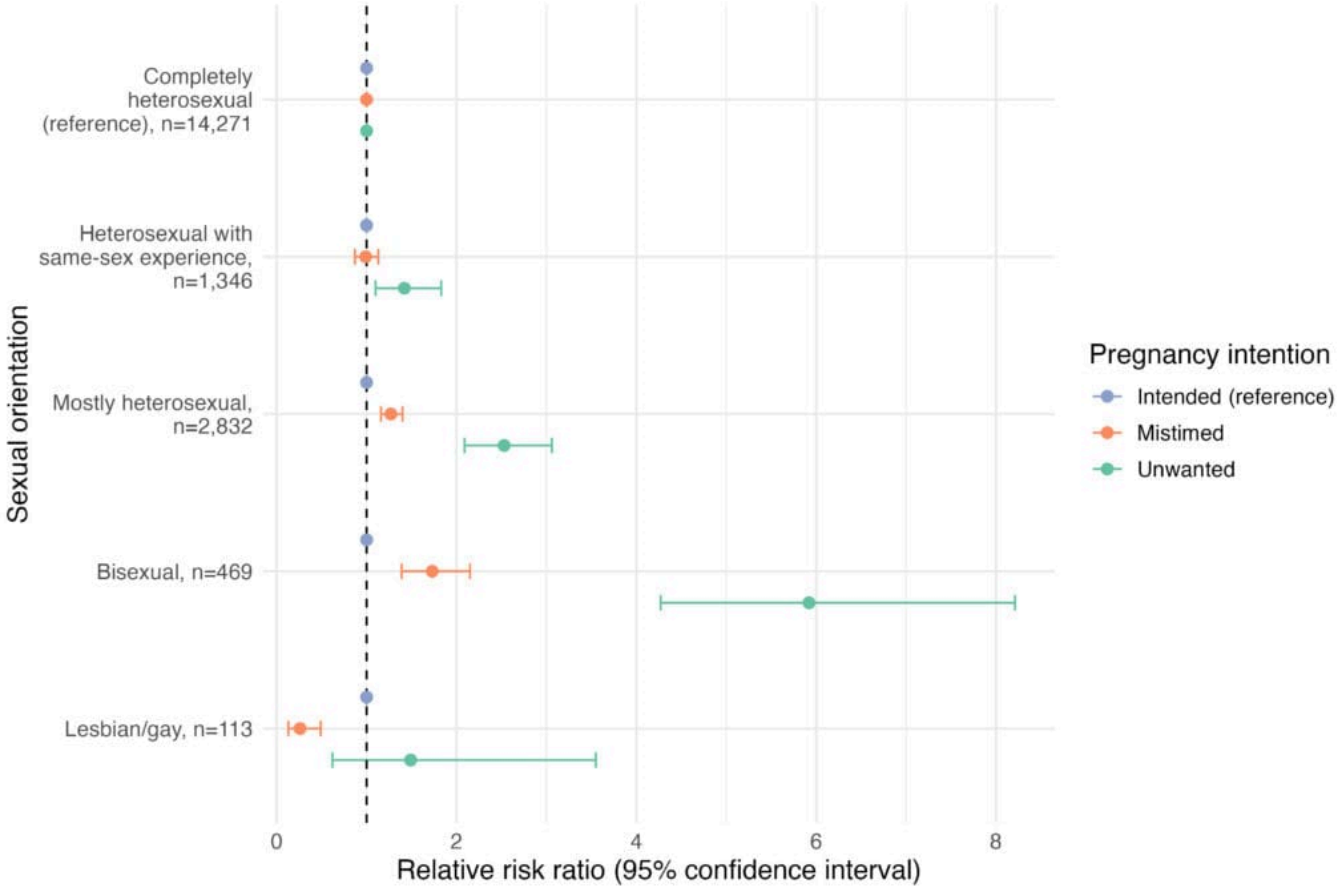
Background: Sexual minority (SM) people may be at increased risk of unintended (mistimed or unwanted) pregnancies. Yet, little research has examined sexual orientation differences in unintended pregnancies and their outcomes.

Methods: We pooled data from two cohorts, the Nurses' Health Study 3 and Growing Up Today Study (analytic N=19,031 pregnancies 1978–2024). We fit multinomial models to estimate associations between mistimed and unwanted (vs. intended) pregnancies comparing completely heterosexual participants and four SM groups (heterosexual with same-sex experience, mostly heterosexual, bisexual, and lesbian/gay). We used generalized estimating equations (GEE) with inverse probability of treatment weights (IPTW) and inverse cluster size weights (ICSW) to address multiple pregnancies per person, confounding, and informative clustering. Within strata of intended, mistimed, and unwanted pregnancies—using log-binomial GEE models with IPTW/ICSW—we examined differences in induced abortion and negative perinatal outcomes (pregnancy loss, preterm birth, low birthweight, gestational hypertension/diabetes, preeclampsia) by sexual orientation.

Results: Compared to pregnancies to completely heterosexual participants, all SM groups had higher unwanted vs. intended pregnancies (RRRs from 1.42–5.92). Those to mostly heterosexual (RRR: 1.27, 95% CI: 1.16–1.40) and bisexual (1.73, 95% CI: 1.39–2.15) participants were more likely to be mistimed vs. intended. Intended, mistimed, and unwanted pregnancies to all SM groups were more likely to end in abortions. Mistimed pregnancies to bisexual (RR: 1.67, 1.07–2.60) and lesbian/gay (3.51, 1.60–7.69) participants were more likely to end in loss.

Conclusions: SM people had higher induced abortion use for unintended pregnancies, possibly suggesting positive care access. SM inequities in pregnancy loss are higher in mistimed pregnancies. Disparities in unintended pregnancies must be addressed to ensure reproductive autonomy for all.

Relative risk ratios of mistimed (vs. intended) and unwanted (vs. intended) pregnancies by sexual orientation*



*Analyses were at the pregnancy-level. Models were fit using multinomial logistic regression via generalized estimating equations with stabilized inverse probability of treatment weights to address confounding by factors related to social origin (i.e., year of birth, race/ethnicity, and U.S. Census division of residence at birth) and inverse cluster size weights to address informative clustering.

Mental Health

Time Out: a scoping review of non-duration based social media use measures and adolescent mental health Jonathan Platt* Jonathan Platt Amanda Sursely Bengi Baran Gerta Bardhoshi

Background: Research to understand the role of social media use (SMU) in explaining deteriorating adolescent mental health has been limited by an overreliance on broad, nonspecific measures of 'time spent on social media'. These measures provide insufficient detail to capture unique risk and protective factors to users.

Methods/Approach: We conducted a scoping review of observational and experimental studies of the relationship between SMU and mental health outcomes in adolescents ≤18 years. Studies that measured SMU solely based on time spent on a platform were excluded.

Results: The initial search returned 868 articles. After inclusion and exclusion, we identified 217 studies, but a further 133 (61%) used duration-based SMU measures and were excluded. Of the 83 remaining studies, most focused on depression (48%), or anxiety (23%). Studies used 85 distinct measures of SMU, and fewer than half (n=37; 45%) provided evidence of validity. SMU measures were grouped into five domains, including SMU habits, addiction-like measures, structural aspects, interactions on SM, and feelings about SM. Social comparison and addiction-related measures were consistently linked with depression and anxiety symptoms. SMU for socialization and was consistently shown to improve loneliness, though evidence of other protective effects was otherwise limited.

Conclusion: The relationship between SMU and adolescent mental health is a dynamic and complex part of adolescent social development, with features that features that may variably influence mental health outcomes depending on the context of use.

Significance/Contribution: These findings contribute to a more complete understanding of specific types of SMU that contribute to adolescent mental health. This specificity may help to identify modifiable targets for use in prevention programs and policy development.

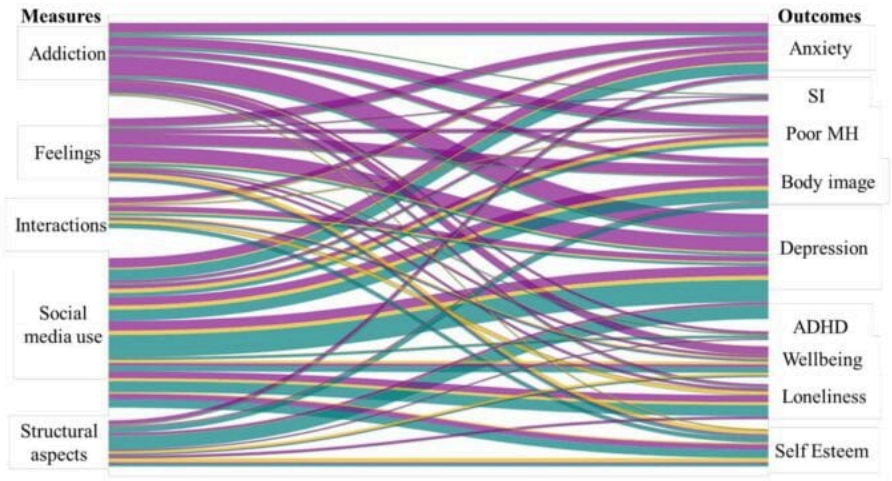


Figure: Associations between social media use domain and mental health outcomes. Purple pathways represent harmful associations, yellow pathways represent protective associations, and teal pathways represent non-significant associations. The thickness of the pathway is representative of the number of studies reporting the association.

Mental Health

Trends in anxiety, depression, and flourishing among American college students by gender identity (2016-2024) Rachel Slimovitch* Rachel Slimovitch Anthony J. Rosellini Jaimie Gradus Sarah Lipson

Background:

Prior research has identified worsening mental health among both cisgender and transgender, nonbinary, and other gender minority (hereafter referred to as TNB) students through 2021, with TNB students experiencing significantly higher prevalence of anxiety and depression. However, trends by gender identity remain unexplored in the years after the emergence of COVID-19. This study expands on prior literature by exploring trends in anxiety, depression, and flourishing from 2016-2024 by gender identity.

Methods:

Using data from the Healthy Minds Study, we examined trends in depression (PHQ-9 ≥ 10), anxiety (GAD-7 ≥10), and flourishing (Flourishing Scale ≥ 48) from 2016-2024 among male, female, and TNB students. Joinpoint regression was used to estimate piecewise log-linear trends and annual percent change (APC) in the survey weighted prevalence estimates of depression, anxiety, and flourishing.

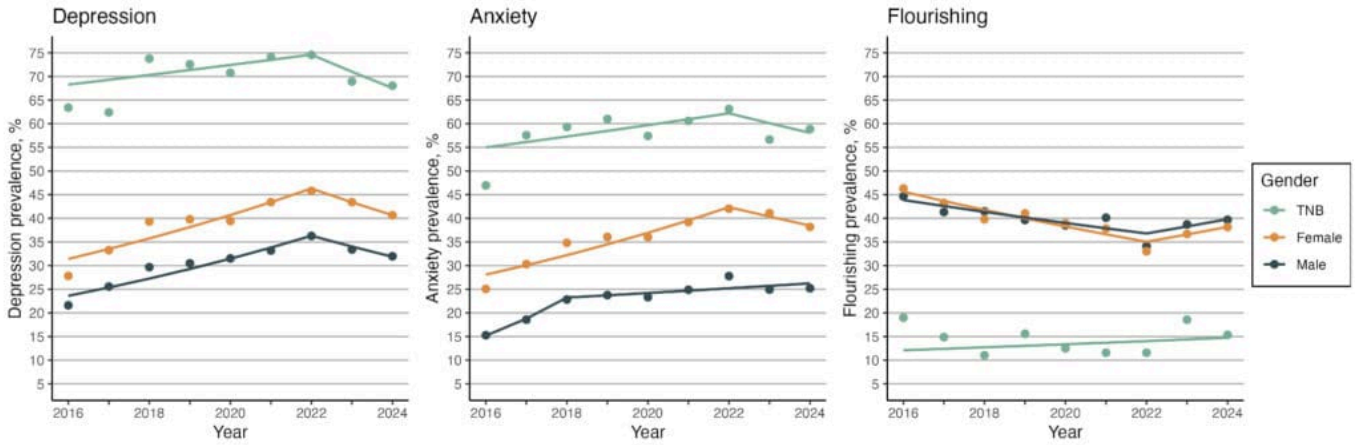
Results:

A total of 669,146 students (3.5% TNB) participated. After an increasing trend in prevalence of depression from 2016-2022 among male (APC 7.4%, 95% CI 6.0 to 10.3), female (APC 6.7%, 95% CI 5.1 to 11.0), and TNB students (APC 1.5, 95% CI 0.8 to 16.2), prevalence of depression decreased for each gender identity from 2022-2024. A similar trend was observed for anxiety among female and TNB students, with trends increasing from 2016-2022 (Female APC 7.1%, 95% CI 5.6 to 11.6; TNB APC 2.1, 95% CI 1.0 to 11.9) before decreasing from 2022-2024 (Female APC -4.7, 95% CI -9.8 to 1.6; TNB APC -3.4, 95% CI -6.4 to 0.1). Flourishing increased among TNB students from 2016-2024.

Discussion:

TNB students continue to experience elevated prevalence of depression and anxiety and lower flourishing compared to cisgender male and female students. However, since 2022, depression prevalence has decreased across all gender identities and anxiety has decreased among female and TNB students. Future research should examine what has been driving these promising recent trends.

Figure 1. Trends in depression, anxiety, and flourishing among male (N =191,408), female (N = 454,096), and TNB (N =23,642) college students, Healthy Minds Study 2016-2024.



TNB = transgender, nonbinary, and other gender minority populations.

Mental Health

Quantifying the Mental Health Impacts of Trauma Exposure among Mental Health Service Users in Lebanon Jennifer Majer* Jennifer Majer Jihane Bou Sleiman Georges Mouawad Fadi Daccache Abdel Karim Khader Georgia Karoutzou Fatima Khachfe Katarzyna Wyka Tania Bosqui

Background

The prevalence of PTSD is well-documented, but broader mental health impacts of traumatic events in lower- and lower-middle-income countries (LLMICs) and complex emergency contexts like Lebanon remain underexplored. This study uses mental health case management data from International Medical Corps (IMC) in a quasi-experimental design. It leverages two traumatic events—the Beirut Port Explosion (October 2020) and the 2024 war in Lebanon—as natural experiments to evaluate trauma's mental health impact.

Methods

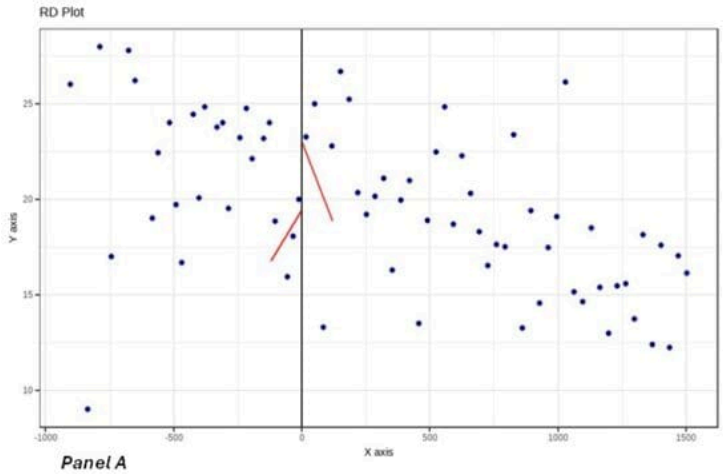
Key research questions are: 1) What are the immediate and short-term mental health impacts of the Beirut Port Explosion on client functioning? 2) How does conflict-related trauma from the 2024 war affect functioning? Primary outcomes include Client Functioning Scale (CFS) scores, assessed through baseline, follow-up, and discharge scores. Two quasi-experimental approaches were used to analyze trauma exposure impacts: 1) Regression Discontinuity Design (RDD) compared outcomes immediately before and after the Beirut Port Explosion. 2) Interrupted Time Series (ITS) tracked deviations in functioning scores over predefined intervals for both events.

Results

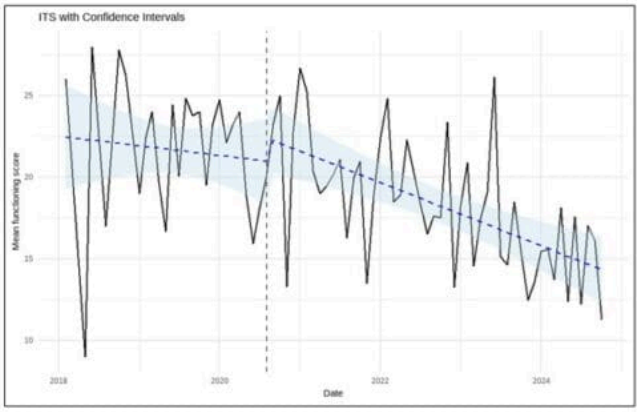
Results from one health facility located in Bekaa governorate (January 2018–October 2024) show that of 1,062 patients, functioning scores dropped significantly post-Beirut Port Explosion by an estimated 8 points (7.99, 95% CI: 2.99–12.99, p = 0.002) in RDD analysis (Fig Panel A). ITS analysis reveals an average decline of 4.8 points (Fig Panel B).

Conclusions

This study aims to address critical gaps in understanding trauma's mental health impacts, providing actionable insights for policymakers to strengthen prevention, mitigation, and post-trauma interventions. Additional analyses will explore variation in the effects depending on geography and social determinants of mental health, as well as the impact of these events on severe mental health disorders, such as Schizophrenia and Bipolar Disorder.



Panel A



Panel B

Mental Health

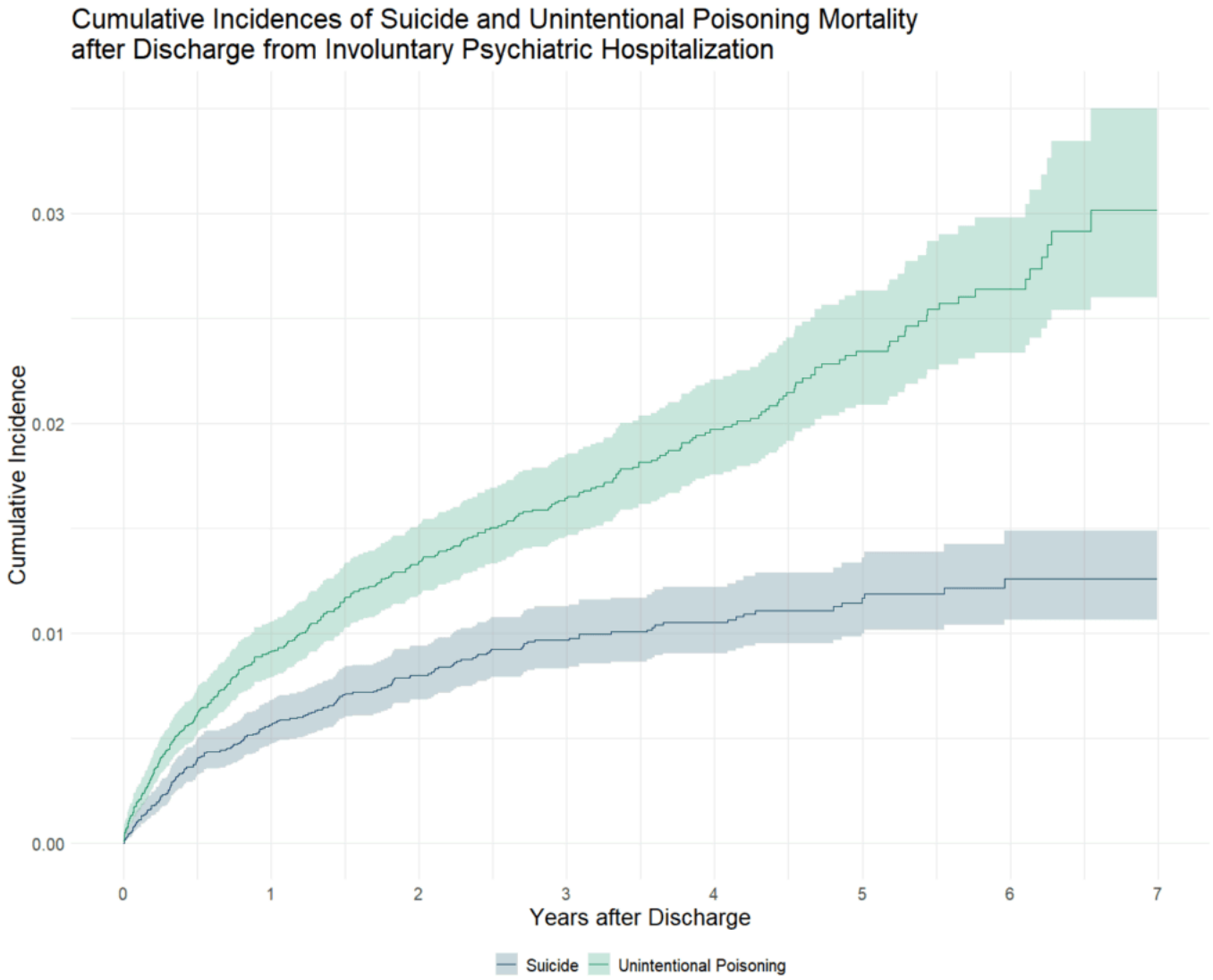
Suicide and Unintentional Poisoning Mortality after Involuntary Psychiatric Hospitalization: A Time-to-Event Analysis with Linked Data from Public Agencies Warren Szewczyk* Warren Szewczyk Spencer Hensley Ali Rowhani-Rahbar Alastair Matheson Isaac Rhew

Background: No studies in the United States have characterized suicide or unintentional poisoning (UP) mortality after involuntary psychiatric hospitalization (IPH). We aimed to estimate the incidences of suicide and UP death after last IPH and investigate factors associated with these outcomes.

Methods: Data for this retrospective cohort study were sourced from the New Opportunities in Health and Resilience Measures for Suicide (NO HARMS) database, which links administrative service utilization records in King County, Washington, and statewide death records. Participants included all people with ≥1 IPH order in King County from January 2016 – December 2022 (N=22,942). We used Kaplan-Meier methods to estimate incidences of suicide and UP death after last recorded IPH and Cox proportional hazards models to estimate associations of these outcomes with age, gender, race, homelessness service use, jail, a history of >1 IPHs, last IPH length of stay, and detainment order type for last IPH.

Results: The 1-year and 7-year cumulative incidences of suicide after last IPH were 0.56% (95% CI=0.47,0.68) and 1.26% (95% CI=1.06,1.48) and of UP death were 0.92% (95% CI=0.79,1.05) and 3.03% (95% CI=2.59,3.49). Asian, Black, and White racial classifications were each associated with greater risk of suicide and UP death compared to not having those classifications (all $p<0.001$). Male gender, homelessness service use, a jail stay before last IPH, and a history of multiple IPHs were associated with UP mortality (all $p<0.05$). Compared to a Danger to Others detainment order, a Danger to Self order was associated with both suicide ($p<0.001$) and UP death ($p<0.05$).

Conclusion: The cumulative incidences of suicide and UP mortality were comparable to published values for patients discharged from voluntary psychiatric hospitalization. The first year after discharge is an important period for intervention. Further research is needed to develop effective suicide and UP prevention strategies.


Cumulative Incidences of Suicide and Unintentional Poisoning Mortality
after Discharge from Involuntary Psychiatric Hospitalization
Cumulative Incidence
0.03
0.02
0.01
0.00
0
1
2
3
4
5
6
7
Years after Discharge
Suicide
Unintentional Poisoning

Mental Health

Characteristics and post-visit suicide outcomes of emergency department patients who screen positive for suicide incidental to their chief complaint Edwin Boudreaux* Alan Ardelean Edwin Boudreaux Joseph Ciminelli Sarah Arias Carlos Camargo Ivan Miller

Background and Objective: Universal screening improves suicide risk detection in individuals presenting to the emergency department (ED) who are not presenting with a psychiatric chief complaint, what we refer to as incidental risk. We sought to better understand characteristics of individuals who present with incidental risk and to evaluate their suicide-related outcomes after the ED visit.

Methods: Two samples from the Emergency Department Safety Assessment and Follow-up Evaluation (ED-SAFE) study were used. Combined, the samples allowed for comparison of baseline characteristics and suicide-related outcomes for participants with incidental risk compared to those with negligible risk (any kind of chief complaint and negative suicide risk) and congruent risk (psychiatric chief complaint and positive suicide risk). We completed univariable and multivariable regression analyses and compared the proportions of participants with a suicide composite outcome over twelve months after the ED visit.

Results: Participants with incidental risk were generally more similar to those with congruent risk than negligible risk across demographics and clinical characteristics. In multivariable analyses, we identified older age, female sex, white race, and non-Hispanic/Latino ethnicity to be positively associated with having incidental risk, in addition to diabetes (aOR=1.97, 95% CI: 1.11-3.49) and chronic pain (aOR=2.05, 95% CI: 1.17-3.57). Those with incidental risk also exhibited similar post-visit suicide-related outcomes compared to those with congruent risk, yet they were far less likely to receive clinical assessments and interventions during the ED visit, such as an evaluation by a mental health professional (91.8% vs. 46.5%), [X2 (1, N =1,362) = 203.78, p <.001].

Conclusion: EDs may need to consider redesigning their clinical approach to address suicide risk among those who present with medical complaints but screen positive for suicide risk.

Mental Health

Does the Nationwide Depression Screening Prevent the Hospitalization for Mood Disorders? A Target Trial Emulation Study Using National Health Insurance Service Database in South Korea Hyejin Kim* Hyejin Kim Sun Jae Jung

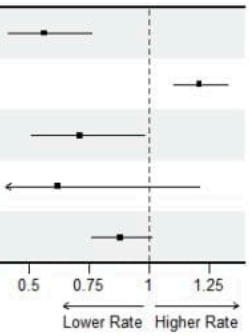
Background: Over the past two decades, previous studies about the effectiveness of organized depression screening at primary care or national level have reached mixed conclusions. Therefore, we conducted a target trial emulation study to analyze the effectiveness of the 2019 nationwide depression screening program in South Korea.

Methods: We used the National Health Insurance Service (NHIS) database to estimate the effectiveness of depression screening based on the modified intent-to-treat approach (n = 53,688). The study period started on January 1, 2019, and ended on December 31, 2022. The primary outcome was the incidence of hospitalization for mood disorders, with secondary outcomes including initial use of antidepressants, emergency department visits for mood disorders, and suicide and suicidal behaviors. Individuals with a psychiatric diagnosis prior to 2019 or those who had participated in the depression screening before 2019 were excluded. Coarsened exact matching (1:1 ratio) based on age, sex, and subscriber types was used to match the screened and non-screened individuals. The multivariate cause-specific Cox regression models were used to estimate the hazard ratios (HRs), which adjusted for urbanicity, prior health check-ups, income, and the Charlson Comorbidity Index. Subgroup analyses were conducted based on sex, age groups (20–50s and 60–70s), and income levels.

Results: After adjusting for confounders, the screened group showed a 44% lower risk of hospitalization for mood disorders compared to the non-screened group (adjusted hazard ratio [aHR] 0.56, 95% confidence intervals [CI] 0.41–0.76). The initiation of antidepressant use was significantly increased in screened individuals than in non-screened (aHR 1.21, 95% CI 1.10–1.33). The hazards of emergency department visits were significantly lower in the screened group than in non-screened group (aHR 0.71, 95% CI 0.51–0.98). No significant difference was observed in suicide and suicidal behaviors between the screened and non-screened groups (aHR 0.62, 95% CI 0.32–1.21).

Conclusion: The nationwide depression screening in South Korea was linked to improvements in depression-related outcomes.

	Non-screened			Screened			
Outcomes (n = 53,688)	Case N	Person-year	Incidence rate (per 1,000 py)	Case N	Person-year	Incidence rate (per 1,000 py)	aHR (95% CI)
Primary outcome: Hospitalization for mood disorders	89	106366.08	0.84	56	106984.51	0.52	0.56 (0.41, 0.76)
Secondary outcomes (1): Use of antidepressants	1111	104411.72	10.64	1365	104500.29	13.06	1.21 (1.10, 1.33)
Secondary outcomes (2): ED visit for mood disorders	122	106298.51	1.15	95	106917.34	0.89	0.71 (0.51, 0.98)
Secondary outcomes (3): Suicide and suicidal behaviors	42	106493.3	0.42	22	107078.96	0.21	0.62 (0.32, 1.21)
Negative control outcome: Hospitalization for cancer	676	105344.12	6.42	575	105980.79	5.43	0.88 (0.76, 1.01)



Causal Inference

Including Trial-Selection Variables in Machine-learning for Generalizable Conditional Average Treatment Effect Estimation Rikuta Hamaya* Rikuta Hamaya Konan Hara Etsuji Suzuki

Machine-learning approaches for estimating the conditional average treatment effect (CATE) can inform individualized treatment decisions. However, generalizing such estimates beyond randomized controlled trial (RCT) participants remains challenging due to potential selection bias through trial participation. Accordingly, we aim to investigate whether including trial participation covariates improves estimation for CATE-estimating algorithms. Using theoretical derivations, we show that unbiased CATE estimation in a source population requires conditioning on trial-selection variables, either when aiming to estimate CATE for specific covariates or individual treatment effect (ITE). Simulation demonstrates that simply including all relevant covariates in a Causal Forest can reduce bias but may inflate variance unless the sample size is large (e.g. >5000 for continuous outcome with 5 CATE covariates). We further evaluate an inverse probability weighting (IPW) approach that leverages data on the source population. IPW reduces selection bias more efficiently than simply adding covariates in high dimensions. In a real-world application using the VITamin D and OmegA-3 TriaL (VITAL), we compare CATEs of omega-3 fatty acid supplementation on coronary heart disease incidence. Including trial-selection variables in the Causal Forest model yields stronger effect estimates among those most likely to benefit, though the evaluation is limited to the trial samples. Our findings highlight that identifying and incorporating variables determining trial participation is crucial for generalizable CATE estimates, and thus RCT may better be designed to collect such variables. However, simply including these variables in Causal Forest may not necessarily lead to better estimates, even when aiming to estimate ITE. Combining RCT data with baseline information from the source population can improve estimation performance, particularly aiming to estimate CATE for specific covariates.

Causal Inference

Estimating vaccine effectiveness in observational studies: a matching alternative Emily Wu*
Emily Wu Elizabeth Rogawski-McQuade Mats Stensrud Razieh Nabi David Benkeser

Matching is a popular approach for estimating vaccine effectiveness in observational studies wherein vaccinated individuals are matched to unvaccinated individuals on key covariates. However, matching can obscure the causal estimand of interest and yield inefficient estimators thereof. In this work, we critically examine the estimand targeted by a matching-based analysis and propose a more general class of causal effectiveness estimands. We further propose G-computation style estimators of these estimands that are shown via simulation to enjoy significantly improved efficiency relative to matching-based estimators. The method is illustrated using a study of the effectiveness of the COVID-19 vaccine in children aged 5-11 years during the 2021-2022 school year. In this application, the proposed method produced point estimates of waning vaccine effectiveness comparable to those obtained through matching-based estimators, but with significantly narrower confidence intervals (Figure 1).

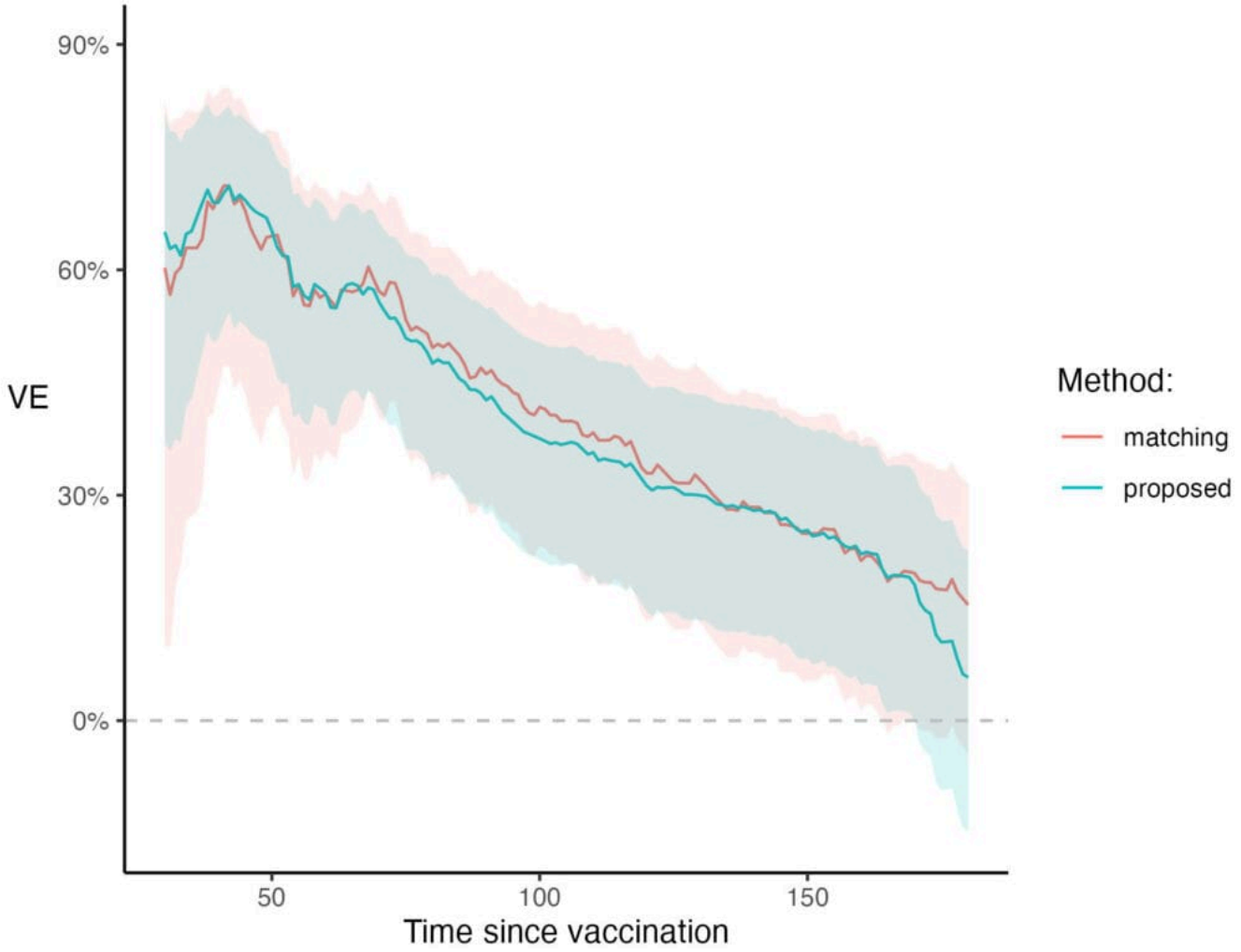


Figure 1. Comparison of proposed and matching-based estimators of VE as a function of time. Shaded areas represent 95% pointwise Wald intervals.

Causal Inference

Framing and Extending Immortal Time Bias with Augmented Causal Diagrams and Annotated Causal Estimands: Immune Time versus Immune Study Population Matthew M Coates* Matthew Coates Onyebuchi A. Arah

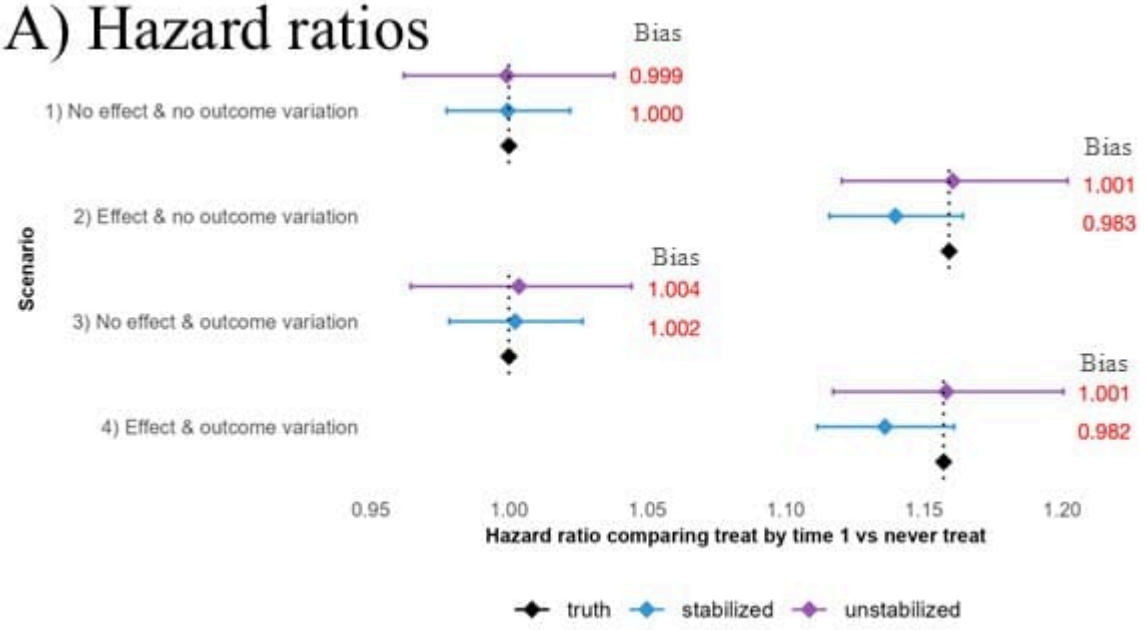
As the increasing availability of large-scale real-world datasets has enabled many studies of causal effects in observational settings that require careful study design, immortal time bias has garnered increased attention. Immortal time is time experienced by study participants during which they are immune to or are not at risk for the outcome. Target trial emulation is a practical strategy that can help avoid inducing immortal time bias by aligning eligibility, treatment assignment, and the start of follow-up for outcome ascertainment. However, this alignment of eligibility, treatment assignment, and the start of follow-up can be more generally described in terms of appropriate definition, timing, and measurement of the target population, treatment, and outcome. Using causal diagrams augmented with selection nodes, treatment misclassification, or both, we show that immortal time bias can occur in a study when the study population sample (so-called eligibility) definition, treatment classification (assignment), or both are based on the study sample, treatment, or both being defined after the start of the study (time zero). We then show how causal estimands can be annotated to see when immortal time bias may be a concern, such as when the study sample differs from the target population based on the timing of sample selection. Finally, we generalize the first type of immortal time bias as an immune study sample bias arising from sample selection based on post-time-zero status that differs from the target population at time zero. The second type of immortal time bias is generalized as immune-to-treatment-effect bias, which arises from treatment misclassification based on post-time-zero exposure assignment. We also investigate whether and how these two biasing mechanisms could co-occur. We conclude by examining the augmented causal structures and estimands that lead to doomed study sample bias versus doomed-to-treatment-effect bias.

Methods/Statistics

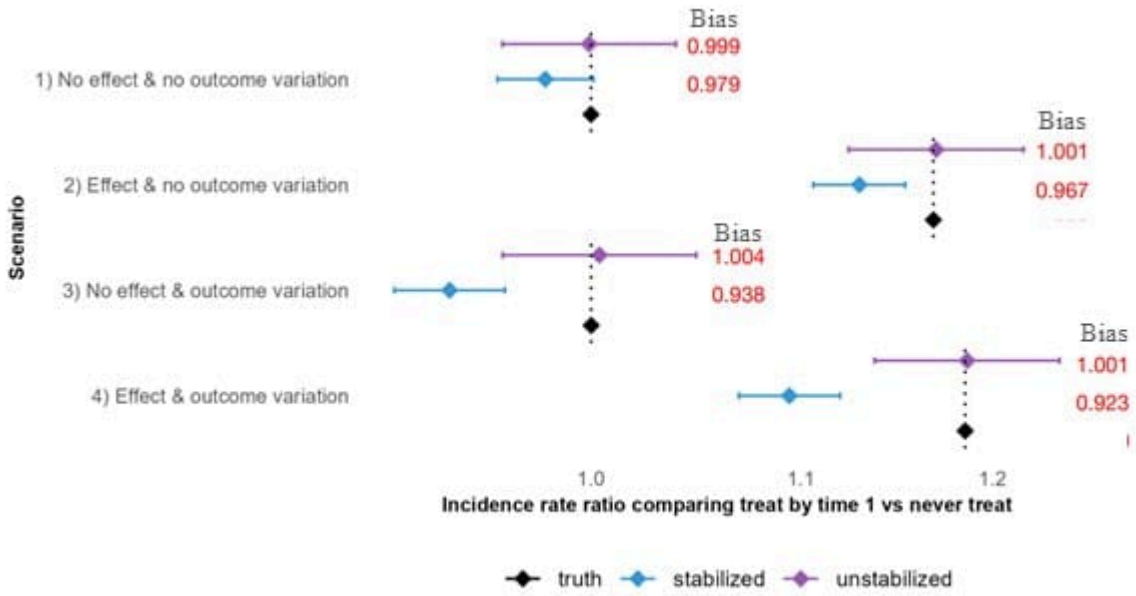
The Dangers of Stabilizing Censoring Weights Michael Webster-Clark* Michael Webster-Clark Alexander Breskin Gwen Aubrac Robert Platt

Weighting is a useful tool for constructing estimators that address confounding and selection bias. When creating inverse probability of treatment weights (IPTW) to address confounding, one very large group will result in large weights for smaller groups. “Stabilizing” IPTW, e.g., by multiplying by the marginal probabilities of treatment, centers weights around 1 and can reduce variability. When addressing selection bias via inverse probability of remaining uncensored weights (a.k.a. “IPCW”), large amounts of censoring can also create very large weights that researchers may be tempted to stabilize by dividing by marginal probabilities of remaining uncensored over time. Unfortunately, stabilizing IPCW (sIPCW) may bias incidence rate ratio (IRR) and hazard ratio (HR) estimates in some situations. This occurs because sIPCW “down-weights” the influence of later segments of person-time compared to what would be observed if the entire population truly remained uncensored. To demonstrate this, we simulated studies using the clone-censor-weight design to compare a “treat with X by time 1” regimen with a “never treat with X” regimen and estimated IRRs and HRs in the presence of a variable W associated with the probability of initiating X. We examined four scenarios: 1) no effect, no association between time and the outcome conditional on W; 2) constant hazard ratio for X; 3) no effect of X with a time-varying hazard conditional on treatment and W; and 4) both potential issues. As **Figure 1** shows, sIPCW always led to more precise estimates. That said, sIPCW yielded biased estimates of the HR in scenarios 2 and 4 and biased estimates of the IRR in all scenarios. Different relationships were observed for incidence rate differences and with other causal contrasts. Under specific circumstances, stabilizing IPCW when estimating IRRs and HRs can lead to increased confidence in biased estimates.

A) Hazard ratios



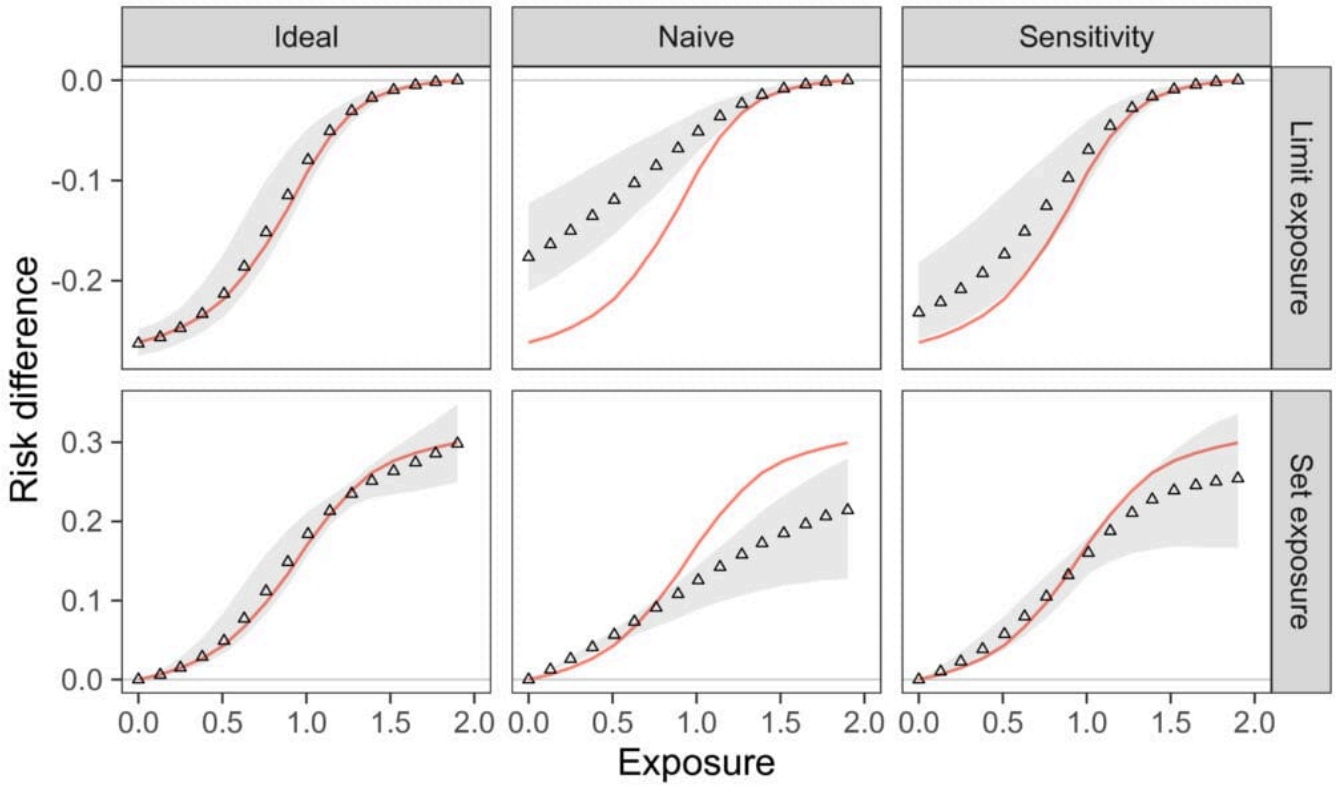
B)Incidence rate ratios



Causal Inference

Bayesian g-formula and causal sensitivity analysis for survival outcomes Kevin Chen* Kevin Chen Sally Picciotto Ellen Eisen Patrick Bradshaw

Background. Parametric g-formula analyses are typically conducted from a frequentist point of view. However, a Bayesian approach can facilitate causal sensitivity analyses that account for systematic sources of error. We extend existing Bayesian formulations of the parametric g-formula to survival outcomes and settings where there may be unobserved time-varying confounding affected by past exposure. Throughout, we considered two types of hypothetical interventions: the first limits exposure to a hypothetical maximum but allows exposures below that limit to vary naturally; the second sets exposure to a hypothetical value.
Methods. We formulated and applied the Bayesian g-formula to simulated data to explore how conclusions might differ under three scenarios. We refer to the first scenario, where we utilized the full data including confounders, as ideal. In the second scenario (naive), we failed to account for unobserved time-varying confounders. In the final scenario (sensitivity), we conducted bias analyses using the Bayesian g-formula by including the unobserved time-varying confounders as latent variables governed by moderately informative priors in the parametric structural causal model.
Results. In our Bayesian g-formula analyses, the average difference between the posterior medians (triangles in the figure) and the true causal risk differences (orange lines) was similar in the sensitivity scenario to that in the ideal scenario. The average difference was several times larger in the naive scenario.
Conclusion. In contrast to the frequentist parametric g-formula, the Bayesian g-formula allows for coherent incorporation of suspected sources of bias to achieve bias-corrected point estimates that are close to the truth. The Bayesian g-formula may offer improved inferences in settings where accounting for an unobserved variable, such as a time-varying confounder, are desirable.



Causal Inference

Comparison of methodological approaches in COVID-19 vaccine effectiveness estimation using observational data Anne Huiberts* Anne Huiberts Bente Smagge Brechje de Gier Henri van Werkhoven Susana Monge Hester de Melker Susan Hahné Janneke van de Wijgert Susan van den Hof Mirjam Knol

Introduction: Target trial emulation (TTE) is an analytical framework to systematically assess and address potential biases in causal inference when using observational data. We aimed to assess vaccine effectiveness (VE) of the Omicron XBB.1.5 booster vaccination against self-reported SARS-CoV-2 infection between 2 October 2023 and 2 April 2024 using two TTE approaches.

Methods: A hypothetical target trial in which eligible participants would be randomized to booster vaccination or no booster vaccination was formulated. Two approaches were used to emulate this hypothetical trial using data of an ongoing prospective cohort study in the Netherlands (VAccine Study COvid-19; VASCO) (**Figure 1**). The first analysis used a single time zero at the start of the booster vaccination rollout and considered booster vaccination as a time-varying variable. The second analysis used multiple time zeros. On each day, all persons who received a booster vaccination on that day were matched 1:1 to persons who had not (yet) received a booster vaccination. Two additional approaches have been planned.

Results: 24,728 participants were eligible for vaccination and 16,295 (66%) were vaccinated. All were included in the single-time-zero analysis and 1,799 and 2,362 infections were reported during vaccinated and unvaccinated follow-up time, respectively. In the multiple-time-zero analysis, 15,138 vaccinated participants were matched to unvaccinated participants, who reported 960 and 1,518 infections, respectively. Overall VE was 39% (95% CI 35-43) using single- and 35% (31-39) using multiple-time-zero analysis. VE decreased as time since vaccination increased, being 46% (41-50), 29% (22-36) and 13% (-8-30) at 1-6, 7-12 and 13-18 weeks post-vaccination using single- and 42% (38-46), 39% (33-46) and 18% (-18-42) using multiple-time-zero analysis, respectively.

Conclusion: Results showed that VE analyses using different approaches within the TTE framework yielded rather similar VE estimates.

Figure 1. Target trial protocol and emulation

Protocol component	Hypothetical target trial	Emulated target trial (single time zero with Cox regression)	Emulated target trial (multiple time zero with covariate matching)
Eligibility criteria	- Age 18-85 years - Eligible for COVID-19 XBB booster vaccination at baseline (HCW, 60+, medical risk; no infection in 90 days prior) - Understanding Dutch	- Age 18-85 years at time zero - Eligible for COVID-19 XBB vaccination (HCW, 60+, medical risk, no infection in 90 days prior) - Understanding Dutch	- Age 18-85 years at time zero - Eligible for COVID-19 XBB booster vaccination (HCW, 60+, medical risk, no COVID-19 vaccine dose received since 2 October 2023 no infection in 90 days prior) - Understanding Dutch
Treatment strategies	1. Administer COVID-19 XBB booster vaccine 2. Do not administer COVID-19 XBB booster vaccine	1. Administer COVID-19 XBB booster vaccine 2. Do not administer COVID-19 XBB booster vaccine	1. Administer COVID-19 XBB booster vaccine 2. Do not administer COVID-19 XBB booster vaccine
Treatment assignment	Randomization	Adjustment for potential time-fixed and time-varying confounders by regression analysis. Potential confounders were age, sex, medical risk condition, educational level and prior infection before 2 October 2023.	1:1 matching on calendar time (sequential trial) and other potential confounders at time zero. Potential confounders were age, sex, medical risk condition, educational level and prior infection before 2 October 2023.
Follow-up	Time zero is when eligibility criteria for inclusion are met, treatment is assigned, and follow-up begins. Follow-up is from time zero to outcome, loss-to-follow up, death, or end of follow-up, whichever occurred first.	Time zero is the start of the vaccination roll-out on 2 October 2023. Follow-up is from time zero to outcome, death of any cause, latest completed questionnaire or administrative end of follow-up, whichever occurred first. To account for treatment assignment not being aligned at time zero, vaccination status was coded as a time-varying variable.	Time zero is date of vaccination or equivalent index date of the matched control who did not receive vaccination on or before that date. Follow-up is from time zero to outcome, death of any cause, latest completed questionnaire, receipt of a vaccine-dose by an individual in the unvaccinated group (with concurrent censoring of the vaccinated member of the pair), or administrative end of follow-up, whichever occurred first.
Outcome	SARS-CoV-2 infection between treatment allocation and end of study	Self-reported positive SARS-CoV-2 test between 2 October 2023 and 2 April 2024	Self-reported positive SARS-CoV-2 test between index date and 2 April 2024
Causal contrast of interest	Per-protocol	Per-protocol	Per-protocol
Statistical analysis	Cumulative incidence (risk) curves using the Kaplan-Meier estimator; vaccine effectiveness = 100% * (1 – risk ratio)	Cox regression model with calendar time as underlying time scale adjusting for covariates; vaccine effectiveness= 100% * (1 – hazard ratio)	Cumulative incidence (risk) curves using the Kaplan-Meier estimator; vaccine effectiveness= 100% *(1 – risk ratio) and bootstrapping to compute 95%CI

Perinatal & Pediatric

Time-related bias when studying perinatal complications after maternal injuries: Application to maternal injuries and preterm birth Asma M. Ahmed* Asma Ahmed Allison Musty Joseph Rigdon Jennifer A. Hutcheon

Background

Injuries affect 1 in 12 pregnancies and are associated with perinatal complications. Some studies that examined associations between maternal injuries and preterm birth (PTB) reported null or counterintuitive protective effects, especially for 3rd-trimester injuries, likely due to time-related biases (**Figure**). We estimated associations between maternal injuries and PTB while appropriately accounting for time-related biases.

Methods

A retrospective cohort study including all births from Atrium Health Wake Forest Baptist system in 2018-2024. Maternal injuries were ascertained using validated diagnostic codes. PTB was defined as gestational age at delivery <37 weeks. We estimated associations between maternal injuries and PTB via two approaches. We used logistic regression for time-fixed analysis (i.e., injury at any point in pregnancy yes/no and PTB yes/no) and Cox proportional hazards models for time-varying analysis (i.e., time-varying injury exposure definition, restricting follow-up to periods when pregnancies were at risk of PTB).

Results

Among 58897 births, 3.1% experienced maternal injuries, and 11.2% were PTB (12.4% among injured and 11.2% among uninjured). With the time-varying approach, maternal injuries were associated with increased risk of PTB (adjusted HR: 1.16 (95% CI: 1.01-1.32)). Trimester-specific analyses showed positive associations for all trimesters, with higher effect estimates for 2nd and 3rd trimester injuries (HR 1.17 (0.97-1.42) and 1.22 (0.92-1.61), respectively). With time-fixed analyses, associations were underestimated, and results for 3rd trimester injuries showed counterintuitive negative associations (HR: 0.74 (0.56-0.97)).

Conclusion

Time-related biases typically underestimate associations between maternal injuries and preterm birth, particularly for 3rd trimester injuries. Rigorous study design and analytical methods that account for time-related biases are crucial in studies investigating adverse outcomes after maternal injury.

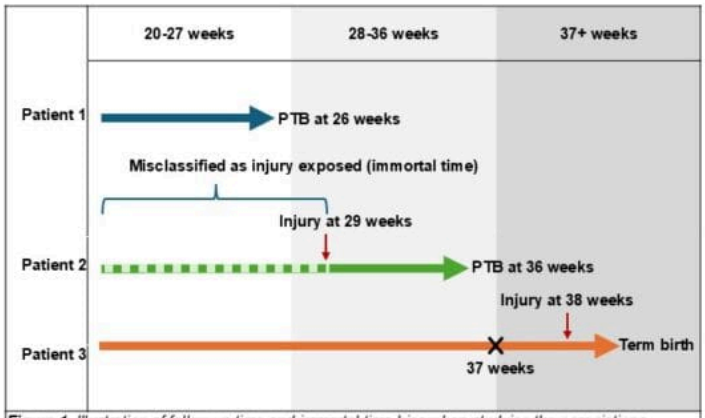


Figure 1. *Illustration of follow-up time and immortal time bias when studying the associations between maternal injury and preterm birth.*

Notes:

- For patient 1, the pregnancy ends before 28 weeks and therefore should be excluded when focusing on 3rd trimester injury.
- For patient 2, the time between the start of follow-up and 29 weeks is misclassified as injury-exposed. The pregnancy must continue to 29 weeks to be classified as injury-exposed, making the time before 29 weeks immortal.
- For patient 3, follow-up should stop at 37 weeks because the pregnancy is no longer at risk of the outcome (PTB) after 37 weeks.
- PTB: Preterm birth

Perinatal & Pediatric

Bias induced by method of pregnancy identification in studies of prenatal exposures using administrative healthcare data Chase D. Latour* Chase Latour Jessie K. Edwards Elizabeth A. Suarez Kim Boggess Mollie E. Wood

Background: Identifying pregnancies in healthcare data has typically required observing pregnancy outcomes (eg, delivery), potentially inducing selection bias in effect estimates for prenatal exposures. Recent efforts use prenatal encounters to identify pregnancies, thus also identifying those with unobserved outcomes (eg, at-home miscarriage). However, including these pregnancies requires appropriate methods to address missing data, which depend on the source of missingness.

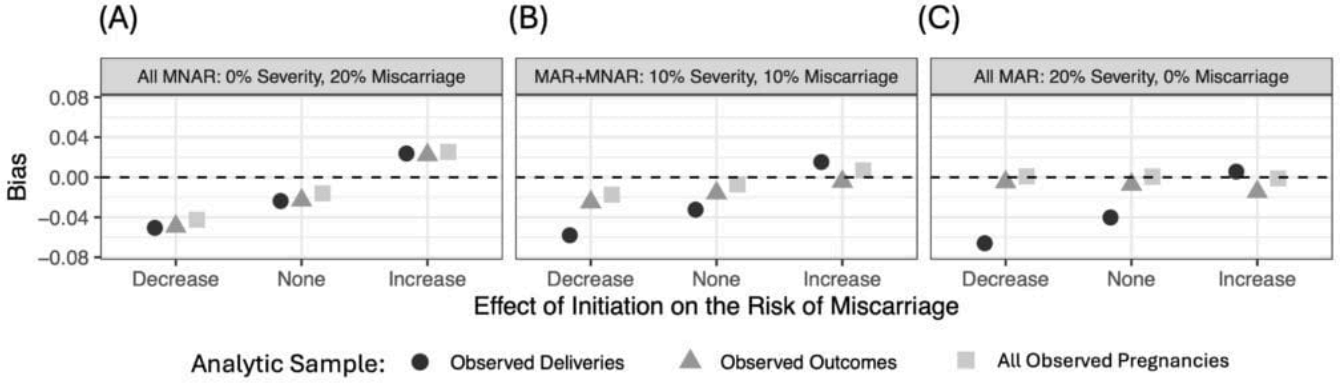
Objective: Evaluate bias under two pregnancy identification approaches (outcome-based, prenatal-based) across measured and unmeasured sources of missingness.

Methods: We simulated 5,000,000 pregnancies and estimated the total effect of initiating antihypertensives on the risk of preeclampsia. We generated data for 9 scenarios characterized by the effect of treatment on miscarriage and the cause of missingness: 1) measured hypertension severity, 2) unmeasured miscarriage, and 3) both severity and miscarriage. Treatment decreased the risk of preeclampsia, and 20% of pregnancies were missing outcomes. We then created 3 analytic samples as possible approaches to deal with missing outcomes: restricting to deliveries (excluding miscarriages), restricting to pregnancies with observed outcomes, and including all pregnancies. Treatment effects were estimated using non-parametric direct standardization.

Results: RDs were most biased when restricted to deliveries (range: -0.07, 0.02) and least among all pregnancies (range: -0.04, 0.03). Within the latter group only, bias decreased as the proportion of missingness due to miscarriage decreased and was zero when all missingness was due to severity (-0.04 to 0.03 when 0% versus 0.00 when 100% of missingness was due to severity).

Conclusions: Incorporating pregnancies with unobserved outcomes did not eliminate bias when missingness was due to unmeasured variables. However, analyzing these pregnancies affords additional analytic approaches to investigate the bias.

Figure. Analytic results from those scenarios where initiation decreased the risk of preeclampsia. Results include bias in the risk difference when pregnancy outcomes were (A) missing due to miscarriage (i.e., Missing Not At Random [MNAR]), (B) due to both severity and miscarriage (i.e., a mix of Missing At Random [MAR] and MNAR), and (C) severity (i.e., MAR). The horizontal, dashed line represents no bias. Estimates in each analytic sample are differentiated according to shape and color.



Perinatal & Pediatric

Impact of increasing midwifery-led prenatal care on birth outcomes among low-risk pregnancies in a claims database: an application of the g-formula and target trial emulation Elizabeth Simmons* Elizabeth Simmons Anna Austin Mollie Wood Alyssa J. Mansfield Karen Sheffield-Abdullah Kavita Singh

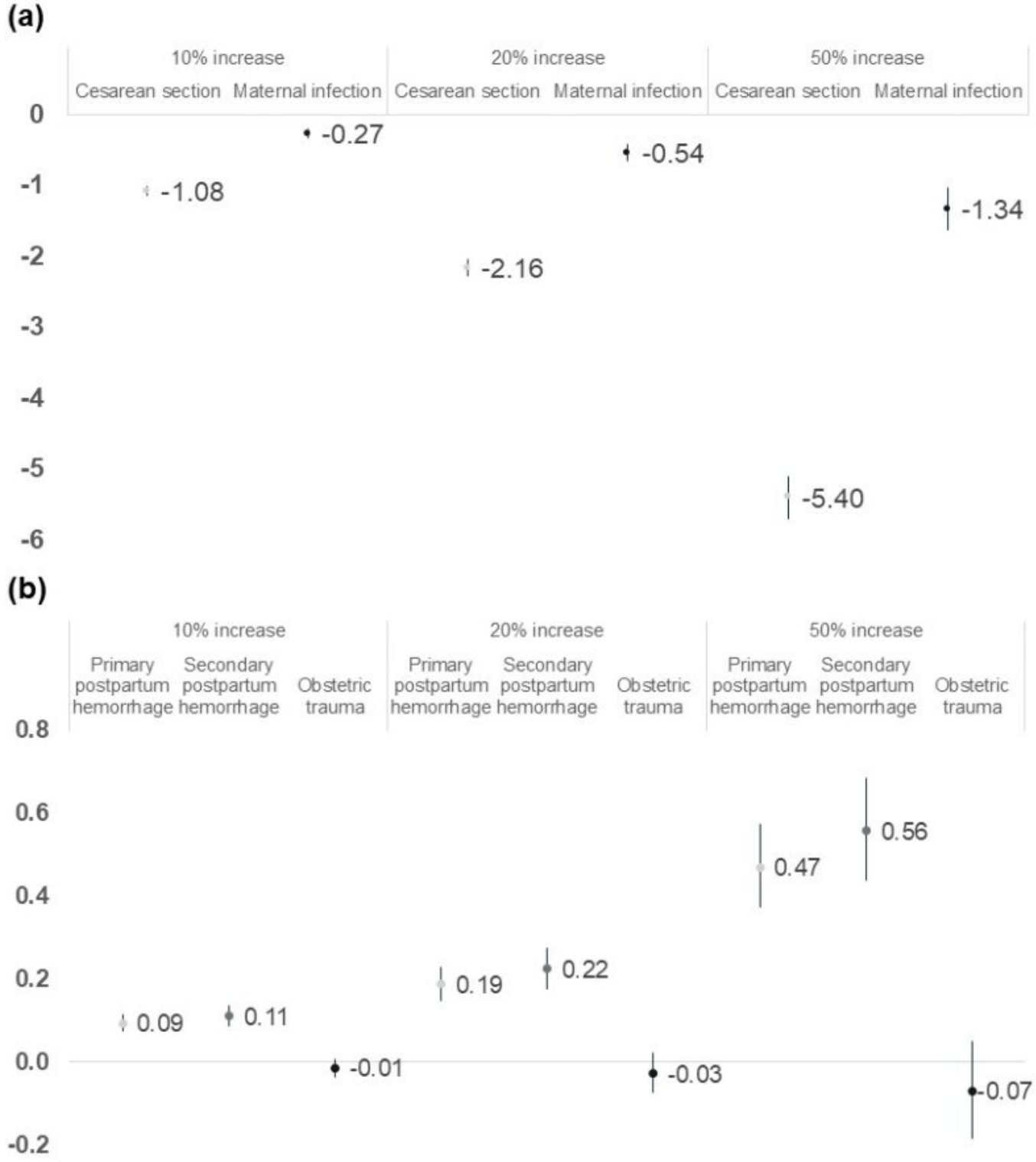
Introduction: Compared to undergoing prenatal care with a physician, prenatal care with a midwife reduces risk of medical interventions and complications during labor and delivery among low-risk pregnant individuals. However, most studies that assess the relationship between midwifery-led care and birth outcomes condition on live births, potentially inducing a type of collider bias. In this study, our objective was to analyze the change in prevalence of birth outcomes under hypothetical scenarios where midwifery-led care is increased by 10%, 20% and 50% among commercially-insured, low-risk pregnant people in the United States.

Methods: We used data from the Merative MarketScan Commercial Claims and Encounters Database. Using a target trial emulation framework, we identified low-risk pregnant people aged 18-55 at delivery who initiated prenatal care in the first trimester with a viable pregnancy and with a midwife or physician. We identified outcomes (cesarean section, maternal infection, primary and secondary postpartum hemorrhage and obstetric trauma) using International Classification of Diseases, Ninth Revision, Clinical Modification diagnosis and procedure codes. Using the nonparametric g-formula, we assessed the change in prevalence of outcomes if 10%, 20% and 50% more pregnant people enrolled in prenatal care with a midwife rather than a physician.

Results: With a 50% increase in the use of midwives compared with the true exposure, we found the prevalence of cesarean sections was reduced by 5.40 percentage points (95% confidence interval (CI): -5.70, -5.09) and of maternal infection decreased by 1.34 percentage points (95% CI: -1.63, -1.03), while the prevalence of primary postpartum hemorrhage increased by 0.47 percentage-points (95% CI: 0.37, 0.58) and of secondary postpartum hemorrhage of 0.56 percentage-points (95% CI: 0.44, 0.69) (Figure 1).

Conclusions: Policymakers should consider removing barriers to improve access to midwives for the US population.

Figure 1. Prevalence difference of (a) cesarean section, maternal infection and (b) primary/secondary postpartum hemorrhage and obstetric trauma, with increase in use of CNMs as providers of prenatal care among low-risk pregnancies with commercial insurance in the United States, 2004-2015



Perinatal & Pediatric

Screen device use and body mass development in children: A causal inference approach to sensitive periods Yuna Koyama* Yuna Koyama Ryan Keen Yena Kyeong Jonathan Bernard Natarajan Padmapriya Falk Muller-Riemenschneider Fabian Yap Yung Seng Lee Law Evelyn Chung Ning Peipei Setoh Henning Tiemeier

Background: “Sensitive periods” are commonly suggested in epidemiological studies but rarely embedded in a causal framework. We examined causal associations of screen time with body mass index (BMI) and possible sensitive periods, leveraging 10 repeated exposure and outcome assessments from ages 1 to 10 years.

Methods: We analyzed data on 1,030 children (546 boys) from a prospective cohort in Singapore. Parents reported children’s screen time. Children’s BMI was derived from anthropometric measures of height and weight. We contrasted a mixed model approach with g-estimation of structural nested mean modeling that estimates average treatment effects while accounting for feedback between chained exposures and time-varying confounders. Average effects at any given age, latent effects, and sensitive period effects were explored.

Results: A 1 standard deviation (SD) increase in screen time at 2 years, but not at other ages, was associated with persistently higher BMI by 0.117 SD (95% confidence interval [CI]: 0.004; 0.230) between ages 2-10 years in boys in mixed modeling. G-estimation showed no sensitive period nor latent effects. However, an average effect across ages exists; if boys increased their screen time by 1 SD at any given age, their BMI at any subsequent age would increase by 0.045 SD (95% CI: 0.002; 0.087). No associations were indicated in girls in both models.

Conclusions: Using g-estimation, we showed an average treatment effect of screen time on subsequent BMI in boys but found no evidence for sensitive periods. Time-varying confounders, chained exposure, and latent effects are key for identifying sensitive period effects.

Perinatal & Pediatric

Calcium supplementation during pre-pregnancy and early pregnancy among women at high risk of preeclampsia: a per-protocol analysis of a randomized trial Kyle Busse* Kyle Busse Long Khuong Gabriela Cormick Stefanie Hinkle José Belizán Enrique Schisterman Sunni Mumford Ellen Caniglia

Calcium supplementation is recommended from 20 weeks' gestation for prevention of preeclampsia. Potential benefits of supplementation before 20 weeks' gestation are less clear. A randomized trial of pre-pregnancy and early pregnancy (<20 weeks) calcium supplementation showed no significant reduction in recurrent preeclampsia (intention-to-treat [ITT] risk ratio [RR]=0.80; 95% confidence interval [CI] 0.61-1.06); however, roughly half of participants took fewer than 80% of expected tablets. Our objective was to estimate the per-protocol effect of pre-pregnancy and early pregnancy calcium supplementation on risk of recurrent preeclampsia in that trial.

This was a secondary analysis of a randomized trial of 500mg daily calcium pre-pregnancy through 20 weeks' gestation on risk of recurrent preeclampsia among 1355 parous women in South Africa, Zimbabwe, and Argentina. Adherence was assessed by pill count every 12 weeks. The parametric g-formula was used to estimate the per-protocol effect of calcium supplementation vs. placebo ≥5 days/week on risk of preeclampsia. Bootstrapping was used to estimate 95% CI. Multiple imputation was used for missing values.

Of the 1355 women, 331 of 678 in the calcium group and 320 of 677 in the placebo group had a pregnancy. Of these, 298 in the calcium group and 283 in the placebo group had a pregnancy beyond 20 weeks' gestation. The percentage of women with adherence ≥5 days/week was 59% in the calcium group and 60% in the placebo group. When adhering ≥5 days/week, the incidence of preeclampsia was 10.5% and 14.9% in the calcium and placebo groups, respectively (RR=0.70 [95% CI 0.44-1.06]). For every 100 women, supplemental calcium ≥5 days/week until 20 weeks' gestation resulted in 4 fewer cases of preeclampsia (risk difference=−4.4 [−9.7-0.6]).

The per-protocol effect suggests that calcium supplementation ≥5 days/week until 20 weeks' gestation may reduce risk of preeclampsia, but, like the ITT effect, it was not statistically significant.

Perinatal & Pediatric

What’s in the Diaper? A Hybrid Targeted and Non-Targeted Analysis of Chemicals in Disposable Diapers Using HPLC-HRMS Elisia White* Elisia White Trevor Johnson Dimitri Abrahamsson Linda Kahn

Infancy is a critical period of development for the reproductive system, which can be dysregulated by exposure to endocrine-disrupting chemicals (EDCs). Infants and toddlers are continuously exposed to exogenous chemicals through commercial baby products including bottles, pacifiers, creams, wipes, and disposable diapers. Most parents in industrialized countries use disposable diapers, yet the diaper manufacturing industry remains unregulated. Research on the chemicals used in commercial diapers is limited, and manufacturers are not required to disclose this information, leaving a gap in oversight by both industry and regulatory bodies. Infants spend 24 hours i.e. all day and night in diapers, which cover a large surface area of their bodies, and the combination of sweat and urine inside the diaper increases dermal absorption. Therefore, it is important to ascertain the chemical constituents of disposable diapers, as they may have adverse effects on infants’ overall health and developing endocrine systems, particularly the gonads. To investigate the chemical components of disposable diapers and identify potential novel compounds for future epidemiologic analyses, we performed a hybrid targeted and non-targeted analysis of 15 popular brands of diapers that included regular, overnight, and eco-friendly types. Each diaper was carefully cut and weighed. The diaper samples were then incubated and extracted in a 50:50 methanol/hexane solution before analysis. The chemical composition of diapers was analyzed using High-Performance Liquid Chromatography (HPLC) coupled with High-Resolution Mass Spectrometry (HRMS) and tandem Mass Spectrometry (MS/MS) in both positive and negative ionization modes. The chemical screening was performed using targeted analysis of known substances, coupled with non-targeted techniques to detect uncharacterized compounds. Bisphenols, phthalates, flavonoids, organophosphates, and polycyclic aromatic hydrocarbons were among the EDCs detected. Identities of bisphenols and phthalates were then confirmed and quantified using analytical standards. This study is an important first step in building an evidence base for regulating chemicals used to produce disposable diapers.

Perinatal & Pediatric

Racial Disparities in Maternal Health and Birth Outcomes in Jefferson County, Kentucky 2017-2022 Felicia Pugh, MS* Felicia Pugh Seyed Karimi, PhD Nick Peiper, PhD Kira Taylor, PhD Laura Schummers, ScD Natalie DuPré, ScD

Severe maternal morbidity (SMM) risk has tripled over the past 30 years. Adverse infant birth outcomes in the U.S. have also increased with substantial Black-White disparities, which interrelated causes may partially explain. This work compares the frequency of adverse maternal and infant birth outcomes by maternal race (Black vs White) in Jefferson County, Kentucky, 2017-2022. We used Jefferson County inpatient hospital delivery and birth certificate records of self-identified Black or White birthing parents. We estimated the incidence of each outcome: SMM, stillbirth, pre-term birth (PTB), and small for gestational age (SGA) with 95% confidence intervals (CI) overall and by race. We used logistic regression to estimate odds ratios (ORs) and 95%CIs, comparing the odds of each outcome by race (Black vs. White), adjusted for a set of explanatory variables and pandemic effects. Among 45,646 deliveries, SMM occurred in 8.0 per 1,000 deliveries (95%CI 8.0, 8.1) to White patients and 14.8 per 1,000 (95%CI 14.6, 15.1) to Black patients. The disparity was similar for stillbirth (White 7.2 per 1,000 [95%CI 7.1, 7.2]; Black 12.7 per 1,000 [95%CI 12.5, 13.0]). Among 46,296 births, PTB and SGA occurred in 7.9% (95% CI 7.8, 8.0) and 6.0% (95%CI 5.9, 6.0) of deliveries to White patients, but 11.4% (95%CI 11.2, 11.6) and 13.7% (95%CI 13.5, 14.0) to Black patients. Disparities persisted after adjusting for maternal, infant, and healthcare factors: OR of SMM: 1.5 (95%CI 1.2, 1.9); stillbirth OR 1.4 (95%CI 1.1,1.7); PTB OR 1.4 (95%CI 1.3, 1.5); SGA 2.3 (95%CI 2.1, 2.4) and considering pandemic effects. Findings confirm substantial Black-White disparities in SMM and adverse birth outcomes, highlighting the need to understand the complex relationship of individual characteristics and socioeconomic status. State and local entities can provide a broader understanding of these indicators through Maternal Morbidity Review (MMR) and Fetal Infant Mortality Review (FIMR) committees.

Abstract Table: Odds Ratios and 95% Confidence Intervals of Severe Maternal Morbidity (SMM) and Adverse Birth Outcomes Comparing Deliveries by Race Among Patients Residing in Jefferson County, Kentucky 2017-2022

		White n/events	Black n/events
Kentucky Health and Family Services Hospitalization Data			
Severe Maternal Morbidity† (n=45,646; events= 468)		**30,736/247**	**14,910/221**
	Crude	Reference	1.86 (1.55, 2.23)
	Model 1	Reference	1.69 (1.40, 2.03)
	Model 2	Reference	1.52 (1.24, 1.86)
Stillbirth (n=45,646; events= 410)		**30,736/220**	**14,910/190**
	Crude	Reference	1.79 (1.47,2.18)
	Model 1	Reference	1.70 (1.39, 2.08)
	Model 2	Reference	1.64 (1.34, 2.00)
	Model 3	Reference	1.40 (1.12,1.73)
Kentucky Vital Statistics Birth Certificate Data			
Preterm Birth (n=46,296; events= 4,172)		**31,642/2,498**	**14,654/1,674**
	Crude	Reference	1.51 (1.41, 1.61)
	Model 1	Reference	1.45 (1.36, 1.55)
	Model 2	Reference	1.38 (1.28, 1.48)
	Model 3	Reference	1.38 (1.28,1.48)
Small for Gestational Age (n=46,296; events=3,894)		**31,642/1,883**	**14,654/2,011**
	Crude	Reference	2.51 (2.35, 2.69)
	Model 1	Reference	2.42 (2.23, 2.59)
	Model 2	Reference	2.25 (2.09, 2.42)
	Model 3	Reference	2.25 (2.09, 2.43)

†Severe maternal morbidity is defined using CDC Index of 21 indicators for deliveries (excluding blood transfusions)

SMM model 1: Adjusted for maternal age (years, 15-20, 21-29, 30-39, 40-54) and maternal comorbidity index score (continuous)
SMM model 2: Adjusted for model 1 variables and payment type (Medicaid, commercial insurance, other or self-pay), teaching hospital delivery (yes, no), and discharge year (2017, 2018, 2019, 2020, 2021, 2022)

Stillbirth model 1: Adjusted for maternal age (years, 15-20, 21-29, 30-39, 40-54) and maternal comorbidity index score (continuous)
Stillbirth model 2: Adjusted for model 1 variables and severe maternal morbidity (yes, no)
Stillbirth model 3: Adjusted for model 2 variables and payment type (Medicaid, commercial insurance, other or self-pay), teaching hospital delivery (yes, no), and discharge year (2017, 2018, 2019, 2020, 2021, 2022)

Pre-term birth model 1: Adjusted for maternal age (years, continuous), maternal body mass index at delivery (kg/m^2, continuous), maternal sexually transmitted infection (yes, no), maternal any diabetes (yes, no), maternal previous pre-term birth (yes, no)
Pre-term birth model 2: Adjusted for model 1 variables and maternal tobacco use (ever, never), maternal education attainment (more than high school, high school, less than high school, missing or unknown), maternal payment type (Medicaid, commercial insurance, other or self-pay)
Pre-term birth model 3: Adjusted for model 2 variables and infant sex (male, female), congenital anomalies at birth (yes, no), birth year (2017, 2018, 2019, 2020, 2021, 2022)

Small for gestational age model 1: Adjusted for maternal age (years, continuous), maternal body mass index at delivery (kg/m^2, continuous), maternal sexually transmitted infection (yes, no), maternal any diabetes (yes, no), maternal previous pre-term birth (yes, no)
Small for gestational age model 2: Adjusted for model 1 variables and maternal tobacco use (ever, never), maternal education attainment (more than high school, high school, less than high school, missing or unknown), maternal payment type (Medicaid, commercial insurance, other or self-pay)
Small for gestational age model 3: Adjusted for model 2 variables and infant sex (male, female), congenital anomalies at birth (yes, no), birth year (2017, 2018, 2019, 2020, 2021, 2022)

Perinatal & Pediatric

Psychosocial profiles in pregnancy predict infant temperament Katherine Ziegler* Katherine Ziegler Christine Hockett Haden Goodwin Santiago Morales Amy Elliott

Background. Infant temperament is one of the best early predictors of future emotional and behavioral difficulties in childhood. Stress and depressive disorders in pregnancy have also been linked to adverse child neurodevelopment. However, maternal mental health and social support have rarely been examined together using person-centered approaches to investigate their impacts on child socioemotional outcomes. This study examines the relations between profiles of maternal psychosocial health and social support in pregnancy with infant temperament.

Methods. Maternal-infant dyads (n=810) enrolled in the Environmental Influences on Child Health Outcomes in South Dakota were included. Psychosocial profiles (PSPs) were determined via latent class analysis based on self-reported responses to mental health and social support questionnaires in pregnancy. Infant temperament was assessed via the Infant Behavior Questionnaire. General linear models assessed the relationship between maternal PSPs and infant temperament adjusting for maternal and infant characteristics.

Results. Four PSPs were identified: high psychological risk and low social support [HPLS] (21.0%), high psychological risk and high social support [HPHS] (15.2%), low psychological risk and low social support [LPLS] (20.6%), and low psychological risk and high social support [LPHS] (43.2%). Infants of mothers with HPLS (β=0.48; 95% CI=0.29-0.67), HPHS (β=0.43; 95% CI=0.21-0.64), and LPLS (β=0.23; 95% CI=0.05-0.43) were higher in negative affect, compared to infants of mothers with LPHS. Infants of mothers with HPLS (β=-0.21; 95% CI=-0.34 to -0.08), and LPLS (β=-0.20; 95% CI=-0.33 to -0.06) were lower in effortful control, compared to infants of mothers with LPHS.

Discussion. Understanding the interplay of prenatal social support and prenatal psychosocial factors on infant neurodevelopment is important and can inform early intervention strategies to mitigate the impact of psychosocial stressors on infant behavior.

Global Health

Sleep health profiles during early infancy are associated with emerging executive function development Ayesha Sania* Ayesha Sania Nicolò Pini Lynn Chen Kirsten A. Donald Michal Zieff Seonjoo Lee Dima Amso William P. Fifer

Background: Infant sleep health is increasingly recognized as a key component of brain maturation and executive function (EF) development in early childhood. Data from low-resource settings remain scarce, where environmental and cultural factors may uniquely shape sleep patterns.

Methods: Data were collected from 200 mother-infant dyads in a prospective cohort study in Gugulethu, Cape Town, South Africa. Infant sleep was assessed using the Brief Infant Sleep Questionnaire at 2–5, 6–10, 12–15, 16–19, and 20–24 months. At 24 months, EF was assessed using the Glitter Wand (GW) task for inhibitory control and the Spin the Pot (STP) task for both inhibitory control and working memory. Nonparametric K-means clustering identified sleep profiles of bedtime, night and day sleep duration, and night-waking frequency. Multiple linear regression models were used to examine associations between sleep clusters at each time point and EF outcomes. Models were adjusted for maternal education, anxiety, depression, family income, and age at EF assessment.

Results: Four sleep profiles emerged: Profile-1 (25.4%) with early bedtime, long night and total sleep, and few night-wakings; Profile-2 (26.3%) with shorter total sleep and longer day sleep; Profile-3 (26.1%) with later bedtime, long day and total sleep, and frequent night-wakings; and Profie-4 (28.3%) with latest bedtime and shortest total sleep. We observed a dose-response relationship between sleep profiles at 2–5 months and STP scores (P for trend = 0.01). On average, the children in profile-4 scored 2.1 points lower (95% CI: -3.6, -0.63) than profile-1 sleepers in the STP task. Sleep clusters at subsequent ages were not associated with STP scores. Sleep clusters were not associated with the GW task scores.

Conclusion: Sleep health in early infancy may critically influence working memory and inhibitory control development. Findings emphasize the need for tailored interventions to promote healthy sleep habits in infancy.

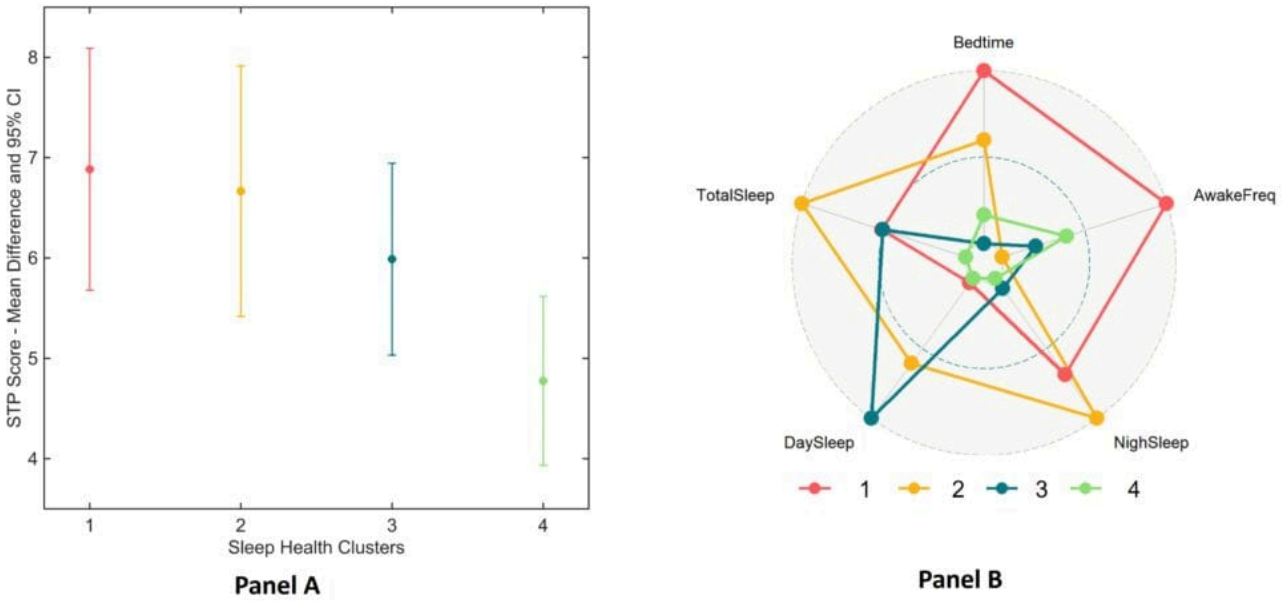


Figure 1. Panel A: The plot displays the marginal means and confidence intervals of STP scores across the different sleep profiles.
Panel B: The radar plot illustrates sleep profiles based on bedtime, total sleep duration, nighttime and daytime sleep, and night-waking frequency. Longer sleep durations are positioned toward the periphery of the plot. Night-waking frequency and bedtime are reverse-coded, with the periphery indicating the lowest night-waking frequency and the earliest bedtime.

Global Health

The Influence of Political Determinants on Antenatal Care and Mortality in LMICs Sueny Paloma* Sueny Paloma Lima dos Santos Dr. Zelalem Haile

Antenatal care (ANC) is critical for improving maternal and child health (MCH) outcomes, yet disparities persist, particularly in low- and middle-income countries (LMICs). This study investigates the impact of political determinants—governance, corruption, and gender inequality—on MCH outcomes, including maternal mortality ratio (MMR), neonatal mortality rate (NMR), infant mortality rate (IMR), and under-5 mortality rate (URMR). Using country-level data from the World Bank, Demographic and Health Surveys, WHO, and UNICEF, we analyzed associations between governance indices and MCH outcomes. Negative binomial regression and mediation analysis were performed. The Global Women's Health Index (HGWHI) and Universal Health Coverage (UHC) scores demonstrated significant negative associations with mortality outcomes (coefficients: -0.03 to -0.07, $p < 0.001$), while CCI showed similar trends (coefficients: -0.03 to -0.06, $p < 0.001$). Countries with higher UHC and CCI scores, such as Brazil and Malaysia, exhibited lower mortality rates, whereas lower scores in Afghanistan and Sierra Leone were associated with worse outcomes. The Gini Index, reflecting income inequality, showed weak and non-significant associations with mortality outcomes (coefficients: 0.00 to -0.01, $p = 0.35$). The Gender Inequality Index (GII) and Women's Peace and Security Index (WPS) were critical determinants, with GII positively associated with mortality outcomes (coefficients: 4.44 to 8.02, $p < 0.001$) and WPS negatively associated (coefficients: -3.1 to -4.36, $p < 0.001$). Mediation analysis revealed UHC and CCI partially mediated the relationship between governance factors and IMR, URMR, and MMR, with significant indirect effects (Estimates: -0.0139 to -0.0251, $p < 0.001$). Sobel tests confirmed that the CCI mediated the relationship in NMR models, whereas CPI did not. These findings highlight the importance of governance and gender equity in reducing mortality and improving access to ANC. Policy recommendations include expanding UHC, addressing gender disparities, and implementing anti-corruption measures to improve equitable healthcare for women and children in LMICs.

Behavior

Associations of financial stressors with disordered eating behaviors and intuitive eating among college students Soyoung Kim* Soyoung Kim Craig Johnston Cynthia Yoon

Associations of financial stressors with disordered eating behaviors and intuitive eating among college students

Soyoung Kim1, Craig Johnston2, Cynthia Y. Yoon1

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Background: College students engage in disordered eating and intuitive eating. Although perceived stress is related to disordered eating behaviors and intuitive eating, how financial stressors relate to such eating behaviors remain unclear.

Objective: To examine associations of financial stressors with disordered eating and intuitive eating among college students.

Methods: Data were drawn from a cross-sectional study of college students (N=1,411 and Mage 20.4± 3.2 years in 2022-2023). Financial stressors, disordered eating behaviors (e.g., overeating, unhealthy weight control behaviors), and intuitive eating were self-reported. Modified Poisson regressions and linear regressions were used to examine associations of financial stressors with disordered eating and intuitive eating, respectively.

Results: For overeating, difficulty affording food was the strongest factor (PR=1.49, 95% CI=1.24-1.79). Anxiety-related binge eating symptoms were associated with difficulty accessing financial aid information and being unable to afford a standard college lifestyle (PR=1.17-1.19). For unhealthy weight control behaviors, all financial stressors except difficulties in obtaining enough money for food or clothing were significant factors (PR=1.16-1.288). For weight and shape concerns, the fear of being identified as financially needy was a significant factor (PR=1.26, 95% CI=1.05-1.49). Intuitive eating score was inversely associated with fearing of being identified as financially needy (β=-4.55, 95% CI=-6.86, -2.24). A cumulative association was observed between the financial stressors and eating behaviors (p value < 0.01).

Conclusion: Financial stressors were related to eating behaviors among college students although the magnitude differed by the type of stressors, level of distress, and number of financial stressors. Future studies should identify strategies to mitigate the adverse effects of financial stress on eating behaviors.

Behavior

Individual and contextual factors associated with active travel to work in England and Wales Jemima Stockton* Jemima Stockton Oliver Duke-Williams

Two thirds of adults in the United Kingdom live with overweight, and whilst around 43% of commuters In England and Wales travel less than 5km to work, only 14% walk or cycle to work. The potential for active travel to improve public health through increased physical activity is huge. A shift away from car dependency, and thereby reduced transport commissions, also plays a role in reducing risks to global health posed by climate change. In previous work, we examined people's travel to work behaviours using the Office for National Statistics Longitudinal Study (LS). The LS is the largest longitudinal data resource in England and Wales, containing linked census and life events data for a largely representative 1% sample from 1971 onwards. Between 2 consecutive decennial censuses, we found that among those travelling by bicycle at one census, a much higher proportion switched to car commuting at the next (43.5%) than retained their commute mode (30.8%). Car drivers had the highest rate of mode retention of all commuters, with 86.3% drivers commuting at one census still commuting by car ten years later at the next. Currently, we are exploiting the unparalleled sample size of the LS to understand the individual and contextual factors – such as age, neighbourhood walkability, distance to work, and workplace and residential stability – associated with propensity to maintain, or switch to, active travel. We also plan to use the LS to study the long-term impacts of commuting on health, using indicators such as mortality. Our findings will provide evidence on which to base pro-environmental and pro-health transport policies.

Behavior

Using Virtual Environments to Study Human Behavior in Two-Lane Roadway Environments in Older Adults Kshitij Sachdev* Kshitij Sachdev Ella Mucciolo Natalie Denburg Shoshannah Eggers Elizabeth O'Neal

Background: Older adults experience disproportionately high rates of pedestrian-motor vehicle collisions, with cognitive and perceptual challenges contributing to this risk. This study examines the relationship between cognitive flexibility and road-crossing decisions in older adults, using a virtual environment to simulate real-world road crossing.

Methods: Participants (N = 43) aged 60-85 completed surveys and cognitive assessments, including tests from the NIH Cognitive Toolbox measuring cognitive flexibility. They crossed two lanes of opposing, continuous traffic 20 times using a head-mounted virtual environment display. For each gap pair (space between moving vehicles) seen, crossing decisions were modeled as a dichotomous outcome (crossed or not). Separate logistic mixed-effects regression models with random intercepts assessed the influence of gap size, cognitive flexibility, and their interaction on crossing decisions for the near and far lanes.

Results**:** The interaction between near-lane gap size and cognitive flexibility was significant (OR: 0.995, 95% CI: 0.992–0.998, $p = 0.016$), such that participants with lower levels of cognitive flexibility were more likely to prioritize larger near-lane gaps when making crossing decisions. Cognitive flexibility did not predict gap selection in the far lane. This significant modification suggests that individuals who have lower cognitive flexibility over-weigh the importance of near lane gap size relative to far lane gaps.

Conclusion**:** Older adults with reduced cognitive flexibility exhibit conservative crossing behavior, focusing primarily on selecting large near-lane gaps and disregarding the size of the far-lane gap. This oversight of the importance of far lane gap size may lead to unsafe collisions. These findings highlight the need for interventions, like Virtual Environment based training programs, targeting cognitive-perceptual calibration to improve crossing safety in older adults.

Behavior

The Association Between Social Activities and Physical Frailty: Cross-Sectional Evidence from Community-Dwelling Older Adults Yu-Kai Lin* Yu-Kai Lin Wan-Yu Lin Chih-Ning Chang

As people age, it becomes more common for them to leave their workplace and reduce connection with the public compared to the younger population. Previous studies suggest the benefits of staying socially active for older adults' cognitive function and mental well-being; however, there is a lack of evidence regarding its impact on physical health. Therefore, our study aims to explore the association between various social activities and physical frailty among community-dwelling older adults in Taiwan.

A cross-sectional study is conducted by recruiting participants from fifty community care stations in Taipei between August and December of 2022. A total of 2,490 adults aged 65 years and older are included in the study. Physical frailty is defined using the Study of Osteoporotic Fractures criteria (SOF ≥ 2), which includes assessments of weight loss, muscle weakness, and decreased energy. Social activity is evaluated based on whether participants volunteer, attend religious or political activities, and engage in study clubs or outdoor leisure activities. Multiple logistic regression and stratified analyses are performed.

After full adjustment, older adults who do not volunteer have a 38% (95% CI: 1.08-1.76) higher risk of being pre-frail; however, other social activities show no significant findings related to frailty. In the stratified results, older adults who are single, live alone, and engage in less exercise have a higher risk of frailty compared to those who volunteer. Furthermore, participants older than 86 years and without taking part in study clubs in their daily lives are found to have a 5.34-fold (95% CI: 1.61-17.72) higher risk of being pre-frail.

In conclusion, our study provides empirical evidence demonstrating the association between volunteering and a lower risk of frailty. It is suggested that governments and health policymakers should place greater emphasis on promoting the incorporation of social activities into the daily lives of older adults.

Health Services/Policy

Policy Exposure Bias: Simulating Information Bias in Legal Epidemiology Research Alina Schnake-Mahl* Alina Schnake-Mahl Gianni Anfuso Ellicott Matthay

Background: Epidemiologists are increasingly investigating the causal effects of social policies on health and health disparities. Previous work has identified potential sources of bias in policy analysis, including policy co-occurrence, time-varying confounders, statistical model misspecification, and limited power. However, less research has assessed the likely magnitude or implications of information bias arising from errors in measuring policy exposures. We use an existing systematic sample of social policy datasets developed by Matthay et al to quantify how much bias in causal effect estimates is likely to be introduced by various theoretical levels and sources of coding errors or date mismeasurement in policy variables.

Methods: Using simulations, we measure variation in the level of bias depending on whether mismeasurement is in the index policy, related policies that are controlled as confounders, or both. We also explore how the magnitude of bias varies when the measurement error is differential versus nondifferential with respect to confounding policies. We report absolute bias, 95% confidence interval coverage, root mean square error (RMSE), and variance for each metric. To complement and ground these simulations, we additionally review the 19 U.S. policy datasets from Matthay et al, and cross-validate the policy data in each database with the original legislative text to identify errors, and potential reasons errors emerged.

Results: In preliminary analyses, absolute bias ranged from 0.1-1.6 depending on the type of information bias. Six of 19 databases incorrectly measured dates, with the percent of incorrect policy dates ranging from 2-40%; differences between the incorrect and correct dates ranged from 2 to 794 days. The most common reasons for incorrect dates included legal battles about legislation, repealed policies, and multiple versions of a bill before the final bill that passed.

Conclusions: Coding errors and date mismeasurement of policy exposure can produce substantial levels of bias. Rigorous application of legal epidemiology and policy surveillance methods can help address these sources of bias. Epidemiologists may benefit from additional training in these areas or partnering with policy experts to mitigate potential information bias.

Health Services/Policy

Quantifying the impact of state-level anti-sanctuary preemption policies on voting patterns, public program participation, and perinatal outcomes Caroline Kravitz* Caroline Kravitz Alina Schnake-Mahl Lita Lillibridge Kalee Fahndrich Alexandra Eastus Brent Langellier

Introduction: Local sanctuary laws limit cooperation with immigration agencies and decrease undocumented persons' fear and risk of deportation. From 2009-2020, states passed anti-sanctuary laws which preempt, or supersede, local laws increasing the fear of immigrant communities. To date, no studies have analyzed the effect of this preemption on civic and health outcomes. Given the anti-immigration focus of the Trump administration, it is important to understand the impact of sanctuary preemption. Furthermore, few studies have developed methods to systematically search local codes to develop local policy exposure data. We hypothesize that preemption will lead to negative civic and health outcomes.

Methods: We used legal mapping to search media and legislative search engines and created a dataset of state anti-sanctuary laws enacted between 2009-2020 and local sanctuary laws enacted between 2000-2020. Previous immigration-themed legal epidemiology studies generally do not include local laws, so we developed a search protocol to identify municipal codes with a sanctuary law. We are merging our policy data with area-level outcomes, including immigration enforcement, voting rates, low weight births, and public program participation. Next, while controlling for policy and sociodemographic covariates, we will use a staggered difference-in-difference design to measure changes in outcomes in sanctuary localities that were preempted versus sanctuary localities that were not preempted.

Results: Between 2009-2020, we identified 19 state laws which preempt local sanctuary laws. Components of these laws we deemed particularly impactful include required compliance with federal detainer requests, required inquiries about immigration status during routine law enforcement activities, and protecting undocumented victims and witness. We further identified 25 local sanctuary laws enacted between 2000-2020. Results from our staggered difference-in-difference analysis are forthcoming.

Health Services/Policy

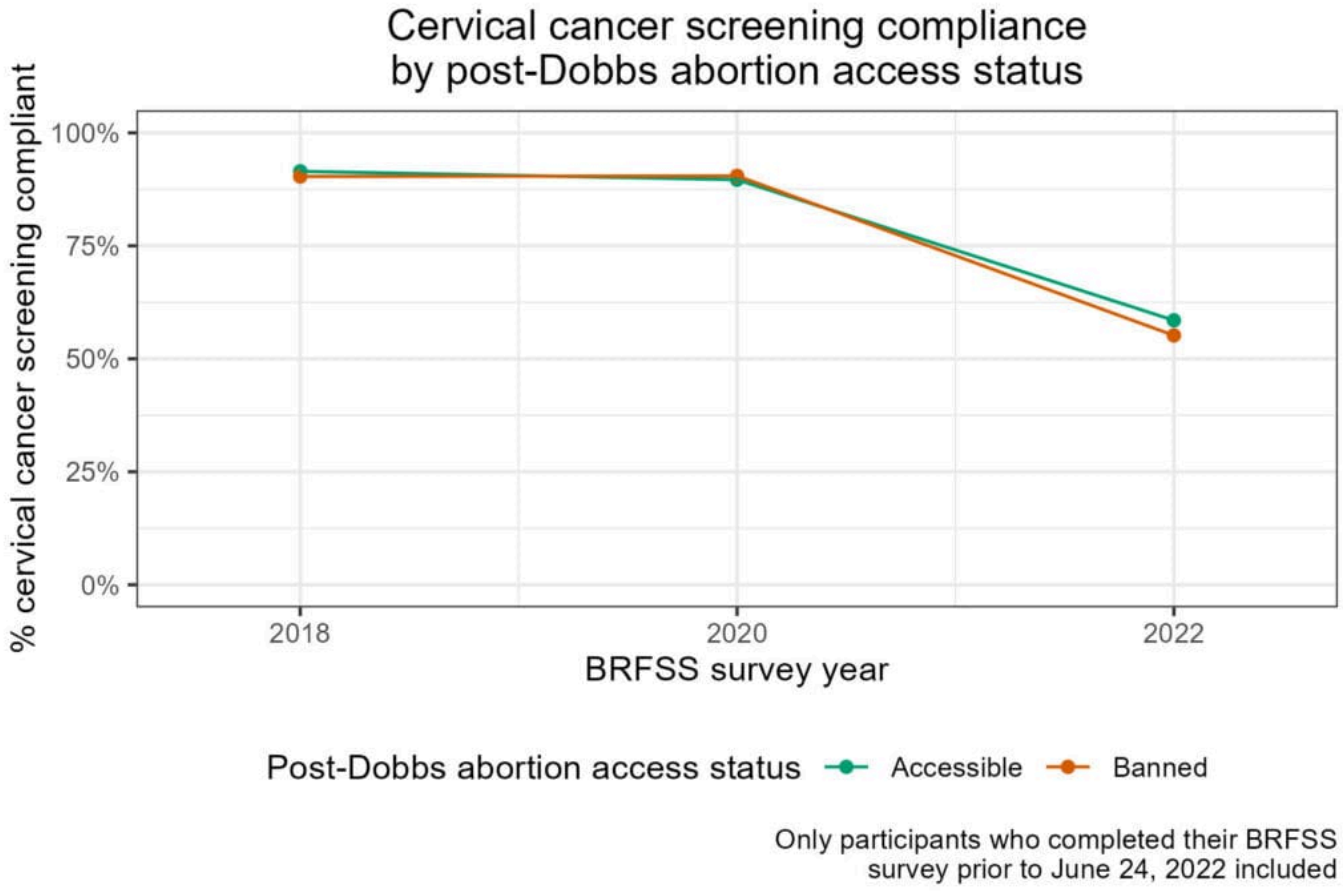
Can BRFSS be used to assess the impacts of the Dobbs v. Jackson Women's Health Organization US Supreme Court decision on healthcare utilization? A preliminary robustness analysis Andrea Molino* Andrea Molino Rachel Winer Vida Henderson Lyndsey Benson Steve Mooney

The June 2022 Dobbs v. Jackson Supreme Court decision created a state-by-state patchwork of abortion policies. Its impact on non-abortion healthcare utilization, such as cervical cancer (CC) screening, is underexplored. When 2024 Behavioral Risk Factor Surveillance System (BRFSS) data become available, we plan to leverage state policy variation and implement a difference-in-differences (DID) design to assess Dobbs' impact. Concerned that COVID-related healthcare changes may affect our ability to estimate causal effects, we performed preliminary robustness checks on available data.

We used 3 pre-Dobbs BRFSS waves (2018, 2020, 2022). Inclusion criteria were identifying as female, 30-49 years, no hysterectomy or CC history, not currently pregnant, and survey completion pre-Dobbs. State inclusion was determined by post-Dobbs abortion access and state Medicaid expansion stability. Robustness checks included: 1) test of prior trends, 2) placebo test (intervention artificially backdated to 2021), and 3) balancing tests for changes in intervention group composition (age, education, urban/rural).

We included 52,085 participants from 27 states, with 88.3% in 22 abortion accessible and 11.7% in 5 abortion banned states. In 2018, 2020, and 2022, 91.3%, 89.7%, and 58.2%, respectively, were considered CC screening compliant, with 2022 decline likely due to COVID. Prior trends F-statistic for year/group interaction terms was statistically significant (p=0.03). The placebo test did not show that artificial 2021 intervention led to greater screening declines in banned states (OR=0.90, 95%CI: 0.75-1.07). Models assessing group composition did not provide evidence that age (F-stat. p=0.52), education (p=0.11), or urban/rural status (p=0.74) changed over time.

Robustness checks support that DID may yield valid estimates of Dobbs' impact on CC screening, which will be crucial when the full analysis is performed with 2024 BRFSS data. Prior trends result may reflect large sample size.


Cervical cancer screening compliance
by post-Dobbs abortion access status
% cervical cancer screening compliant
100%
75%
50%
25%
0%
2018
2020
2022
BRFSS survey year
Post-Dobbs abortion access status
Accessible
Banned
Only participants who completed their BRFSS
survey prior to June 24, 2022 included

Health Services/Policy

The Impact Of Medicaid Coverage Of Gender-Affirming Care On Use Of Gender Affirming Surgery Among Transgender And Gender Diverse Medicaid Enrollees Alex McDowell* Alex McDowell J. Wyatt Koma Pang-Hsiang Liu Mary Beth Landrum Vicki Fung

Research Objective: Use of gender affirming care has been shown to improve health outcomes among transgender and gender diverse (TGD) adults. Many Medicaid programs have implemented policies requiring coverage of gender affirming care. However, no research has examined use of gender affirming care among TGD Medicaid enrollees or the impact of these policies on access. Using national Medicaid claims, we evaluated the impact of Medicaid coverage policies on use of gender affirming surgery among TGD Medicaid enrollees.

Study Design: We identified a sample of adult TGD Medicaid enrollees in the 2016-2019 Medicaid T-MSIS Analytic Files using a previously validated diagnosis-based algorithm. We used a difference-in-differences design to assess the impact of Medicaid coverage policies on gender affirming surgery use. Treatment states were those with no previous Medicaid coverage of gender affirming care that implemented a coverage policy between 2016-2019; comparison states were those that had implemented coverage before 2016. We estimated multivariable logistic regression models with state and year fixed effects and adjusted for age, race, and ethnicity.

Principal Findings: The number of TGD Medicaid enrollees increased from 2016-2019 from 66/100,000 (n=6,714) to 132/100,000 enrollees (n=13,351) in treatment states and from 84/100,000 (n=9,714) to 163/100,000 enrollees (n=17,620) in comparison states. Use of gender-affirming surgeries rose from 4.6/100,000 Medicaid enrollees to 30.9/100,000 in treatment states and from 22.2/100,000 Medicaid enrollees to 66.0/100,000 in comparison states from 2016-2019. In adjusted analyses, TGD Medicaid enrollees had greater odds of gender affirming surgery use after the implementation of a Medicaid coverage policy (Odds Ratio: 1.54; 95% CI: 1.37-1.74).

Conclusions: The percentage of TGD Medicaid enrollees increased about two-fold in treatment and comparison states from 2016-2019. While levels of use of gender affirming surgeries were higher in states with coverage policies before 2016, the rate of use grew more steeply among treatment states that adopted coverage policies during the study period. Our analysis suggests that Medicaid coverage of gender-affirming care increases access to and use of gender-affirming surgery.

Health Services/Policy

The Impact of the Canada Child Benefit on Acute Mental Health Service Use Among Parents: An Interrupted Time Series Design Jasleen Arneja* Jasleen Arneja Brice Batomen Arijit Nandi

The Canada Child Benefit (CCB) is a means-tested tax credit implemented across Canada in 2016. The CCB is more generous than prior child tax benefits, is targeted towards low-and middle-income families, and has led to reductions in childhood poverty and food insecurity.

In the context of resource constraints (e.g., poverty and food insecurity), parents make trade-offs between food and other basic necessities, leading to stress, anxiety, and depression. Additional income received through the CCB may increase parents' disposable income and reduce financial stress. It may also increase the flexible use of resources for the use of preventive care, allowing parents to address mental health concerns through visits to psychologists and physicians, and reducing their risk of acute mental health service use (AMHSU), including hospital and ED visits. We aim to examine the impact of the CCB on AMSHU use among parents using an interrupted time series (ITS) design.

We are using data from a retrospective cohort of adult Canadian Community Health Survey respondents from 2005-2019 with children <18y, followed from January 2010 to December 2019 using annual tax files and health administrative databases. The CCB was implemented in July 2016. AMHSU outcomes include hospitalizations and emergency department visits for anxiety-, mood-, and substance-related-disorders. The ITS impact model will allow for both slope and level changes. Count regression models accounting for overdispersion and auto-correlation will be used to calculate prevalence rate differences.

Ancillary analyses will use a controlled ITS design to compare changes in outcomes among parents vs. non-parents with similar sociodemographic characteristics, as well as in subgroups who receive a larger vs. smaller CCB benefit payment (i.e., parents of children aged 0-5 vs. 6-18 years).

The results of this study will guide evidence-based policies to improve health and reduce health disparities.

Substance Use

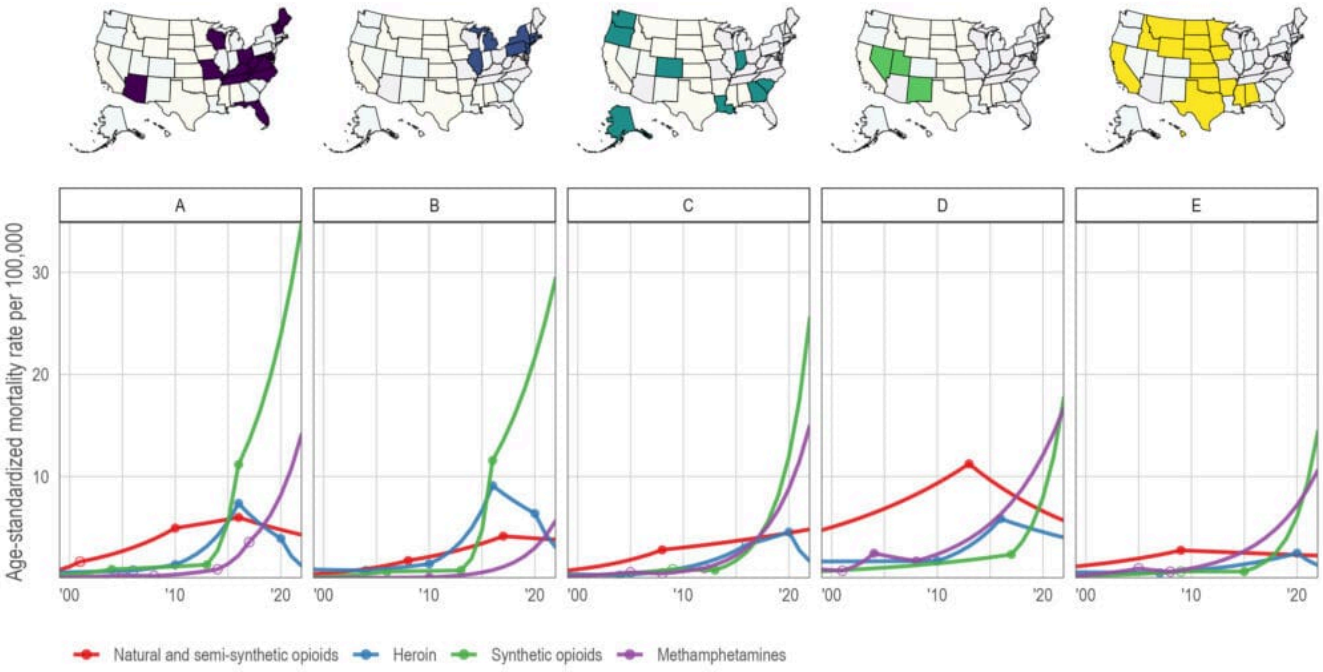
Quantifying the five American drug crises Meekang Sung* Meekang Sung Lucia Pacca Anusha M. Vable Monica J. Alexander Keith Humphreys Mathew V. Kiang

Background: The United States suffers from a decades-long drug addiction and overdose crisis, resulting in over a million deaths since 1999. In the common narrative, the drug epidemic is often described as four “waves” of drug mortality. Briefly, the first wave began with prescription opioids, shifting to the second wave of heroin around 2010, followed by the ongoing third wave of synthetic opioid (i.e., fentanyl) in 2013, and the recent fourth wave of methamphetamine-related deaths. We evaluate if this national mortality pattern holds true across states.

Methods: We used 1999-2022 data from the CDC to calculate annual state-level age-standardized mortality rates for deaths involving natural/semi-synthetic (i.e., prescription) opioids, heroin, synthetic opioids, and methamphetamine. We grouped states with similar drug mortality trajectories using multichannel sequence analysis with hierarchical clustering. We fit joinpoint regression models to quantify drug mortality trajectories within each cluster.

Results: We identified five distinct clusters. Clusters A and B comprise states mostly east of the Mississippi and generally follow the common four-wave narrative, with higher methamphetamine mortality in Cluster A. The other 3 clusters, comprising 27 states, diverge from the four-wave narrative. For example, Cluster E never experienced high prescription or heroin mortality but is experiencing high and rapidly increasing synthetic opioid and methamphetamine mortality.

Discussion: The “drug epidemic” is not a monolith but varies widely across states. These findings have significant implications for public policy. National drug control strategies may only address some states and potentially harm others. For example, policies to reduce opioid prescribing may prevent prescription opioid mortality in some states while reducing effective pain treatment in others. Likewise, variation across states suggests national metrics may be too crude to adequately evaluate impact.


A
B
C
D
E
Age-standardized mortality rate per 100,000
30
20
10
'00
'10
'20
Natural and semi-synthetic opioids
Heroin
Synthetic opioids
Methamphetamines

Substance Use

Impact of the New York City Overdose Prevention Centers on Neighborhood Commercial Activity: A Synthetic Control Analysis Bennett Allen* Bennett Allen Cale Basaraba Czarina N. Behrends Laura C. Chambers Alex Harocopos Brandon D. L. Marshall Magdalena Cerdá

Background: On November 30, 2021, the first overdose prevention centers (OPCs) in the United States opened in the East Harlem (EH) and Washington Heights (WH) neighborhoods of New York City (NYC). In NYC, OPCs are incorporated into syringe service programs (SSPs) and include monitored spaces for drug use to prevent overdose deaths. OPCs face opposition over possible negative neighborhood impacts, including reduced economic activity. Prior OPC research has evaluated their effects on health and crime, but few studies have measured consumer economic impacts. We evaluated changes in consumer mobility and spending around the NYC OPCs before and after implementation.

Methods: This retrospective study used linked, anonymized foot traffic and spending data from SafeGraph for NYC points of interest (POIs, e.g., retail stores and restaurants). Our study period was June 2021-June 2022, with the untreated period ending November 30, 2021. Catchment areas were Business Improvement Districts (BIDs) and 250- and 500-meter buffers around OPCs. Primary outcomes were median biweekly foot traffic and spending. Confounders included neighborhood demographics, gentrification measures, arrests, COVID-19 hospitalizations, and POI features. We used an augmented synthetic control approach to compare OPC areas to counterfactuals constructed from non-OPC BIDs (N=74) and buffers around SSPs (N=18) and opioid treatment programs (N=41). A conformal inference procedure estimated effects at post-OPC timepoints, with placebo testing to estimate overall effects.

Results: We found no changes in foot traffic or spending at any post-OPC timepoint, and overall effects in OPC BIDs were no different from those noted in non-OPC BIDS for foot traffic (EH p=0.284; WH p=0.784) and spending (EH p=0.157; WH p=0.343). Preliminary findings using 250- and 500-meter buffers were similar.

Conclusions: This study provides the first evidence globally that OPCs have minimal impact on neighborhood consumer economic activity.

Substance Use

Violence, criminal legal system contact, and incidence of nonfatal overdose among sex workers who use criminalized drugs: Findings of a recurrent event analysis (2010-2024)

Shira Goldenberg* Shira Goldenberg Andrea Krüsi Wiebke Bartels Charlie Zhou Sarah Moreheart Kate Shannon

Background: While prior research has highlighted impacts of a toxic drug supply on overdose risk, limited work has examined the gendered impacts of violence and criminal legal system contact among women, which are determinants of health for people who use drugs. We prospectively evaluated the impacts of violence and criminal legal system contact on nonfatal overdose events in a marginalized occupational cohort of women who use drugs.

Methods: Baseline and semi-annual data were drawn from a community-based cohort of women sex workers in Vancouver (2010-2024). Analyses were restricted to participants who used criminalized drugs with valid outcome data; analyses of violence and criminal legal system contact while working were further restricted to visits during which participants did sex work. We used the Andersen-Gill method to develop recurrent time-to-event models of the association between recent gender-based, workplace, and neighborhood violence, criminal legal system contact and nonfatal overdose over 15-years.

Results: Among 600 participants (4647 observations), 39.3% (n=236) experienced at least one nonfatal overdose over 15-years, contributing 511 events and an event rate of 18.95/100PY. The proportion who experienced one, two, or ≥three overdoses over follow-up was 20.8%, 8.5%, and 10%, respectively. In separate models, experiencing recent gender-based (Adjusted Hazard Ratio (AHR): 1.95, 95% CI: 1.63,2.33), workplace (AHR: 1.96, 95%CI: 1.54,2.50), and neighborhood (AHR: 1.38, 95%CI: 1.06,1.79) violence, and police harassment without arrest (AHR: 1.74, 95%CI: 1.18,2.56) were associated with elevated hazard of nonfatal overdose.

Discussion: Sex workers face high incidence of nonfatal overdose, with almost one in five experiencing multiple overdoses over this 15-year study. Structural interventions to reduce criminal legal system contact and violence exposure are recommended, alongside scale-up of women-specific and sex worker-tailored overdose prevention services.

Substance Use

Impact of Pre-admission Opioid Abuse on In-Hospital Mortality in Traumatic Brain Injury Patients: A Counterfactual and Mediation Analysis Sepideh Saroukhani* Sepideh Saroukhani Jie Liang Fatemeh Movaghari Pour Hongyin Lai Yuan Li Syeda Amna Kazmi Kelly West Rabail A. Chaudhry George W. Williams Vahed Maroufy

Pre-admission opioid abuse and dependence (POAD) have acute and chronic impacts on outcomes of patients with Traumatic brain injuries (TBIs). Based on traditional association models, previous research suggested an inverse association between POAD and in-hospital mortality in TBI patients. However, these models are limited in establishing unbiased estimates of direct effects, especially from retrospective data due to unmeasured or residual confounding. On the other hand, conducting prospective studies such as randomized clinical trials (RCTs), is neither ethical nor feasible for this type of research questions that involve opioid abuse as the exposure. Using a large retrospective observational dataset (N=455,843) from the National Inpatient Sample (NIS) between 2004-2015, we conducted counterfactual distribution analysis and mediation analysis with multiple mediators (MMA) to discern the direct and indirect effects of POAD on in-hospital post-TBI mortality. While POAD had no significant direct effect [Quantile estimate (95% confidence interval): – 0.07 (-0.15, 0.02), P = 0.15], other covariates and mediators had significant effects (P < 0.001) on in-hospital post-TBI mortality. Specifically, smoking, alcohol abuse, depression and anxiety showed the relative mediatory effect on in-hospital mortality [the relative mediation effect estimate (95% CI): 0.17 (0.14, 0.20), 0.14 (0.12, 0.17), 0.02 (0.017, 0.03) and 0.05 (0.047, 0.06), respectively] suggesting that if smoking, alcohol abused, depression and anxiety had the same distributions between POAD and non-POAD patients, the disparity of in-hospital mortality would have been reduced by 17%, 14%, 2% and 5% among the respective groups. These findings highlight potential avenues for enhancing clinical outcomes in TBI patients with POAD and reinforce the importance of employing statistical approaches to unveil potential causal relationships when randomized clinical trials are not feasible.

Substance Use

Gender-based differences in harm reduction practices among people who use drugs in Rhode Island: A latent class analysis Leah Shaw* Leah Shaw Anusha Kumar Carolyn Park Yu Li Catherine Lenox Alexandra Collins Susan Sherman Brandon Marshall Alexandria Macmadu

Background: Previous research has documented differing drug use patterns and risk behaviors by gender identity and sex assigned at birth, but differences in harm reduction practices remain underexplored.

Methods: We utilized data from the Rhode Island Prescription and Illicit Drug Study (RAPIDS), which enrolled adults who used drugs (2020-2023). Participants were analyzed based on gender identity: men, women, and other (including those identifying as non-binary or something else). Participants reported typical harm reduction practices (e.g., use fentanyl test strips, keep naloxone nearby) to avoid accidental overdose. Latent class analysis (LCA) identified harm reduction practice typologies and a correlation matrix examined pairwise relationships between practices.

Results: Among 503 eligible participants, 64% were men, 34% were women, and 2% were non-binary or something else (n=9). Harm reduction practices were comparable between men and women, although men were less likely to keep naloxone nearby ($p=0.02$). Group membership in latent classes (no/low, moderate, and high utilization of harm reduction practice typologies) did not vary by gender identity. However, those belonging to the no/low utilization subgroup were significantly more likely to have ever been incarcerated ($p=0.03$) and to be single ($p<0.01$). Those belonging to the high utilization group were significantly more likely to have ever witnessed an overdose, performed rescue breathing, and administered naloxone (all $p<0.001$). Correlations showed pairwise relationships, with ‘use fentanyl test strips’ and ‘keeping naloxone nearby’ being positively and significantly correlated ($r=0.33$, $p<0.05$).

Conclusions: We found that engagement in harm reduction practices were largely comparable between men and women; however, men who use drugs are significantly less likely to keep naloxone nearby. Gender-attentive strategies to increase naloxone carriage and usage among men may be warranted to mitigate overdose risk.

Substance Use

The COVID-19 pandemic and opioid overdose deaths in Kentucky: An analysis of demographics and comorbidities in 2016-2021. Venetia Aranha* Venetia Aranha Dr. Jovita Murillo Dr. Kira Taylor Dr. Seyed Karimi

Purpose: Kentucky has one of the highest drug overdose death rates . This study assesses the association of the COVID-19 pandemic with opioid overdose deaths among hospitalized patients (2016-2021).

Methods: We captured inpatient hospitalizations from Kentucky Health Facility and Services (KHFS) database in 2016 to 2021, utilizing ICD-10-CM codes for opioid overdose T40.0-T40.6. Quarterly analysis was performed to identify the seasonal surges of opioid overdose deaths. The probability and 95% CIs of opioid overdose deaths, adjusted for demographic and social factors, admission type, drug type, Charleson Comorbidity Index (adopted from Glashen et al.), were calculated. Linear probability models were used to test interactions between period (exposure of interest) and demographic and social factors on overdose death (outcome of interest). The analysis was conducted for opioid use disorder reported as the 1st or 2nd diagnosis, or as any of the 1st-25th diagnosis.

Results: Compared to the pre-pandemic period (2016-2019), during the pandemic (2020-2021), hospitalizations for synthetic opioid users rose (15.5% vs. 8.8%) for the 1st or 2nd diagnosis, and for the 1st-25th diagnosis (7.64% vs 5.69%). Adjusted models showed that the probability of opioid overdose deaths was not associated with COVID-19 pandemic. Also, associations of dependent variable with opioid overdose deaths did not change with the COVID-19 pandemic. These overdose deaths may be underreported due to exclusions of fentanyl and methamphetamine-related cases.

Conclusion: The COVID-19 and opioid crises underscore the need for improved harm reduction services and support for Community-Based Participatory Research to combat the epidemic.

Mental Health

Trauma, trust, and ties: exploring the impact of social support on mental health in Afghanistan Emma Sexton* Emma Sexton Ajmal Sabawoon Katherine M. Keyes Sabrina Hermosilla Elie Karam Viviane Kovess-Masfety

Exposure to potentially traumatic events (PTEs) is associated with increased rates of depression, anxiety, and post-traumatic stress disorder (PTSD). While social support has been shown to buffer the effect of PTEs on psychiatric outcomes, little is known about this moderation in contexts of prolonged conflict. Afghanistan, with its ethnic diversity, persistent exposure to conflict, and strong communal structures, presents a unique context to examine the buffering hypothesis of social support. Using data drawn from a nationally representative study of 4,359 adults in Afghanistan, we assessed the relationship between PTEs (measured by LEC-5), social support (OSSS-3), and mental health symptoms of depression, anxiety, and PTSD (CIDI-SF and PCL-5). Logistic regression models were stratified by social support, and interactions between PTEs and social support were examined relative to any psychiatric disorders (specifically depression, anxiety, or PTSD) and stratified by sex. Strong social support was significantly associated with being male (RRR = 1.69; 95% CI: 1.30-2.17), higher education attainment (RRR = 2.49; 95% CI: 1.58-3.93), higher income (RRR = 1.57; 95% CI: 1.25, 1.98), and rural residence (RRR = 1.75; 95% CI: 1.30-2.35). Males who experienced collective violence with strong social support had lower odds of any psychiatric disorders versus those with poor social support (OR = 0.43; 95% CI: 0.19-0.94). Females who experienced sexual violence with strong social support had lower odds of any psychiatric disorders versus those with poor social support (OR = 0.23; 95% CI: 0.06-0.89). Social support’s relationship with PTEs and psychiatric outcomes varies by sex and PTE type. These factors should be taken into consideration to ensure adequate mental health care and support is provided. Given social support’s protective effects, strengthening support systems should also be considered when planning and providing mental health services in conflict-affected areas.

Global Health

Adverse childhood experiences, socioeconomic position and mental health in middle-income countries: analyses of Brazilian and Filipino birth cohorts Lucy Barrass* Lucy Barrass Lucy Riglin Theresa Maria Redaniel Nanette R Lee Duleeka Knipe Laura Howe Alicia Matijasevich

Adverse childhood experiences (ACEs) are associated with poorer mental health. However, most evidence comes from high-income settings, despite most children residing in low- and middle-income countries, where the burden of mental disorders is also highest. We aimed to explore the association between ACEs and mental health, and whether associations were modified by socioeconomic position (SEP), in two middle-income countries. We hypothesized that the effects of ACEs would be exacerbated in those with socioeconomic disadvantage.

We used data from the Pelotas 2004 birth cohort (Brazil) and the Cebu Longitudinal Health and Nutrition Survey (CLHNS) (Philippines). Self-reported ACEs were measured prospectively up to age 15 years (Pelotas) and retrospectively recalled at age 35 (CLHNS). ACEs were explored individually, cumulatively and using the dimensional approach to adversity and psychopathology (DMAP). Mental health outcomes were measured at age 18 (depression in both cohorts, anxiety in Pelotas). Logistic regression was used to explore associations between ACEs and outcomes and we assessed the modifying effect of maternal education.

Analysing data from 1620 and 1217 participants from Pelotas and CLHNS respectively, we found strong evidence of associations between experiencing physical and emotional abuse, emotional neglect, witnessing domestic violence, higher cumulative scores or threat ACEs and having depression in both cohorts. All individual, cumualtive and DMAP categorisations of ACEs were associated with anxiety, with odds ranging from 1.36 for parental separation (95%CI: 1.06,1.75) to 4.90 for 4+ ACEs (95%CI: 3.21,7.48), except parental death (OR: 0.91 95%CI: 0.57,1.44). We found inconsistent evidence that SEP modifies associations.

Consistent with HIC evidence, ACEs are linked to depression and anxiety in LMICs, suggesting a need for population-level prevention interventions and support for those exposed to ACEs to promote good mental health.

Mental Health

Network Analysis of Korean Happiness: A Comparative Study by Generation, Gender, and Income Level Doo Woong Lee* Doo Woong Lee Alexander C. Tsai Soyeon Sarah Oh

Background: South Korea faces significant mental health challenges, with one of the highest suicide rates among OECD countries. Various socio-cultural, economic, and political factors, including generational conflict, gender inequality, and socio-economic disparities, contribute to the mental well-being of the population. Understanding how these factors interconnect to influence happiness across different demographic groups is critical to designing effective interventions for improving well-being.

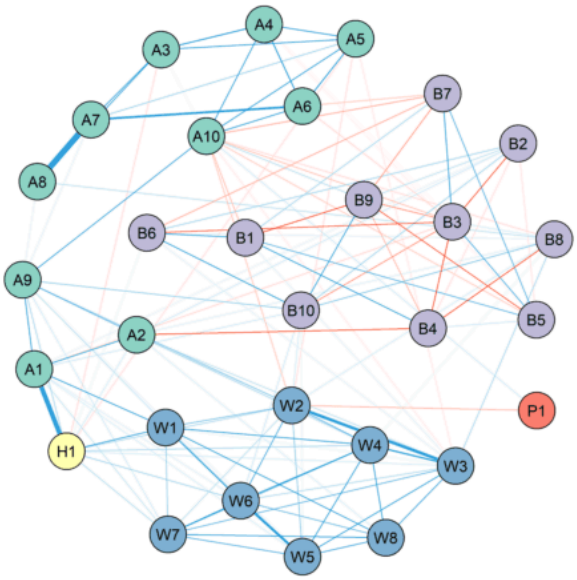
Objective: This study aims to analyze the determinants of happiness in South Korea using a network analysis approach, focusing on the interrelationships between psychosocial and personality factors. It seeks to uncover how happiness is structured across different demographic segments, including gender, income, and generation, to provide insights that can inform social, and policy interventions aimed at enhancing well-being.

Methods: A cross-sectional study was conducted using data from the 2020-2023 Koreans' Happiness Survey (KHS), which includes a nationally representative sample of 64,531 individuals. Network analysis using the graphical Gaussian model (GGM) and the Least Absolute Shrinkage and Selection Operator (LASSO) method was applied to explore the relationships between happiness, emotional states, personality traits, and socio-economic factors. Subgroup analyses were performed to compare network structures by gender, income, and generation groups.

Results: The network analysis revealed significant connections among variables related to emotional well-being, satisfaction, and personality traits. Strong relationships were identified, such as between stress and tiredness, happiness and enjoyment, and depression and anger. Gender differences were observed, with males exhibiting a more diversified network structure, connecting happiness to socio-economic factors such as standard of living and future security, while females' happiness was more closely tied to emotional factors like depression and loneliness. Income disparities also influenced network structures, with lower-income groups showing a stronger link between happiness and standard of living, while higher-income groups exhibited more complex connections. Generational analysis showed that the "MZ generation" (Millennials and Generation Z) prioritized both affective experiences and economic conditions in their happiness assessment, with strong connections between enjoyment and standard of living.

Conclusion: This study provides a multidimensional analysis of happiness in South Korea, highlighting the complex interplay of emotional, economic, and personality factors across different demographic groups. The findings underscore the importance of tailored policy interventions that address both emotional well-being and socio-economic stability, with specific approaches for men, women, income groups, and younger generations. These insights contribute to a deeper understanding of the determinants of happiness in South Korea's socio-cultural context and inform efforts to promote well-being across diverse population segments.

Keywords: Happiness; Mental health; Network analysis; South Korea; Gender differences; Generational differences; Income inequality



- **Happiness**: 'Overall, how satisfied are you with life as a whole these days?'
  - H1: 'Happiness'
- **Affect**: 'How much have you felt ___ yesterday?'
  - A1: 'Enjoyment'
  - A2: 'Calm'
  - A3: 'Worry'
  - A4: 'Sadness'
  - A5: 'Depression'
  - A6: 'Anger'
  - A7: 'Stress'
  - A8: 'Tiredness'
  - A9: 'Vitality'
  - A10: 'Loneliness'
- **Modified Personal Wellbeing Index**: 'How satisfied are you with your ___?'
  - W1: 'Standard of Living'
  - W2: 'Health Satisfaction'
  - W3: 'Relationships Satisfaction'
  - W4: 'Safety'
  - W5: 'Community Belonging'
  - W6: 'Future Security'
  - W7: 'Hobbies'
  - W8: 'Local Environment'
- **Political Orientation**: 'People can be politically progressive or conservative. Which of the following do you think you belong to?'
  - P1: 'Political Orientation'
- **Big Five Inventory-10**: 'I see myself as someone who ___.'
  - B1: Extraversion 1, 'is reserved.' (reverse coded)
  - B2: Extraversion 2, 'is outgoing, sociable.'
  - B3: Agreeableness 1, 'is generally trusting.'
  - B4: Agreeableness 2, 'tends to find fault with others.' (reverse coded)
  - B5: Conscientiousness 1, 'tend to be lazy.' (reverse coded)
  - B6: Conscientiousness 2, 'does a thorough job.'
  - B7: Neuroticism 1, 'is relaxed, handles stress well.' (reverse coded)
  - B8: Neuroticism 2, 'gets nervous easily.'
  - B9: Openness 1, 'has few artistic interests.' (reverse coded)
  - B10: Openness 2, 'has an active imagination.'

Mental Health

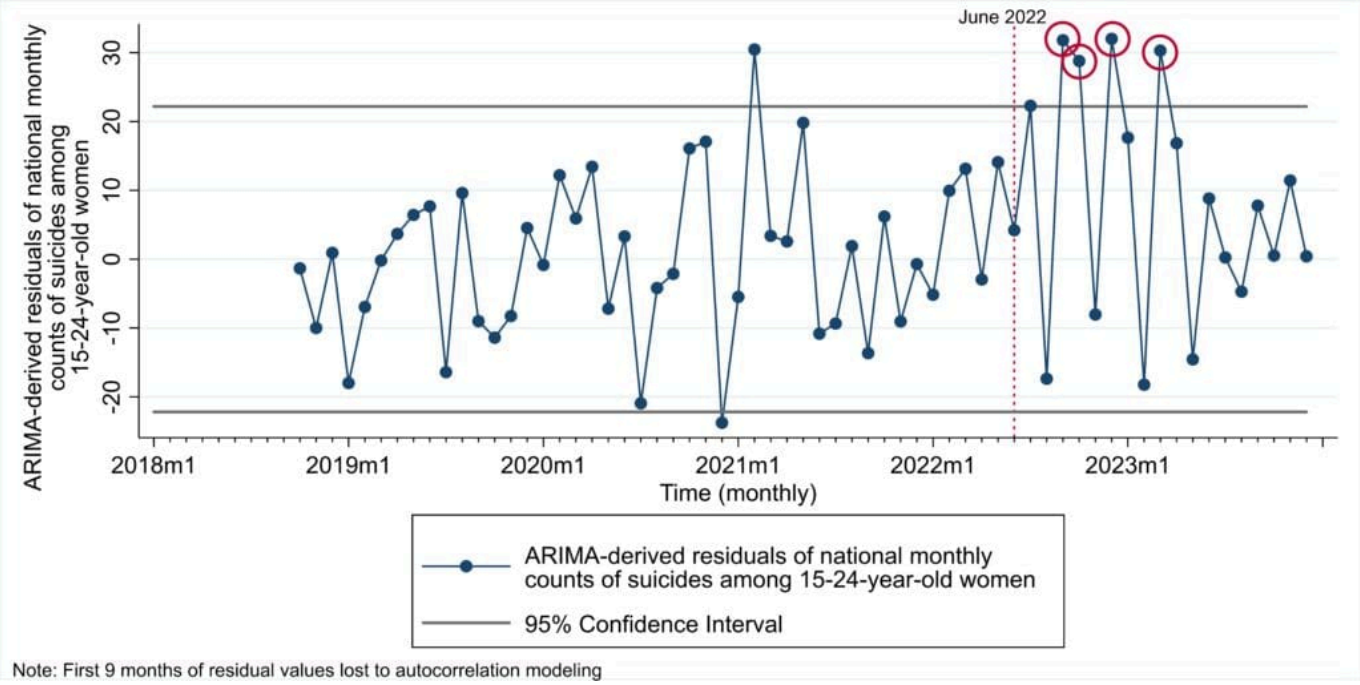
Suicide deaths among reproductive-aged women in the US post-Dobbs: A national time-series analysis Parvati Singh* Parvati Singh Alaxandria Crawford Sarah Crow Jonathan R. Powell Maria F. Gallo

Purpose: The United States Supreme Court's Dobbs decision in June 2022 may have worsened mental health among reproductive-aged women nationally. We examined whether the Dobbs decision preceded an increase in suicides among reproductive-aged women using national, monthly data, from January 2018-December 2023.

Methods: We retrieved national monthly suicide counts from January 2018 to December 2023 for women and men 15-49 years of age (overall and stratified by two age groups- 15-24 years, 25-49 years) from the Centers for Disease Control and Prevention's Wide-ranging Online Data for Epidemiologic Research Multiple Cause of Death database. We used time series analyses to examine whether residuals of nationally aggregated counts of monthly suicides among women 15-49, 15-24- and 25-49-years of age (outcomes) exhibited higher-than-expected values following the Dobbs decision, controlling for autocorrelation and concomitant monthly series of suicides among men.

Results: We observed higher-than-expected residuals of suicides in July and September 2023 among 15-49-year-old women and in September, October, December 2023 and March 2024 among 15-24-year-old women. No residual outliers were observed among 25-49-year-old women post-Dobbs. Results from time-series analyses indicate an average of 52.5 additional suicides in outlier months among 15-49-year-old women post-Dobbs (95% confidence interval [CI]: 14.85, 90.15). The increase appeared pronounced among younger age (15-24 years) women (coefficient = 19.6, 95% CI: 11.17, 28.03). Results suggest 104 additional suicides among 15-49-year-old women, and 78 excess suicides among 15-24-year-old women, nationally, post-Dobbs.

Conclusions: Findings highlight the adverse impact of the Dobbs ruling on mental health among reproductive-aged women.

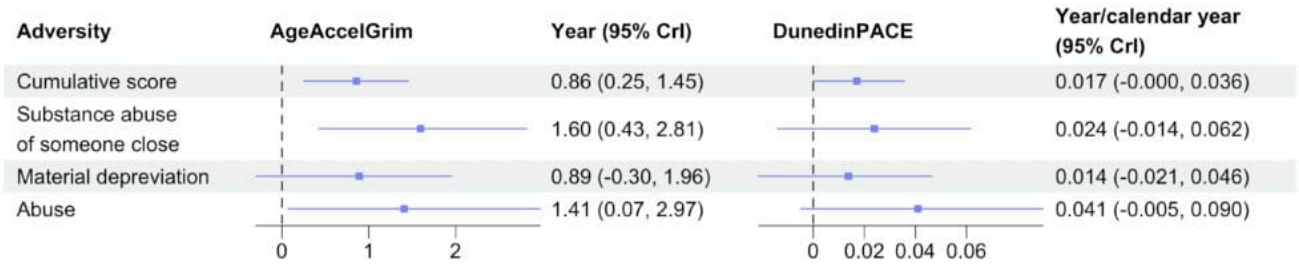


Aging

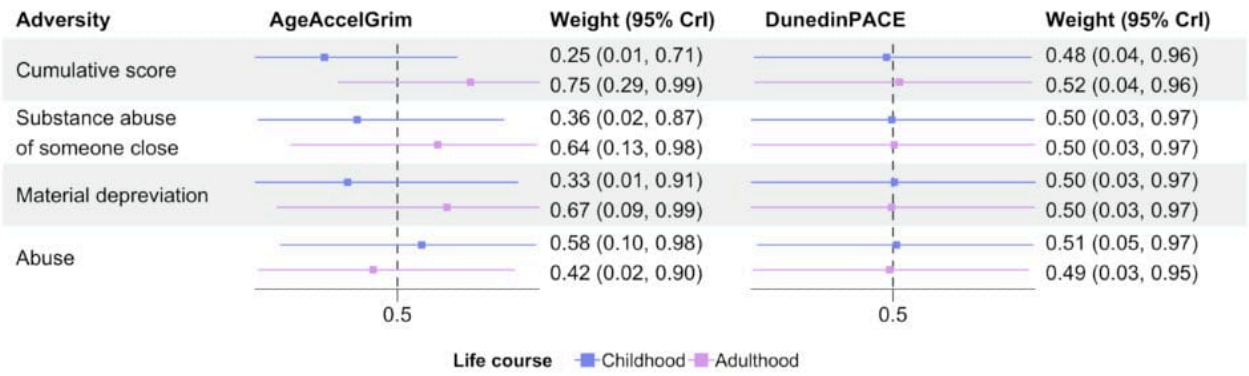
Life-course Adversity and Biological Aging in the Hispanic Community Health Study / Study of Latinos: A Life-course Model Analysis Yinxian Chen* Yinxian Chen Sarina Abrishamcar Krista Perreira Maria Argos Andrea Baccarelli Jianwen Cai Christian Dye Maria M. Llabre Linda C. Gallo Martha Daviglus Bharat Thyagarajan Carmen R. Isasi Karen N. Conneely Timothy L. Lash Anke Huels Shakira F. Suglia

The effect of adversity on aging may vary over the lifespan. Assessing the associations among life-course adversity (LA), biological aging, and the relevant life-course model may reveal mechanisms of LA in aging and inform prevention. We included 970 individuals with DNA methylation profiles at Visit 2 (2014-2017) from the Hispanic Community Health Study/Study of Latinos to calculate GrimAge epigenetic age and DunedinPACE pace of aging. The LA was defined as the weighted sum of exposure to childhood (CA) and adulthood adversity (AA), which were assessed at Visit 1 (2008-2011) as a sum of physical and sexual abuse, material hardship, and substance abuse of someone close (scored 0-4). The Bayesian relevant life-course model (BRLM) was used to estimate the association between LA and epigenetic aging, examining three hypothetical life-course models: critical period (Weight[W]CA=1/WAA=1), sensitivity period (WCA>WAA / WCA<WAA), and accumulation (WCA=WAA) model. We further examined the pathway model by causal mediation analysis of the indirect effect of CA through AA. After addressing confounders, one unit increase in LA was associated with a 0.86-year increase in GrimAge acceleration (AgeAccelGrim) (95% credible interval [CrI]: 0.25, 1.45) and 0.017-year/calendar year in DunedinPACE (95%CrI: 0.000, 0.036). WCA was 25% (95% CrI: 1%, 71%) and WAA 75% (95%CrI: 29%, 99%) for AgeAccelGrim, while WCA 48% (95% CrI: 4%, 96%) and WAA 52% (95% CrI: 4%, 96%) for DunedinPACE. We found an indirect effect of CA through AA (0.13 years, 95%CI: 0.03, 0.24) on AgeAccelGrim but not DunedinPACE. For AgeAccelGrim, BRLM identified the sensitive period model as the most relevant, but mediation analysis supported the pathway model. For DunedinPACE, the accumulation model best explained the life-course association. The varied importance of CA and AA by aging markers suggests that LA may have distinct pathways affecting different aging outcomes and should be explored.

A


Adversity
AgeAccelGrim
Year (95% CrI)
DunedinPACE
Year/calendar year (95% CrI)
Cumulative score
0.86 (0.25, 1.45)
0.017 (-0.000, 0.036)
Substance abuse of someone close
1.60 (0.43, 2.81)
0.024 (-0.014, 0.062)
Material depreviation
0.89 (-0.30, 1.96)
0.014 (-0.021, 0.046)
Abuse
1.41 (0.07, 2.97)
0.041 (-0.005, 0.090)
0
1
2
0
0.02
0.04
0.06

B


Adversity
AgeAccelGrim
Weight (95% CrI)
DunedinPACE
Weight (95% CrI)
Cumulative score
0.25 (0.01, 0.71)
0.75 (0.29, 0.99)
0.48 (0.04, 0.96)
0.52 (0.04, 0.96)
Substance abuse of someone close
0.36 (0.02, 0.87)
0.64 (0.13, 0.98)
0.50 (0.03, 0.97)
0.50 (0.03, 0.97)
Material depreviation
0.33 (0.01, 0.91)
0.67 (0.09, 0.99)
0.50 (0.03, 0.97)
0.50 (0.03, 0.97)
Abuse
0.58 (0.10, 0.98)
0.42 (0.02, 0.90)
0.51 (0.05, 0.97)
0.49 (0.03, 0.95)
0.5
0.5
Life course
Childhood
Adulthood

Aging

Intimate partner violence and aging outcomes: an application of transportability using an observational, occupational cohort study Audrey R. Murchland* Audrey R. Murchland Sebastien Haneuse Karestan C. Koenen M. Maria Glymour Eleanor Hayes-Larson

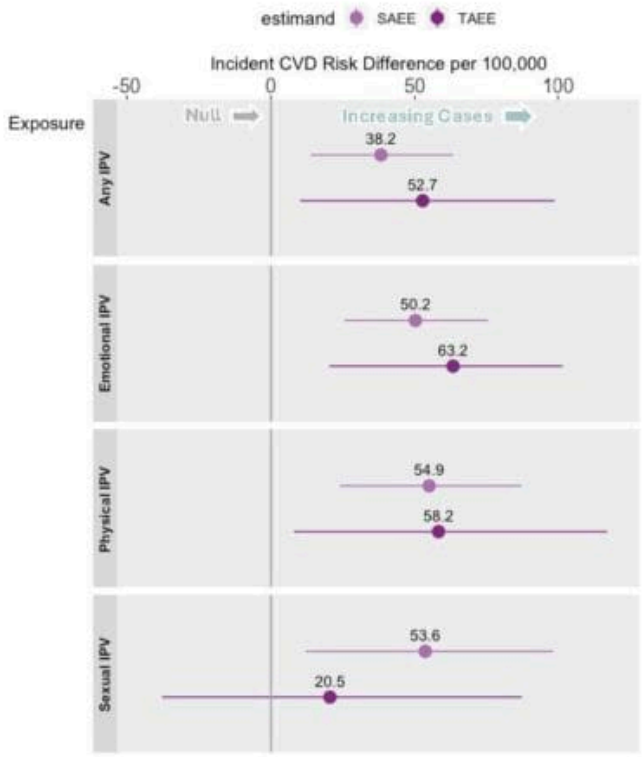
Background: Few population-based aging cohorts measure intimate partner violence (IPV). Transportability methods may facilitate extrapolation of results from selected observational cohorts to US nationally representative target populations. However, there has been little use of these methods in observational settings to date.

Methods: To obtain US population average effects of IPV victimization on incident stroke or myocardial infarction events (CVD), we used data from the Nurses' Health Study II (NHS2) and a US population survey-weighted sample, the Health and Retirement Study (HRS). The target population-average estimands included RRs and RDs of incident CVD (2001-2019), comparing individuals exposed and unexposed to IPV by 2001. We used inverse odds of selection weight (IOSW) estimators to transport sample average exposure effects, while accounting for confounding and censoring in NHS2.

Results: Compared to the weighted HRS (unweighted n=2,475; weighted n=16,998,380), NHS2 participants (n=64,615) were born earlier, more likely to be White, and higher socioeconomic status. IPV victimization was reported among 46.5% of NHS2 (42% emotional, 23% physical, and 11% sexual). If the entire NHS2 sample had been exposed versus unexposed to IPV victimization, risk of incident CVD would have been significantly higher (RR=1.23 (95% CI 1.08, 1.40) and RD=38/100,000 (95% CI: 14, 63)) over follow-up. After applying IOSW, if the entire US female target population was exposed versus unexposed to IPV victimization, magnitude of incident CVD risk would be slightly higher relative to NHS2 (RR=1.33 (95% CI: 1.05, 1.70) and RD=53/100,000 (95% CI: 10, 99)). Results were generally consistent across IPV subtypes (Figure 1) though CIs are wide.

Conclusions: Exposure to IPV victimization was associated with increased CVD risk in NHS2. The magnitude of associations generally increased when transporting estimates, but increased precision is needed for improved evaluation of differences.

Figure 1. Estimated study average exposure effects (SAEE) and target population average exposure effects (TAEE) of IPV experiences on incident CVD risk difference per 100,000 persons (2001-2019) using NHS2 (N=64,615)



Aging

Prevalence of subjective cognitive decline among the US Multiracial population, 2019-2023

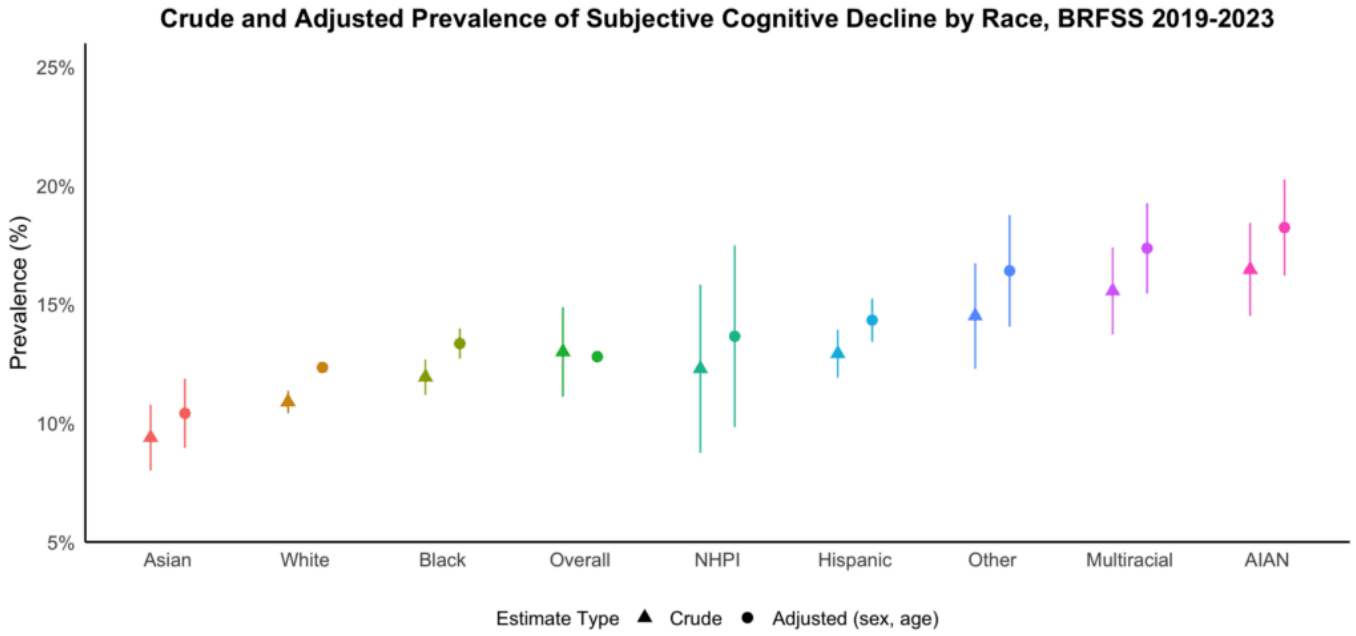
Tracy Lam-Hine* Tracy Lam-Hine Michelle C. Odden Bryan D. James David H. Rehkopf

Background: The prevalence of dementia and cognitive impairment in the growing US Multiracial population is unknown. Subjective cognitive decline (SCD), a self-reported measure of worsening memory, is a proxy for dementia risk. We compared SCD prevalence nationally between Multiracial adults and other racial groups.

Methods: We analyzed Behavioral Risk Factor Surveillance System (BRFSS) data from 52 US states and territories (2019–2023) among adults aged 50+ identifying as White, Black, American Indian/Alaska Native (AIAN), Asian, Native Hawaiian/Pacific Islander (NHPI), Other, Multiracial, or Hispanic. Weighted survey designs accounted for complex sampling, and Taylor linearization calculated standard errors (SEs) for adjusted prevalence. Logistic regression adjusted for age and sex. Multiply imputed and complete case analyses had similar results.

Results: Among 723,497 participants, overall crude prevalence of SCD was 12.8% (95% CI: 12.6%–13.0%). Crude prevalence was highest for AIAN (18.2%, 95% CI: 16.2%–20.3%) and Multiracial adults (17.4%, 95% CI: 15.5%–19.3%). Other groups ranged from 10.4% (Asian, 95% CI: 8.9%–11.9%) to 13.7% (NHPI, 95% CI: 9.9%–17.5%). Overall age- and sex-adjusted prevalence was 13.0% (95% CI: 11.1%–14.9%). AIAN adults had the highest adjusted prevalence (16.5%, 95% CI: 14.5%–18.4%), followed by Multiracial adults (15.6%, 95% CI: 13.7%–17.4%), Hispanic adults (13.0%, 95% CI: 11.9%–13.9%), and Black adults (11.9%, 95% CI: 11.2%–12.7%). Asian adults (9.4%, 95% CI: 8.0%–10.8%) and White adults 10.9% (95% CI: 10.4%–11.4%) had the lowest adjusted prevalence.

Conclusions: We provide the first estimates of SCD prevalence for the Multiracial population, revealing high rates comparable to AIAN adults. We could not disaggregate the Multiracial category using the publicly available BRFSS race data, a limitation. Future studies should examine cognitive impairment disparities in this group using clinical data and explore targeted preventive interventions.


Crude and Adjusted Prevalence of Subjective Cognitive Decline by Race, BRFSS 2019-2023
Prevalence (%)
25%
20%
15%
10%
5%
Asian
White
Black
Overall
NHPI
Hispanic
Other
Multiracial
AIAN
Estimate Type
Crude
Adjusted (sex, age)

Aging

The Impact of Crises on Delayed Healthcare Access Among Older Adults in Lebanon Mira Bekdache* Mira Bekdache Abla M Sibai Adina Zeki Al Hazzouri Amani Zaidan Martine Elbejjani

Background Delays in healthcare can have important consequences for morbidity and mortality risks, particularly among older adults, and these effects are exacerbated in contexts of crises and emergencies. During the COVID-19 pandemic, nearly one third of older persons reported postponing or forgoing necessary medical care. Lebanon, a low to middle-income country, faced the pandemic amidst multisectoral crises including a record financial collapse and the Beirut Blast, leading to immense strains on social protection and healthcare resources. This study aims to examine delays in healthcare among older adults in a polycrisis setting and to assess how various aspects of different crises (financial, pandemic, and security/humanitarian) influence these delays.

Methods Data come from a cross-sectional online survey (n= 576 individuals aged 50 and above). Delayed healthcare was evaluated across three subtypes: delayed doctor's visit, delayed medical test (laboratory, imaging, and any other medical test), and delayed operations. We used logistic regressions to assess the relation of delayed healthcare with various crises indicators, namely the pandemic (concerns about contracting the virus, physical/social distancing, and financial hardships), the Beirut Blast (occurrence of physical injury, home damage, business loss), and financial crisis impact (decreased income). We used multiple imputation by chained equations for missing data and logistic models included adjustment for relevant confounders including sociodemographic and socioeconomic factors, living conditions, and health-related factors.

Results 47.8% of older adults reported delaying a doctor visit, 31.5% had to delay medical tests, and 11.4% had to delay medical operations. The most self-reported reason for delays was financial difficulties (59%) and the most prevalent crisis-related difficulty was decreased income due to the financial crisis (88.95%). Adjusted analyses showed that decreased income due to the financial crisis was related to higher odds of delayed doctor visits and medical tests (OR=1.50, 95% CI: [0.93-2.41] and OR=1.87, 95% CI: [1.07-3.28], respectively). Business loss (due to the Beirut blast) was associated with higher odds of delaying a doctor's visit (OR=1.81, 95% CI: [1.02-3.22]) and pandemic related financial concerns were related to higher odds of delaying medical tests (OR=1.47, 95% CI: [1.00-2.16]).

Conclusion Results indicate that compounded crises have led to substantial delays in healthcare for older adults, with financial hardships being a predominant driver of delay across different crises indicators. Results emphasize the central role of improving financial support mechanisms for impacted populations and healthcare systems to mitigate the immediate and long-term impact of crises on health and health disparities.

Aging

Examining 20-year income volatility and 10-year memory decline in a longitudinal synthetic cohort. Katrina Kezios* Katrina Kezios Scott Zimmerman Peter Buto M. Maria Glymour Adina Zeki Al Hazzouri

Income volatility from young to middle adulthood predicts worse midlife cognition, but its impact on cognitive decline is unknown. Examining this association in a single cohort is difficult: few studies span early-adulthood to later-life, and those that do lack detailed, repeated, and prospective data on finances and cognition. To fill this gap, we created a synthetic cohort by linking two US national cohorts of baby boomers: the National Longitudinal Survey of Youth 1979 (NLSY79) and the mid-Baby Boomer Health and Retirement Study (HRS) subcohort. In NLSY79, we defined income volatility as the number of income drops >25% between successive surveys from 1990-2010 (0 vs. 1, 2, ≥3). In the HRS, we examined memory function every 2 years from 2010-2020 via a composite score that incorporated direct and proxy assessments. To create the synthetic cohort, each HRS participant was matched to and assigned the income volatility history of their 20 most similar NLSY79 counterparts based on the following matching variables measured in 2010 (when age~50 in each cohort) and harmonized: family income, memory score, education, age, sex, race/ethnicity, parental education, employer-provided health insurance, age first married, marital status, wealth, self-rated health, and chronic health conditions. Each of the 20 pairs for a given HRS participant was redistributed into 1 of 20 analytic datasets. In each dataset, we used confounder-adjusted linear mixed models to estimate the effect of income drops on 10-year memory decline, pooling results across datasets using Rubin’s Rules. In the synthetic cohort, experiencing more income drops was associated with faster memory decline in a dose-response fashion (β1_v_0_drops=-0.0015, 95% CI: -0.005, 0.002; β2_v_0_drops=-0.0035, 95% CI: -0.007, -0.0003; β3_v_0_drops=-0.0065, 95% CI: -0.009, -0.004). The synthetic cohort approach allowed evaluation of a novel question, but its validity depends on strong assumptions about matching across cohorts.

Aging

Association of depressive symptoms with cognitive decline in the presence of truncation by death among adults age 90+ Alexander Ivan B. Posis* Alexander Ivan B. Posis Hilary L. Colbeth L. Paloma Rojas-Saunero Ruijia Chen Rifat B. Alam Kristen M. George Paola Gilsanz María M. Corrada Rachel A. Whitmer

Background: Depressive symptoms are associated with faster cognitive decline and earlier mortality. This association is unclear among those aged 90+. We tested associations of depression with cognitive decline, while accounting for death as a truncation event, among the oldest-old.

Methods: Baseline depressive symptoms were assessed in the *LifeAfter90* Study (2018-2022) using the 15-item Geriatric Depression Scale (GDS) where greater scores suggest greater depressive symptoms. Executive function (EF), semantic memory (SM), and verbal episodic memory (VM) were measured every 6 months using the Spanish and English Neuropsychological Scales and z-scored to baseline. Time to all-cause mortality was calculated from time from enrollment to death. We fit linear mixed-effects (LME) models for cognitive outcomes. To account for death as a truncation event, we also fit joint models (JM) using LME and Cox proportional hazards submodels. All models adjusted for age, gender, race, ethnicity, and education.

Results: At baseline, the average age of the 944 participants was 92.4 (SD=2.4) with average baseline GDS score of 2.9 (SD=2.6). Mean follow-up time was 1.8 (SD=1.3) years and 26% died over follow-up. Overall, 23.5% of the sample identified as African American/Black, 23.9% as Asian, 17.5% as LatinX, 8.5% as Multiracial/Other, and 26.6% as White. Greater GDS was associated with a greater hazard of mortality (HR=1.10, 95% CI 1.05-1.14). Longitudinal results were similar for LME and JM. Every 1-point increase in GDS was associated with faster decline in EF (βLME=-0.02, 95% CI -0.02,-0.01; βJM=-0.01, 95% CI -0.02,-0.001), SM (βLME=-0.01, 95% CI -0.02,0.001; βJM=-0.01, 95% CI -0.02,-0.001), and VM (βLME=-0.01, 95% CI -0.02,0.001; βJM=-0.01, 95% CI -0.02,-0.003).

Conclusion: Greater depressive symptoms were associated with faster time to mortality and cognitive decline. Findings highlight the negative cognitive health consequences of depressive symptoms.

Environment/Climate Change

Wildfire smoke and fetal loss in California Dana Goin* Dana Goin Marianthi-Anna Kioumourtzoglou Tarik Benmarhnia Rachel Morello-Frosch Michael Leung Amy Padula

Background: Wildfires in California have been increasing in number and severity over the last several decades, and there is mounting evidence that they adversely affect reproductive health. However, there is a gap in the literature about the relationship between wildfire smoke and fetal loss.

Objective: To evaluate the effect of increased wildfire smoke during pregnancy on the rate of fetal loss using live birth-identified conceptions (LBIC).

Methods: We used California birth records from 2017-2019 and linked pregnancies to Census places using geocoded addresses. We estimated the week of conception for each birth and calculated the weekly count of LBICs for each Census place. We then linked this cohort of LBICs (identified by each Census place and week) to wildfire particulate matter (PM2.5) data for 40 weeks of pregnancy. We used a quasi-Poisson regression model with distributed lag terms to estimate the rate ratio of LBICs. We also estimated the fetal loss count difference (CD) using G-computation with nonparametric bootstrap for inference. We included weekly non-wildfire PM2.5 and temperature as confounders.

Results: For a given week of pregnancy, wildfire PM2.5 had a right-skewed distribution with a mean (SD) of 5.2 (33.2) µg/m3. Approximately 30% of the Census place-weeks had non-zero wildfire PM2.5 levels. We observed a reduction in livebirths and thus an increase in fetal loss associated with higher wildfire PM2.5 exposure. We identified three gestational periods for which associations were the strongest: weeks 1-3, 26-28, and 37-40 of pregnancy. We observed the largest effect estimates during gestational week 1 (RR=0.996, 95% CI 0.992, 1.000 ;and CD = 0.15, 95% CI 0.11, 0.22) and week 40 (RR = 0.995, 95% CI 0.991, 0.999; and CD=0.20, 95% CI 0.13, 0.31) associated with a 5 µg/m3 increase in wildfire PM2.5.

Conclusions: Wildfire smoke exposure, especially during gestational weeks 1-3, 26-28, and 37-40, is associated with an increased risk for fetal loss.

Environment/Climate Change

Prenatal exposure to phthalate mixtures and birthweight – Findings from an Ethnically Diverse U.S. Pregnancy Cohort (2010-2015). Shabnaz Siddiq* Shabnaz Siddiq Jeanette A. Stingone Andrew Rundle John Meeker Virginia Rauh Susannah Leisher Pam Factor-Litvak

Background: Prenatal exposure to phthalate metabolites (PthM) is widespread and may affect maternal-fetal health. This study investigates associations between a prenatal PthM mixture and birthweight in a diverse U.S. sample.

Methods: We analyzed 951 controls (without pregnancy complications) from a nested matched case control study embedded in the Nulliparous Mothers to Be Study who provided 1-3 urine samples (total n=2723) throughout pregnancy. Eleven PthM were measured. . Birthweight (in grams) was recorded at delivery. Bayesian Weighted Quantile Sum (BQWS) regression estimated associations between PthM mixtures and birthweight, with stratification by maternal BMI and race/ethnicity and infant sex.

Results: Mean infant birthweight was 3393.8g (SD=473.9g). Each quartile increase in PthM mixture was associated with lower infant birthweight (β = -72.9g, 95% CI -116.6, -28.5), with Mono-isobutyl phthalate (MiBP) (weight (w) = 0.18), Monoethyl phthalate (MEP) (w = 0.18), and Monobenzyl phthalate (MBzP) (w = 0.10) contributing most to the mixture's effect. Among underweight/normal weight women, increase in the mixture was associated with a -85.3g (95% CI: -137.0, -35.9) decrease in infant birthweight. The decrease was -71.3g (95% CI: -128.6, -14.5) for women carrying female infants and -45.8g (95% CI: -101.2, 9.6) for women carrying male infants. Among infants born to Non-Hispanic White women, the decrease in birthweight was -71.8g (95% CI: -125.5, -19.6); -52.4g (95% CI: -110.7, 5.9); for infants born to Hispanic women; and -36.2g (95% CI: -90.8, 18.4) for infants born to Non-Hispanic Black women. MBZP and MiBP played prominent roles in the stratum-specific results.

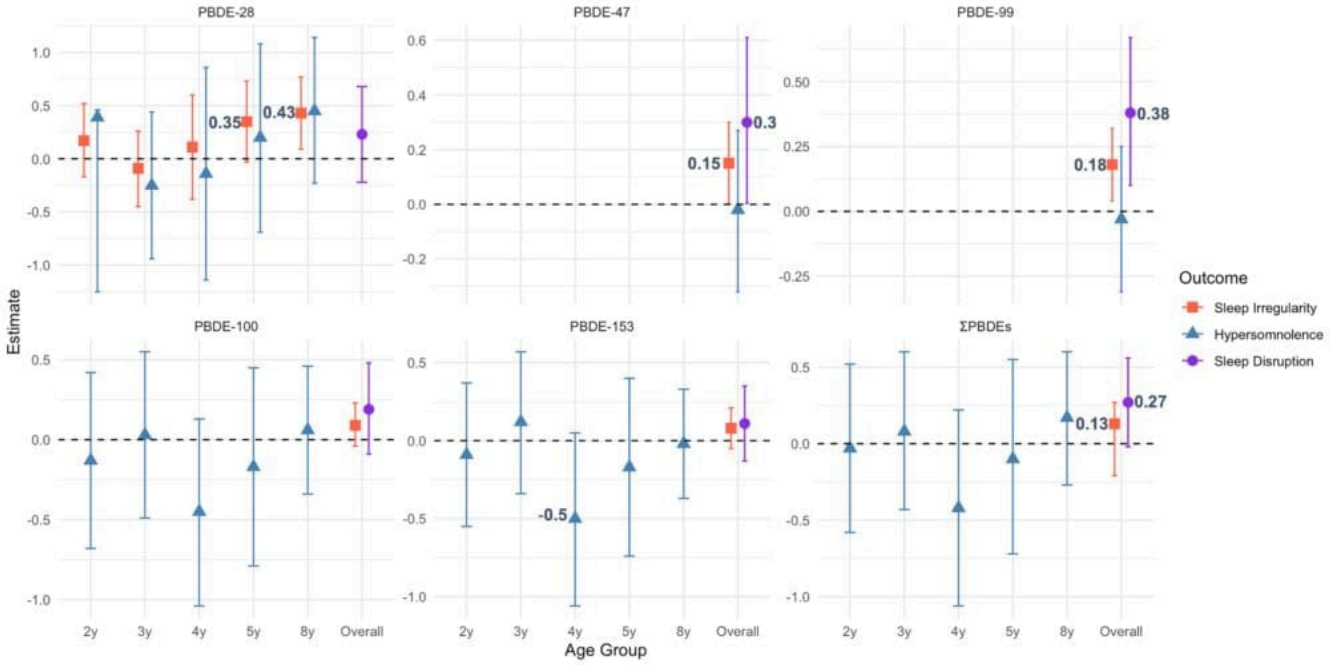
Conclusions: The findings suggest that prenatal exposure to a PthM mixture decreased infant birthweight, with MiBP and MBZP playing important roles. Given the pervasiveness of phthalate exposure, even modest decreases in average infant birthweight could have significant population-level impacts.

Environment/Climate Change

Gestational Polybrominated Diphenyl Ether (PBDE) Concentrations and Sleep Patterns in Children Kelli Williams* Kelli Williams Jagadeesh Puvvula John Holmes Wei Yang Sigrid Veasey Jianghong Liu Kimberly Yolton Kim M. Cecil Yingying Xu Joseph M. Braun Bruce P. Lanphear Clara Sears Ann M. Vuong Andreas Sjödin Aimin Chen

Gestational polybrominated diphenyl ethers (PBDEs) exposures have been associated with thyroid disruption in pregnant women and adverse neurobehavioral outcomes in their children, but it is unknown if they interfere with children's sleep patterns. We assessed gestational PBDE exposure (16 weeks) and child sleep patterns from ages 2 to 8 years using 410 mother-child dyads in the Health Outcomes and Measures of the Environment (HOME) Study. Gestational biomarkers of serum PBDEs include PBDE-153 (GM±GSD: 5.2±2.8 ng/g lipid), PBDE-100 (4±2.6), PBDE-99 (4.6±2.7), PBDE-47 (20.2±2.6), PBDE-28 (1.3±2.2), and ∑PBDEs (37.03±2.52). We measured child sleep patterns using the adapted Child Sleep Health Questionnaire, which measures sleep irregularity (mean±SD: 2.5±0.8), hypersomnolence (4.7±1.5), sleep disruption (6.7±1.6), and sleep duration. We assessed longitudinal associations between gestational PBDEs and sleep patterns using generalized estimating equations, adjusting for covariates. For PBDE-visit interactions ($p < 0.1$), visit-specific estimates with 95% CIs were calculated; otherwise, the overall estimate was reported. Every 10-fold increase in PBDE-99 (β=0.18, 95% CI: -0.04, 0.23), PBDE-47 (0.15, 95% CI: 0.001, 0.3) and ∑PBDEs (0.13, 95% CI: -0.21, 0.27) was associated with increased sleep irregularity for all years, and PBDE-28 was associated with this outcome at age 5 and 8 years. PBDE-153 (-0.5, 95% CI: -1.06, 0.05) was associated with decreased hypersomnolence at age 4 years. PBDE-47 (0.3, 95% CI: 0.004, 0.61), PBDE-99 (0.38, 95% CI: 0.1, 0.67 and 0.62), and ∑PBDEs (0.27, 95% CI: -0.02, 0.56) were associated with increased sleep disruption for all ages. We observed no significant associations between PBDEs and sleep duration. We found that gestational PBDEs were associated with sleep irregularity, hypersomnolence, and sleep disruption in children, highlighting the need to explore sleep as a mediator of PBDE-associated neurobehavioral problems.

Adjusted differences and 95% CI of child sleep outcomes at 2-8 years by a 10-fold increase in gestational PBDE concentrations



*Adjusted covariates: Serum Cotinine, Blood Lead, Child Sex, Child Race, HH Income, Marriage Status, Maternal IQ, HOME Inventory Score, Age at Delivery, Parity, Breastfeeding Status, Baseline Beck Depression Inventory (BDI), Baseline region, Neighborhood Deprivation Index (NDI) at Birth

*If interaction term had $p<0.1$, we performed linear combination to calculate visit-specific estimates and 95% CI. If interaction term has $p \geq 0.1$, dropped interaction term, and reported regression estimate as the overall effect

-Estimates are provided for significant and marginally significant p-values

Environment/Climate Change

Prenatal and early childhood exposure to biothermal stress and developmental vulnerability at school entry: A population-based study in Western Australia Kendalem Atalell* Kendalem Atalell Gavin Pereira Bereket Duko Sylvester Nyadanu Gizachew Tessema

Backgrounds: Evidence shows that temperature is rising across Australia and globally, increasing biothermal stress. However, the impact of prenatal and childhood exposure to adverse biothermal stress, measured by the Universal Thermal Climate Index (UTCI), on early childhood developmental vulnerability remains unclear. This study examined the long-term effect of biothermal stress on early childhood developmental vulnerability at school entry.

Methods: A population-based retrospective cohort study of 59,771 children from the 2009-2015 Australian Early Development Census (AEDC) was used to investigate the role of biothermal stress on early childhood developmental vulnerability. Biothermal stress, measured using the Universal Thermal Climate Index (UTCI), was spatiotemporally linked to maternal residential addresses at the statistical area 1 (SA1) level. The UTCI incorporates air temperature, wind speed, humidity, and solar radiation. The average UTCI exposure from conception to the census date was calculated for each child. Exposure during pregnancy and childhood was also separately assigned to everyone. Mixed-effect logistic regression models examined the association between developmental vulnerability and biothermal stress levels.

Result: After adjusting for confounders, children exposed to long-term heat stress (>26°C) had 29% higher odds of being developmentally vulnerable in at least one developmental domain (DV1) compared to those exposed to optimal thermal conditions (9–26°C) (OR: 1.29; 95% CI: 1.05–1.58). Prenatal exposure to heat stress was associated with a 34% higher likelihood of DV1 than optimal thermal conditions exposure (OR: 1.34; 95% CI: 1.10–1.65).

Conclusion: Exposure to heat stress during and after pregnancy was associated with an increased risk of developmental vulnerability, with particularly significant effects observed in pregnancy. Policymakers and healthcare providers may prioritise creating supportive environments for pregnant individuals and young children, integrating heat exposure considerations into maternal and child health strategies.

Environment/Climate Change

Air Pollution Exposure and Blood Pressure in Children of the NIH ECHO Consortium Yu Ni* Yu Ni Catherine Karr Miranda Jones Andrew Law Xingyu Gao Arpita K. Vyas Ruby Nguyan Mingyu Zhang Hooman Mirzakhani Assiamira Ferrara Alicia K. Peterson Judy Aschner Scott Collingwood Margaret R. Karagas Tom O'Connor Michelle Katzow Annemarie Stroustrup Mehtap Haktnair Tina V. Hartert Brittney M. Snyder Sophia Jan Anne Marie Singh Anne Marie Singh Dana Dabelea Angela M. Malek Jennifer K. Straughen Carlos. A. Camargo, Jr. Miatta A. Buxton Rosalind Wright Kecia Carroll Keia Sanderson Daphne Koinis Mitchell Viren D'Sa Christine Hockett Anne L. Dunlop Shohreh Farzen Alison Hipwell Sunni L. Mumford Akram N. Alshawabkeh Hudson P. Santos Jr Christine T Loftus Adam Szpiro Sindana Ilango Logan C Dearborn Allison Sherris Kaja LeWinn Nicole Bush Qi Zhao Marnie Hazlehurst Akhgar Ghassabian Anne Starling

Background: There is growing interest in linking early life exposures to ambient air pollution to child blood pressure; however, existing findings, largely from single site or cohort studies, are inconclusive.

Methods: We examined the association between exposures to two ambient air pollutants – fine particulate matter (PM2.5) and nitrogen dioxide (NO2) – and blood pressure in 4,863 U.S. children from 20 study sites of the NIH ECHO Cohort. Point-based residential exposures were derived from spatiotemporal models with a biweekly resolution and averaged over each trimester, the whole pregnancy, and in offspring at aged 0-2 years. We converted systolic (SBP) and diastolic blood pressure (DBP) to age-, sex-, and height-specific percentiles and classified children with SBP and/or DBP 90th percentile as high blood pressure (HBP). Linear and Poisson regressions were fitted to estimate the associations of PM2.5 (per 5-g/m3) or NO2 (per 10-ppb) exposures in each window with BP percentiles and HBP, adjusting for sociodemographics, lifestyle factors, and temporal and spatial confounders.

Results: Mean PM2.5 ranged from 7.6 to 7.9 g/m3 across windows, while mean NO2 ranged from 8.1 to 8.8 ppb. We found positive associations of PM2.5 in the first trimester with SBP percentile (: 1.92, 95%CI: 0.02, 3.83) and risk of HBP (RR: 1.16, 95%CI: 1.02, 1.33). Results also indicated that higher PM2.5 exposures averaged over pregnancy and age 0-2 years were related to elevated SBP percentiles and a higher risk of HBP, but with lower precision. Contrary to our hypotheses, inverse associations of pregnancy average NO2 averaged with both SBP (: -2.42, 95%CI: -4.70, -0.14) and DBP (: -1.94, 95%CI: -3.81, -0.08) percentiles were suggested.

Conclusion: The study provides evidence reinforcing the detrimental effects of PM2.5 on childhood cardiometabolic health. There remains a need in future research to understand the counterintuitive inverse association between NO2 and blood pressure.

Environment/Climate Change

Effects of metal mixtures on thyroid function in Bangladeshi children aged 5 to 7 years: Evidence from the BiRCH cohort Yingyue Ni* Yingyue Ni Syed Emdadul Haque Tariqul Islam Mohammad Hasan Shahriar Golam Sarwar Alauddin Ahmed Farzana Jasmine Muhammad G Kibriya Habibul Ahsan Maria Argos

Studies have demonstrated the adverse impact of metals on thyroid function. However, limited research has evaluated this relationship in children despite the importance of thyroid hormones during this stage of development. This study aims to investigate the cross-sectional associations of metal co-exposures on thyroid function in 496 children aged 5 to 7 years participating in the Bangladesh Environmental Research in Children's Health (BiRCH) cohort. Linear regression models were used to estimate the individual associations of 17 toenail metal concentrations with free thyroxine (FT4), adjusted for potential confounding by sex, age, body mass index and second-hand smoke exposure. Weighted Quantile Sum (WQS) regression was conducted to evaluate the joint effect of the metal co-exposures. Arsenic, zinc, selenium, and cadmium were individually positively associated with FT4 levels (arsenic β=0.03, 95% CI: 0.01, 0.05; zinc β=0.06, 95% CI: 0.01, 0.11; selenium β=0.10, 95% CI: 0.03, 0.17; and cadmium β=0.02, 95% CI: 0.00, 0.04), while mercury was inversely associated (β=-0.05, 95% CI: -0.07, -0.02). In WQS regression, we observed an association with the positive metal mixture index on FT4 (β=0.06, 95% CI: 0.02, 0.10), primarily driven by selenium, arsenic, and zinc. This study provides evidence of early-life associations of metal exposures on thyroid function based on FT4 in children. Further research is needed to elucidate the mechanisms underlying these associations and the potential long-term health impacts across the life course.

Social

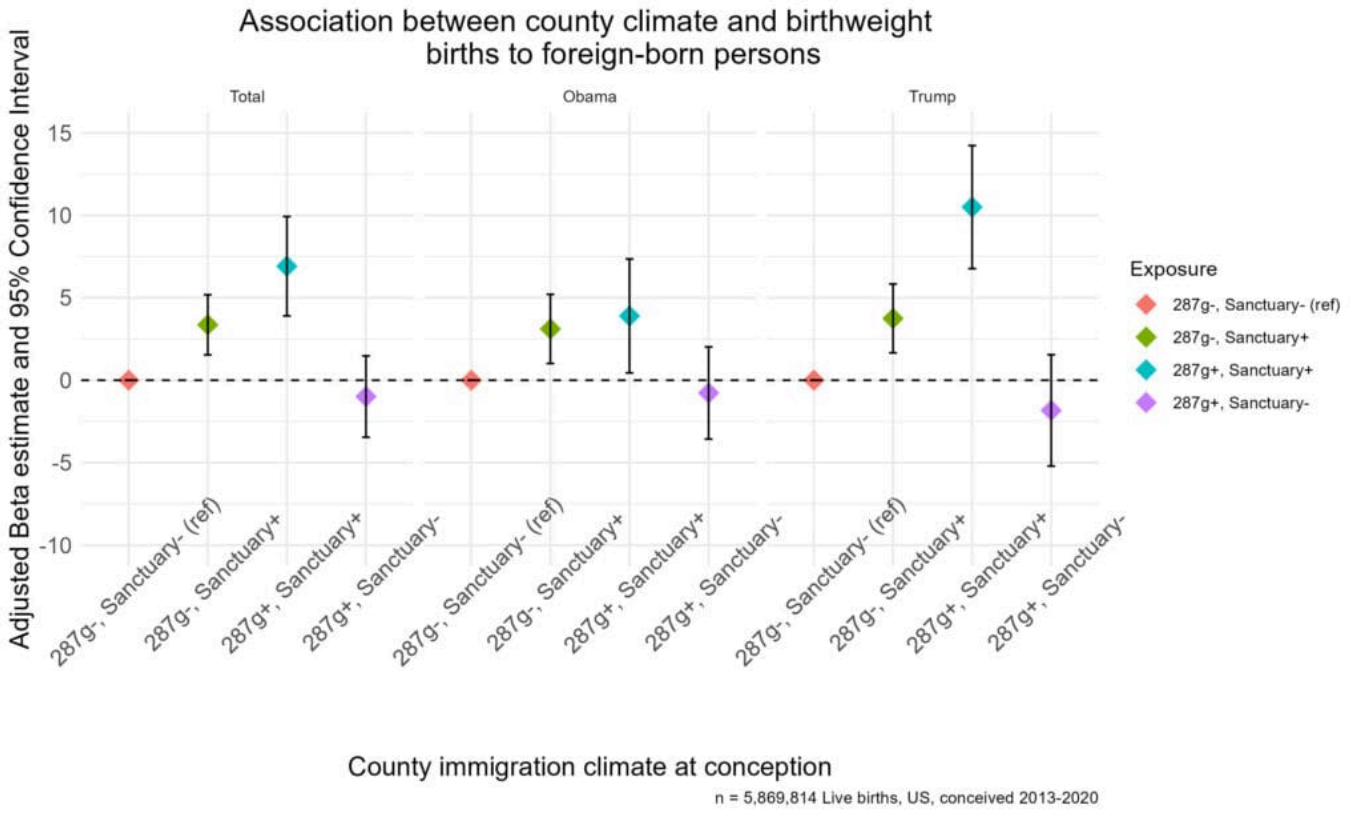
Understanding the impact of county immigration climate on birthweight among immigrant birthing people across restrictive and supportive federal and state immigration policy climates Kaitlyn K Stanhope* Kaitlyn Stanhope Margot Moinester

Goal: While a growing body of work shows impacts of state policies on immigrant health, only limited research examines local climates. Our goal was to quantify the effect of county immigration policy climate on birthweight and determine whether the effect was modified by overarching state or federal climate among foreign-born birthing people, 2012-2020.

Methods: We used data from the U.S. restricted use natality files, 2012 to 2020, linked to county- and state-level characteristics using resident county and birth year. We create a joint exposure based on the presence of a 287g agreement with Immigration Customs Enforcement and/or sanctuary policy active in the county at the time of delivery. We fit multivariable linear models including random effects for state, parity, age, insurance, race/ethnicity, year, county rurality, poverty, percent foreign-born, percent unemployed, percent with a high school education, and percent of households below federal poverty level. We examined potential effect modification by state climate (measured using the Immigration Policy Climate score, in quartiles) or federal climate (Obama’s (2012-2015) vs. Trump’s presidency (2016-2020)) by including multiplicative interaction terms.

Results: We included 6,033,418 births to foreign born birthing people. Living in a county with a sanctuary policy was associated with increased birthweight compared to a county without a sanctuary policy, both without and with a 287g policy in place (adjusted beta: 3.4, 95% confidence interval: (1.5, 5.2); 6.9, (3.9, 9.9), respectively). The estimates were stronger during the Trump presidency. There were not differences by state climate.

Conclusions: These results do not support the hypothesis that county climates can buffer against restrictive state or federal climate. However, they do support the role of counties in impacting immigrant health, possibly uniquely through passing inclusively policies in otherwise restrictive state and federal climates.


Association between county climate and birthweight
births to foreign-born persons
Total
Obama
Trump
Adjusted Beta estimate and 95% Confidence Interval
15
10
5
0
-5
-10
287g-, Sanctuary- (ref)
287g-, Sanctuary+
287g+, Sanctuary+
287g+, Sanctuary-
Exposure
287g-, Sanctuary- (ref)
287g-, Sanctuary+
287g+, Sanctuary+
287g+, Sanctuary-
County immigration climate at conception
n = 5,869,814 Live births, US, conceived 2013-2020

Social

The 2021 Child Tax Credit expansion and perinatal health: a quasi-experimental study Rita Hamad* Rita Hamad Deborah Karasek Daniel F. Collin Justin S. White Guangyi Wang

Objective: Poverty alleviation policies play an important role in mitigating socioeconomic and racial/ethnic disparities in perinatal health. The 2021 temporary expansion of the Child Tax Credit (CTC) provided monthly payments of up to $300 per child during July-December 2021 and allowed the most economically disadvantaged families to qualify. It has been linked to decreased material hardship and food insecurity, but few studies have examined effects on perinatal health. The goal of this study was to estimate impacts of the 2021 CTC expansion on perinatal health, including differences among minoritized populations.

Methods: Data were drawn from national birth certificate files (January 2021-February 2022; N=3,487,943) and the Pregnancy Risk Assessment Monitoring System (PRAMS; January-December 2021; N=28,874). Using quasi-experimental difference-in-differences analyses in each data set, we compared changes in perinatal outcomes before versus after the 2021 CTC expansion for CTC-eligible versus ineligible individuals. Outcomes included gestational hypertension, gestational diabetes, birthweight, preterm birth (<37 weeks' gestation), low birthweight (<2,500 grams), small-for-gestational-age (SGA), and large-for-gestational-age (LGA).

Results: In birth certificates, the CTC expansion was associated with reduced birthweight (-5.54 grams, 95%CI: -7.83, -3.25) and reduced LGA births (-0.26 percentage points, 95%CI: -0.38, -0.14). In PRAMS, the CTC expansion was associated with reduced SGA (-2.77 percentage points, 95%CI: -4.99, -0.55). There was no association for other outcomes. Among subgroups, individuals without Medicaid had decreased birthweight; individuals with lower education, Medicaid, and those who were unmarried had reduced SGA births.

Conclusions: The 2021 CTC expansion was associated with improvements in birthweight distribution, perhaps due to decreased financial insecurity, with more positive impacts on SGA among those of lower socioeconomic status.

Social

Caste-based social inequalities in child undernutrition in India: exploring the role of environmental and health services interventions using mediation analyses Arijit Nandi* Arijit Nandi Sam Harper

Child undernutrition has improved in India over the past 30 years, but social inequalities persist. Children from historically disadvantaged groups, including those designated by the Indian Government as belonging to a scheduled caste (SC), scheduled tribe (ST), or other backward caste (OBC), have higher rates of stunting, wasting, and underweight than other children. Mediation analysis can help to identify interventions for eliminating these inequalities.

Using a sample of 490,986 under 5-year-old children born between 2010-2020 and included in the Indian National Family Health Survey, we quantified caste-based inequalities in stunting, wasting, and underweight, defined using measured height and weight. We then used marginal structural models with inverse probability weights (IPWs) to examine if two distinct potential interventions, increasing coverage of delivery in a health sector facility with assistance from health personnel and improved household drinking water and sanitation facilities, mitigated these inequalities.

82.6% of children belonged to a SC, ST, or OBC, and 37.0% of children were stunted, 19.5% were wasted, and 32.8% were underweight. The prevalence of stunting, wasting, and underweight were 8.6 (95%CI: 8.2, 9.0), 2.7 (95%CI: 2.3, 3.0), and 8.1 (95%CI: 7.7, 8.5) percentage-points higher, respectively, among children belonging to a SC, ST, or OBC compared to those who did not, representing the total effects. Mediation models using IPWs to estimate controlled direct effects (CDE) on the prevalence difference scale showed that setting coverage of the interventions to 100% eliminated nearly one-half of the inequality for wasting (CDE=1.3, 95%CI=-0.6, 3.2 for health facility delivery; CDE=1.3, 95%CI=-0.5, 3.2 for improved water and sanitation), but had a minimal effect on disparities in stunting and underweight. Results were compared to analyses using the “product method” and randomized intervention analogues to natural direct and indirect effects.

Social

Heat-Related Mortality among Incarcerated Individuals in Texas Jails, 2013–2023 Shreya Patel* Shreya Patel Jaquelyn L. Jahn

The relationship between heat and mortality is well-established in the general population, but research examining heat-related mortality among incarcerated individuals remains limited, particularly among those who are confined in local jails. Incarcerated people have very limited control over their thermal environment, outdoor time, ventilation, and healthcare, contributing to elevated risk of heat-related mortality.

In this study we explored the effect of heat during summer months on mortality in Texas jails between 2013-2023. We obtained daily maximum temperature data at 4 km × 4 km resolution from the PRISM Climate Group and linked it using date and location coordinates with publicly available individual-level data on all deaths in custody from the Texas Justice Initiative. We used a distributed lag model to estimate the 10-day cumulative association between daily maximum temperature (90th, 95th, 97.5th, and 99th percentiles of the maximum temperature distribution) and mortality, with fixed effects for jail facility, month, and year.

Among 797 in-custody jail deaths (excluding deaths during arrest), 359 occurred during summer months (May-September). The study population was predominantly male (85%), with a mean age of 45 years. Findings indicated a clear dose-response association between heat and mortality. Compared to days with a maximum temperature of 20°C, the risk of death was 2.7 times higher at 37.7°C (95% CI: 1.18, 6.22), 2.88 times higher at 38.8°C (95% CI: 1.19, 6.99), 3.05 times higher at 39.8 °C (95% CI: 1.20, 7.76) and 3.25 times higher at 41°C (95% CI: 1.21, 8.71) across ten-day lag periods.

These findings suggest that higher temperatures are significantly associated with mortality among incarcerated people in Texas. Despite existing legislation mandating Texas jails be kept between 65-85 degrees Fahrenheit, these results indicate that facilities incarcerated individuals may still be vulnerable to high ambient temperatures in these settings.

Social

Social Isolation and Cognitive Aging: Are Operational Definitions Creating a Reproducibility Crisis? Ruijia Chen* Ruijia Chen Dylan Tran Jingxuan Wang Peter T. Buto Erin Ferguson Mary Thoma Scott Zimmerman Ashwin Kotwal Jacqueline M. Torres M. Maria Glymour

A substantial body of research on the impact of social isolation on health has emerged; however, conflicting findings are common, even when using the same data. Discrepancies may arise from methodological choices, including operationalization of social isolation. We conducted multiverse analyses to investigate how varying definitions of social isolation influence associations with cognitive function and decline.

Using the 2010 to 2020 Health and Retirement Study (n=12,975), social isolation was defined using 16 items related to marital status, living arrangements, social interaction frequency, and participation in social activities. We created continuous and binary composite scores for social isolation based on all possible combinations of these items (n=196,587 combinations), using top tertile and quartile cutoffs for the binary definitions. Cognitive function was assessed by the Telephone Interview for Cognitive Status, with scores standardized to baseline mean and SD. Linear mixed-effects models evaluated associations of each definition with cognitive level and decline.

Across all model choices, most models suggested a negative association between social isolation and level of cognitive function: point estimates ranged from very large to close to the null (e.g. associations with binary social isolation measures ranged from -0.31 to 0.01 SD of average difference across all binary social isolation specifications, see Figure). Most models indicated that social isolation was associated with faster cognitive decline (e.g. from -0.001 to 0.03 standard deviations average annual difference across the range of binary social isolation specifications).

While social isolation appears associated with lower levels of cognitive function and faster cognitive decline, the magnitude of these associations varies widely depending on how social isolation is defined.

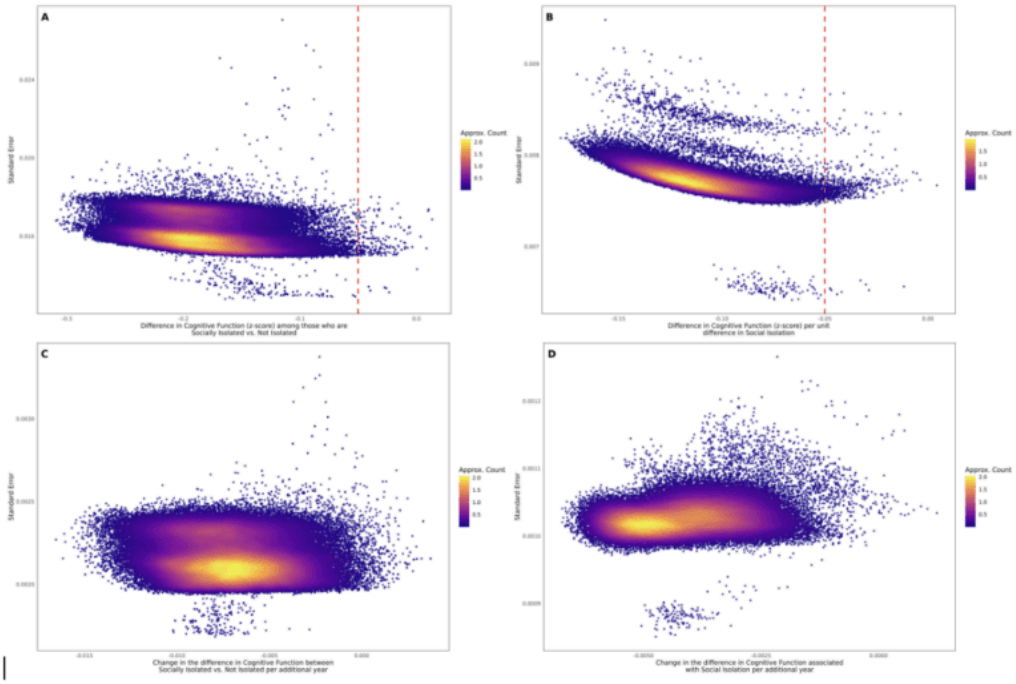


Figure. Scatter plots of the associations of social isolation with level and decline in cognitive function across multiverse analyses. Each dot represents the result of a single model, with the x-axis displaying the estimated coefficients and the y-axis representing the associated standard errors. The top two plots show the estimated coefficients of social isolation in binary (left) and continuous (right) forms for levels of cognitive function. The bottom two plots display the coefficients of the interaction terms between social isolation (binary on the left and continuous on the right) and time. For the models examining cognitive decline, time since baseline was used as the time scale, and models were adjusted for age, sex, race, education, and their interactions with time. The red dashed line represents the average difference in cognitive function scores by age.

Social

Who is lonelier? An Age-Period-Cohort and Generational Analysis Rosanne Freak-Poli*
Rosanne Freak-Poli Haoxiong Sun Trong-Anh Trinh

When taking office, Surgeon General Murthy heard “if I disappear tomorrow, no one will even notice” repeatedly. Murthy has declared loneliness in America an “epidemic,” identifying it as a root cause contributing significantly to numerous social issues. Unfortunately, the USA is not alone, with the World Health Organization also declaring loneliness a ‘global public health concern’.

Aim

To investigate patterns of loneliness and social isolation across age, period, cohort and generations in a nationally representative longitudinal cohort.

Methods

We use 19 annual waves of data from the Household, Income and Labour Dynamics in Australia (HILDA) Survey, incorporating 337,630 participants aged 15 years and older between 2001 and 2022. Age-Period-Cohort and generational differences in loneliness (≥5/7 for “I often feel very lonely”) and social isolation (meeting friends/relatives outside household ≤2-3 times monthly and being single) were analyzed using logistic regression with $p<0.05$.

Results

Women reported greater loneliness (mean±SD 13%±34 vs 11%±31) and lower social isolation than men (28%±45 vs 29%±45). AGE: Loneliness was greatest among older adults (>18% prevalence) but also high for women aged 15-20 years. Social isolation was greatest for ages 40-60 years (>40%), and for men these high rates continued into later life. PERIOD: Loneliness prevalence decreased from 2001 (13.5%) to 2009 (10.5%), and then increased by 2022 (13.8%). Social isolation steadily increased across the observation period from 24.5% to 35%. Patterns were similar across binary gender. COHORT: More recent birth cohorts report less loneliness and less social isolation, which were consistent across genders. GENERATION: Generational and gender differences in loneliness and social isolation were observed across age groups (Figure).

Discussion

The high rates of loneliness and social isolation are concerning, especially social isolation which is increasing over time with no plateau observed.

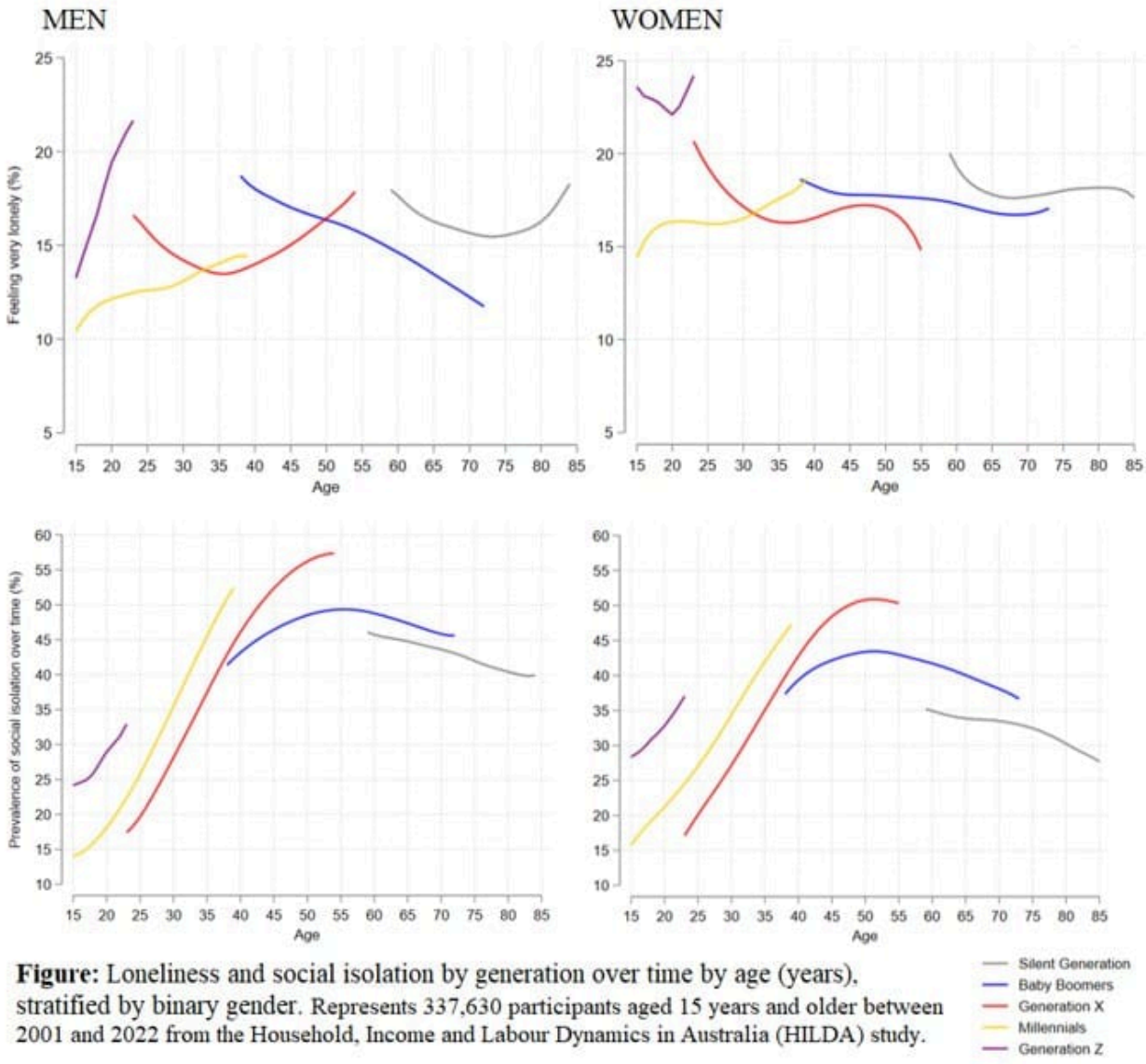


Figure: Loneliness and social isolation by generation over time by age (years), stratified by binary gender. Represents 337,630 participants aged 15 years and older between 2001 and 2022 from the Household, Income and Labour Dynamics in Australia (HILDA) study.

HIV / STI

Geographic changes in drive time access to pre-exposure prophylaxis (PrEP) in the United States, 2017 to 2024 Noah Mancuso* Noah Mancuso Patrick Sullivan

Background: HIV incidence has fallen drastically in the US in the past decade. However, disparities in uptake of pre-exposure prophylaxis (PrEP) – an HIV prevention drug – exist among several minority populations. Studies have found associations between lower geographic accessibility of PrEP and reduced uptake, which is important given new formulations – like injectable PrEP – require bimonthly administration in-person. Our objective was to assess current drive times to the nearest PrEP provider in each county in the contiguous US and examine changes since the last national analysis (2017).

Methods: Data on PrEP providers was obtained from PrEPLocator. Geospatial analyses calculated the shortest one-way drive time between population-weighted centroids and providers. Counties with drive times >30 minutes were defined as PrEP deserts. Linear regression with natural cubic splines was used to assess differences in drive time by urbanicity controlling for median income, region, and proportion of men who have sex with men (MSM) and racial/ethnic minorities.

Results: Among 3108 counties, median drive time in 2024 was 30.2 minutes, which increased as urbanicity decreased (p-value <0.05). Roughly half (49%) of all counties were PrEP deserts (**Figure 1**), accounting for 37 million people and 40% of all PrEP-eligible MSM. Drive times in micropolitan/non-metro counties in 2024 were 5-8 times as high as larger metro areas. Between 2017 and 2024, drive time decreased by 29.5 minutes. Predominantly due to lower initial (2017) drive times, the magnitude of change in drive times significantly decreased as urbanicity increased (p-value <0.01).

Conclusions: Most counties have seen sizable reductions in drive time to the nearest PrEP provider. Nonetheless, the ongoing concentration of providers in urban areas has led to persistence of the urban-rural divide. Programs and policies must prioritize expanding PrEP provider access to less urban areas to end the HIV epidemic in the US.

HIV / STI

Pre-exposure prophylaxis accessibility beyond driving: a case study of Dallas-Fort Worth, Texas Hui Luan* Hui Luan

Spatial accessibility to pre-exposure prophylaxis (PrEP) is associated with PrEP uptake. Existing studies, however, predominantly use driving time or distance to measure PrEP accessibility. Those measures are not optimal from a health equity perspective. Not all people have access to private transportation, and communities at high risk for HIV infections may be more likely to rely on public transit. This study compares driving- and public transit-based PrEP accessibility and relate public transit accessibility with social determinants of health (SDOH) variables in Dallas-Fort Worth, Texas at the Zip Code Tabulation Area (ZCTA) level using Bayesian spatial statistical modeling. Results indicate that disparities exist between driving and public transit travel time to access PrEP providers. By public transit, residents in ZCTAs with higher socioeconomic deprivation or higher HIV risk are more likely to have access to PrEP providers within 30 minutes. In contrast, residents in ZCTAs with higher percentages of Black or Hispanic populations were less likely to have access to PrEP providers within 30 minutes by public transit. Six ZCTAs warrant special attention, because they are in the highest tertile of new HIV diagnosis risks, socioeconomic deprivation, and travel time to the nearest PrEP provider by public transit (>60 minutes). It is insufficient to evaluate PrEP accessibility by driving only. Accounting for different transportation modes in PrEP accessibility is warranted to identify areas most in need of interventions. The Dallas-Fort Worth area should continue its efforts to improve PrEP accessibility to areas with higher percentages of Black and Hispanic populations.

HIV / STI

Experiences of housing instability, HIV, and mortality among transgender women in the United States: a multistate analysis of prospective cohort data from the LITE study Dorothy Apedaile* Dorothy Apedaile Sari L Reisner Erin Cooney Tonia Poteat Susan Bondy Amaya Perez-Brumer Andrea L Wirtz on behalf of the American Cohort to Study HIV Acquisition Among Transgender Women (LITE) Study Group

Housing insecurity among transgender women can be highly dynamic, with individuals moving between housing stability and instability. Unstable housing can lead to serious health issues, including HIV acquisition and mortality. This analysis uses multistate modelling to estimate the probability of transitions between states of stable housing, unstable housing, and HIV seroconversion or death among transgender women in the United States. A total of 725 HIV-negative transgender women were enrolled in a prospective cohort study from March 2018 to May 2020 in 6 cities across the eastern and southern United States. Participants completed surveys and HIV testing every 3 months for up to 2 years, contributing 1078 person-years of follow up time. Participants were censored at death or HIV seroconversion. Housing instability was defined as experiencing homelessness in the past 3 months. Multi-state models under a time-homogenous Markov assumption were used to estimate the probability of transition between states, presented over 6-month periods. Confidence intervals were estimated using 1000 bootstrap replications. At enrollment, the median age of participants was 29 (IQR: 24-37), 45% had experienced lifetime homelessness, and 11% were currently experiencing housing instability. Over follow up, 6 participants died, 7 acquired HIV, and 169 (23%) experienced housing instability at least once. Participants who were unstably housed had a 57.2% (95% CI: 50.2%-63.7%) probability of being housed at the end of 6 months and a 2.1% (95% CI: 0.3%-4.3%) probability of dying or acquiring HIV while participants who were stably housed had only a 0.4% (95% CI: 0.2%-0.8%) probability of death or HIV seroconversion after 6 months. These results demonstrate housing instability is highly dynamic among transgender women and multistate modelling can be used to better understand changes in housing status. Furthermore, interventions to improve housing stability are needed to prevent HIV and mortality.

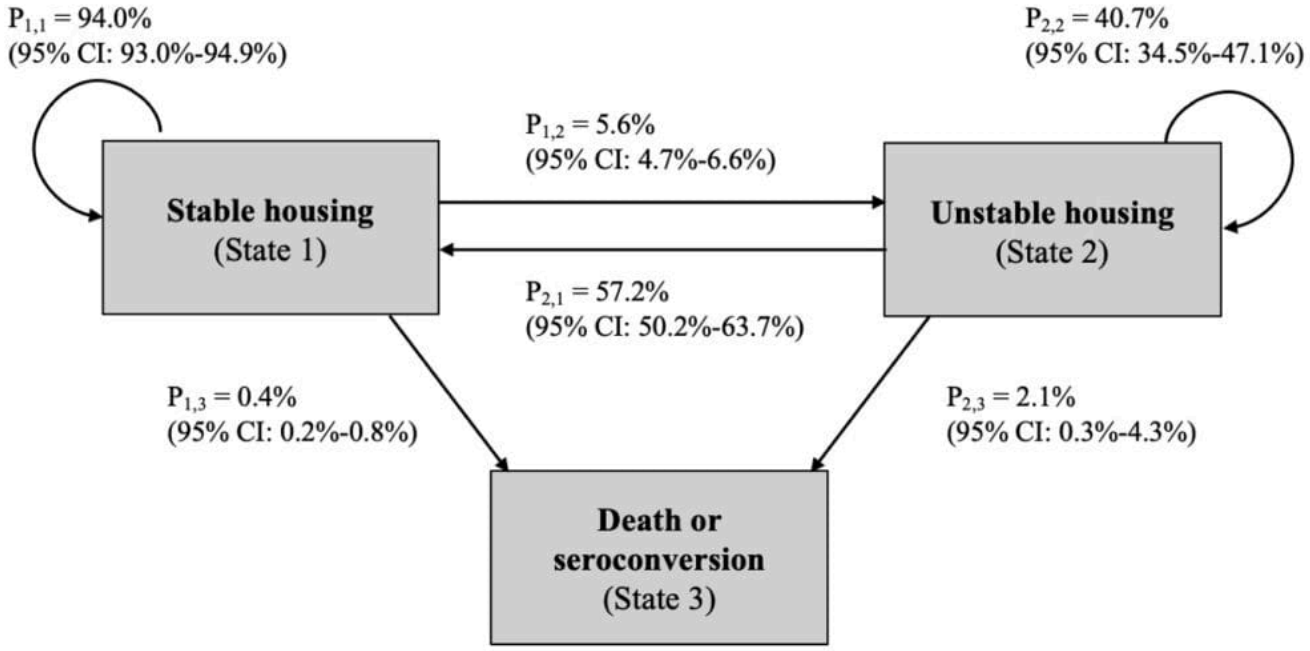


Figure 1: 6-month transition probabilities between states of stable housing, unstable housing, and death or HIV seroconversion among transgender women in the United States

HIV / STI

The impact of intimate partner violence and relationship safety on HIV care engagement in GBMSM Alison Walsh* Alison Walsh Erin Kahle

Intimate partner violence (IPV) is known to reduce healthcare utilization, yet its impact on HIV care among gay, bisexual, and other men who have sex with men (GBMSM) remains underexplored. This study examined associations between IPV, relationship safety, and HIV care engagement using baseline data from a cohort of 330 partnered GBMSM (US, 2022-2024). Participants reported demographics, psychosocial factors, viral suppression, and HIV care engagement, defined as attending all scheduled HIV appointments in the past 3 months. IPV over the past 3 months was assessed with the IPV-GBMSM scale; victimization was categorized as experiencing ≥1 of the scale's 18 items. Participants also indicated whether they felt safe in their relationship. Logistic models evaluated associations between HIV care engagement, IPV, and relationship safety. 90% of participants had attended all recent HIV care appointments. Sample IPV prevalence was 41%, and 7% felt unsafe in their relationship; only 14% of those experiencing IPV reported feeling unsafe. In unadjusted models, the odds of care engagement were 58% lower for those experienced IPV compared to those who had not (95% CI: 0.21-0.87) and 74% lower for those who felt unsafe versus safe (95% CI: 0.10-0.72). After adjusting for demographics, psychosocial and behavioral factors, and viral suppression, experiencing IPV was associated with 72% higher odds of care engagement (95% CI: 0.47-6.22), though this result was not statistically significant. The adjusted odds of care engagement associated with feeling unsafe were 83% lower than the odds associated with feeling safe (95% CI: 0.03-0.96; p = 0.04). These findings emphasize the complex interplay between care engagement, relationship violence, and safety among GBMSM living with HIV and suggest that enhancing feelings of safety, irrespective of IPV, may improve HIV care engagement. Further investigations are needed to understand measured IPV and its incongruency with perceived safety.

HIV / STI

The effect of depressive symptoms on six month antiretroviral therapy adherence among women with HIV of reproductive age Karen Diepstra* Karen Diepstra Andrew Edmonds Paul N. Zivich Catalina Ramirez Maria L. Alcaide Deborah L. Jones Seble Kassaye Deborah Konkle-Parker Anandi N. Sheth Elizabeth F. Topper Aadia Rana Daniel J. Westreich

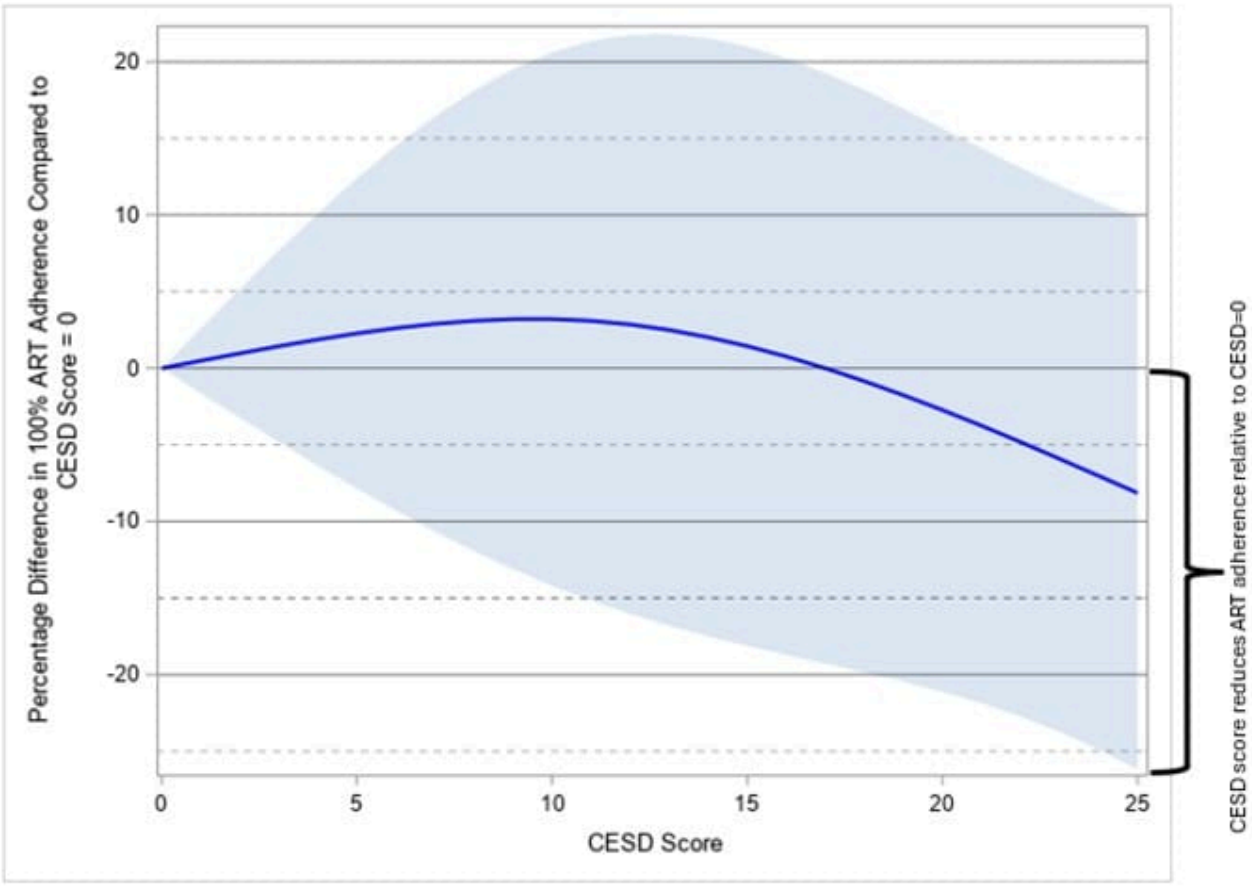
Background: Depression can negatively impact antiretroviral therapy (ART) adherence. We examined the effect of depressive symptoms on ART adherence among women with HIV (WWH) of reproductive age in the Southern US.

Methods: Using the Study of Treatment and Reproductive Outcomes cohort data, we identified WWH receiving ART at enrollment. Self-report of baseline depressive symptoms were measured using the Center for Epidemiologic Studies Depression (CESD) scale. The outcome was self-reported ART adherence (100% adherence vs. <100% adherence) at the 6-month visit. Using g-computation, we estimated the dose-response effect of CESD. We also compared the probability of 100% adherence given the observed CESD scores in the sample vs. the probability under two hypothetical depression interventions (e.g., cognitive behavior therapy) which reduced CESD scores in all participants by 3 and 6 points.

Results: Of 513 WWH receiving ART, we identified 480 with complete baseline data, of whom 311 (61%) had outcome data at the 6-month visit. The median CESD score was 11 (interquartile range: 5-21); 184 (38%) had a CESD score >16 – a cutoff traditionally used to detect clinical depression. Among those with a 6-month visit, 172 (55%) reported 100% ART adherence. Compared to CESD=0, the probability of 100% ART adherence was 0.8 points higher for CESD=16 (95% CI: -18.7, 20.2) and 5.9 points lower for CESD=23 (95% CI: -23.7, 11.9) (Figure). The interventions to reduce CESD score by 3 or 6 points increased the probability of 100% ART adherence by 0.9 (95% CI: -1.2, 3.0) and 1.4 (95% CI: -1.7, 4.5) percentage points, respectively.

Conclusions: We found high depressive symptom prevalence among WWH of reproductive age in the Southern US. Above the threshold of 16, higher CESD scores (compared to CESD=0) were associated with lower probability of 100% ART adherence, though 95% CIs were wide. Depression interventions for individuals with clinical symptoms may have an impact on HIV-related care in this population.

Figure. Risk differences and 95% confidence intervals for the effect of continuous CESD score (compared to a CESD=0) on 100% ART adherence among women with HIV in the Southern U.S.



CESD: Center for Epidemiologic Studies Depression, ART: antiretroviral therapy. Risk difference comparing all women having CESD score shown versus CESD=0. Line is risk difference and shaded regions are 95% confidence intervals.

HIV / STI

Antiretroviral Therapy Adherence Among Patients at a Specialized Long-Term Care Facility for People with HIV Brianne Olivieri-Mui* Brianne Olivieri-Mui Aneeka Ratnayake Mark Brennan-Ing Laura Senier

Background: Evidence suggests that HIV antiretroviral therapy (ART) adherence is suboptimal in long-term care (LTC) settings. We studied a LTC facility specializing in HIV care to understand how they meet the ART needs of people with HIV (PWH).

Methods: We conducted semi-structured, in-depth interviews with 11 PWH and 5 LTC staff/clinicians to ask about facility-level routines, medical care, and observed/perceived culture. Interviews were recorded, transcribed verbatim, and analyzed using deductive and inductive coding matrices.

Results: Three themes emerged from the data: 1) maintaining adherence to an HIV routine is only one of many competing priorities for PWH including housing insecurity, drug use, and justice system involvement; 2) social support and loneliness are widely experienced and pose a challenge to complying with HIV regimens; and 3) staff members at this LTC facility provide material and emotional support to PWH to facilitate compliance. We highlight how routines and procedures complement organizational culture to support PWH in this setting.

Conclusions: Even in a facility that is designed to deliver consistently high-quality care to PWH, we still find that patients suffer numerous challenges in adhering to HIV medication protocols. Our findings show how a multidisciplinary team can support optimal adherence to ART.

Methods/Statistics

Multilevel network meta-regression for population-adjusted treatment comparisons: transporting treatment effects to target populations for decision-making David Phillippo* David Phillippo

Network meta-analysis (NMA) and indirect comparisons combine aggregate data from multiple randomised controlled trials to estimate relative treatment effects, assuming that any effect modifiers are balanced across populations. Population adjustment methods aim to relax this assumption, using individual patient data available from one or more studies to adjust for differences in effect modifiers between populations. These methods are closely related to those in the causal inference literature for transporting estimates from trials to target populations, and to recent developments in causally-interpretable meta-analysis.

We introduce multilevel network meta-regression (ML-NMR), a general method for synthesising individual and aggregate data in networks with any number of studies and treatments, extending the standard NMA framework. An individual-level regression model is defined, and aggregate study data are incorporated appropriately by integrating this model over the covariate distributions of the respective studies, which avoids aggregation bias. This marginalisation integral is evaluated using Quasi-Monte Carlo integration, providing a general approach that is applicable to models and likelihoods of any form. Crucially for decision making, estimates may be transported into any target population with a given covariate distribution.

We demonstrate this approach with a network of trials and treatments for moderate-to-severe plaque psoriasis, transporting estimates into a decision population with characteristics informed by a representative registry study. We discuss the links between population adjustment methods like ML-NMR and the literature on transportability and causally-interpretable meta-analysis, and suggest areas for future research and cross-pollination. A user-friendly R package multinma is available for performing ML-NMR analyses.

Methods/Statistics

Leveraging electronic health record data to evidence collider stratification bias and inform clinical epidemiology: Type-1 diabetes and rotator cuff tears Ayush Giri* Ayush Giri Simone Herzberg Katherine Hartmann Hann-Heui Ong Max Breyer Wei-Qi Wei Nitin Jain

Background: Electronic health record (EHR) data are ever popular for case-control investigations. Imaging is often required for affirmative diagnosis of rotator cuff tears and due to high estimates of asymptomatic tears, many argue imaging should be required for control selection. Leveraging de-identified EHR-data to construct multiple control groups (with/without imaging), we evaluate evidence for selection bias through collider stratification using type-1 diabetes (T1D) and rotator cuff tears as an illustrative example.

Methods: We developed EHR-based algorithms to identify imaging-verified cases, and two control groups: one reliant on imaging data to confirm lack of tear (control group 1), and one without such requirement (control group 2). We compared key characteristics between cases and controls, and between the two control groups, and performed multivariable logistic regression analyses to compare associations between T1D and rotator cuff tears across two case-control designs.

Results: Cuff tear cases (Group 1) were older, more likely to have arthritis (57%), ligamentous disease (9%) and prior shoulder injury (99%) than either of the control groups (Fig. 1). However, control group 1 was more similar to cases than control group 2 with higher proportion of arthritis (Control group 1: 9% vs. Control group 2: 1%), ligamentous disease (6% vs. 2%), and prior shoulder injury (54% vs. 7%). T1D was present in 3% of cases, 4% of control group 1 and 1% of control group 2. The prevalence of T1D is ~1% in the US. T1D was positively associated with rotator cuff tears when using control group 2 (aOR=1.78; 95% CI = 1.64-1.92); and inversely associated when using control group 1 (aOR=0.75; 0.57-0.97).

Discussion: Imaging in EHR-data, indicated due to symptomology, is not systematic. Using multiple control groups in EHR-data we evidence how conditioning on imaging (descendent of a collider: symptomology) can perturb exposure estimation in controls, enough to reverse conclusions.

Table 1 Characteristics of rotator cuff tear cases and controls by imaging requirement using electronic health record data from Vanderbilt University Medical Center

	Imaging Required		Imaging Not required	
	Cases (Case Group 1)	Controls (Control Group 1)	Cases (Case Group 2)	Controls (Control Group 2)
Total Count (N)	2,632	10,528	8,482	33,928
Female N (%)	1,248 (47%)	5,251 (50%)	3,802 (45%)	18,568 (55%)
Age Mean (SD)	61.43 (10.47)	56.83 (11.58)	60.52 (10.24)	59.22 (12.42)
Race/Eth				
NH-White	1,751 (67%)	7,117 (68%)	5,853 (63%)	116,685 (53%)
NH-Black	171 (6%)	965 (9%)	552 (7%)	13,746 (2%)
NH-Asian	9 (0%)	82 (1%)	40 (0%)	1,424 (1%)
Hispanic	57 (2%)	280 (3%)	157 (2%)	639 (1.9%)
Other	644 (24%)	2,084 (20%)	1,880 (22%)	12,968 (38%)
Any Diabetes	476 (18%)	1589 (15%)	1197 (14%)	2546 (8%)
Type 1	83 (3%)	382 (4%)	232 (3%)	393 (1%)
Type 2	246 (9%)	651 (6%)	560 (7%)	1132 (3%)
Ligamentous Disease	234 (9%)	682 (6%)	595 (7%)	803 (2%)
Prior Shoulder Injury	2,594 (99%)	5,710 (54%)	8,260 (97%)	2,450 (7%)
Arthritis	1,499 (57%)	986 (9%)	3,959 (47%)	351 (1%)

Methods/Statistics

Trends in statistical results presentation of benefits and harms in abstracts of published randomized controlled trials with a focus on asymmetric framing Andreas Stang* Andreas Stang Jennifer Rauscher

Background: Asymmetric framing means that results on the benefits and harms of a new therapy are not presented in the same level of detail. In most cases, the benefits are presented in more detail than the harms. The aim of this study was to investigate how often results of randomized controlled trials (RCTs), phase 3, are presented asymmetrically in abstracts of peer-reviewed publications.

Methods: All 1225 abstracts of RCTs, phase 3, published in PubMed in 2000, 2010 and 2020 were identified. After excluding noneligible abstracts, 698 abstracts remained in the analysis. Two independent raters extracted features (presence of frequency and effect measures, confidence intervals, p-values and significance terminology for benefit and harm) of the abstracts.

Results: In the context of benefit, the presentation of effect measures (2000: 18.2%, 2010: 36.4%, 2020: 63.3%) and p-values (2000: 56.4%, 2010: 69.1%, 2020: 70.4%) increased over time; confidence intervals were reported in 80%, 63.2% and 56.7% in 2000, 2010, and 2020, respectively. The use of significance terminology decreased over time (2000: 54.6%, 2010: 50.6%, 2020: 47.2%). In the context of harm, the use of significance terminology has decreased (2000: 25.5%, 2010: 14.6%, 2020: 5.4%) and the reporting of the frequency of harm per study arm has increased (2000: 36.4%, 2010: 39.3%, 2020: 56.0%). A total of 89% of all abstracts provided benefit information (effect measures, confidence intervals, p-values, significance terminology) without corresponding harm information. Journals with higher impact factors tended to report more statistical features of both benefits and harms.

Conclusion: Even though the reporting of benefits and harms has improved somewhat, there is still a very strong asymmetry in the reporting of benefits and harms in abstracts of RCTs, phase III. Obviously, recommendations of the CONSORT statements are not sufficiently implemented.

Methods/Statistics

Transfer Learning for Improving Local Predictive Performance in Small Datasets Carine Savalli* Carine Savalli André Henrique Alves Carneiro Fabiano Barcellos Filho Murilo Afonso Robiati Bigoto Roberta Moreira Wichmann Alexandre Dias Porto Chiavegatto Filho

Transfer learning is a machine learning technique that incorporates knowledge from a pre-trained model to enhance the training and performance of a new model in a distinct but related context. This study focused on predicting admissions to the intensive care unit (ICU) for COVID-19 patients in a hospital with a small sample size (H1, n=72). We employed a transfer learning approach and compared two competitive source models trained in two different hospitals in Brazil (H2: n=1,330; and H3: n=148). All hospitals collected the same demographic and laboratory variables. The dataset was divided into training and testing (70%/30%) subsets using a hold-out approach, while ensuring stratification based on the outcome variable. Pre-processing steps were applied to prepare the data for modeling, followed by training the XGBoost algorithm. Hyperparameter tuning was performed through a randomized search strategy combined with 3-fold cross-validation on the training set to optimize model performance. The metric adopted was the area under the curve ROC (Receiver Operating Characteristic). Both source hospitals demonstrated excellent predictive performance for the task (H2: AUC=0.9410; AUC=0.9316), while the hospital H1 presented an unsatisfactory performance (AUC=0.6239). Using the transfer learning approach, each source model was updated with 20 additional trees trained on data from H1 to capture local patterns. Using H2 as the source model resulted in an AUC of 0.7863, representing a 26.0% increase in predictive performance in H1, and using H3 as the source model yielded an AUC of 0.7094, representing a 13.7% increase. This study demonstrates the effectiveness of transfer learning in improving predictive performance in resource-limited settings with small datasets. Leveraging knowledge from source hospitals with high-performing models yielded substantial AUC gains, highlighting its potential to improve decision-making in healthcare.

Methods/Statistics

The Impact of Census-Tract Level Mortgage Discrimination on Cognitive Function: Accounting for Measurement Error in Small-Area Data via Joint Modeling Yueying Hu*
Yueying Hu Michael R. Elliott Helen C.S. Meier Liang Chen Monica E. Walters Laura B. Zahodne

Racial disparities in cognitive health reflect entrenched structural inequalities. This study investigates the association between census-tract level mortgage discrimination, operationalized as the Mortgage Density Index Ratio (MDIR), and cognitive outcomes among racially diverse older adults. Using data from the Michigan Cognitive Aging Project (MCAP), a cohort of 644 participants was analyzed across six cognitive domains, taking into account individual demographics and neighborhood characteristics.

Hypersegregation, driven in part by historical redlining and contemporary racial discrimination in housing and lending, introduces instability in ratio indices like MDIR, particularly in census tracts with extreme racial imbalances. To address this, we employed a joint modeling approach that simultaneously estimates cognitive outcomes and latent mortgage rates for Black and White households, effectively mitigating measurement error. This method identified a significant association between MDIR and processing speed only among Non-Hispanic Black participants, with a one-unit MDIR increase corresponding to a 0.48 standard deviation (SD) improvement in processing speed (95% CI: 0.05-0.93 SD). That is, a more equitable mortgage lending environment is associated with faster cognitive processing. Traditional regression methods, in contrast, failed to detect such effects.

Simulations further demonstrated the advantages of joint modeling in managing measurement error, showing notably lower bias and greater robustness in small- to moderate- sized census tracts compared to traditional regression approaches. These findings underscore the importance of advanced statistical methods in quantifying structural racism and highlight the disproportionate effects of mortgages discrimination on cognitive outcomes among Black adults.

Health Disparities

Area Deprivation as a Modifier of Racial and Income-Based Disparities in Stroke Risk: A Population-Based Analysis Jiajun Luo* Jiajun Luo Briseis Aschebrook-Kilfoy

Background: Prior research has consistently shown that minority populations and lower-income groups experiencing a higher burden. However, less is known about how broader contextual factors, such as neighborhood-level deprivation, interact with individual characteristics to exacerbate or mitigate these disparities. This study investigates the interaction between area deprivation, race, and household income in determining stroke risk in the US.

Methods: The study used data from the All of Us Research Program. Participants aged above 35 and with valid data on electronic health records (EHR), household income, and race/ethnicity identity were included for analysis. Stroke incidence was measured based on EHR records. Cox proportional hazards models were used to estimate the hazard ratio (HR) and 95% confidence interval for stroke according to racial/ethnic and household income groups.

Results: A total of 178,026 participants were included in this study. Race/ethnicity and household income were significantly associated with stroke incidence (Table). When stratified by area deprivation index, the associations of race and ethnicity were strengthened in the high-deprivation area (non-Hispanic Black: HR=2.21, 95% CI: 1.73-2.82), nonetheless, became null in the low-deprivation area (non-Hispanic Black: HR=0.99, 95% CI: 0.75-1.30). The difference was significant (P for interaction <0.01). The associations of household income were also more pronounced in the high-deprivation area (≥100k: HR=0.61, 95% CI: 0.43-0.87) compared to the low-deprivation area (≥100k: HR=0.73, 95% CI: 0.58-0.93).

Conclusion: The finding that racial and income-based disparities in stroke risk are only present in high-deprivation areas suggests that structural inequalities embedded in disadvantaged neighborhoods may amplify the effects of individual-level risk factors.

Table. Hazard ratio and 95% confidence interval for stroke incidence according to racial/ethnic and household income groups in the study population

Characteristics	Hazard ratio (95% confidence interval)[a]			
	Total	High deprivation index	low deprivation index	P for interaction
Race and ethnicity				
Non-Hispanic white	Ref	Ref	Ref	
Non-Hispanic black	1.63 (1.38-1.92)	2.21 (1.73-2.82)	0.99 (0.75-1.30)	<0.01
Hispanic/Other	0.83 (0.68-1.02)	0.64 (0.45-0.91)	1.08 (0.84-1.39)	0.01
Annual household income				
<25k	Ref	Ref	Ref	
25k to 50k	0.87 (0.72-1.03)	0.74 (0.56-0.98)	0.98 (0.77-1.25)	0.16
50k to 100k	0.70 (0.58-0.84)	0.71 (0.53-0.96)	0.72 (0.56-0.92)	0.96
≥100k	0.70 (0.57-0.84)	0.61 (0.43-0.87)	0.73 (0.58-0.93)	0.33

[a] Model adjusted for hypertension status, history of atherosclerotic cardiovascular diseases, sex at birth, age at enrollment, alcohol drinking, and smoking status.

Cardiovascular

Gender-specific population attributable fractions for cardiovascular disease and all-cause mortality associated with living arrangement in community-dwelling older people Rosanne Freak-Poli* Rosanne Freak-Poli Achamyeleh Birhanu Teshale Htet Lin Htun Alice J. Owen James R. Baker Irja Isaksen

Background: Living alone poses significant social and health risks. No studies have yet examined the population attributable fraction (PAF) for cardiovascular disease (CVD) and all-cause mortality associated with living alone.

Aim: To assess the PAF for CVD and all-cause mortality related to living alone, and not living with a partner/spouse.

Methods: This study used longitudinal data from the Aspirin in Reducing Events in the Elderly (ASPREE) trial and its sub-study, the ASPREE Longitudinal Study of Older Persons (ALSOP), which included 5,853 men and 6,998 women followed for up to 12 years. The participants were community-dwelling healthy older adults aged >70 years without CVD, dementia, or significant physical disability. Adjusting for social determinants and clinical risk factors, the gender-specific PAFs of CVD and all-cause mortality attributable were determined. Not living with a partner/spouse was defined as living alone or with someone other than a partner/spouse.

Results: Living alone was more prevalent among women (41%) than men (17%, p<0.001). Among men, the PAFs for CVD and all-cause mortality attributable to living alone were very low and not statistically significant (only 2.9% of CVD events and 3.6% of all-cause mortality rates, Figure). In contrast, for women, these PAFs were higher and statistically significant, 13.5% of CVD events and 9.8% of all-cause mortalities were attributed to living alone. Patterns were similar for PAFs associated with not living with a partner/spouse but slightly greater in magnitude and reached statistical significance for all-cause mortality for men (6.0%).

Conclusion: Our findings demonstrate that living alone contributes to the population CVD risk and all-cause mortality. Our findings demonstrate that older women are more likely to live alone and their risk is greater, when compared to men. These findings have critical implications for “Ageing in Place” policies.

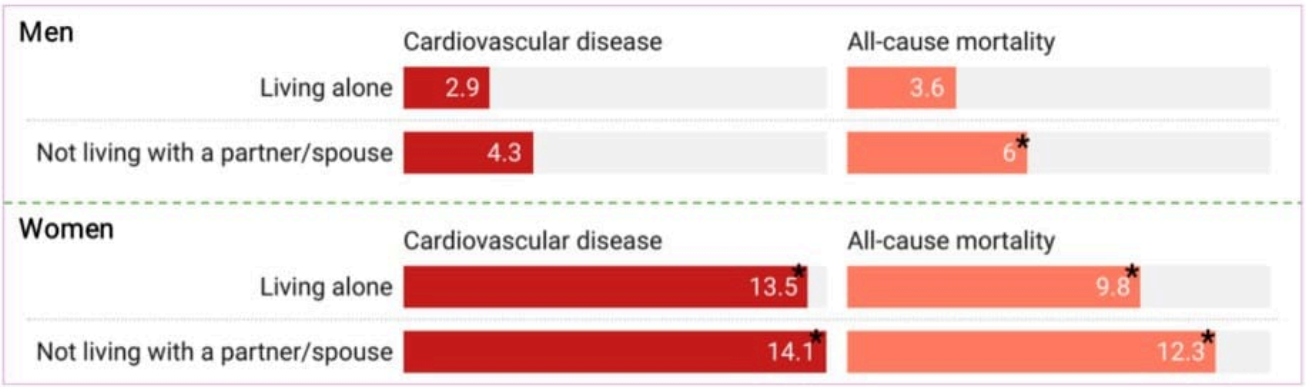


Figure. Gender-specific population attributable fractions (PAFs) for cardiovascular disease and all-cause mortality associated with living alone and not living with a partner/spouse. *The PAFs are statistically significant (p<0.05).

Health Disparities

Exploring the Association Between Perceived Neighborhood Environment and Overweight and Obesity in Adolescents: Findings from the National Health Interview Survey Yangyang Deng* Yangyang Deng Mohammad Moniruzzaman Breanna Rogers Lu Hu Ram Jagannathan Kosuke Tamura

PURPOSE: Despite the effects of neighborhood contexts on adolescents' overweight and obesity, limited research has explored how their perceptions of neighborhood characteristics affect overweight/obesity. We aimed to examine the associations between perceived neighborhood environments and adolescents' overweight/obesity and whether these associations varied by age, sex, and racial/ethnic groups.

METHODS: Data (n=4,099; female=48.5%; Mage=14.2 years) were obtained from 2020-2022 National Health Interview Survey. Overweight and obesity status was defined as BMI≥25.0 kg/m2 (Yes/No). Perceived neighborhood features (Yes/No) included unsafe walking conditions due to traffic and crime, and availability of parks. Analyses were stratified by age groups (10-14 and 15-17 years), sex, and racial and ethnic groups. Weighted generalized logistic regression was used to examine the relationships between each factor and overweight/obesity, adjusting for age, sex, racial/ethnic groups, region, and survey year, stratified by age, sex, and racial/ethnic groups.

RESULTS: Adolescents who reported the presence of sidewalks and the availability of parks had a 29% (OR=0.79, 95% CI 0.58–0.88) and 15% (OR=0.85, 95% CI 0.72–0.99) lower odds of being overweight/obese, respectively, compared to the ones who did not. Those reporting unsafe traffic conditions and high crime rates had a 28% (OR=1.28, 95% CI 1.09–1.51) and 43% (OR=1.43, 95% CI 1.15–1.79) higher odds of being overweight/obese, respectively. Similar patterns of associations were consistent across age and sex groups, while analyses by race/ethnicity revealed more complex relationships.

CONCLUSION: Adolescents with favorable perception of sidewalks and parks had lower prevalence of overweight/obesity, while perceptions of unsafe traffic or higher crime had an increased prevalence. Improving neighborhood physical and social environmental characteristics may be critical for addressing disparities in adolescents' overweight/obesity.

Cardiovascular

Beating the Odds: A Randomized Controlled Trial of a School-Based Prevention Education Program on Lifestyle Modifications for Cardiovascular Risk Reduction Among Adolescents

Alina Yang* Alina Yang

Background: Contemporary epidemiological trends indicate escalating cardiovascular risk factors among adolescent populations, necessitating effective preventive interventions. This investigation evaluates the implementation of a comprehensive educational program for secondary school students.

Methods: A randomized controlled trial design was used to assign 858 students aged 14–18 from a suburban high school to either an intervention group (n=429) or a control group (n=429). The intervention group received a year-long CVD prevention curriculum integrated into health classes, including weekly sessions on healthy eating and regular physical activity, supplemented by activities such as cooking demonstrations, fitness challenges, and discussions with professionals. The control group continued with the standard curriculum. We collected data at baseline, immediately post-intervention, and three months post-intervention.

Results: The intervention group showed increased fruit and vegetable intake by 1.5 servings/day (95% CI: 1.2–1.8, $p < 0.001$) and reduced fast food consumption by 1.1 servings/week (95% CI: 0.9–1.3, $p < 0.001$). Physical activity increased by 30 minutes/day (95% CI: 25–35, $p < 0.001$). These changes were associated with a BMI reduction of 0.7 kg/m² (95% CI: 0.5–0.9, $p < 0.001$), decreases in systolic blood pressure by 2.8 mmHg ($p < 0.05$), diastolic blood pressure by 1.5 mmHg ($p < 0.01$), and total cholesterol by 7 mg/dL ($p < 0.01$). Self-perceived CVD knowledge increased by 20.3 points (95% CI: 18.7–21.9, $p < 0.001$). The control group showed minimal changes. Qualitative data from 13 focus intervention groups indicated that the program was engaging and informative, and motivated healthier lifestyles.

Conclusions: The intervention demonstrated statistically significant efficacy in modifying cardiovascular risk factors and health behaviors among adolescents, suggesting the viability of school-based preventive cardiology programs for population-level health promotion.

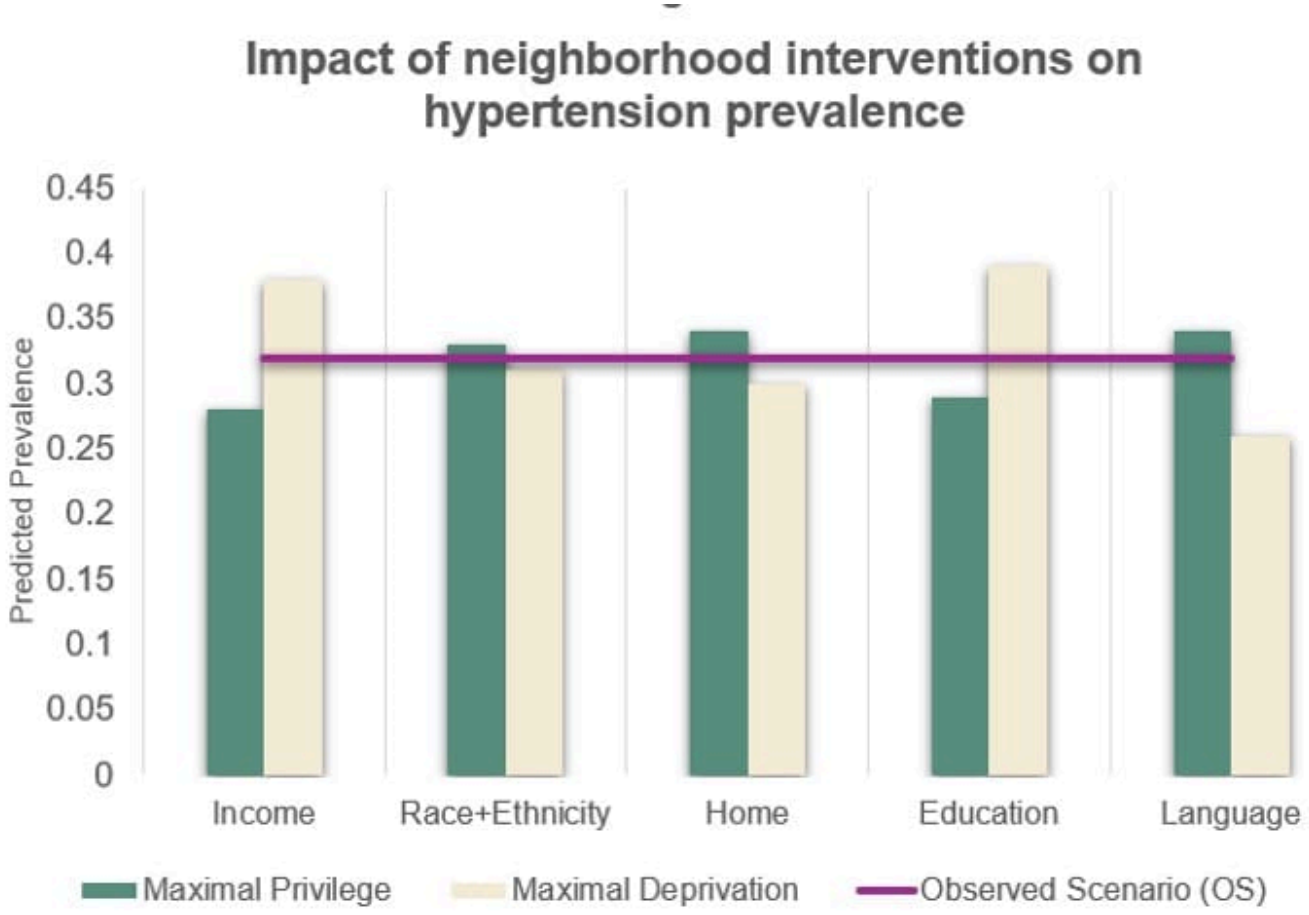
Cardiovascular

Population Intervention Effects of Spatial Social Polarization on Hypertension Disparities
Hoda Abdel Magid* Hoda Abdel Magid Mengya Xu Gina S. Lovasi Suzanne Judd Michelle C. Odden

Background: Spatial social polarization (SSP)—the unequal geographic distribution of privilege and deprivation—is hypothesized to drive hypertension disparities in the United States. Using the Index of Concentration at the Extremes (ICE), SSP was measured across six domains: income, education, homeownership, primary language, race/ethnicity, and joint race/ethnicity with income. This study used 2019 claims data (N=644,707) to estimate the population-level impact of eliminating SSP disparities on hypertension outcomes through counterfactual modeling in Black and White adults.

Methods and Results: Population Intervention Models (PIMs) with the parametric g-formula simulated counterfactual scenarios where SSP disparities were eliminated, allowing comparisons of current exposure levels with idealized distributions (e.g., universal privilege or deprivation). Analyses at the ZIP code level were adjusted for demographic factors and clinical comorbidities, including diabetes, hyperlipidemia, and myocardial infarction. Observed hypertension prevalence was 32%. Results demonstrated significant SSP-related gradients. In a hypothetical scenario where everyone lived in high-income neighborhoods, hypertension prevalence would decrease by 4.3%, while residence in income-deprived areas would increase prevalence by 5.8%. Neighborhood racial composition effects varied: among White participants (70% of the sample), moving to predominantly White neighborhoods increased prevalence from 33.2% to 33.6%. Among Black participants (11%), relocating to predominantly White neighborhoods decreased prevalence by 0.3%, while residence in predominantly Black neighborhoods increased prevalence by 0.3%. Living in neighborhoods with higher educational attainment reduced hypertension prevalence by 3.8%, while residence in neighborhoods with lower educational attainment increased it by 6.3%.

Conclusion: Eliminating SSP disparities could significantly reduce hypertension prevalence, with the greatest benefits observed in socioeconomically deprived communities. These findings highlight SSP as a critical determinant of hypertension disparities and underscore the potential for targeted, neighborhood-level interventions to reduce polarization and advance cardiovascular health equity


Impact of neighborhood interventions on hypertension prevalence
Predicted Prevalence
0.45
0.4
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0
Income
Race+Ethnicity
Home
Education
Language
Maximal Privilege
Maximal Deprivation
Observed Scenario (OS)

Cardiovascular

Characterization of the Course of Heart Disease in a Large Cohort Study Ming Ding* Ming Ding Feng-Chang Lin Michelle Meyer

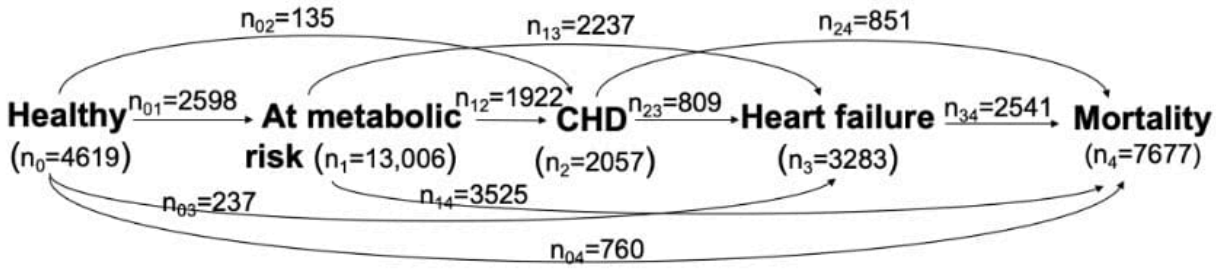
Background. In cardiovascular epidemiology, studies have largely focused on the prevention and prediction of a single endpoint (e.g., hypertension). However, the development of heart disease is a long-term process that involves multiple endpoints, which are biologically inseparable. Limited studies have considered the entire disease course.

Method. We modeled the course of heart disease in five states: healthy, at metabolic risk, coronary heart disease (CHD), heart failure, and mortality. We characterized the disease course using two novel estimates: disease path and Multimorbidity-adjusted Life Year (MALY). Both estimates were derived from a new multi-state modeling method that we developed (Ding et al. BMC Medical Research Methodology. 2025). We used the Atherosclerosis Risk in Communities (ARIC) study data obtained through NHLBI BioLINCC.

Results. In this mid- to old-age population, participants' course of heart disease is shown in the **Figure**. The projected MALY was 24.13 years (95% CI: 16.55, 32.06) and the corresponding multimorbidity-adjusted life expectancy was 78.23 years (95% CI: 75.95, 80.96). For healthy participants at baseline, the most likely disease paths were: "Healthy → at metabolic risk → mortality" (37%), "Healthy → mortality" (21%), followed by "Healthy → at metabolic risk → heart failure → mortality" (19%). The MALY was higher among women than men and higher among Whites than Blacks. The distribution of disease paths was similar across sex and race subgroups.

Impact. This study characterized the course of heart disease at the population level. For future research, MALY can be used to compare the effect of intervention regimes over the disease course to identify personalized optimal intervention; and disease path enables us to predict a person's entire disease course, rather than just the risk of a single endpoint. These two summary estimates have potential applications in precision prevention and prediction of heart disease.

Figure. Participants' course of heart disease in the Atherosclerosis Risk in Communities (ARIC) Study from 1987-2019 (n=15027).



CHD: Coronary heart disease.
n is the number of participants transitioned through each state.

Nutrition/Obesity

Identification and estimation of the average causal effects under dietary substitution strategies Yu-Han Chiu* Yu-Han Chiu Lan Wen

The 2020-2025 Dietary Guidelines recommend that most individuals can improve their diet by making some changes to what they eat and drink. In many cases, these changes can be made through simple substitutions, such as choosing chicken instead of processed red meat to decrease sodium intake. The question about such dietary substitution strategies seeks to estimate the average counterfactual outcome under a hypothetical intervention that replaces a food an individual would have consumed in the absence of intervention with a healthier substitute. While substitution analyses have been widely used in nutritional epidemiology using observational data, the studies have not explicitly considered the definition of their causal estimand and the assumptions necessary for identifying and consistently estimating the average causal effect. In this work, we outline a framework for estimating the average causal effect of dietary substitution strategies using observational data. We derived nonparametric identification of these strategies and proposed new estimators that can be used in conjunction with parametric or nonparametric estimation procedures. In contrast to existing research, our approach considers each individual's natural dietary intake and can be readily translated into real-world interventions or recommendations. Moreover, our estimators avoid imposing unrealistic assumptions of linearity and the absence of interaction terms commonly imposed in parametric outcome regression models. We evaluated the performance of our proposed methods via simulation studies and applied them to estimate the effect of substituting processed red meat with chicken on mortality using data from the Nurses' Health Study.

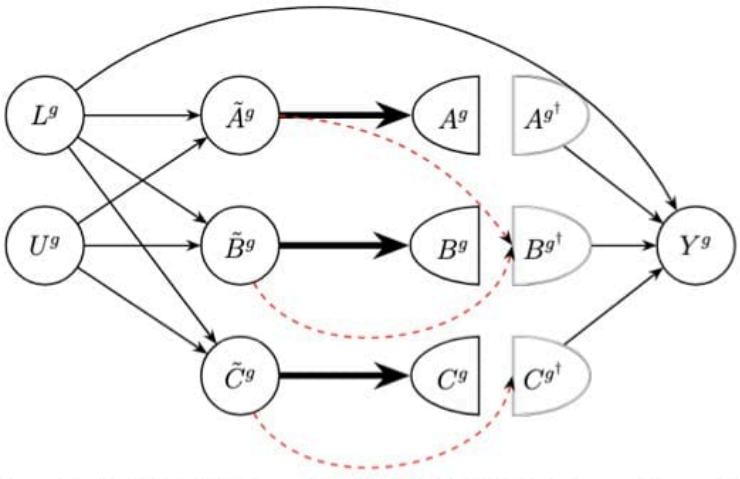


Figure 1: Single World Intervention Graph (SWIG) depicting an intervention g: If an individual plans to eat a servings of A and b servings of B per week, then ensure they eat 0 serving of A and a+b servings of B. The intake of C should remain unchanged from their intended levels. Here, $\tilde{A}$, $\tilde{B}$, and $\tilde{C}$ denote the planned weekly portions of food intake in groups $\mathcal{A}$, $\mathcal{B}$ and $\mathcal{C}$; A, B, and C denote the actual weekly portions of food intake in groups $\mathcal{A}$, $\mathcal{B}$ and $\mathcal{C}$; Y a binary outcome; L a set of potential baseline confounders that affect planned dietary intake and outcome; and U a set of potential baseline common causes of planned dietary intake decisions. Bold arrows are used to emphasize equivalence relationships.

Diabetes

Emulation of the PREDIMED Protocol in two US cohorts: Could sample differences explain disagreements between trial and observational results? Octavio Pano Espinola* Octavio Pano Espinola Prof Dalia Stern Arturo Aguilar Prof. Martin Lajous Prof. Deirdre K Tobias Prof. Yu-Han Chiu

The PREDIMED trial concluded that a Mediterranean, compared to a low-fat diet, can effectively reduce the incidence of type 2 diabetes (T2D). However, it remains unclear whether these findings are applicable to other populations, where diet and the distribution of risk factors might differ. Given that conducting randomized trials in diverse populations may not be efficient, we applied the target trial framework (TTF) to emulate the PREDIMED protocol in two US cohorts. **Methods** We adapted the PREDIMED trial to the Nurses' Health Study and Health Professionals Follow-up Study data. A similar high-risk population was selected to estimate the observational analogue of the intention-to-treat effect over 4-years on the incident of T2D had everyone initiated a Mediterranean or a Low-fat diet. The interventions were defined using similar foods as the PREDIMED protocol. We estimated the absolute cumulative incidence, risk differences (RD) and risk rations (RR) using the g-formula. **Results** Applying the protocol we selected a sample of 10,627 participants (77% female). Compared to the PREDIMED, our population had a higher prevalence of smokers (15.6% vs. 7.9%), dyslipidemia (92.3% vs. 51.2%) and hypertension (93.9% vs. 90.0%), but lower prevalence of overweight/obesity (84.1% vs. 94.6%). Overall, adherence to the Mediterranean diet differed between studies, with a mean score of 6.2 (SD 1.9) in the US cohorts and 8.7 (1.9) in the PREDIMED. Moreover, the foods characterizing the dietary patterns were different between studies. The 4-year cumulative incidence of T2D in the Mediterranean arm was 6.9 (5.5–8.6) in the PREDIMED trial and 3.8 (2.8 – 5.1) in the US cohorts. Preliminary results show a RR of 1.4 (95% CI 1.0-2.3) for the ITT comparing a mediterranean diet versus a low-fat diet. **Conclusions** Using TTF to emulate PREDIMED, we found differences in risk factors, diets and adherence to food groups. Further exploration of these differences, unmeasured confounding and adherence patterns between studies is necessary to understand conflicting results

Cardiovascular

Effect of sustained alcohol abstinence versus moderate consumption of wine on cardiovascular disease: emulating a target trial using data from NHS and HPFS Shuyuan Yang* Shuyuan Yang Eric Rimm Kenneth Mukamal Edward Giovannucci Dalia Stern Miguel A. Martínez-González Yu-Han Chiu

Background: Numerous observational studies have reported a “J-shaped” relationship between alcohol consumption and cardiovascular disease, while only a few recent non-original studies have supported complete abstention as the best cardio-preventive strategy. However, all these comparisons lack actionable guidance for decision-making regarding the best advice to be given to drinkers. This study addressed this gap by emulating a target trial to assess the effect of quitting versus maintaining moderating wine consumption among baseline drinkers.

Methods: Using biennially collected data from Nurses’ Health Study (NHS) and Health Professionals Follow-up Study (HPFS), we identified men (50-70 years old) or women (55-75 years) consuming ≥3 but ≤40 servings/wk of any alcoholic beverage and without prior history of liver or breast cancer at baseline. We compared two sustained strategies: 1) complete abstention from any alcoholic beverage, and 2) moderation with wine, limiting it to no more than 14 servings/wk for males and 7 servings/wk for females, with no more than one serving/wk of other alcoholic beverages. The primary outcome was the 12-year risk of major atherosclerotic cardiovascular events (MACE), defined as a composite of non-fatal myocardial infarction, non-fatal stroke, and cardiovascular death. We used the parametric g-formula to estimate MACE risk under these interventions.

Results: Of the 24,753 participants who met the eligibility criteria, 2,852 had MACE during follow-up. The estimated 12-year risks of MACE were 12.7% under abstention versus 11.4% under moderation with wine in the NHS (RD = -1.3%, 95% CI: -1.9% to -0.9%), and 20.5% versus 18.8% in the HPFS (RD = -1.7%, 95% CI: -2.8% to -0.8%). The corresponding risk ratios were 0.89 (95% CI: 0.86-0.93) in the NHS and 0.92 (95% CI: 0.87-0.96) in the HPFS.

Conclusions: We estimated that drinkers remaining moderate consumers of wine may have a slightly lower risk of MACE than those who abstain completely.

Nutrition/Obesity

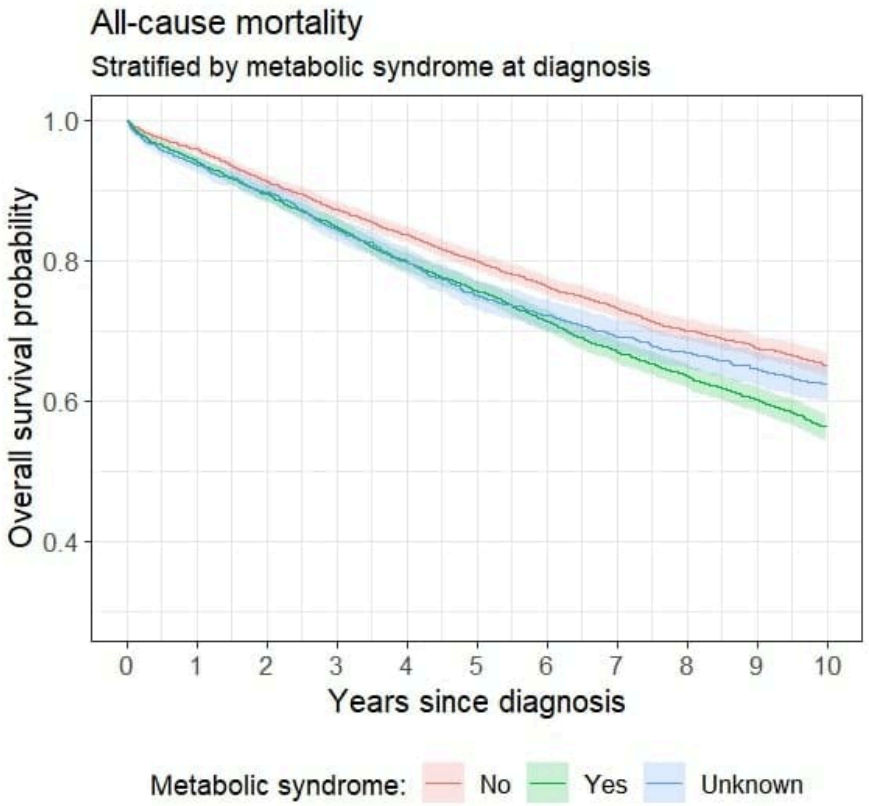
Into the Unknown – missing data in real-world analyses of metabolic syndrome and colorectal cancer survival Anlan Cao* Anlan Cao Kristina L. Johnson Jeffrey A. Meyerhardt Edward Giovannucci Elizabeth M. Cespedes Feliciano

Metabolic syndrome (MetSyn) is a cluster of risk factors that increase incidence and mortality of multiple conditions, including cancer. Electronic health records can be used to assess MetSyn , but incomplete measurement of the five components is common. Understanding the impact of missing data is essential as unmeasured cannot be presumed to be healthy.

We included patients aged 18+ diagnosed with stage I-III colorectal cancer (CRC) at Kaiser Permanente Northern California (2005-2020). MetSyn was defined as having ≥3 of 5 components as abnormal within 24mo pre- to 6mo post-diagnosis and before systemic anticancer therapy: 1) body mass index ≥27.7, 2) elevated blood pressure, 3) low high-density lipoprotein cholesterol, 4) hypertriglyceridemia, and 5) diabetes/impaired glucose tolerance. Patients with insufficient data for a definitive diagnosis were classified as unknown. We addressed the unknown group using various approaches: complete case analysis, missing indicator, multiple imputation (MI) and inverse probability weighting (IPW). We used Cox proportional hazards models to calculate the HR for MetSyn and survival adjusted for confounders.

Among 9,343 patients (mean age: 66, 50% female), 3,594 had definitive MetSyn, 4,004 did not, and 1,745 were unknown. Over a median follow-up of 7 years, 3,644 patients died. Complete case analysis showed MetSyn was associated with higher all-cause mortality (HR= 1.27 [1.18-1.36]). Using a missing indicator for unknown, HRs for MetSyn remained similar, while the unknown group also had worse survival (HR=1.20 [1.09-1.32]). MI and IPW yielded similar MetSyn HRs with slightly wider confidence intervals (MI: HR=1.20 [1.11-1.29]; IPW: HR=1.24 [1.13-1.36]). CRC-specific mortality followed a similar pattern.

Missingness in MetSyn components is informative, but predictable by measured variables. Rather than presuming patients with missing components to be healthy, they should be included in analyses as a separate group or using MI or IPW.


All-cause mortality
Stratified by metabolic syndrome at diagnosis
Overall survival probability
1.0
0.8
0.6
0.4
0
1
2
3
4
5
6
7
8
9
10
Years since diagnosis
Metabolic syndrome:
No
Yes
Unknown

Nutrition/Obesity

Harnessing Social Media to Analyze Temporal and Co-occurrence Trends of GLP-1 Agonists Side Effects from 2022 to 2024 Vidur Jain* Vidur Jain Amrutha Alibilli Thu Thi Xuan Nguyen

Background: In recent years, there has been a dramatic influx in the use of glucagon-like peptide 1 (GLP-1 RAs) receptor agonists for weight loss. However, there has been limited research regarding short-term, long-term, and co-occurrent side effects associated with GLP-1 RAs medications.

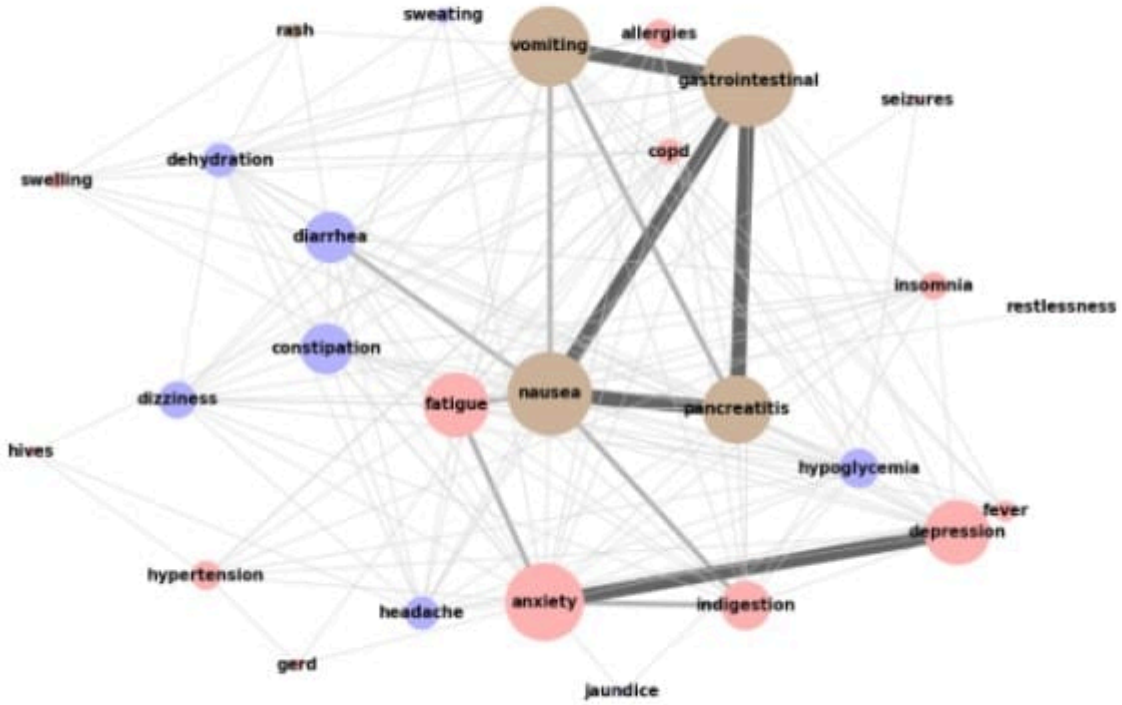
Objective: This study aims to quantitatively analyze temporal and co-occurrent side effect trends through discussions of GLP-1 RA weight loss medications on Facebook and Instagram from 2022 to 2024, a recent period following the FDA approval of GLP-1 RAs medications, such as Tirzepatide.

Methods: We collected 63,023 posts from January 1, 2022, to May 31, 2024 from Facebook and Instagram posts through CrowdTangle, a public insights tool from Meta. Using English language social media posts from the United States, we examined the effect of side effects in relation to six weight loss medications. All analyses were conducted using Python (version 3) in a Google Colab environment.

Results: Among posts, 13.8% mentioned side effects. Gastrointestinal (GI) side effects were most common, with 6.5% of Mounjaro posts, 4.3% of GLP-1 RA posts, and 3.6% of Wegovy posts reporting them. Ozempic (Semaglutide) posts linked to depression at 2.49% versus other GLP-1 RAs at 0.16%. Headache (2.00%) and joint pain (1.80%) were the most reported in Tirzepatide and Wegovy posts (0.96%; 0.87%). Node network analysis found GI symptoms (nausea, vomiting, pancreatitis, diarrhea, indigestion) strongly associated together (≥100 mentions), while neurological symptoms (anxiety, depression, insomnia) were moderately correlated together (50-100 mentions).

Conclusion: This social media study highlighted adverse side effects, along with side effect co-occurrence patterns related to GLP-1 RAs medications. These findings underscore the importance of monitoring social media discussions to predict novel, underreported GLP-1 RAs side effects to improve patient care and guide informed public health policy interventions.

Figure 1. Network Analysis of Adverse Side Effect (ASE) Co-Occurrences and Community Clusters



LATEBREAKER

Methods/Statistics

Crisis Methods for Crisis Settings: An Innovative, Flexible Randomised Controlled Trial Testing a Psychosocial, Mental Health, Parenting, and Violence Prevention Support Group for Ukrainian Families Affected by War Sydney Tucker* Sydney Tucker Susan Hillis Lucie Cluver Jamie Lachman Oliver Ratmann Seth Flaxman Nicole Baldonado

Background

More than two-thirds of the world's children live in a conflict-affected country, and 19% of the world's children live within 50 kilometres of war zones. There is urgent need to identify effective approaches to protect children. However, war-time threats present immense challenges in rigorously evaluating child protection programming – creating an urgent need for innovative, flexible methods to enable simultaneous prioritisation of 1) estimation of causal effects to ensure investment in 'what works' to protect children and 2) expedited delivery of beneficial services to war-affected children. Therefore, we designed an innovative, flexible randomised controlled trial evaluating the effectiveness of Hope Groups – a psychosocial and violence prevention support group for Ukrainian families in war – compared to wait-list controls.

Methods

We conducted a matched cluster RCT of 510 Ukrainians. Primary outcomes were assessed prior to randomisation (baseline) and 1-week post-intervention (endline). Our primary model was a 2-level generalised linear mixed-effects model nesting person within cluster, utilising wild bootstrapping to estimate mean differences and percentile-based confidence intervals. Bayesian interim analyses were conducted after the first 20 clusters reached endline, to inform delivery to wait-list controls. To assess sustained benefits over time: We innovatively compared participants 6-weeks post-intervention (clusters originally randomised to the intervention arm) and 1-week post-intervention (clusters originally randomised to the wait-list control arm – which became a 'delayed intervention' arm).

Results

At endline, Hope Groups caused 57% reductions in caregiver depression/anxiety (β=-2.85;95% CI=-3.49,-2.22) and 53% reductions in violence against children (β=-.5;95% CI=-.64, -.36). In follow-up analyses comparing participants 6-week vs 1-week post-intervention, we observed no significant differences, indicating the benefits of Hope Groups are sustained over time.

Discussion

This study contributes an important blueprint for randomised controlled trials in an era of polycrisis, where delays in crisis evidence cause delays in urgently needed evidence-based crisis action. The following methods may serve as promising tools: 1) Matching to simultaneously ensure covariate balance while also honouring the implementation preferences of participants and facilitators; 2) Bayesian interim analyses to expedite scaling of beneficial programming; 3) Innovative approaches to long-term follow-up analyses to assess sustained benefits over time without delaying delivery to control arms.

LATEBREAKER

Perinatal & Pediatric

Acute exposure to wildfire smoke and fetal death risk in California Sneha Ghimire* Sneha Ghimire Sandie Ha

Background: Evidence suggests wildfire has detrimental impacts on pregnant people and their developing fetus. However, its effect on fetal death risk is unclear. The increase in wildfire frequency and intensity underscores the critical need to examine the relationship between acute exposures to wildfire PM2.5 and fetal death.
Methods: In this case-crossover study, we examined 7,849 singleton fetal deaths (death of a fetus between 20-42 weeks of gestation) in California during the fire season (May-October)2009-2019.Wildfire PM2.5 was estimated using a previously published machine learning model that incorporates Environmental Protection Agency monitoring data, satellite plume classifications, and meteorological variables. Daily ZIP code-level concentrations of wildfire PM2.5 were calculated using population and area-weighted averages. Conditional logistic regression models compared exposures shortly before fetal death(case period) with times when no such event occurred(control periods) for the same mothers, accounting for time-invariant factors. Case periods were the event day(lag0) and the preceding 6 days(lag1-lag6), with control periods selected by a time-stratified approach. Odds ratios(OR) and 95% confidence intervals(CI) were calculated for smoke days (any day with wildfire PM2.5 concentrations>0 mg/m3) versus non-smoke days while adjusting for temperature, humidity, ambient PM2.5 and ozone.
Results: Wildfire PM2.5 was associated with 1-6% increased odds of fetal death within a week of exposure, but these associations were not statistically significant. The strongest associations were observed within the same day of exposure (aOR lag0 1.05, 95% CI: 0.95,1.16) and six days prior (aOR lag6 1.06, 95% CI: 0.96,1.17).Stratified analyses indicated mothers aged >35 years were more impacted.
Conclusions: Acute exposure to wildfire PM2.5 may increase fetal death risk, among older mothers, indicating further investigation and protective measures amid rising wildfires.

LATEBREAKER

Methods/Statistics

Two-Stage Interrupted Time Series Analysis with Machine Learning: Evaluating the Health Effects of the 2018 Wildfire Smoke Event in San Francisco County as a Case Study Yiqun Ma* Yiqun Ma Arnab K. Dey Gabriel Carrasco-Escobar Changwoo Han François Rerolle Tarik Benmarhnia

Randomized controlled trials (RCTs) are considered a key identification strategy for establishing causal relationships between exposures and outcomes. When evaluating the health impacts of extreme weather events, however, RCTs are generally infeasible due to ethical issues, costs, and the lack of a suitable control group. Quasi-experimental designs capitalizing on the timing of natural experiments, such as Interrupted Time Series (ITS), offer a valuable alternative to estimate causal effects when control groups are not available. This paper explores the application of a two-stage ITS framework that compares traditional autoregressive integrated moving average (ARIMA) models and two machine learning algorithms: Neural Network Autoregressive (NNETAR) and Prophet-Extreme Gradient Boosting (XGBoost). As a case study, we assess the impacts of the 2018 wildfire smoke event on respiratory hospitalizations in San Francisco County, California. We split the data into pre- and post-event periods to train and evaluate the models, perform cross-validation for hyperparameter tuning, and predict hospitalizations under the counterfactual scenario. Data and R code are provided for reproducibility. In the case study, the Prophet-XGBoost shows the best model performance and was used to generate the counterfactual trends. We estimate that the 2018 smoke event resulted in a total of 115 (95% empirical confidence interval: 99, 131) excess respiratory hospitalizations (15.5% of the hospitalization count during the event period). Our proposed approach offers a powerful tool for assessing the effects of extreme weather events and can be broadly applied to other epidemiological contexts, such as public health policy evaluation.

LATEBREAKER

Health Disparities

Evaluating the Impact of Varying Bias Thresholds in Pulse Oximeter Performance on Racial and Ethnic Disparities: A Simulation Study in COVID-19 Patients Xinyi Sun* Xinyi Sun Xinyi Sun Theodore J Iwashyna Emmanuel Drabo Deidra Crews Kadija Ferryman John Jackson

Background

Pulse oximeters often overestimate oxygen levels in individuals with darker skin, potentially driving racial disparities in clinical care. The FDA's 2025 draft guidance highlights the need for evidence on acceptable bias thresholds, but how varying bias levels influence disparities remains unclear.

Objectives

To evaluate racial and ethnic bias in SpO_2 measurement and assess the impact of different "acceptable" bias thresholds on disparities.

Methods

We conducted a target trial emulation using EHR data from COVID-19 patients treated at Johns Hopkins Health System from March 2020 to June 2024. Race/ethnicity was self-reported and categorized per 2024 OMB standards, focusing on non-Hispanic Black (NHB) and White (NHW) groups. Exposure was SpO_2 measurement error, defined as SpO_2-SaO_2 difference. Hypothetical interventions varied by racial bias thresholds, each with assigned SpO_2 error distributions. Outcomes included supplemental oxygen and dexamethasone use (24 hours) and hospital readmission (30 days). We used G-computation to estimate average potential outcomes, standardized to the distribution of allowable covariates (e.g., measures of clinical indications) in NHB.

Results

Among 15,122 SpO_2-SaO_2 pairs (7,350 NHB; 7,772 NHW), NHB patients had greater measurement error (mean: 1.99% vs. 0.56%, $P < 0.001$) and a higher probability of occult hypoxemia (4.80% vs. 2.34%, $P < 0.001$). Supplemental oxygen use (~98%) was similar between groups, with no significant differences across interventions. NHW patients were more likely to receive dexamethasone (28.19% vs. 20.05%), with a disparity of -8.14% (95% CI: -15.60%, -1.12%), which decreased after adjusting for allowables. Hospital readmission rates were higher in NHB (14.10% vs. 8.73%), with a persistent disparity (~4%) across intervention scenarios.

Conclusions

Varying our specified racial bias thresholds in SpO_2 measurement had no impact on treatment disparities, while disparities in hospital readmission persisted.

Study Design

Has the “obesity paradox” been resolved by semaglutide trials Zhu Liduzi Jiesisibieke* Zhu Liduzi Jiesisibieke Zhu Liduzi Jiesisibieke Mary Beth Terry C Mary Schooling

Background: Semaglutide reduces weight and cardiovascular disease in older people with obesity, diabetes, or heart failure. Although, some benefits could be pleiotropic effects, these findings, consistent with previous small trials in older people, question the ‘obesity paradox’, which posits that higher body mass index (BMI) may be beneficial for older people or patients with heart disease. Here, we consider the role of selection bias, specifically survival bias, in the ‘obesity paradox’.

Methods: We clarified the role of different instances of survival bias using directed acyclic graphs (DAGs), which are often used to identify confounding. Specifically, we focused on different ways survival to recruitment, in general or amongst patients, could generate bias alone or as the result of the interplay of survival with confounders and competing risk.

Results: We developed a prototype DAG comprehensively identifying when survival bias could potentially occur, including due to selection on potential confounders. Typical situations where unrecoverable survival bias might occur, include selection on exposure and competing risk of the outcome, for example, the association of BMI with stroke cannot be observed when death from heart disease precludes occurrence of a stroke, making heart disease a competing risk before recruitment for stroke. The best way to mitigate selection bias is to address it at the study design stage, and to consider birth cohort studies, studies in younger people and target trial designs, apart from randomized trials which obviates both confounding and selection bias.

Conclusion: Selection bias due to survival, like confounding, can occur in many ways and may be difficult to recover from, especially if not addressed during study design. Survival bias may be inevitable in observational studies when selecting exposure and outcome, or a competing risk of the outcome, on survival to recruitment, such as in studies of patients.

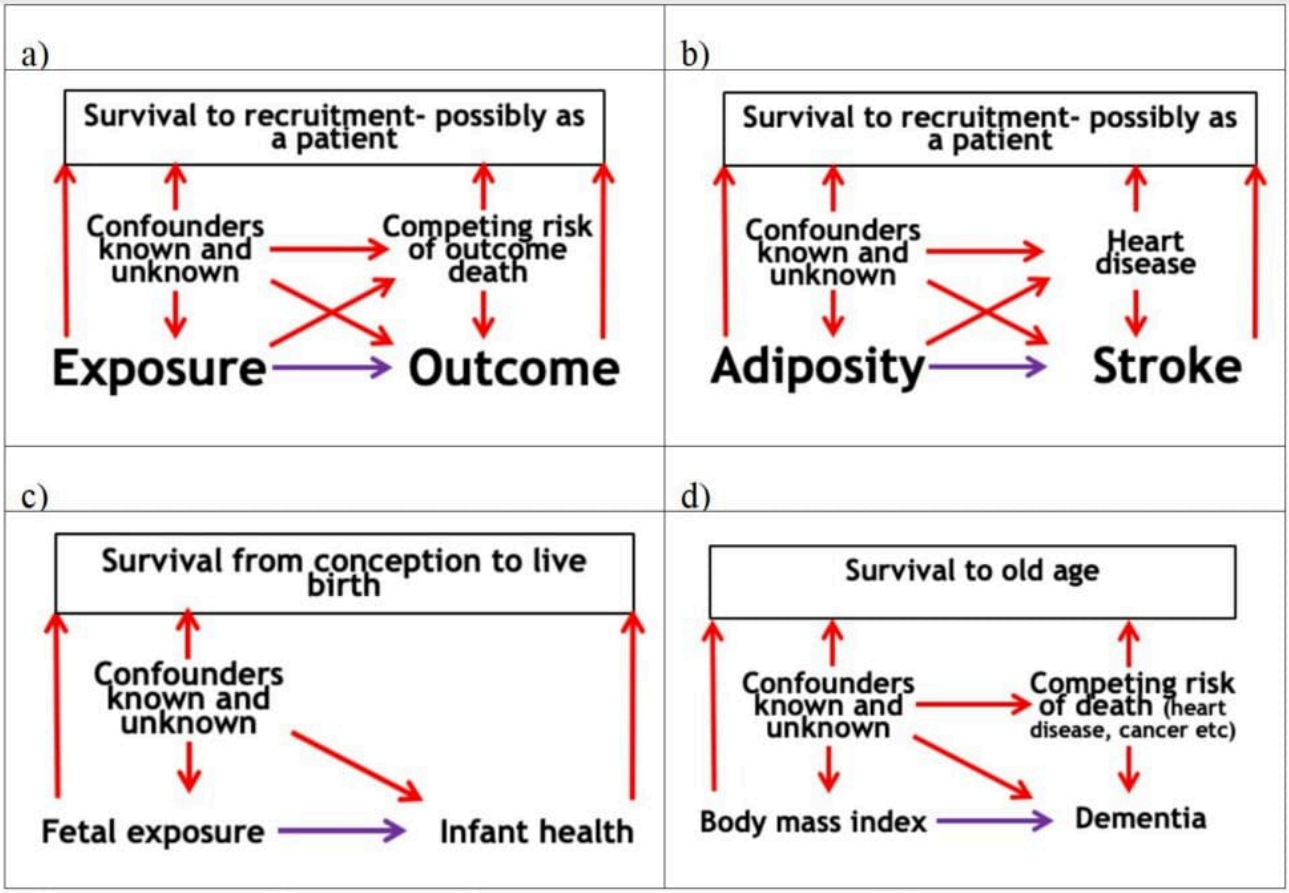


Figure 1. Directed acyclic graph showing a) the structure of bias induced by selection on survival, indicated by a box around the item, b) potential survival bias from competing risk by heart disease for a study of adiposity on stroke, c) potential survival bias for fetal exposures on infant health and d) potential bias from competing risk by heart disease and cancer for adiposity on dementia

Nutrition/Obesity

Association of Adiposity Measures and Metabolic Health with All-Cause Mortality in the Cooper Center Longitudinal Study Kimberly N. Doughty* Kimberly Doughty Qing Li David Leonard Carolyn E. Barlow Clare Meernik Tammy Leonard Valentine Y. Njike David L. Katz Jarett Berry Andjelka Pavlovic Laura DeFina Kerem Shuval

The validity of body mass index (BMI) as an indicator of health risk has been criticized, particularly when applied to those without obesity-associated metabolic dysfunction (i.e., “metabolically healthy obesity”). Some have proposed that BMI should be replaced by alternative measures of adiposity. However, how well alternative adiposity measures indicate health risk at the population level has not been clearly established. Long-term mortality risk related to metabolically healthy obesity also remains uncertain.

We analyzed data from 59,778 men and women who received examinations between 1978 and 2017. We used a parametric (Gompertz) proportional hazards mortality model to examine associations between adiposity measures (BMI, body fat, waist circumference, waist:height ratio, waist:hip ratio, and relative fat mass) and all-cause mortality, independently and jointly with metabolic health (0 vs. ≥ 1 metabolic syndrome criteria, excluding WC).

All adiposity measures were associated with increased mortality. As z-scores, body fat had the weakest association (aHR 1.11, 95% CI 1.08-1.14) and WC the strongest (aHR 1.21, 95% CI 1.18-1.24), although similar to BMI and waist:height (both aHR 1.19, 95% CI 1.16-1.22). Among metabolically healthy individuals (i.e., those with no metabolic syndrome criteria), increasing adiposity was associated with increased mortality for all adiposity measures. Risk associated with adiposity was further increased among those who also met ≥ 1 metabolic syndrome criteria. For example, BMI z-score was associated with mortality among metabolically healthy individuals (aHR 1.25, 95% CI, 1.09-1.41) and those with any metabolic syndrome criteria (aHR 1.51, 95% CI 1.32-1.69).

In this study, all adiposity measures were associated with mortality, even among metabolically healthy individuals and were more strongly associated with mortality among those with additional metabolic risk factors. BMI was one of the strongest predictors of mortality overall.

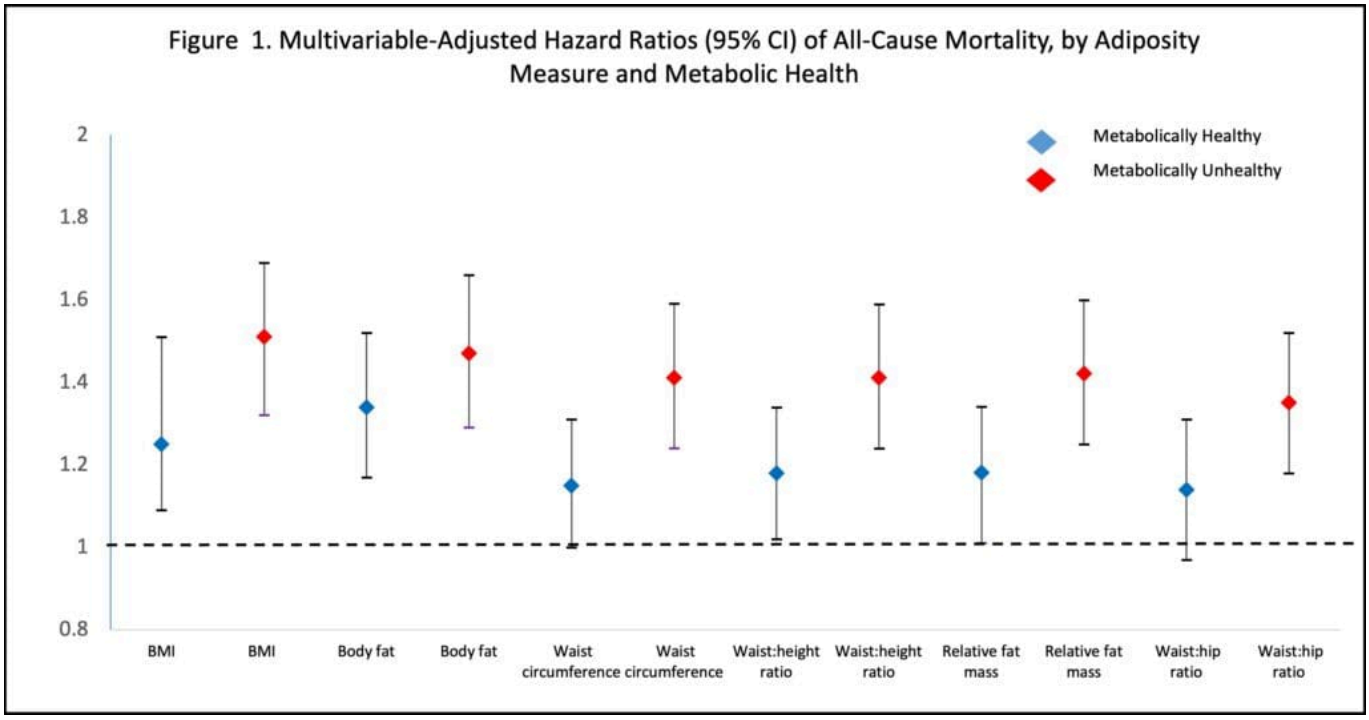


Figure 1. Multivariable-Adjusted Hazard Ratios (95% CI) of All-Cause Mortality, by Adiposity Measure and Metabolic Health
Metabolically Healthy
Metabolically Unhealthy
2
1.8
1.6
1.4
1.2
1
0.8
BMI
BMI
Body fat
Body fat
Waist circumference
Waist circumference
Waist:height ratio
Waist:height ratio
Relative fat mass
Relative fat mass
Waist:hip ratio
Waist:hip ratio

Reproductive

Preconception Cannabis Use and Total Gestational Weight Gain in a North American Prospective Cohort Lauren A Wise* Lauren A Wise Krystal E Kuan Alyssa F Harlow Kenneth J Rothman Lisa M Bodnar

Background: The effects of preconception cannabis use on gestational weight gain (GWG) are not well studied.

Methods: We assessed the association between preconception cannabis use and total GWG in a North American prospective cohort of 5,423 females aged 21-45 years who delivered singleton births during 2014-2024. Participants reported their average frequency of cannabis use in the previous 2 months on baseline and bimonthly follow-up questionnaires during preconception. On the postpartum questionnaire, participants reported GWG in 5-lb categories, which we validated against birth records from 7 US states. We converted GWG (kg) to z-scores using gestational age- and BMI-specific charts and defined excess GWG as >1 SD (equivalent to >50 lb at term for normal-weight female). We used log-binomial regression to estimate risk ratios (RRs) for excess GWG and linear regression to estimate mean differences (β) in GWG z-scores by prepregnancy BMI (kg/m2), adjusted for preconception behaviors, SES, race, ethnicity, and medical history.

Results: Mean GWG was 31 lbs (SD: 13.6); 7% and 5% used cannabis <1 and ≥1 time/wk, respectively. Cannabis users were more likely than non-users to be younger, less educated, smoke cigarettes, and report higher perceived stress, depressive symptoms, and prepregnancy BMI. There was moderate agreement between self-reported and birth-record-abstracted GWG (weighted Kappa=0.64, 95%CI: 0.60-0.67). Cannabis use (≥1 time/wk vs. non-use) was associated with a higher risk of excess GWG: RR=1.47, 95%CI: 1.08-2.02 and the β in GWG (lbs) for a 40-wk delivery increased with greater prepregnancy BMI (BMI 18.5-24.9: 2.16, 95%CI: -0.09, 4.47; BMI 25-29: 3.08, 95%CI: -0.31, 6.64; and BMI ≥30: 4.09, 95%CI: 0.11, 8.32).

Conclusions: Preconception cannabis use ≥1 time/week was associated with a clinically-relevant increase in total GWG. The magnitude of the increase was larger among participants with greater prepregnancy BMI.

Nutrition/Obesity

Examining dietary changes across pre-, post- and pregnancy time periods in the Nurses' Health Study 3 Kristen Lyall* Kristen Lyall Juliette Rando Jaime Hart Loni Tabb Marc Weisskopf Heather E. Volk Jorge Chavarro

Background: Prior work has documented the reproducibility of dietary intake captured by Food Frequency Questionnaires (FFQ), but data across the pre-, post-, and pregnancy periods, which may help guide longitudinal studies and inform practice, are lacking.

Methods: Using validated semi-quantitative FFQs collected pre, during, and post-pregnancy from the Nurses' Health Study 3 (NHS3), a prospective cohort of registered nurses in the US and Canada, we evaluated group-level mean nutrient and food group intake across these times. Correlation coefficients were calculated to assess agreement and compare to previously reported metrics.

Results: 2,757 participants had FFQs at all 3 time points, collected approximately 3 years before and after pregnancy (SD=1.5yrs). Mean intake of most factors increased during pregnancy relative to other time points, and was similar in pre- and post- periods, with the notable exceptions of decreases in alcohol and caffeine during pregnancy (mean 0.2gm/day and 66mg/day). The most substantial nutrient increases during pregnancy were for folate and iron (Figure 1; increases of 66% and 61% from pre-pregnancy, respectively; folate exceeded recommended levels: mean DFE= 2321mcg/day, SD=885). Servings/day of food groups changed little over time periods, with the exception of vegetables and dairy, which decreased and increased respectively during pregnancy by approximately ½ serving/day. Correlations across times were comparable to lower (0.2-0.5 for most nutrients and foods; .1 for folate, iron and zinc) than previously-published metrics in other populations not across pregnancy.

Conclusions: Expected changes in dietary intake were observed during pregnancy relative to pre- and post-pregnancy periods in this large national sample of women. Stability in food group intakes over time was supported across these childbearing periods, but higher than recommended average levels of certain nutrients such as folate may warrant further consideration.

Figure 1: Average nutrient changes over pre-pregnancy, pregnancy, and post-pregnancy in NHS3

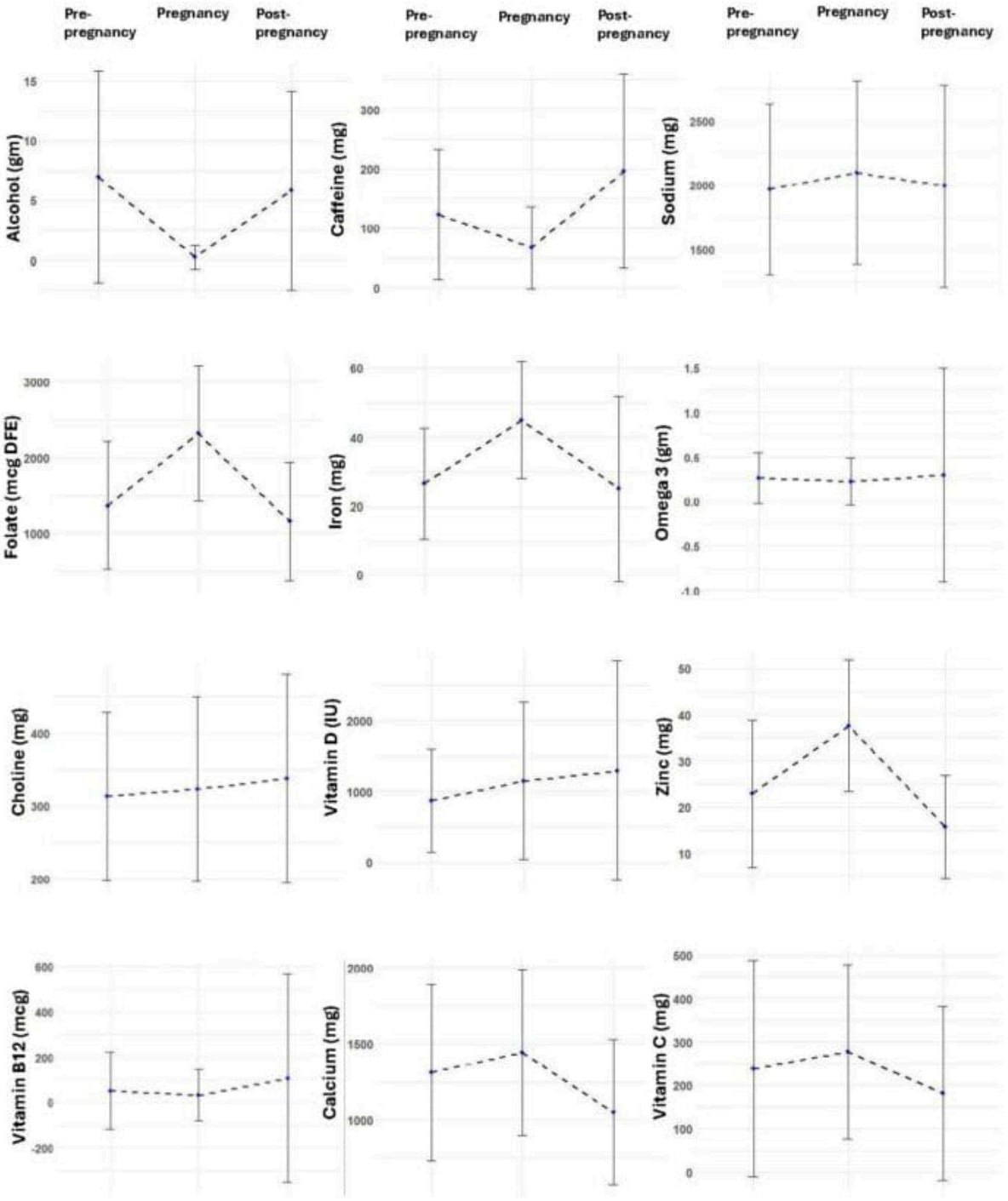


Figure legend: Graphs show mean nutrient values at each time point. Error bars show SD from the mean.

Nutrition/Obesity

The per-protocol effect of adherence to the low-fat dietary pattern intervention on visceral adipose tissue levels in the Women's Health Initiative Dietary Modification Trial Anais Elena Fernandez Calzavara* Anais Elena Fernandez Calzavara Jiarui Li Matthew J. Landry Jennifer W. Bea Marian L. Neuhouser Matthew Allison Thomas E. Rohan Lesley F. Tinker Linda G. Snetselaar Jean Wactawski-Wende JoAnn Manson Andrew O. Odegaard

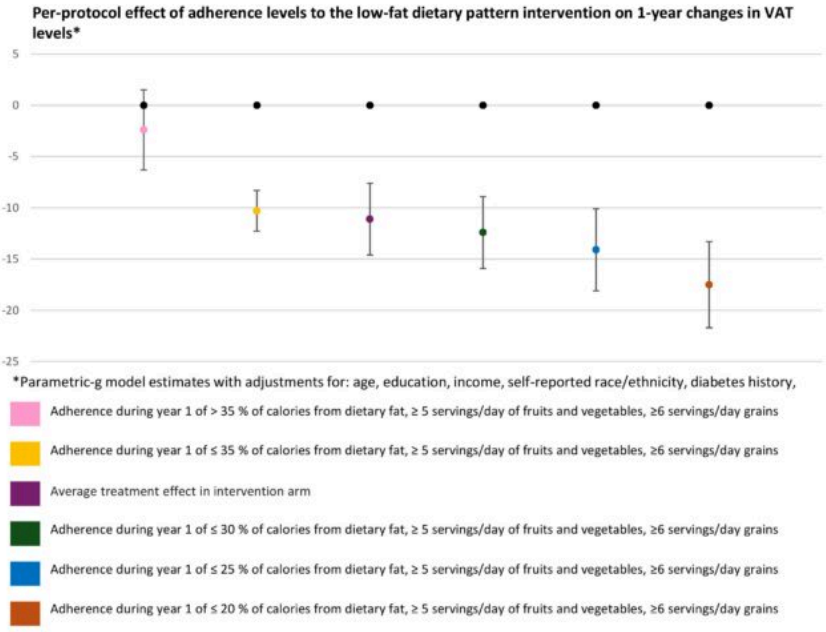
Objective: Strong evidence supports that higher levels of abdominal visceral adipose tissue (VAT) drive obesity-related chronic disease risk. Yet, there is little evidence of the impact of specific dietary interventions, and in particular, decreasing dietary fat levels, on VAT. We estimated the per-protocol effects of adherence to the low-fat dietary intervention among postmenopausal women in the Women's Health Initiative (WHI) Dietary Modification (DM) trial on 1-year changes in VAT levels.

Methods: The DM trial was designed to reduce total fat intake to 20% of total energy, and increase both vegetable/fruit intake to ≥5 and grain intake to ≥6 servings/day. We analyzed equation-derived estimates of VAT in participants in the DM intervention group who had baseline and year 1 whole-body dual-energy X-ray absorptiometry scans for body composition (n=1043). Adherence during this year was assessed via the year 1 food-frequency questionnaire. We used the parametric g-formula to estimate the per-protocol effect of adherence to varying levels of dietary fat intake (% of total energy), while meeting the fruit/vegetable and grain intake aspects of the intervention on 1-year VAT changes, adjusting for pre and post-randomization predictors of protocol deviation and loss to follow-up.

Results: On average, participants randomized to the DM intervention arm had a reduction of 10.3 cm2 (95% CI, -12.3, -9.0) of VAT at year 1. When classifying participants according to adherence levels of dietary fat intake during the intervention (% of total energy: > 35, ≤35, ≤30, ≤25, ≤20%), there was a respective stepwise decrease in VAT (Table), with the greatest effect aligning with adherence to the targeted intervention of ≤20%: -17.5 (95% CI, -21.7, -13.3).

Conclusions: Among postmenopausal women in the WHI DM trial, greater levels of adherence to the low-fat dietary pattern intervention corresponded to greater decreases in VAT.

Women's Health Initiative (WHI) Dietary Modification Trial: Per-protocol effect of adherence levels to the low-fat dietary pattern intervention on 1-year changes in VAT levels



Health Services/Policy

Using difference-in-difference analysis and decision trees to examine the efficacy of overdose prevention policies on opioid overdose mortality Chinelo Onyebeke* Chinelo Onyebeke John Pamplin

More than 500,000 people have died of opioid overdose in the US since 1999 and the number is still increasing per year. Rates of opioid overdose death are rising faster for Black people than any other racial/ethnic group, possibly due to reduced access to quality healthcare (including naloxone access), financial barriers, and mistrust of medical and other systems that are discriminatory and stigmatizing. Overdose prevention policies (i.e., Good Samaritan Laws and Naloxone Access Laws) are policy interventions enacted to reduce overdose mortality. Good Samaritan laws are state laws that provide legal protections for individuals who call 911 for the person experiencing the overdose. Naloxone access laws permit prescribing and dispensing of naloxone (i.e., Narcan, etc.) by health care providers and encourage its use by laypersons in a position to assist a person experiencing a drug overdose.

The goal of our study was to identify the set of harm reduction law provisions that provided the greatest reductions in opioid overdose mortality, both for the overall population and specifically among Black people. We generated difference-in-difference (DID) estimates of the effect of a policy enactment on overdose rates, as well as conducted a decision tree regression to show the predicted DID estimate based on which policy provisions were enacted.

In the preliminary decision tree results, the largest decrease in overdose deaths per 100,000 population was seen for Black individuals (including only enactments in which the parallel trends assumption was met for the DID analysis), where there was a predicted average decrease of 0.112 overdose deaths per 100,000 population when enactments contained the following policy provisions: “NAL Prescriber Immunity (civil)” and “NAL Prescriber Immunity (criminal)”. The findings of this study will aid in implementing sets of policies that best reduce opioid overdose rates for the overall population and Black individuals.

Health Services/Policy

A randomized study of cash transfers on biomarkers of inflammation and infection among the ultra-poor Rebecca Stebbins* Rebecca Stebbins Audrey Pereira Allison E. Aiello Sudhanshu Handa

The immune system is highly sensitive to stressors, with economic hardship being a significant source of stress, particularly for individuals living in resource-limited settings. In this study, we examine the effects of a government cash transfer program, and its impact of alleviating economic stress, on immune function and infectious disease biomarkers in Malawi. Using data on 1,788 youth participants (mean age = 24 years) and 2,118 adult caregiver participants (mean age = 59 years) in the Malawi Social Cash Transfer Project (SCTP), we described the distribution of C-reactive protein (CRP), cytomegalovirus (CMV), and herpes simplex virus (HSV)-1 in a low resource setting and tested whether these biomarker levels were associated with a randomized cash transfer treatment. The Malawi SCTP is an unconditional poverty-targeted cash transfer program administered by the Ministry of Gender, Community Development and Social Welfare, reaching approximately 10% of the population. The transfer size varies by household size and averages approximately US$8 per month per household (18% of pre-program consumption). Households were randomized to begin receiving cash transfers either in 2013 (treatment group) or 2016 (delayed-entry control group). Biomarkers were measured from dried blood spot samples collected in 2021-2022. We found that over 99% of all participants were seropositive to both CMV and HSV-1. Average CRP levels were high at 296.8 (SD 286.72) pg/mL for adults and 252.6 (SD 279.0) pg/mL for youth. While levels CRP (pg/mL), CMV IgG, and HSV IgG levels were roughly 4% higher among participants in the cash transfer treatment group versus the control group, respectively, but the associations were not statistically significant. These findings highlight the extreme viral and immune burden experienced by this population, which in turn explains why the three additional years of cash support had no impact.

Health Services/Policy

Access to and health outcomes associated with pharmacist-initiated prescribing services among equity-deserving groups Fiona Chan* Fiona Chan Colin Dormuth

Evidence suggest that certain equity-deserving groups (EDGs) have reduced access to independent pharmacist prescribing services, such as those support by the Pharmacist Prescribing for Minor Ailments and Contraceptives policy (PPMAC) in British Columbia, Canada. More rigorous studies are needed to assess for access issues and differences in outcomes for these groups. The study objective is to evaluate, by social strata, the differences in rates of access to PPMAC for treatment of uncomplicated urinary tract infections (UTI) and in the outcome of the consult. In the first year since policy implementation on Jun 1, 2023, there were approximately 83,000 PPMAC claims for UTIs, representing the most common PPMAC claim. A cohort of PPMAC service recipients for UTI from Jun 1, 2023 to Dec 31, 2024 will be assembled using administrative health data. Key EDGs of interest include older adults, females, rural residents, and lower income individuals. To understand the effects at various intersections of social identity, social strata will be defined for each patient as the combination of status in each EDG. The main outcome of whether a prescription was issued and/or the patient referred following the consult will be identified through unique claims codes. Rate of visitation will first be calculated by social strata. To estimate the odds of prescription and/or referral receipt for each social strata adjusted for health status, fixed effect logistic regression models will be used with interaction terms for status in various EDGs included. ORs, predicted probabilities, and their 95%CIs will be reported. Multilevel analysis of individual heterogeneity and discriminatory accuracy (MAIHDA) will also be conducted to understand the extent that the variation between social strata is not explained by the additive effects of the individual social identities. The results will be crucial to guide policymakers on how to revise the current policy to reduce inequities.

Cardiovascular

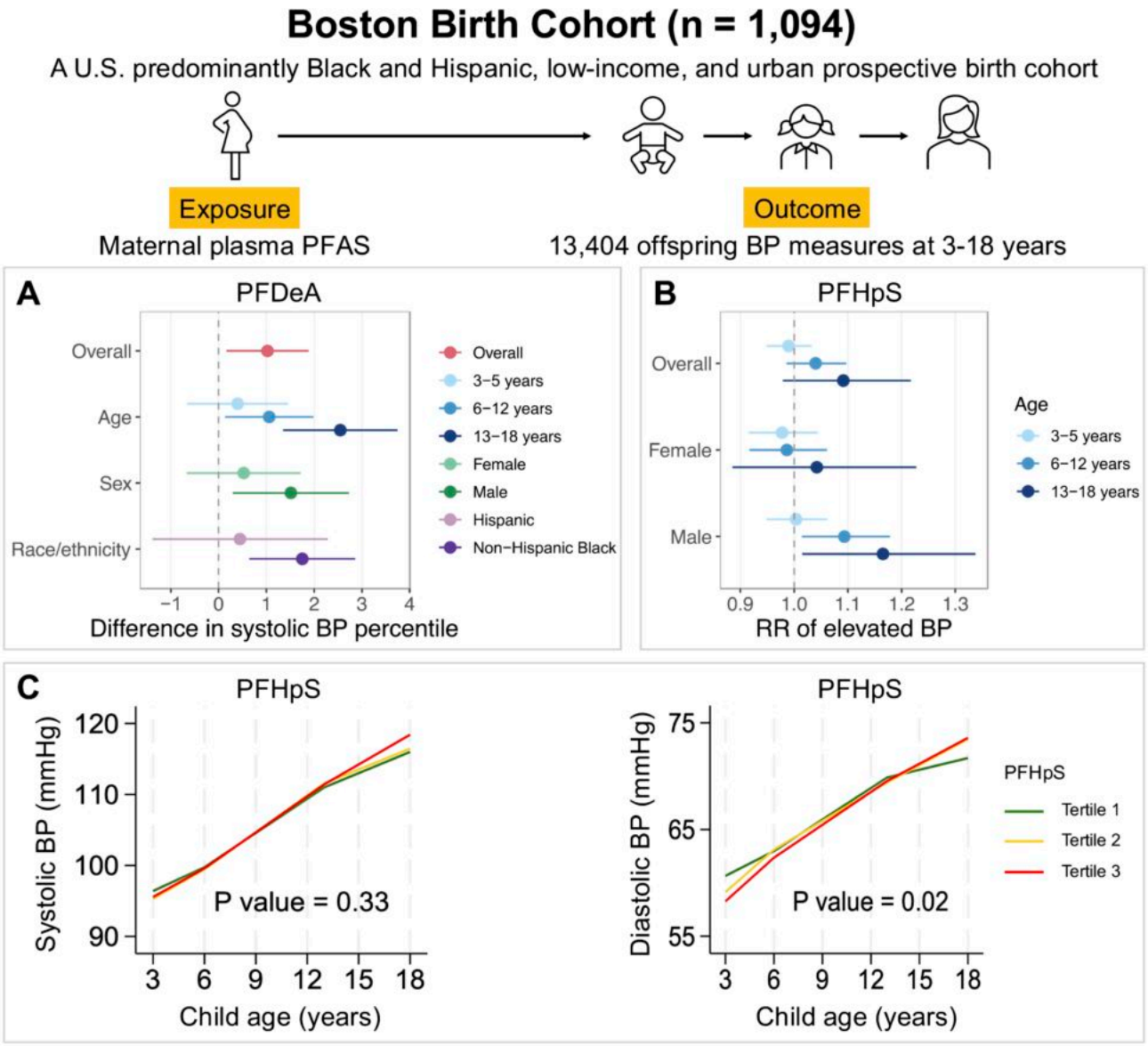
Prenatal per- and polyfluoroalkyl substances (PFAS) exposures and longitudinal blood pressure measurements in children aged 3-18 years: Findings from a racially and ethnically diverse U.S. prospective birth cohort Zeyu Li* Zeyu Li Guoying Wang Xiumei Hong Tammy M. Brady Colleen Pearson Jessie P. Buckley Xiaobin Wang Mingyu Zhang

Background: Prenatal PFAS exposures may increase offspring blood pressure (BP), but long-term studies in diverse populations are limited.

Methods: Participants were from the Boston Birth Cohort, a predominantly Black and Hispanic, low-income, and urban cohort. We measured PFAS in maternal plasma collected at delivery and extracted offspring BP from medical records. We derived age-, sex-, and height-specific BP percentiles and defined elevated BP as systolic/diastolic BP ≥90th percentile (ages 3-<13y) or ≥120/80 mmHg (ages 13-<18y). We used linear and modified Poisson mixed-effects models to examine associations of PFAS with BP percentiles and elevated BP. We used linear spline mixed-effects models to predict BP trajectories at ages 3-18y by PFAS levels. We adjusted for covariates listed in the **Figure** footnote.

Results: We analyzed 13,404 BP measures from 1,094 children (median follow-up: 12y [IQR: 9-15y]), with 61% Black and 22% Hispanic participants. Overall, each doubling of PFDeA, PFNA, and PFUnA was associated with a 1.02 (95% CI: 0.16-1.88), 1.15 (95% CI: 0.10-2.19), and 0.76 (95% CI: 0.14-1.39) percentile higher systolic BP, respectively. There were age-, sex-, and race/ethnicity-specific associations for PFDeA, PFHpS, PFNA, and PFUnA. For example, associations of PFDeA with systolic BP percentile were stronger in older (β3-5y=0.40; β6-12y=1.06; β13-18y=2.55), male (βmale=1.51; βfemale=0.52), and Black (βBlack=1.75; βHispanic=0.45) participants (**Panel A**). In males, each doubling of PFHpS was associated with a 1.09 times risk of elevated BP at ages 6-12y and a 1.17 times risk at ages 13-18y, with no increased risk at ages 3-5y (**Panel B**). PFHpS was associated with dose-dependent divergence in BP trajectories beginning at 13y (**Panel C**).

Conclusions: Prenatal PFAS exposures are associated with higher offspring BP, with stronger associations in adolescents, males, and Black children. Prenatal PFAS may have intergenerational, long-term, and latent hypertensive effects.



Footnote: Models were adjusted for maternal age, race/ethnicity, education, marital status, pre-pregnancy BMI, smoking history during pregnancy, parity, delivery mode, and maternal hypertensive disorders. The models stratified by race/ethnicity did not adjust for race/ethnicity.
Abbreviations: PFAS: per- and polyfluoroalkyl substances; BP: blood pressure; PFDeA: perfluorodecanoic acid; PFHpS: perfluoroheptanesulfonic acid.

Women’s Health

Gestational hypertension and risk of cardiovascular disease development in women who have had infants with congenital heart defects in Arkansas, 1997 to 2011 Emine Bircan*
Emine Bircan Mohammed Orloff Laura Hays Jun Ying Hari Eswaran Wendy N Nembhard

Preeclampsia and gestational hypertension are common hypertensive pregnancy disorders, with preeclampsia a recognized risk factor for future cardiovascular disease (CVD). Similarly, adverse pregnancy outcomes, including carrying a fetus with congenital heart defects (CHDs), are linked to an increased CVD risk later in life. Women with pregnancies complicated by both CHDs and gestational hypertension may face an elevated CVD risk. This study examines the association between gestational hypertension and CVD risk in women with CHD-affected pregnancies.

Data from the Arkansas site of the National Birth Defects Prevention Study (1997–2011) included 1,423 women with a CHD-affected pregnancy, 1,426 women with a non-CHD birth defect pregnancy, and 1,020 women who delivered infants without structural defects. Maternal sociodemographics, pregnancy complications, and periconceptional risk factors were obtained via telephone interviews. These data were linked to the 2000–2022 Arkansas All-Payers Claims Database to identify subsequent CVD cases. CVD, classified using ICD-9/10-CM codes, included ischemic heart disease, cerebrovascular disease, hypertension, and other heart conditions. Cox proportional hazards models were used to estimate unadjusted and adjusted hazard ratios (HRs) with 95% confidence intervals (CIs) based on time to the first CVD event.

Among women with gestational hypertension (n=521), CHD was found no impact on the CVD risk. Among women without gestational hypertension (n=3,348), those with CHD-affected pregnancies had a hazard ratio (HR) of any CVD of 1.4 (95% CI of HR: 1.1–2.1) against women with pregnancies without structural birth defects.

In women with gestational hypertension, CHD-affected pregnancies were not associated with an increased risk of CVD, likely due to the dominant influence of gestational hypertension as a primary risk factor, potentially obscuring additional effects.

Cardiovascular

Age at Type 2 Diabetes Diagnosis, Depression, and Risk of Cardiovascular Disease: Findings from the Women's Health Initiative Godness Biney* Godness Biney Matthew Allison Tomas Nuño3 Elizabeth Bertone-Johnson Cassandra Spracken

Cardiovascular diseases (CVD) are a leading cause of morbidity and mortality globally and in the United States (US). Type 2 Diabetes (T2D), which affects over 37 million Americans, and depression, impacting more than 21 million US adults, have been identified as significant risk factors for CVD. Epidemiological evidence suggests a bidirectional relationship between T2D and depression. However, their compounded risk on CVD is largely understudied, with no study to date assessing the interaction between T2D or age at T2D diagnosis and depression and their impact on CVD risk. This study aimed to investigate how age at T2D diagnosis and potential interactions with depression can impact the relationship between T2D and cardiovascular events among participants in the Women's Health Initiative (WHI) cohort. WHI is a large, multi-racial cohort of postmenopausal women in the US. At baseline and follow-up, participants self-reported their depression status (Yes/No), T2D status (Yes/No), and the age group they were diagnosed with T2D. Based on this information, we categorized age at onset into early (30-49) versus late (>=50). We also categorized our T2D duration into five years intervals. Incident CVD events (i.e., any CVD event, CHD, CHF, MI, and stroke) were all adjudicated outcomes and binary in nature (Yes/No). Cox proportional hazard regression models were used to estimate the unadjusted and adjusted hazard ratios (HR) and their 95% confidence intervals (95% CI) for the association between Age at T2D and incident CVDs, considering depression as an effect modifier. After adjusting for crucial covariates, we found that individuals with early onset T2D (30-49) who also have depression are at a heightened risk for any CVD, specifically CHF compared to their counterparts with depression and late (>=50) onset T2D. We also found that individuals with a longer duration of T2D who also had depression were at a progressively increasing risk of any CVDs with every five-year increase in the duration of T2D. These results support the bidirectional relationship between T2D and depression and their compounded risk on CVD. Our study emphasizes the need for a comprehensive, multidisciplinary approach to care.

Cardiovascular

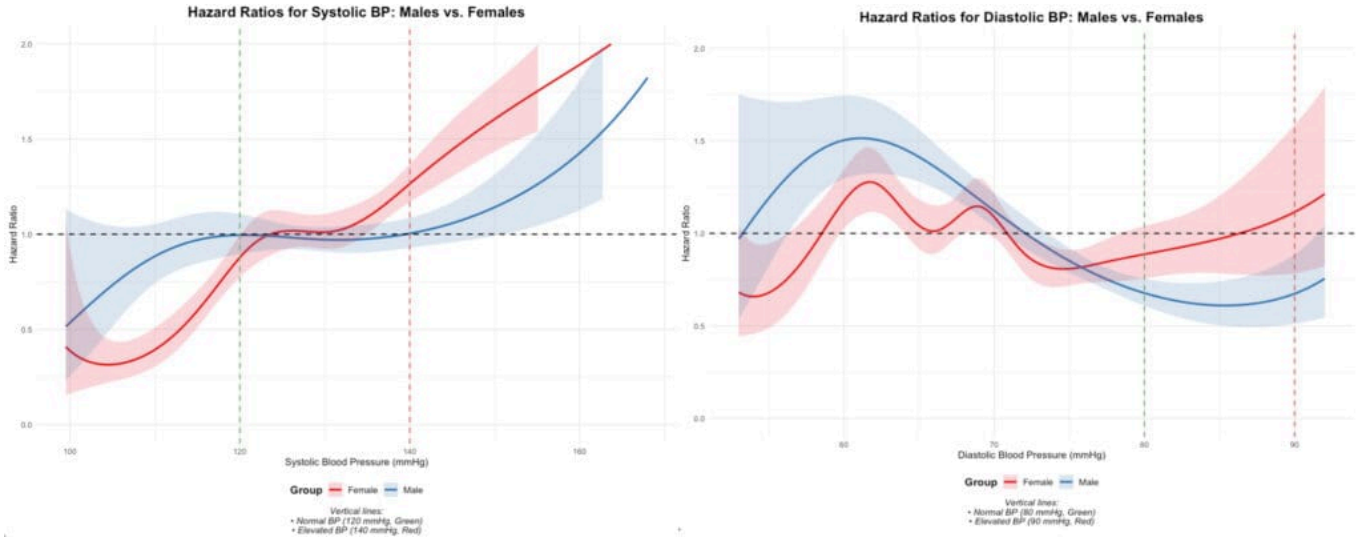
The Association of Systolic and Diastolic Blood Pressure with Progression from Mild Cognitive Impairment to Dementia Silvia Miramontes* Silvia Miramontes Erin L. Ferguson Hunter Mills Evan Phelps Boris Oskotsky Elena Tsoy Maria Glymour Marina Sirota

Introduction: Mild cognitive impairment (MCI) is considered a transitional stage between normal cognition and dementia. Blood pressure (BP) is an accepted dementia risk factor, but its association with progression from MCI to Alzheimer's Disease and Related Dementias (ADRD) is uncertain.

Methods: For 8,026 UCSF patients diagnosed with MCI, we calculated median BP over the 5 years preceding diagnosis (M=18 measurements per person) from electronic health records. Cox proportional hazards models assessed the association of systolic and diastolic BP (linear and restricted cubic splines) with incident ADRD, stratified by sex and race/ethnicity.

Results: Participants (mean age=70.7) were 57% female, 54% White, 22% Asian, 8% Black or African American, 8% Latinx, and 8% Other. Higher systolic BP (SBP) was more strongly associated with ADRD risk (HR:1.10 per 10 mmHg; 95% CI:1.06-1.13) than diastolic BP (DBP) (HR:1.01 per 10 mmHg; 95% CI:0.95-1.07). In sex-specific models, higher SBP was linearly associated with elevated ADRD risk in females (HR:1.14 per 10 mmHg increase; 95% CI:1.09-1.20), but not males (HR:1.03; 95% CI:0.97-1.10). DBP was similarly associated with ADRD risk in females (HR:1.08 per 10 mmHg increase; 95% CI:0.99-1.20) but not males (HR:0.92; 95% CI:0.84-1.00). Interaction models showed weaker BP effects in males (SBP interaction HR:0.90, p=0.003; DBP interaction HR:0.864, p=0.016) compared to females. DBP was more strongly associated with ADRD risk in Asians than in Whites (DBP interaction HR:1.18, p=0.028), with no differences observed in other groups. Spline models suggested non-linear associations for both BP types, with higher ADRD risk at extreme BP levels, particularly in females (Fig).

Conclusion: SBP was associated with progression to ADRD in females but not males. Diastolic BP may play a stronger role in ADRD risk in Asians compared to Whites. BP may influence which patients develop ADRD, though the causal nature of these findings remains uncertain.



Cardiovascular

Cardiovascular health and its association with all-cause dementia, parkinson's disease and mortality among UK older adults: a multistate analysis Michael F. Georgescu* Michael Georgescu May A. Beydoun Jordan Weiss Jagdish Kubchandani Sri Banerjee Alyssa A. Gamaldo Michele K. Evans Alan B. Zonderman

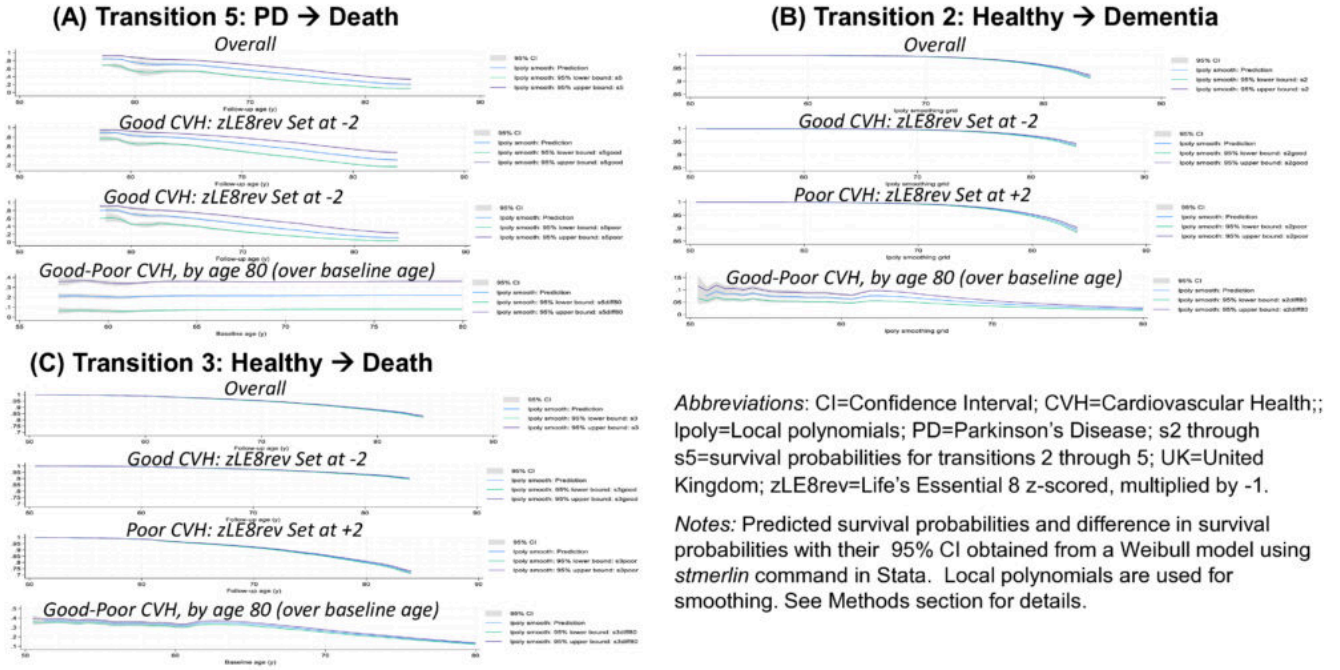
Background: The study investigated the relationship between cardiovascular health (CVH), all-cause dementia, Parkinson's disease (PD) and mortality, identifying associations and transitions.

Methods: Using data from the UK Biobank (n=269,816, Age = 60+y individuals, ≤15y follow-up). We investigated the relationships between cardiovascular health and PD, dementia, and mortality using Cox Proportional Hazards with sequential covariate adjustment. Finally, we used multistate parametric models to identify health state transitions: healthy (state 1; dementia- and PD- free), PD (state 2; irrespective of dementia status), dementia (state 3; irrespective of PD status), death (state 4). Transition rates between the states were modeled using fully parametric Weibull regression.

Results: Full models found poor CVH associated with a 14% increased risk of all-cause dementia and 31% increased risk for all-cause mortality. Healthy and PD transition had no association; however, poor CVH and transition PD and death, Healthy and dementia, Healthy and death had a positive relationship. Transitions PD Dementia and Dementia Death was not associated with poor CVH z-score.

Conclusions: CVH was associated with transition from PD to death and from "Healthy" to Dementia/Death. In conclusion, poor CVH was directly associated with increased risk of mortality from PD into Death, Healthy into Dementia, and Healthy into Death.

FIGURE 1: Transition probability for all 4 states, overall, among good cardiovascular health, poor cardiovascular health and differences in survival (good-poor): UK Biobank 2006-2021



Abbreviations: CI=Confidence Interval; CVH=Cardiovascular Health;; lpoly=Local polynomials; PD=Parkinson's Disease; s2 through s5=survival probabilities for transitions 2 through 5; UK=United Kingdom; zLE8rev=Life's Essential 8 z-scored, multiplied by -1.

Notes: Predicted survival probabilities and difference in survival probabilities with their 95% CI obtained from a Weibull model using *stmerlin* command in Stata. Local polynomials are used for smoothing. See Methods section for details.

Methods/Statistics

Sampling for computational efficiency when conducting analyses in big data Jacqueline E Rudolph* Jacqueline Rudolph Yiyi Zhou Steven Xu Eryka Wentz Maylin Palatino Karine Yenokyan Anyue Ruan Keri Calkins Corinne Joshu Bryan Lau

Background. A challenge to research in big data is the inherent computational intensity of analyses, particularly when using rigorous methods to address biases. We demonstrate the use of sampling methods in big data to estimate parameters using fewer resources. Our motivating question was whether lung cancer incidence differs by HIV status, in nearly 30 million Medicaid beneficiaries.

Methods. We built a cohort of Medicaid beneficiaries, aged 18-64, who enrolled 2001-2015 in 14 US states and had 6 months of enrollment (run-in period) with no evidence of cancer. HIV status at baseline was based on presence of an HIV diagnosis during the run-in period. Beneficiaries were followed from baseline until lung cancer diagnosis or censoring. We targeted three parameters: IRR (Poisson model), HR (Cox model), and RR (Kaplan-Meier). We controlled for confounders using inverse probability weights. We ran the analysis using the full sample and several sampling schemes: divide and recombine (10, 20, 50 samples), sub-cohort, and case-cohort. We compared point estimates, standard errors, computation time (hours), and memory used (GB). Analyses were run on one server node with four CPUs, 64 cores, and 660GB of RAM.

Results. We included 29,360,920 beneficiaries, of whom 180,980 beneficiaries (0.6%) had HIV at baseline. We observed 1113 incident lung cancer diagnoses among beneficiaries with HIV and 33,106 among beneficiaries without HIV. Our findings for the risk ratio are summarized in the Table. Inferences were similar across target parameters, although findings obtained using Poisson and Cox modeling required fewer resources (time and memory).

Conclusions. Sub-cohort and case-cohort were more reliable than divide and recombine. The latter performed poorly when estimating the RR and only improved computation time when parallelized (at the cost of memory). Between sub-cohort and case-cohort, including non-sampled cases resulted in increases in computation time and memory.

Table. Comparing sampling approaches for estimating the weighted risk ratio at 5 years

Approach	Risk Ratio	Absolute Error	Standard Error: 100 B	Computation Time: 100 B (hours)	Estimated Computation Time: 500 B (hours)	Memory Used (GB)
Full sample	1.39	0.00	0.09	74.10	367.26	145.2
Divide (10; NP)	1.24	0.15	0.08	53.66	267.14	42.5
Divide (10; P)	1.23	0.15	0.07	15.38	76.48	161.9
Divide (20; NP)	1.17	0.22	0.07	41.83	206.75	32.5
Divide (20; P)	1.17	0.22	0.07	12.00	59.58	136.0
Divide (50; NP)	0.84	0.54	0.05	40.72	201.41	20.8
Divide (50; P)	0.87	0.52	0.05	11.41	56.87	70.9
Sub-cohort (25%)	1.38	<0.01	0.09	14.63	72.52	67.5
Sub-cohort (10%)	1.41	0.03	0.10	4.83	23.93	37.5
Case-cohort (25%)	1.38	0.01	0.09	25.32	125.35	78.5
Case-cohort (10%)	1.39	<0.01	0.09	9.68	48.00	36.9

Abbreviations: B, bootstraps; GB, gigabytes; NP, no parallelization; P, parallelization

Methods/Statistics

Differentially Private Modeling of Disease Transmission within Human Contact Networks

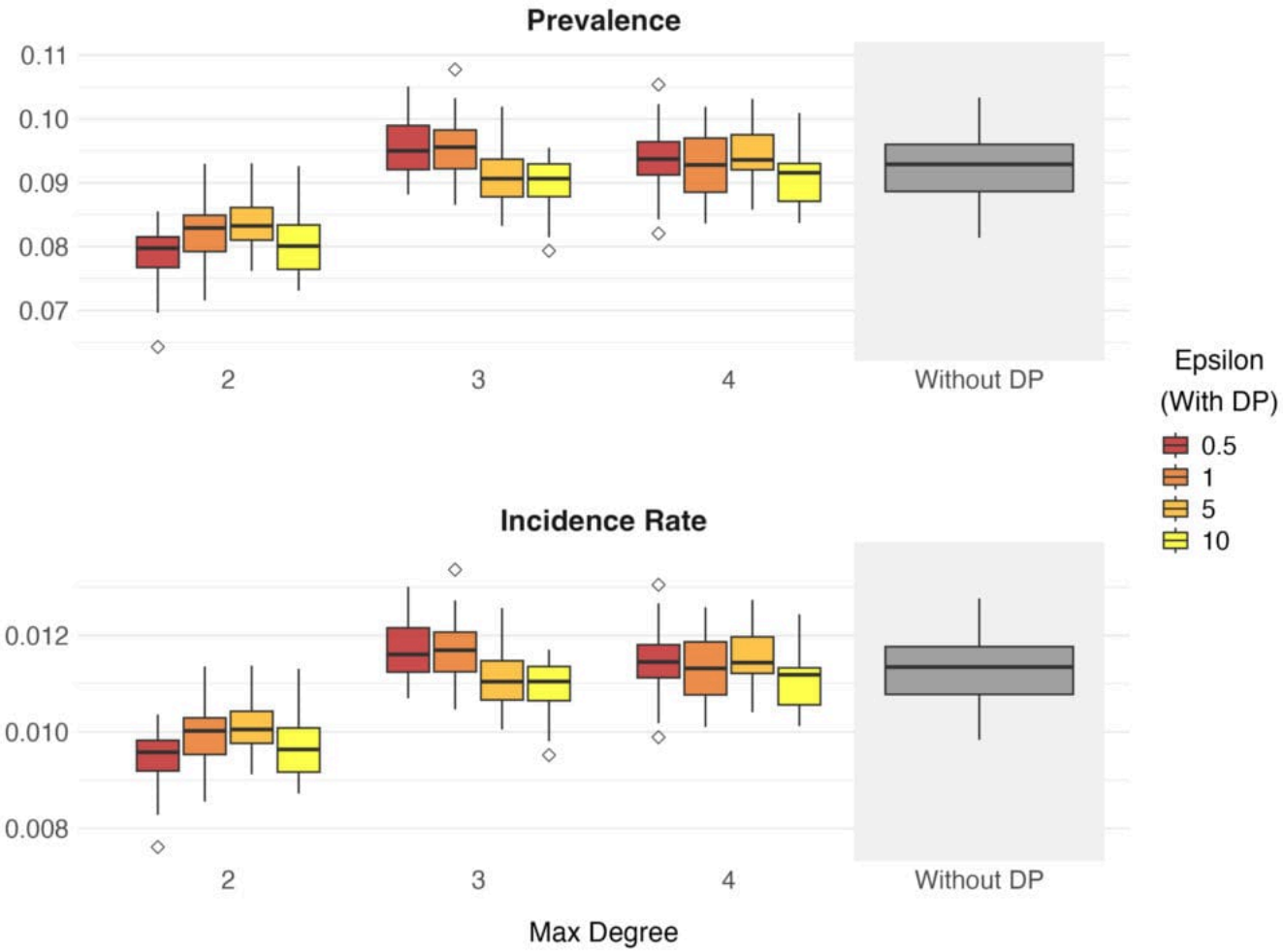
Debanuj Nayak* Shlomi Hod Debanuj Nayak Iden Kalemaj Jason R. Gantenberg Thomas A. Trikalinos Adam Smith

Epidemiologic studies of infectious diseases often rely on models of contact networks to capture the complex interactions that govern disease spread. Data on how people interact may include sensitive information about sexual relationships or drug use behaviors. Protecting individual privacy while maintaining the scientific usefulness of the data is crucial.

Differential privacy (DP) is a mathematical framework that protects sensitive data by limiting the influence of a given person's data on an aggregate statistic. In general, DP involves adding random noise—calibrated to control the tradeoff between privacy and accuracy—to the calculation. In the context of network data, where individuals are modeled as nodes of a network, node-DP safeguards both an individual's data and their social connections.

We propose a privacy-preserving pipeline for simulating disease spread on network data which integrates node-DP with exponential random graph models (ERGMs). Our pipeline comprises three steps: (1) compute network statistics using node-DP, (2) fit an ERGM to these statistics to generate synthetic networks reflecting the structure of the original network, and (3) simulate disease spread on the synthetic networks using an agent-based model.

We evaluate the effectiveness of our approach using a simple Susceptible-Infected-Susceptible (SIS) disease model under multiple configurations. We compare simulated disease incidence and prevalence on networks generated with and without node-DP, based on egocentric sexual network data from the ARTNet study (a survey about HIV-related behaviors among MSM in the US). Our results show that the noise added for privacy is small relative to the other sources of error (sampling and modeling, for example). They suggest that, in principle, our pipeline can provide valuable epidemiologic insights while maintaining privacy. Future work will explore more complex networks and simulators.



Boxplots of simulated epidemic outcomes from the agent-based model (average prevalence and incidence rate over the final 100 time steps) across ERGM network samples. ERGMs were fitted using network statistics calculated either with or without differential privacy (DP). Epsilon indicates the level of privacy protection, where lower epsilon values translate into stronger privacy protection. We preprocessed the network to restrict maximum node degree (in this case, number of sexual partners) to a predefined value (max_degree), due to the requirements of the differential privacy algorithm.

Methods/Statistics

Comparison of immortal time bias across four time-zero settings Hiroya Morita* Hiroya Morita Masataka Taguri

Introduction

In epidemiological research, time-related biases can have a substantial impact on the results. One prominent example of such a bias is immortal time bias, for which various strategies have been proposed to address. One such approach is the prevalent new user design (PNUD), which can be used when non-users are selected as the comparison group. In this method, matching is performed between the non-user group and the treatment group based on the time elapsed since the cohort entry date (CED).

Purpose

In the PNUD, individuals who will eventually receive treatment could be matched as non-users. An inappropriate method is to exclude those subjects from being matched as the non-user, as this approach cannot eliminate bias. We call this method inappropriate PNUD. The aim of this study is to compare scenarios through simulation: inappropriate PNUD and another in which immortal time bias arises without using PNUD, in order to assess the degree of bias generated when PNUD is used incorrectly.

Method

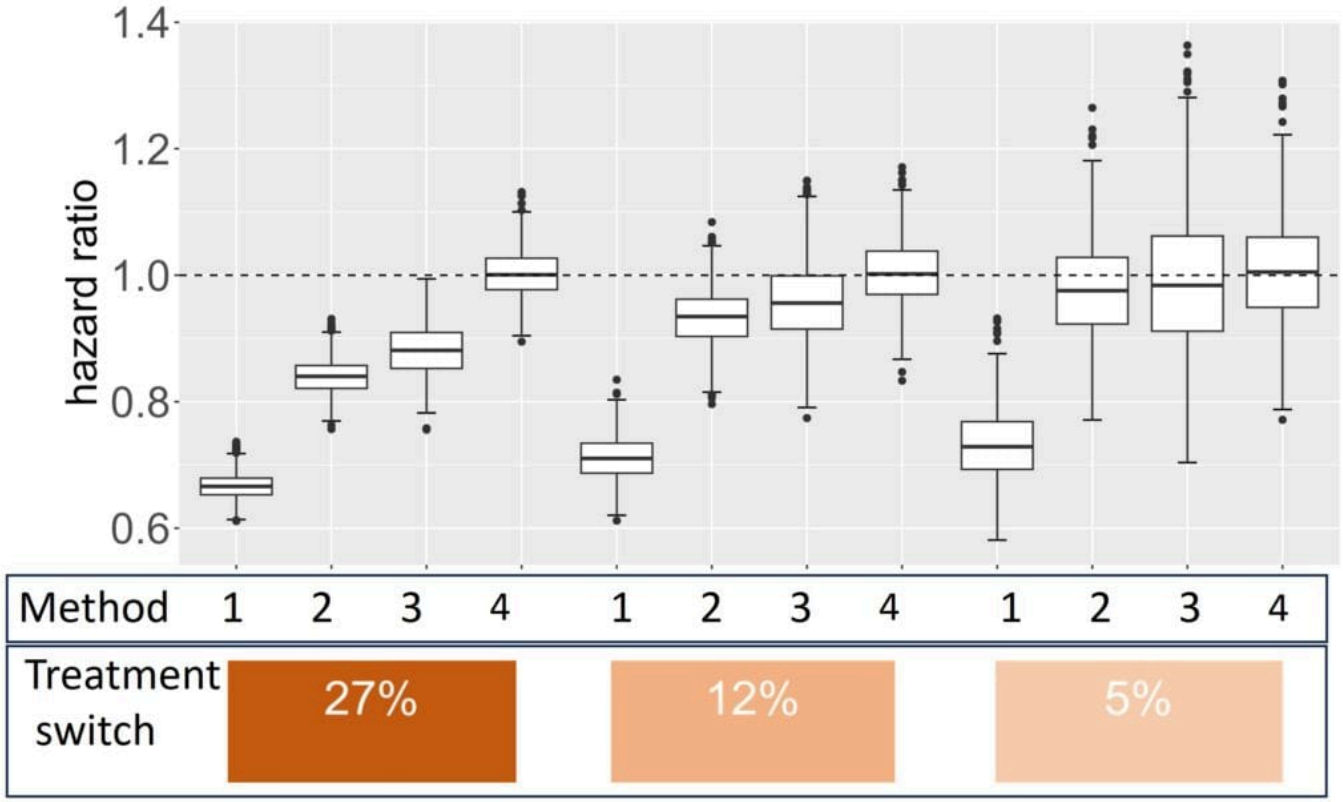
For simplicity, our simulation is based on the situation that there is no confounding and no treatment effect. We compare four different settings of time-zero for treatment and control groups: (1) CED vs CED (misclassified immortal time bias), (2) treatment initiation date (TID) vs CED (excluded immortal time bias), (3) using an inappropriate PNUD, and (4) using appropriate PNUD.

Results:

Our simulation shows that both methods (1) and (2) exhibit large apparent preventive effects of the treatment due to immortal time bias. The magnitude of the bias is greater for method (1) than for method (2). In method (3), a bias similar in magnitude to that of method (2) was observed. Conversely, method (4) shows almost no bias. (Figure)

Discussion/Conclusion:

When PNUD is used inappropriately, it fails to eliminate the bias, highlighting the importance of using the method correctly.

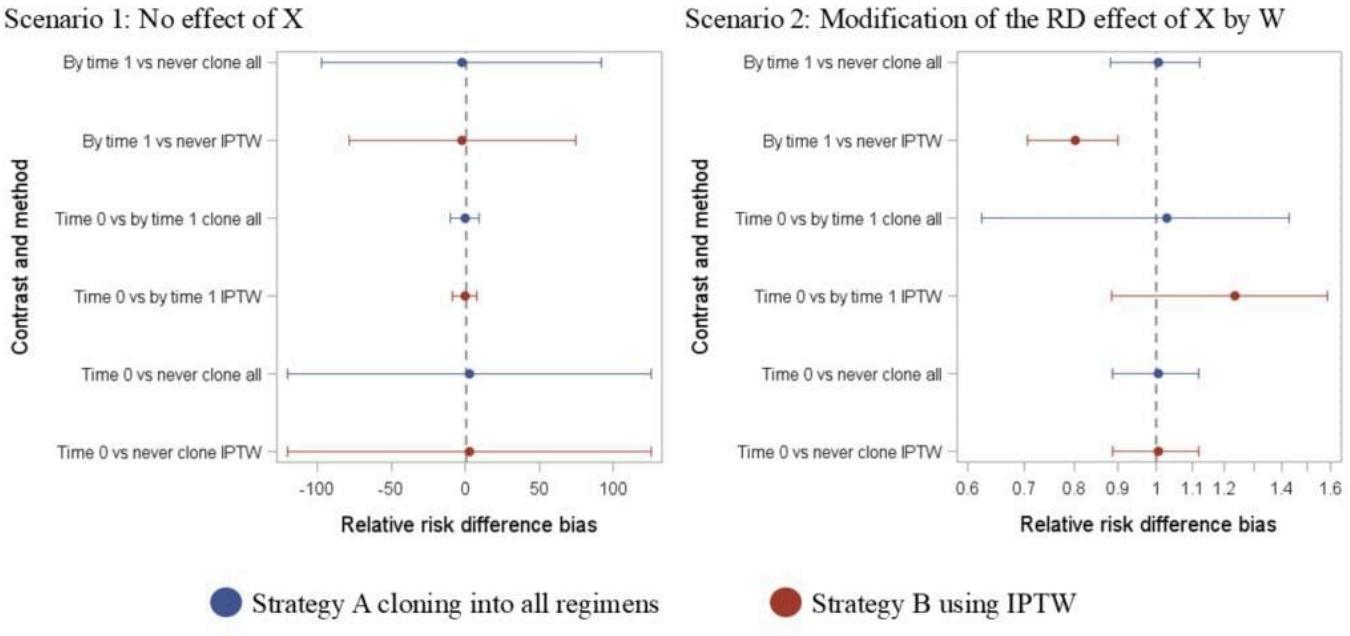


Simulation results comparing Methods 1, 2, 3, and 4.
(1) CED vs CED (misclassified immortal time bias)
(2) treatment initiation date (TID) vs CED (excluded immortal time bias)
(3) using an inappropriate PNUD
(4) using appropriate PNUD
The figure shows box plots of estimated hazard ratios over 1,000 simulation runs, with the true value set at 1. The probabilities of receiving treatment at each time point are set at 27%, 12%, and 5%, respectively.

Methods/Statistics

To Clone or not to Clone into Incompatible Regimens in Non-experimental Settings Michael Webster-Clark* Michael Webster-Clark Alexander Breskin Robert Platt

Cloning, censoring, and weighting (CCW) is a great tool to contrast regimens that cannot be distinguished at baseline. The origins of CCW involved emulating target trials contrasting regimens like “never treat with X” (Regimen 0) with multiple protocols like “with X for time ” (Regimens) with people randomized to X=1 or X=0 at baseline. As t0 treatment was random, there is no need to clone patients randomized to X=0 to Regimens or clone patients randomized to X=1 to Regimen 0. Observational studies, however, may be confounded by non-random t0 treatment assignment. They have two options: A) clone all patients into all regimens, censor incompatible patients at time 0, and create censoring weights for them; and B) do not clone into incompatible regimens, create CCW in each regimen, and account for confounding between regimens as in nonexperimental studies (e.g., inverse probability of treatment weights). While both can generate unbiased estimates, approach 1 ensures consistent target populations across comparisons. To demonstrate, we simulated using CCW to compare risk of an outcome Y by time 3 under three regimens: “start X at t0 or t1,” “start X at t0,” and “never start X.” The probability of starting X at each time was associated with a variable W associated with Y. We calculated risk differences (RDs) between regimens using A and B in the presence and absence of risk difference-scale heterogeneity and compared them to true RDs (**Figure 1**). RDs using A estimated the full study population RDs. RDs using B, however, only estimated full population RDs absent treatment effect heterogeneity or if comparing “start treatment X at t0” to “never start X” because those compatible with multiple regimens at t0 appear multiple times in the IPTW pseudopopulation while those compatible with a single regimen appear once. If applying CCW to nonexperimental data, clone participants into all regimens at baseline unless regimens are exclusive and exhaustive.



Methods/Statistics

Comparison of disease risk score methods to study treatment effect heterogeneity: a simulation study Haedi Thelen* Haedi Thelen Wei Yang Sean Hennessy Jordana Cohen Wensheng Guo Todd Miano

Background: Estimation of treatment effects across levels of predicted baseline disease risk (i.e., the disease risk score (DRS)) is a popular method for evaluating treatment effect heterogeneity in randomized trials (RCTs). Although prior studies suggest that trial data can be used for DRS derivation, the optimal approach to using data to both fit DRS models and estimate treatment effects is uncertain. This simulation compares three approaches to fitting DRS models in RCT data.

Methods: We simulated repeated RCTs of a binary treatment by drawing samples of 3600 from a population of one million subjects with 12 binary covariates. We evaluated ground truth treatment effects of OR=1, 0.8, 0.5, and 0.5 with treatment-covariate interactions on the OR scale. In each scenario, we fit a DRS model on 1) controls only (CO), 2) the full-sample (treated and controls (FS)), and 3) a 50% random sample of controls, who were then removed from the sample for treatment effect estimation (split-sample (SS) method). We estimated treatment effects within strata of predicted DRS on the risk difference scale. We calculated within strata percent bias and overall percent bias (OPB), defined as the average absolute percentage bias across strata. We repeated simulations varying outcome incidence, trial sample size, and randomization ratio (treated to control 1:1 and 2:1).

Results: In the base case with null treatment effect, the CO method was substantially biased, while FS and SS exhibited reduced bias. Bias increased with the FS method as treatment effect increased, and when there were treatment-covariate interactions (Figure, panels b, e, h); whereas the SS remained minimally biased (panels c, f, i). Bias with the FS method was greatest with uneven randomization (OPB 21.4%).

Conclusion: These findings encourage re-evaluation of existing guidance in favor of split-sample methods which were less biased across studied scenarios.

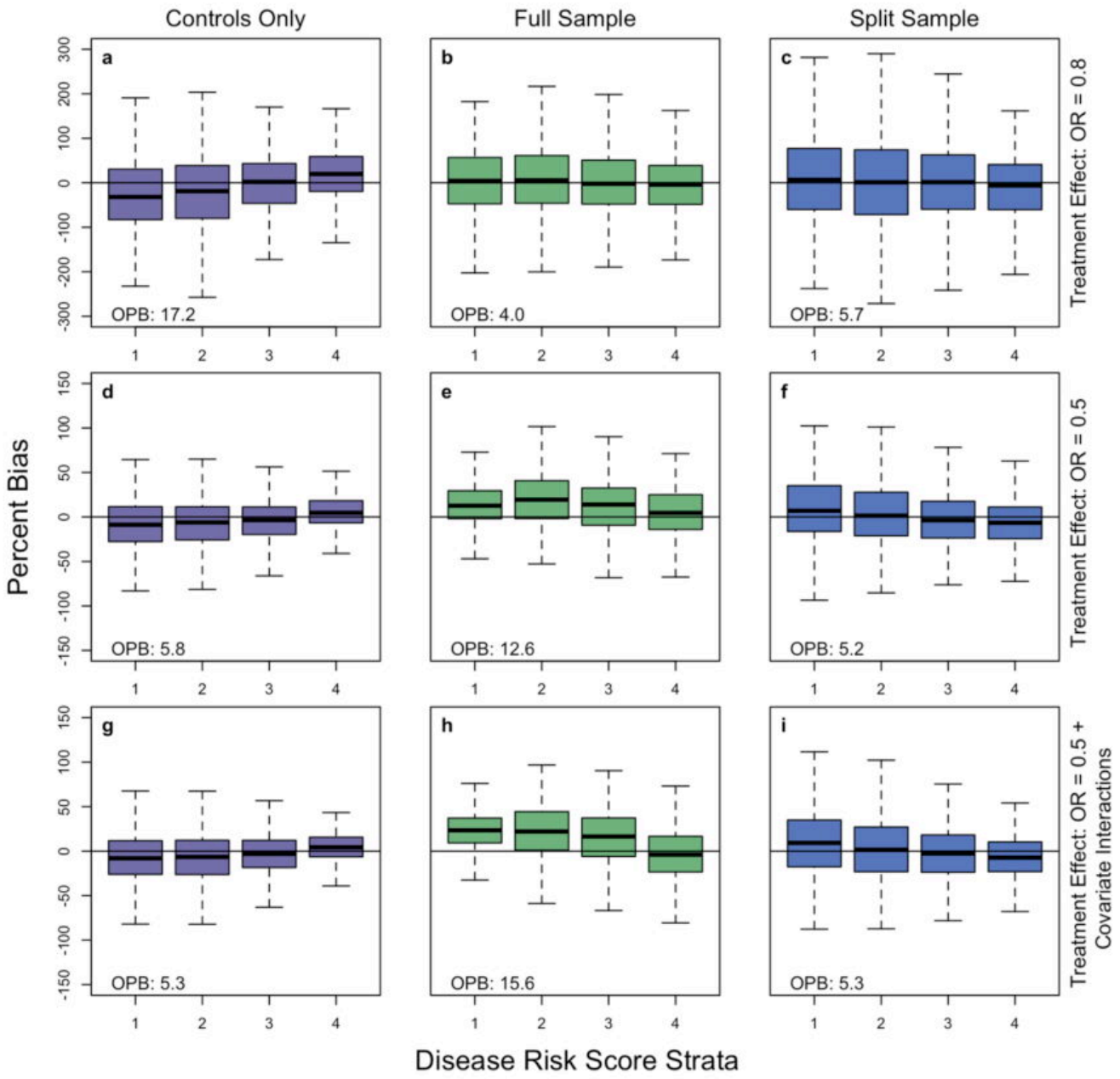


Figure: **Percent bias in DRS strata-specific treatment effect estimates among DRS methods in the base case.** Base case simulation parameter settings include outcome rate of 25%, 12 binary covariates with 20% prevalence each, subjects randomized 1:1 treated to control, and a trial sample of 3600. Abbreviations: OPB, overall percent bias; OR, odds ratio.

Occupational

Counting the Carnage: How Sensitive are State Data Systems for Occupational Fatality?
Chelsea Martin* Chelsea Martin Catherine Wolff Maryalice Nocera Elizabeth McClure Shabbar Ranapurwala Morgan Richey Stephen Marshall

Background: Occupational fatalities are a significant public health concern. Attaining accurate records of occupational fatalities is essential to discern the true number of occupational fatalities, and better target prevention programs. The purpose of this study was to estimate the sensitivity of fatal occupational injury ascertainment based on flags that indicate death “on the job” and “at-work” as recorded in the Chief Medical Examiner (OCME) data system and on death certificates in North Carolina (NC) from 1992 to 2017.

Design: Validation Study

Methods: NC fatal occupational injuries were identified between 1992-2017 from flags in the NC OCME and death certificates data and reviewed for accuracy. Next, we sampled 5% of non-occupational deaths from alternating calendar years between 1992-2017 to identify occupational fatalities that had been inaccurately flagged. We estimated misclassified non-occupational fatalities using the inverse probability of the sampling fraction. Sensitivity of the classification of fatal occupational injuries based on the data systems’ flags was calculated.

Results: From 1992-2017 there were 3,202 occupational fatalities originally classified in the combined database and verified by the study investigative team. We extracted and adjudicated 2,129 non-occupational deaths. Following adjudication, 41 non-occupational deaths were determined to have been misclassified in the sample, suggesting an estimated 1,500 misclassified occupational deaths and an overall sensitivity of 66.0% (95% CI: 64.6%, 67.4%). Sensitivity of the OCME data for civilian adult occupational fatality differed by intent and means [unintentional driving fatality: 61.2%, (58.5%, 63.8%); unintentional non-driving fatality: 71.4%, (69.5%, 73.3%); intentional fatality: 59.6%, (56.2%, 63.0%)].

Conclusion: An estimated 28-41% of occupational fatalities may have been misclassified in OCME systems, with unintentional driving and intentional fatalities being most affected.

Methods/Statistics

A novel heat exposure metric from work history data: Estimating occupational heat exposure in a low-resourced region Samantha Hall* Samantha Hall Selene Vences Brown Juan José Amador Velasquez Damaris López-Pilarte Maria Argos Luis Carvalho Madeleine K Scammell Daniel R Brooks Jessica H Leibler

Interview-based work histories can be an important tool to estimate individual-level environmental exposure profiles over time, particularly in low-resourced settings where research infrastructure may restrict personal monitoring and satellite datasets may lack spatial resolution. We used work history to estimate longitudinal occupational heat exposure in a prospective study of adolescents at high risk for chronic kidney disease of uncertain etiology in Central America (n=450). We developed a novel categorical heat burden metric that incorporated local knowledge of strenuousness of tasks, radiant and machine-based heat sources, and access to cooling strategies, which we used to classify each self-reported occupational activity and experiences of worksite attendance with an adult in youth as having low (0), moderate (1), or high (2) heat burden. To model exposure duration, we summed months in moderate or high heat paid jobs as full weight and months attending a worksite with an adult as half weight. A dichotomous ever/never variable of occupational heat exposure and the more nuanced exposure duration metric were modeled separately in adjusted regression models to evaluate associations with longitudinal kidney function. We evaluated spatial temperature datasets and residential regions to address effect measure modification by climate trends. More than a quarter of the population (26.7%) had ever worked in moderate or high heat and median exposure duration was 17 months (IQR 24.1). Occupational heat exposure (ever/never) was associated with 0.7% decline/year in estimated glomerular filtration rate in males (95% CI -1.4, -0.1) and 0.9% incline/year in females (95% CI 0.0, 1.7). Work duration was unrelated to kidney outcomes, potentially due to short duration of occupational histories. Our approach suggests detailed work history aligned with climate data assessment can be used to generate cost-effective estimates of occupational heat burden in under-resourced regions.

Occupational

Coronary Heart Disease Attributable to Psychosocial Stressors at Work Mathilde Lavigne-Robichaud* Mathilde Lavigne-Robichaud Trudel, X. Talbot, D. Milot, A. Gilbert-Ouimet, M. Brisson, C.

Background. Psychosocial stressors at work, including job strain and effort-reward imbalance (ERI), have been associated with an increased risk of coronary heart disease (CHD). However, the proportion of CHD events attributable to these work-related stressors has not been quantified in a prospective cohort study.

Methods. This 15-year prospective cohort study was conducted among employees from public and semi-public organizations in Quebec City, Canada, between 2004 and 2018. A total of 6,295 participants without cardiovascular disease at baseline were included, with essential eligibility criteria encompassing employment in the specified organizations and absence of pre-existing cardiovascular conditions. Psychosocial stressors were assessed using validated instruments measuring job strain and ERI. The primary outcome was the incidence of CHD events, identified through universally covered healthcare databases. Attributable fractions were estimated using the Kaplan-Meier method, with multiple imputation and inverse probability weighting applied to address selection and confounding biases.

Results. Over the 15-year follow-up, 669 CHD events occurred among the participants, who contributed a total of 112,297 person-years, yielding a CHD incidence rate of 5.96 per 1,000 person-years. The attributable fraction for job strain was 18.2% (95% confidence interval [CI]: 1.8% to 34.7%), and for ERI, it was 3.3% (95% CI: -1.6% to 8.2%). Combined exposure to both stressors resulted in an attributable fraction of 19.5% (95% CI: 0.7% to 38.4%).

Conclusions. In this cohort, combined exposure to job strain and ERI accounted for approximately one-fifth of CHD events. Implementing strategies to reduce these work-related stressors may effectively decrease the burden of CHD.

Cardiovascular

Associations of shift work and eating duration with cardiometabolic health and biological age acceleration among U.S. workers Xuyuehe Ren* Xuyuehe Ren Liwei Chen Jian Li

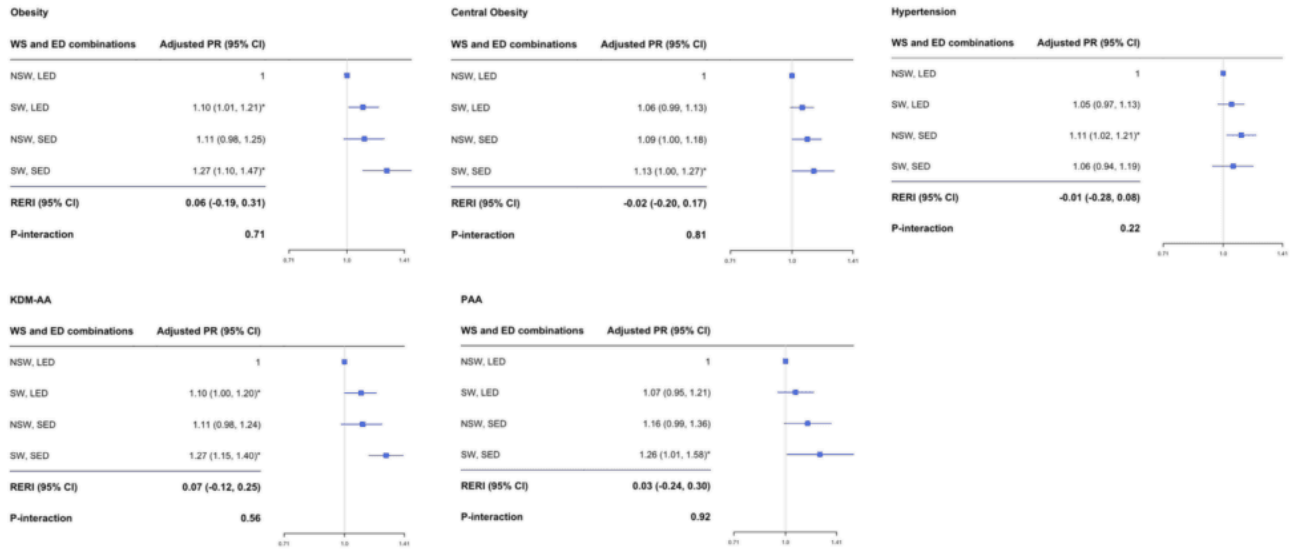
Objectives: Shift work schedules and eating duration can both influence circadian rhythm, which is crucial for cardiometabolic health and longevity. We aimed to examine the independent and joint associations of shift work (SW) and short eating duration (SED) with cardiometabolic diseases (CMD) and biological age acceleration (BAA) in a nationally representative sample of U.S. workers.

Methods: We included 30,299 eligible workers from the National Health and Nutrition Examination Survey 1999-2020. Work schedules were self-reported and classified as SW vs. non-shift work (NSW). Time of eating occasions were accessed by 24-hour dietary recalls, and eating duration was classified as SED (<11h) vs. long eating duration (LED: ≥11h) based on exploratory analyses for threshold effects. CMD were ascertained by self-reported physician diagnosis, medication use, or clinical markers. BAA was calculated as the difference between biological age (estimated using Klemera and Doubal method (KDM-AA) and PhenoAge algorithms (PAA)) and chronological age, then dichotomized at zero. Adjusted Poisson regressions were used to cross-sectionally examine the independent and joint associations of SW and SED with the prevalence of obesity, central obesity, hypertension, and BAA.

Results: SW was associated with higher prevalences of obesity (PR, 1.22; 95%CI, 1.10-1.35), central obesity (PR, 1.18; 95%CI, 1.03-1.34), and positive BAA (KDM-AA: PR, 1.14, 95%CI, 1.08-1.21; PAA: PR, 1.12, 95%CI, 1.04-1.19). Similarly, SED was associated with higher prevalences of obesity (PR, 1.11; 95%CI, 1.10-1.35), central obesity (PR, 1.09; 95%CI, 1.04-1.14), and positive BAA (KDM-AA: PR, 1.13, 95%CI, 1.07-1.21; PAA: PR, 1.19, 95%CI, 1.08-1.33). There was suggestive evidence that workers exposed to both SW and SED had higher prevalences of obesity, central obesity, and positive BAA than those with NSW and LED.

Conclusions: Workers with SW, SED, or both were more likely to have obesity, central obesity, and BAA.

Figure 1. Joint associations of work schedules and eating duration with cardiometabolic diseases and biological age acceleration



Abbreviations: WS: work schedule; ED: eating duration; KDM-AA: KDM Age Acceleration; PAA: PhenoAge Acceleration; SW: shift work; NSW: non-shift work; SED: short eating duration; LED: long eating duration; RERI: relative excess risk due to interaction.
[1] Models were adjusted for age, gender, race/ethnicity, education, poverty-income-ratio, marital status, smoking status, alcohol drinking, physical activity, total energy intake, and preexisting comorbidities.
[2] Eating duration: short (<11 hours) vs. long (≥11 hours).
* p-value<0.05

COVID-19 Pandemic

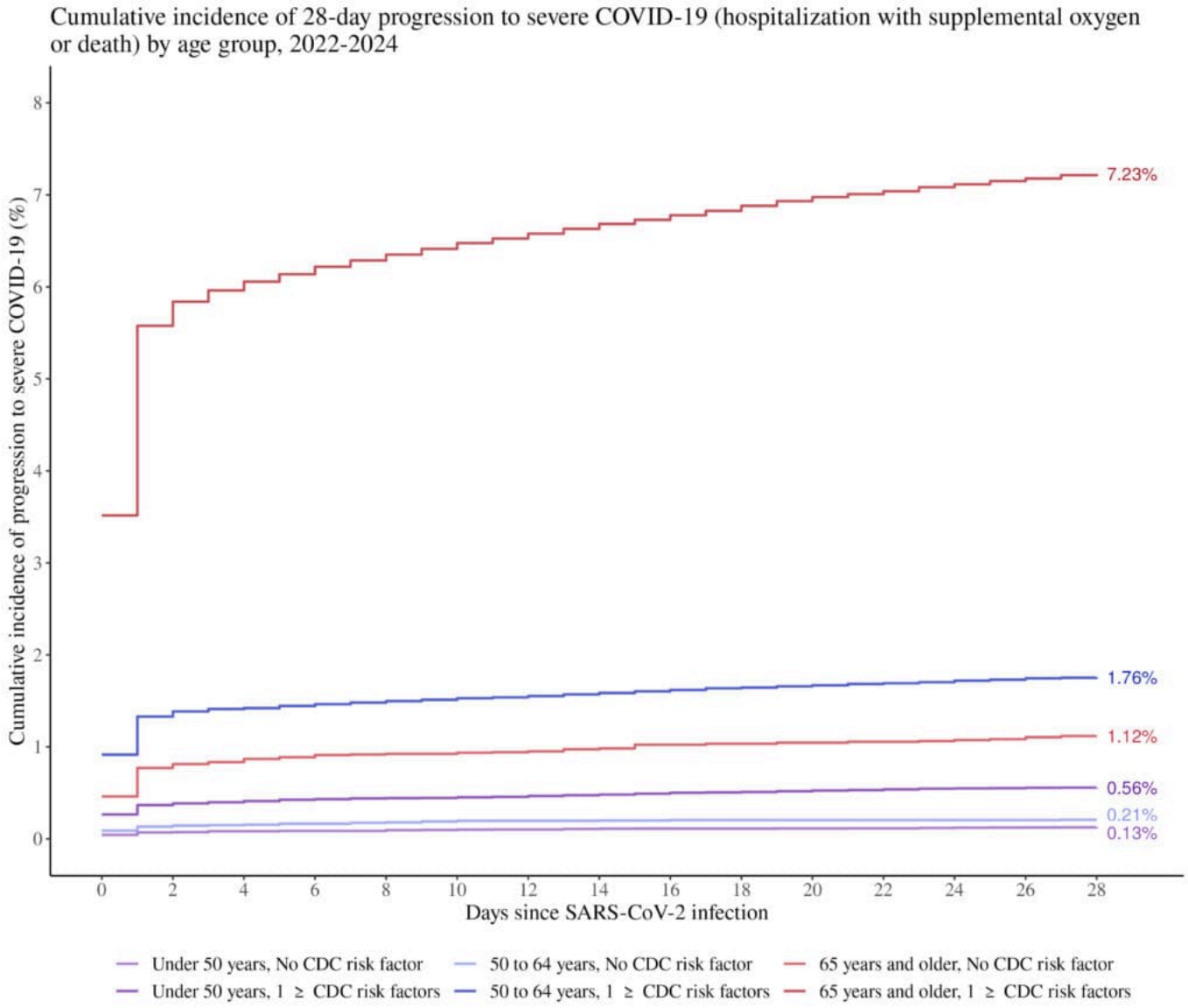
Risk factors for progression to severe COVID: a retrospective cohort study of 994,397 persons, 2022-2024 Jorge R Ledesma* Jorge Ledesma Liyan Liu Jacek Skarbinski Joshua R Nugent

Background: Currently, providers and patients are unsure about who should receive antiviral treatment for preventing progression to severe COVID. These ambiguities arise from the following: CDC's expansive guidelines indicate that 75% of US population is eligible for therapy, new clinical trial data showing no benefit for lower risk patients, and gaps in evidence for several risk factor-severe COVID links. A clearer understanding of who is at greatest risk for disease progression can optimize care delivery and ensure people at high risk receive treatment. We therefore aimed to describe the relationships between 30+ CDC risk factors and severe COVID.

Methods: We conducted a retrospective cohort study including Kaiser Permanente Northern California (KPNC) members aged > 18 years with (1) incident SARS-CoV-2 infection and (2) > 1 year of continuous enrollment between January 2022 and December 2024. We used inverse probability weighting to create a population where treatment naïve risk (risk in the absence of future antiviral therapy) can be estimated followed by marginal standardization to derive risk differences (RD) associated with CDC risk factors and 28-day risk of severe COVID (hospitalization with supplemental oxygen or death).

Results: Among 994,397 people, 20,526 (2.06%) experienced severe COVID over 28 days: 18,991 (1.91%) were hospitalized with oxygen support and 3,542 (0.36%) died. Age was the largest risk factor (e.g., 60-69 years: RD=1.62% [95% CI 1.56-1.69]; 70-79 years: 3.12 [3.02-3.20]). Clinical risk factors with the largest excess risks were chronic lung disease (1.76% [1.63-1.91]), schizophrenia (1.71 [1.19-2.41]), and dementia (1.63% [1.50-1.76]). Risk factors with the least excess risks were mood disorders (0.56% [0.51-0.63]), asthma (0.38% [0.30-0.43]), ever smoker (0.33% [0.28-0.38]).

Conclusions: Our analysis provides new data for beginning to redefine broad treatment guidelines and optimize treatment prescribing to reduce COVID morbidity.


Cumulative incidence of 28-day progression to severe COVID-19 (hospitalization with supplemental oxygen or death) by age group, 2022-2024
Cumulative incidence of progression to severe COVID-19 (%)
0
1
2
3
4
5
6
7
8
7.23%
1.76%
1.12%
0.56%
0.21%
0.13%
0
2
4
6
8
10
12
14
16
18
20
22
24
26
28
Days since SARS-CoV-2 infection
Under 50 years, No CDC risk factor
50 to 64 years, No CDC risk factor
65 years and older, No CDC risk factor
Under 50 years, 1 ≥ CDC risk factors
50 to 64 years, 1 ≥ CDC risk factors
65 years and older, 1 ≥ CDC risk factors

COVID-19 Pandemic

The Role of Workplace Presence in Racial Disparities in COVID-19 Mortality During the Pandemic: A Mediation Analysis Elisabeth Gebreegziabher* Elisabeth Gebreegziabher Charsey Porse Gar-Wei Lee Matthew Frederick Kristin J. Cummings Ximena Vergara

Objective: To examine the relationship between being black, indigenous, and other people of color, including Latino origin (BIPOC) and presence at workplace, the effect of physical presence on COVID-19 mortality and whether and to what extent racial disparities in COVID-19 mortality were mediated through presence at the workplace.

Methods: Using a case-control study design, we identified all COVID-19 deaths in California (CA) through linkage to the CA COVID-19 registry, as well as non-COVID-19 deaths between January 2020 and March 2021, prior to the widespread availability of vaccines. We included decedents who were aged 18-64 years and confirmed to be working through Employment Development Department (EDD) records. We assigned occupations to in-person presence or not based on an in-house job-exposure matrix. The relationships between BIPOC status, presence at work, and death from a COVID-19 cause were assessed using logistic regression, adjusting for key demographics, while CAUSALMED in SAS was used for mediation analysis.

Results: Compared to non-Hispanic white decedents, BIPOC decedents had 39% (95%CI: 30–49%) higher odds of being present at work and 4.34 (95%CI: 3.93-4.79) times the odds of dying from COVID-19. Workplace presence increased the odds of dying from COVID-19 by 22% (95%CI: 11-33%). However, the effect of being BIPOC on dying from COVID-19 was predominantly through direct effect (NDE: OR=4.29, 95%CI: 3.87-4.73) and not mediated by the indirect path through presence (NIE: OR=1.01, 95%CI: 1.0-1.02).

Conclusion: BIPOC individuals were overrepresented in occupations requiring physical presence and were disproportionately affected by COVID-19 mortality. While workplace presence increased the risk of death from COVID-19, we did not detect a mediation effect of this presence in the effect of being BIPOC on COVID-19 death. Other social determinants may have a larger role in racial disparities in COVID-19 death. The workplace remains an important focal point for transmission interruption of communicable diseases.

COVID-19 Pandemic

Public health funding, vulnerable groups, and COVID-19 hospitalizations and deaths: a time-to-event analysis in Ontario, Canada Samantha Forbes* Samantha Forbes Naomi Schwartz Stephen Hunter Roman Pabayo Brendan Smith

Background: The COVID-19 pandemic disproportionately impacted health across sociodemographic groups. Areas with higher pre-pandemic public health funding may have better protected population and vulnerable group health. The objective was to estimate the association between public health unit (PHU) funding and COVID-19 hospitalization or death, and whether it differs among vulnerable groups in Ontario, Canada.

Methods: A population-based cohort study was conducted using linked health administrative data from all Ontario residents covered by government health insurance (March 1, 2020-December 31, 2022). PHU funding per capita in 2019, a measure of pre-pandemic preparedness, was linked from the Ontario Public Health Information Database (OPHID). The association between PHU funding per capita and COVID-19 hospitalization or death was estimated using Fine and Gray subdistribution hazard models, with non-COVID-19 death as a competing risk. Interactions between PHU funding per capita and neighborhood socioeconomic status (SES) quintile, neighbourhood racialized population quintile, and individual immigrant status on COVID-19 hospitalization or death were estimated. Quintile 1 (Q1) was the referent and represented the highest SES/lowest racialized population neighborhoods. Models were adjusted for individual- and area-level covariates and included robust sandwich co-estimators by PHU.

Results: A $10 increase of PHU funding per capita was associated with a 5% decreased risk of COVID-19 hospitalization or death (HR=0.95, 95%CI:0.90-0.99). The protective effect of increased PHU funding on COVID-19 hospitalization or death was stronger in neighborhoods with lower SES (Q5 vs, Q1: HR=0.94, 95%CI:0.90-0.99) and higher racialized populations (Q4 vs. Q1: HR=0.92, 95%CI:0.87-0.97), and among immigrants (recent immigrant [≤5 years] vs. Canadian born: HR=0.92, 95%CI:0.84-1.01).

Conclusion: Public health funding plays an important role in mitigating harm and reducing health inequities.

COVID-19 Pandemic

Modeling Study Impact of Lifting Isolation Measures on COVID-19 Infected Individuals in South Korea Suyoung Jo* Suyoung Jo Kyung-Duk Min Sung-il Cho

From the early stages of the COVID-19 pandemic, South Korea effectively controlled incidence and mortality through the TTIQ strategy. Starting in 2022, the country gradually lifted isolation periods, reflecting an exit strategy that balanced public health and socioeconomic burdens. This study evaluated the impact of lifting isolation measures on COVID-19 control in South Korea from both perspectives.

A deterministic mathematical model for SARS-CoV-2 transmission dynamics was developed using data from the Korea Disease Control and Prevention Agency (KDCA) on daily age-specific confirmed cases and vaccination rates (January 16, 2022, to August 31, 2023) and population data from Statistics Korea for 2021. The V-SEIR model was parameterized using prior literature and calibration.

In 2022, scenarios compared reducing isolation from 10 to 7 days (starting February 10) with maintaining 10 days, reducing it to 5 days, or delaying the reduction by two months. In 2023, scenarios assessed lifting isolation on June 1 against earlier or later dates. Outcomes were compared with the strictest scenarios using additional cases and economic savings calculated via average daily wages. Cost-effectiveness was assessed using the Incremental Cost-Effectiveness Ratio (ICER).

Results showed that in 2022, delaying the reduction by two months minimized cases, but the real-world scenario yielded the greatest economic savings, saving $4,341 per case and making it the most cost-effective. In 2023, lifting isolation one month later than the real-world scenario saved $244 per case, proving more cost-effective.

This study highlights the importance of adjusting isolation policies based on population immunity and economic activity to optimize policy outcomes. These findings underscore the critical importance of timing in lifting isolation measures to effectively mitigate trade-offs between public health and socioeconomic burdens, offering evidence-based insights for future decision-making.

COVID-19 Pandemic

Old symptoms, new diagnoses: Frequent care-seeking behaviour predict subsequent diagnosis of Post Covid Condition and Post Viral Fatigue Syndrome in Swedish women

Agnes af Geijerstam* Agnes af Geijerstam Lauren Lissner Ailiana Santosa Maria Åberg Kirsten Mehlig Annika Rosengren

Background
Recent data shows that women are at higher risk of being diagnosed with Post Covid Condition than men. As of February 2022, 2,3% of all registered female COVID-19 cases in Sweden had been given this diagnosis, the majority in primary care without prior hospitalization. SARS-CoV-2 is not unique in its ability to cause post-acute sequelae, as shown by the use of the diagnosis Post-Viral Fatigue Syndrome. Both diagnoses are symptom based with vocal patient groups.
Aims
To compare risk factors for Post Covid condition (PCC) and post-viral syndrome in primary care. Particular attention will be given to prior medically unexplained symptoms, BMI and socio-economic status.
Methods
This is a registry based prospective cohort study including 318 541 women in the Swedish Medical Birth Registry, linked to registries with primary care data and demographic data. Logistic regression was used to calculate odds ratios for receiving a diagnosis of PCC or Post-viral syndrome. Baseline was set at first measurement of BMI. Follow-up was until 3 months prior to diagnosis, or until June 2024. Main exposure value was monthly rate of general practitioner visits with a symptom diagnosis.
Results
We found a clear prediction of both PCC and Post-viral syndrome by the rate of primary care contacts with a symptom diagnosis. Having more than 0,1 visits to a physician with a symptom diagnosis per month of follow-up gave OR 5,4 (95% CI 4,7-6,2) of later diagnosis with PCC, with less than 0,01 as reference. For Post-viral syndrome, the OR was 18,7 (95% CI 14,8-23,6).
BMI had no association with PCC. For Post-viral syndrome there was a trend of lower odds ratios for higher BMI. Higher education was positively associated with both diagnoses.
Conclusions
Symptom diagnoses are common in our population and are predictors of both PCC and Post-viral syndrome. Simultaneously, many diagnosed patients had no prior contact with primary care, raising questions about differing ethology of the symptoms leading to diagnose.

COVID-19 Pandemic

Impact of the COVID-19 pandemic on routine childhood healthcare in Oklahoma Jessica Beetch* Jessica Beetch Laura Beebe Amanda Janitz Katrin Kuhn

Introduction: The COVID-19 pandemic disrupted routine healthcare for children, but its impact has not been thoroughly studied, especially in low-income populations. Apart from the direct effects of the pandemic, such as COVID-19-associated hospitalizations and deaths, children's health was also indirectly impacted. After the emergence of the pandemic, there were disruptions to routine services leading to delays in screening, vaccination, and treatment. Low-income children and those living in low-income settings were at risk of prolonged delays in care and worse health outcomes during the pandemic. Oklahoma is a state with a high poverty rate, high vaccine hesitancy, and low health ranking compared to other states in the US. We hypothesized that these factors contributed to poor childhood routine care during the pandemic in Oklahoma. Given this, the objective of this research study was to examine the impact of the COVID-19 pandemic on routine childhood vaccination and well-child visits in populations in Oklahoma.

Methods: First, we used data from the Oklahoma State Immunization Information System on children 18 years of age and younger to evaluate changes in DTaP and MMR vaccination during the pandemic (March 1, 2020 to July 31, 2022) compared to before it began (March 1, 2017 to July 31, 2019). We calculated percentage change in total vaccine doses administered separately for DTaP and MMR vaccines overall and by pandemic phase. The phases were named initial impact (March 1, 2020 to September 30, 2020), initial recovery (October 1, 2020 to May 31, 2021), Delta variant predominance (June 1, 2021 to November 30, 2021), and Omicron variant predominance (December 1, 2021 to July 31, 2022), and were compared to previous years before the COVID-19 pandemic (pre-initial impact: March 1, 2019 to September 30, 2019, pre-initial recovery: October 1, 2018 to May 31, 2019, pre-Delta: June 1, 2019 to November 30, 2019, pre-Omicron: December 1, 2018 to July 31, 2019). Log-binomial regression was performed with a sub-cohort of unique children <1 to 11 months of age that received a single DTaP vaccine or more than one DTaP vaccine before and during the COVID-19 pandemic. Race, ethnicity and income were examined as potential effect modifiers and confounders.

Next, we utilized data on children enrolled in Oklahoma's Medicaid (SoonerCare) from the Oklahoma Health Care Authority. We examined changes in well-child visits in low-income children under 1 year of age. Percentage change in well-child visits was calculated overall, by pandemic phase, and month. Log-binomial regression was performed with children <1 month of age at first recorded visit that attended 6 or more well-child visits or less than 6 well-child visits in their first year of life before and during the pandemic. SoonerCare recommends 6 well-child visits in the first year of life. Sex, race, and ethnicity were explored as potential effect modifiers and confounders. Statistical analyses were performed using SAS (version 9.4; SAS Institute) and a type 1 error rate of 0.05.

Results: We observed declines in Oklahoma in childhood DTaP and MMR vaccinations administered during the pandemic. Overall, there was a 16% decline in DTaP vaccines administered and 16.7% decline in MMR vaccines administered during the pandemic compared to before the pandemic began. There were declines in DTaP and MMR vaccination counts during all pandemic phases studied. initial impact: DTaP = -18.1%, MMR = -23.9%; initial recovery: DTaP = -12.4%, MMR = -13.6%; Delta variant predominance: DTaP = -9.9%, MMR = -8.9%; Omicron variant predominance: DTaP = -19.9%, MMR = -22.0%. Children receiving more than one dose of DTaP vaccine in their first

year of life decreased during the pandemic (RR = 0.92, 95% CI: 0.92,0.93).

We also observed declines in well-child visit attendance for low-income children less than 1 year of age in Oklahoma during the pandemic. Overall, well-child visit attendance declined by 10.4% (initial impact: -5.2%; initial recovery: -6.0%; Delta variant predominance: -1.1%; Omicron variant predominance: -13.8%). Substantial declines occurred in the initial months of the pandemic (March: -7.2%; April: -17.9%; May: -7.3%). We found racial disparities in attending well-child visits for low-income children in Oklahoma. In all races besides American Indians, children attending the full number of recommended well-child visits was reduced during the pandemic.

Conclusion: Our findings contribute to the body of evidence on the indirect effects of the pandemic on low-income children and children living in low-income settings. The pandemic substantially disrupted routine childhood care, particularly in the early months and during Omicron predominance. Racial disparities were evident for well-child visit attendance during the pandemic. This research study advises guidance on preparedness and response efforts during future outbreaks or public health emergencies.

Reproductive

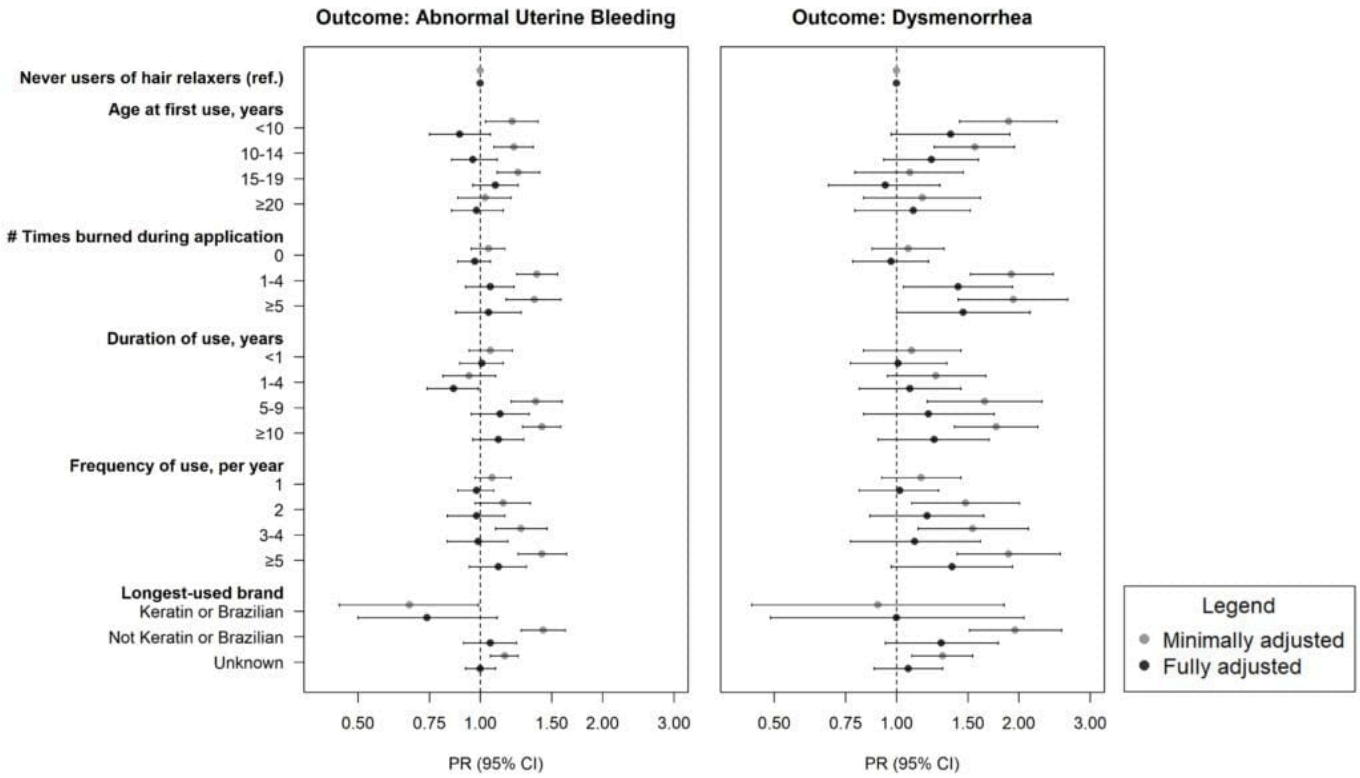
Hair relaxer use and menstrual disturbances in a North American cohort Ruth Geller* Ruth Geller Amelia Wesselink Samantha Schildroth Tamarra James-Todd Nyia Noel Donna Baird Lauren Wise

Background: Use of hair relaxers (chemical straighteners) is associated with higher risks of hormonally mediated conditions, but its relation to menstrual function during adulthood has not been studied. We hypothesized that current and former use of hair relaxers would be associated with abnormal uterine bleeding (AUB) and dysmenorrhea.

Methods: We analyzed baseline data from Pregnancy Study Online (PRESTO), an internet-based preconception cohort study of North American pregnancy planners. We included 14,366 participants aged 21-39 years who enrolled during 2014-2024 and reported on their typical menstrual cycle characteristics during the past couple years when not using hormonal contraceptives. We queried details of lifetime hair relaxer use including age at first use, frequency per year, duration of use, number of burns, and the longest-used brand. We defined AUB as cycle length <24 or >38 days, flow ≥7 days, irregular cycles, and/or heavy flow (≥30 pads/tampons per menses). We defined dysmenorrhea as severe cramps requiring medication and bed rest. We used log-binomial regression to estimate prevalence ratios (PR) and 95% CIs for the associations of hair relaxer use with AUB and dysmenorrhea, adjusted for potential confounders.

Results: Overall, 2% of participants were current users and 10% were former users of hair relaxers; 75% of ever users initiated use before age 20 years. The frequencies of AUB and dysmenorrhea were 31% and 8%, respectively. Compared with never use of hair relaxers, PRs for current use were 1.16 (95% CI 1.00-1.33) for AUB and 1.30 (95% CI 0.94-1.80) for dysmenorrhea; former use was not strongly associated with either outcome. Compared with never use of hair relaxers, participants who reported ever experiencing burns had a higher prevalence of dysmenorrhea (1-4 burns: PR=1.42, 95% CI 1.04-1.93; ≥5 burns: PR=1.46, 95% CI 1.00-2.13).

Conclusion: Some measures of hair relaxer use were associated with a higher prevalence of menstrual disturbances.



Minimally adjusted model: Adjusted for current age in years (21-24, 25-29, 30-34, 35-39) and year of enrollment (2014-2015, 2016-2020, 2021-2024).

Fully adjusted model: Adjusted for current age, year of enrollment, race/ethnicity (Black, Non-Black People of Color, Non-Hispanic White), parent's educational attainment (≤ high school, some college, ≥ college), history of anxiety or depression diagnosis (yes, no), participant's educational attainment (≤ high school, some college, college, graduate school), and current smoking (yes, no).

The fully adjusted model for *age at first use* is adjusted for current age, year of enrollment, race/ethnicity, and parent's educational attainment.

Reproductive

Neighborhood Disadvantage and Menstrual Pain Among Black/ African-American Women

Sydney Carolan* Sydney Carolan Ruth J. Geller Kristen Upson Quaker E. Harmon Chandra Jackson Anne Marie Jukic Ganesa Wegienka Lauren A. Wise Amelia K. Wesselink

Dysmenorrhea (severe menstrual pain) affects 16-29% of menstruating individuals. Stress is an established risk factor for dysmenorrhea and neighborhood environment can drive chronic stress; yet, there is little research on neighborhood context and menstrual health. We estimated the association of neighborhood disadvantage with menstrual pain among individuals in the Study of Environment, Lifestyle, and Fibroids. Participants self-identified as Black/ African-American, had an intact uterus, were aged 23-35 years, and lived in the Detroit, MI area in 2010-2012 (n=1693). Participants provided their residential address and data about the severity and impact of menstrual pain in the last year. We calculated a census tract level standardized neighborhood disadvantage score, a measure of disadvantage within the Detroit area, by linking addresses to 2011 American Community Survey data. We excluded participants who had no menses in the past year, or who used medication that could alter menstrual cycle frequency, for a final sample of 883. We fit age-adjusted log-binomial regression models to estimate prevalence ratios (PR) and 95% CIs for associations between neighborhood disadvantage scores (tertiles) and three menstrual pain outcomes: 1) menstrual pain is a “big problem”, 2) menstrual pain interferes “a lot” with daily activities, and 3) missed any days of work or home activities due to menstrual pain. Living in a more disadvantaged neighborhood was associated with a higher prevalence of menstrual pain outcomes. Relative to the lowest tertile, those in the highest tertile of neighborhood disadvantage were more likely to report menstrual pain being a big problem (PR=2.32, CI: 0.84-6.38), menstrual pain interfering a lot with daily activities (PR= 5.36, CI: 1.28-22.43), and missing any days of work or home activities due to menstrual pain (PR=2.02, CI: 0.95-4.30). Neighborhood disadvantage is associated with more severe menstrual pain that adversely impacts quality of life.

Table 1. Age-adjusted prevalence ratios and 95% CIs for the association between neighborhood disadvantage and menstrual pain outcomes comparing tertiles 2 and 3 to tertile 1

	Tertile	PR	95% CI
Menstrual pain as a big problem	2	1.75	(0.89, 3.43)
	3	2.32	(0.84, 6.38)
Interference from pain (a lot)	2	3.06	(1.18, 7.95)
	3	5.36	(1.28, 22.43)
Interference from pain (some)	2	1.31	(0.82, 2.10)
	3	1.50	(0.74, 3.04)
Days missed due to pain: Any	2	1.60	(0.97, 2.64)
	3	2.02	(0.95, 4.30)
Days missed due to pain: ≥ 3	2	1.74	(0.87, 3.48)
	3	2.29	(0.81, 6.48)
Days missed due to pain: ≥ 12	2	0.92	(0.23, 3.64)
	3	0.88	(0.11, 6.93)

Women’s Health

The association between perimenopausal depression and risk of mortality Alicia Nevriana* Alicia Nevriana Donghao Lu

Introduction

Perimenopausal depression is a common condition, affecting around 30% of women going through menopausal transitions. However, there is a lack of understanding of the potential long-term consequences following perimenopausal depression, including the risk of mortality.

Objectives

To determine the association between perimenopausal depression and mortality.

Methods

Population-based matched cohort study using linkage of Swedish healthcare registers. We included women aged 45-55 and identified the first episode of perimenopausal depression between 1 January 2003 and 31 December 2022 recorded in specialist/primary care. To ensure that it is a new episode instead of a routine follow-up, for those with history of depression, we only included depression diagnosis recorded as unplanned visit. Using incidence density sampling, we randomly matched by birth year (+/- 1 year) and county of residence to 10 unexposed women. Participants were followed from index (matched) date until death, emigration, diagnosis of perimenopausal depression (for the unexposed group), or 31 December 2022, whichever was earliest. We estimated hazard ratios (HRs) using Cox regression.

Results

We included 104,758 women with perimenopausal depression and 1,047,580 unexposed women. Women with perimenopausal depression received the diagnosis at an average age of 49.6 years. During a mean follow-up of 10 years (SD: 5.5 years), we observed 5,197 deaths among women exposed to perimenopausal depression (rate 4.7 per 1,000 person-years) and 28,033 deaths among unexposed women (rate 2.7 per 1,000 person-years). Compared to unexposed women, women with perimenopausal depression had a higher risk of mortality (HR 1.79, 95% CI 1.73-1.84).

Conclusion

Preliminary findings from this study indicated that perimenopausal depression was associated with a higher risk of early death overall. We plan to control for a range of potential confounders and stratify the risk by cause of death in the next step of the study.

Women’s Health

Association of migraine and vasomotor symptom severity and duration in midlife in Nurses’ Health Study 2 Holly Crowe* Holly Crowe Janet Rich-Edwards Kathryn Rexrode Hadine Joffe

Objective: Migraine and vasomotor symptoms (VMS) are prevalent brain conditions linked to female sex hormones and negatively impact quality of life for middle-aged women. We aimed to quantify the association between migraine phenotype and VMS severity and duration across the final menstrual period.

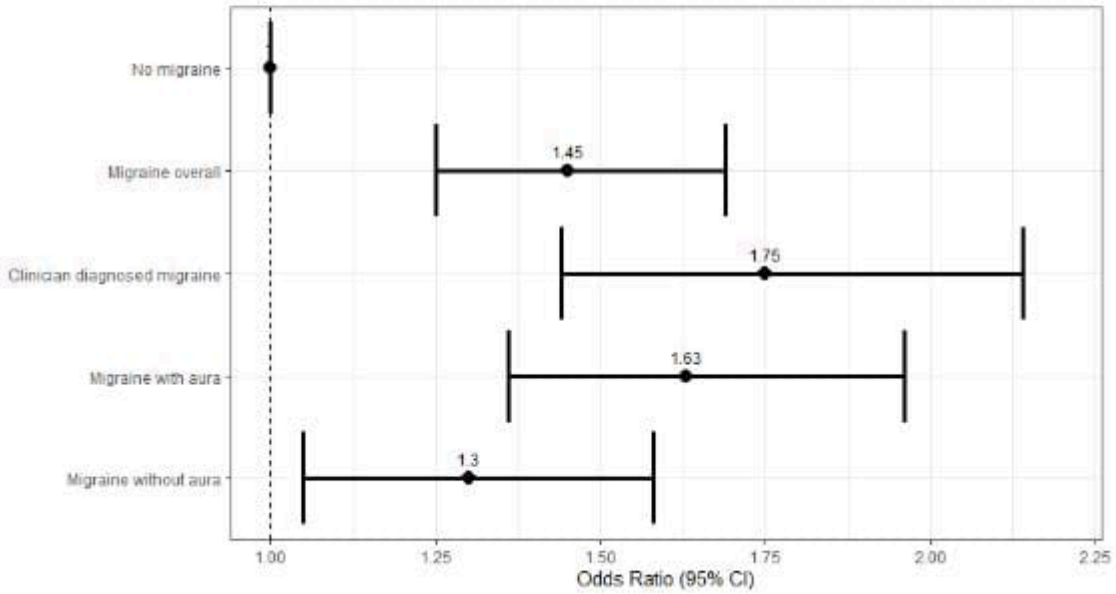
Methods: We analyzed data from 21,648 participants in Nurses’ Health Study II, an ongoing prospective cohort study of female registered nurses aged 25-42 at baseline in 1989. We included individuals who were within 2 years before or after self-reported cessation of menses from 2007-2015. We analyzed their self-reported migraine and VMS from 2009-2017, stratifying by history of clinician-diagnosed migraine and migraine phenotype (with and without aura) and estimated the cross-sectional association between migraine and VMS in midlife using logistic regression, adjusting for demographic, lifestyle, and reproductive health factors.

Results: Overall, 64% of the cohort reported VMS in the past four weeks (4% severe VMS) and 36% reported VMS lasting ≥5 years. Individuals with recent (past two years) migraine in midlife (29%) had 25% (17%-34%) greater odds of reporting VMS than those without migraine. Recent midlife migraine was also associated with severe (OR=1.45, 95% CI=1.25-1.69) and prolonged (≥5 years; OR=1.18, 95% CI=1.08-1.29) VMS. Migraine with aura and clinician-diagnosed migraine were more strongly associated with severe VMS than was migraine without aura or self-reported migraine. VMS duration did not materially differ across migraine phenotypes.

Discussion: While the nature of the association remains unclear, our findings highlight the importance of risk assessment and screening for VMS among women with migraine.

Figure 3. Recent migraine and VMS severity and duration among 21,468 women ±2 years from Final Menstrual Period in NHS II with VMS

a. Severe vs. Mild or Moderate VMS



LATEBREAKER

Aging

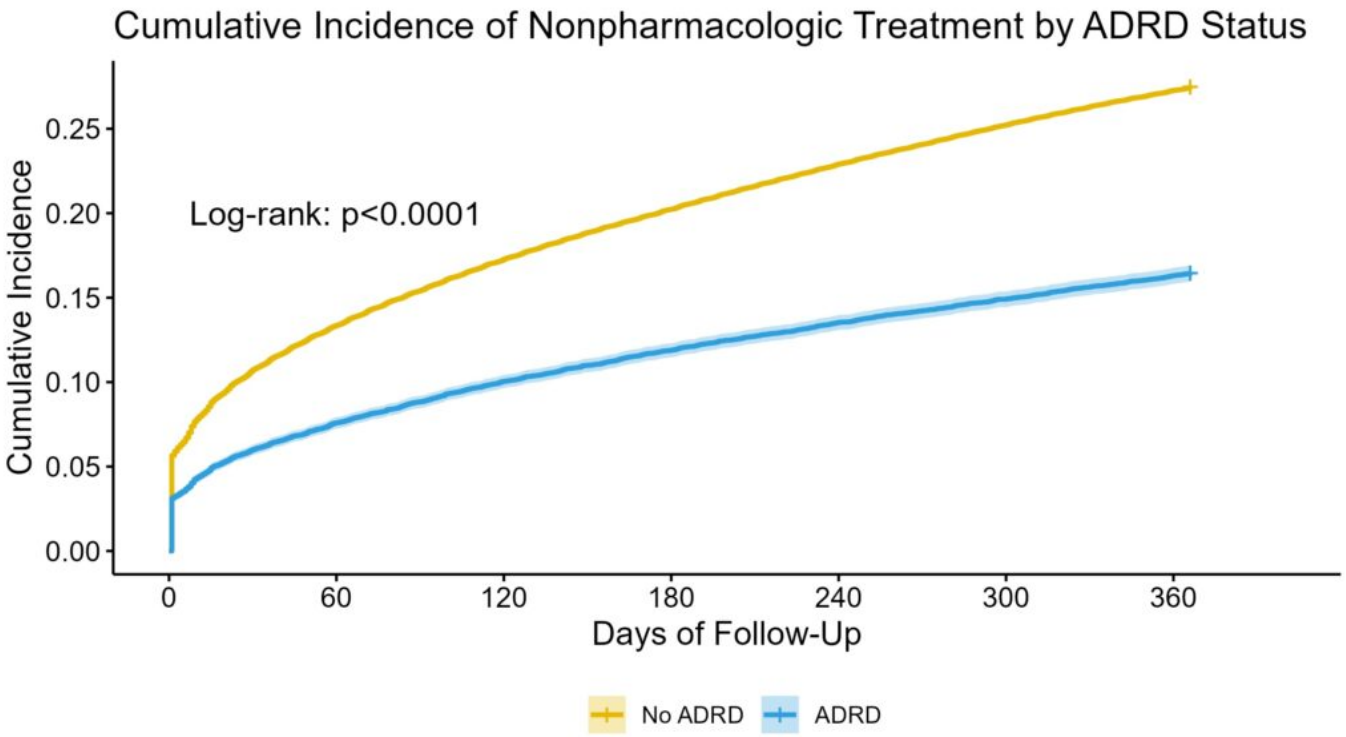
Disparities in nonpharmacologic chronic pain treatments for older adults with Alzheimer's disease and related dementias Fiona Bhondoekhan* Fiona Bhondoekhan Patience M. Dow Brandon D.L. Marshall Kaleen N. Hayes Nina Joyce

Background: Chronic pain is a major disability in adults with Alzheimer's disease and related dementias (ADRD). As analgesics increase adverse drug events, nonpharmacologic treatments are recommended as safer options for chronic pain; however, their use in adults with ADRD is unknown. We compared the 1-year incidence of nonpharmacologic treatment by ADRD status.

Methods: We designed a retrospective cohort study with Medicare fee-for-service claims (January 2017-December 2021). Participants were community-dwelling adults aged ≥66 years with newly diagnosed chronic non-cancer back pain. We defined new chronic pain as ≥2 claims for radicular/nonradicular back pain 90-183 days apart, with no claims 6 months prior. Excluding those with nonpharmacologic treatment 6 months prior to the pain diagnosis, we used the 1-year Bynum Standard algorithm to classify ADRD and current procedural terminology codes to find nonpharmacologic treatments (physical therapy [PT], chiropractic care, acupuncture). Follow-up was 1 year or until nonpharmacologic treatment receipt, death, or disenrollment from Medicare. We used weighted Kaplan-Meier curves to measure nonpharmacologic treatment incidence by ADRD status.

Results: We identified 333,125 new chronic pain diagnoses, of which 30,297 (9.1%) involved ADRD. More adults with ADRD were female (71.6% vs. 66.6%) and Hispanic (8.5% vs. 5.8%). The 1-year incidence of nonpharmacologic treatment was 13.7% and 25.3% for those with and without ADRD, respectively ($p<0.001$). Median time to treatment was 76 days (IQR: 9, 195) for those with ADRD and 65 days (IQR: 7, 188) for those without ADRD ($p= 0.079$). PT was the most common treatment type (ADRD: 62.7%, no ADRD: 61.0%). Chiropractic care was more common for those without ADRD (19.8% vs. 14.5%), while acupuncture was higher in those with ADRD (22.8% vs. 19.2%).

Conclusion: Nonpharmacologic treatments were less common in those with ADRD, suggesting a gap in guideline-recommended pain treatments for a population vulnerable to adverse drug events.



Number at risk

No ADRD	269980	234044	223523	215407	208228	201955	196415
ADRD	23129	21379	20810	20384	20005	19683	19363

LATEBREAKER

Aging

The Impact of Loneliness on Insomnia and Depression among Older Adults: Role of Smoking in these Associations RoiSan Nhpang* RoiSan Nhpang

Background: Loneliness is an increasing public health concern among the growing population of older adults, with research indicating its associations with sleep disturbances, mental health issues, and smoking. This study examines associations between loneliness and insomnia, as well as loneliness and depression, while also exploring the potential moderating effect of smoking among adults aged 50 and older.

Method: This secondary data analysis of the early-release 2022 Health and Retirement Study (HRS) examines relationships between loneliness (3-item UCLA Loneliness Scale), insomnia (four self-reported sleep-related questions), and depression (self-reported physician diagnosis). Smoking status was categorized as ever or never smoker. Chi-square tests and logistic regression were used to assess associations between loneliness, health outcomes (insomnia and depression), and smoking. Multivariable logistic regression further assessed these relationships, including testing moderating effect of smoking, and with the addition of relevant covariates.

Result: Among 3,843 adults included in the study, 25.03% reported loneliness, 23.95% reported depression, and 42.91% reported insomnia. Chi-square tests showed significant associations between loneliness and both depression and insomnia ($p < 0.0001$). After adjusting for covariates, loneliness was significantly associated with insomnia (OR: 1.67, 95% CI: 1.43–1.96), indicating that lonely individuals were 67% more likely to report insomnia. Similarly, loneliness was associated with depression (OR: 2.23, 95% CI: 1.87–2.65), suggesting a 2.2-fold increased likelihood of reporting a depression diagnosis. Smoking did not moderate these associations.

Discussion: This study underscores the significant impact of loneliness on insomnia and depression among older adults. Given its widespread prevalence and adverse health effects, addressing loneliness should be a public health priority to improve overall well-being in this population.

Aging

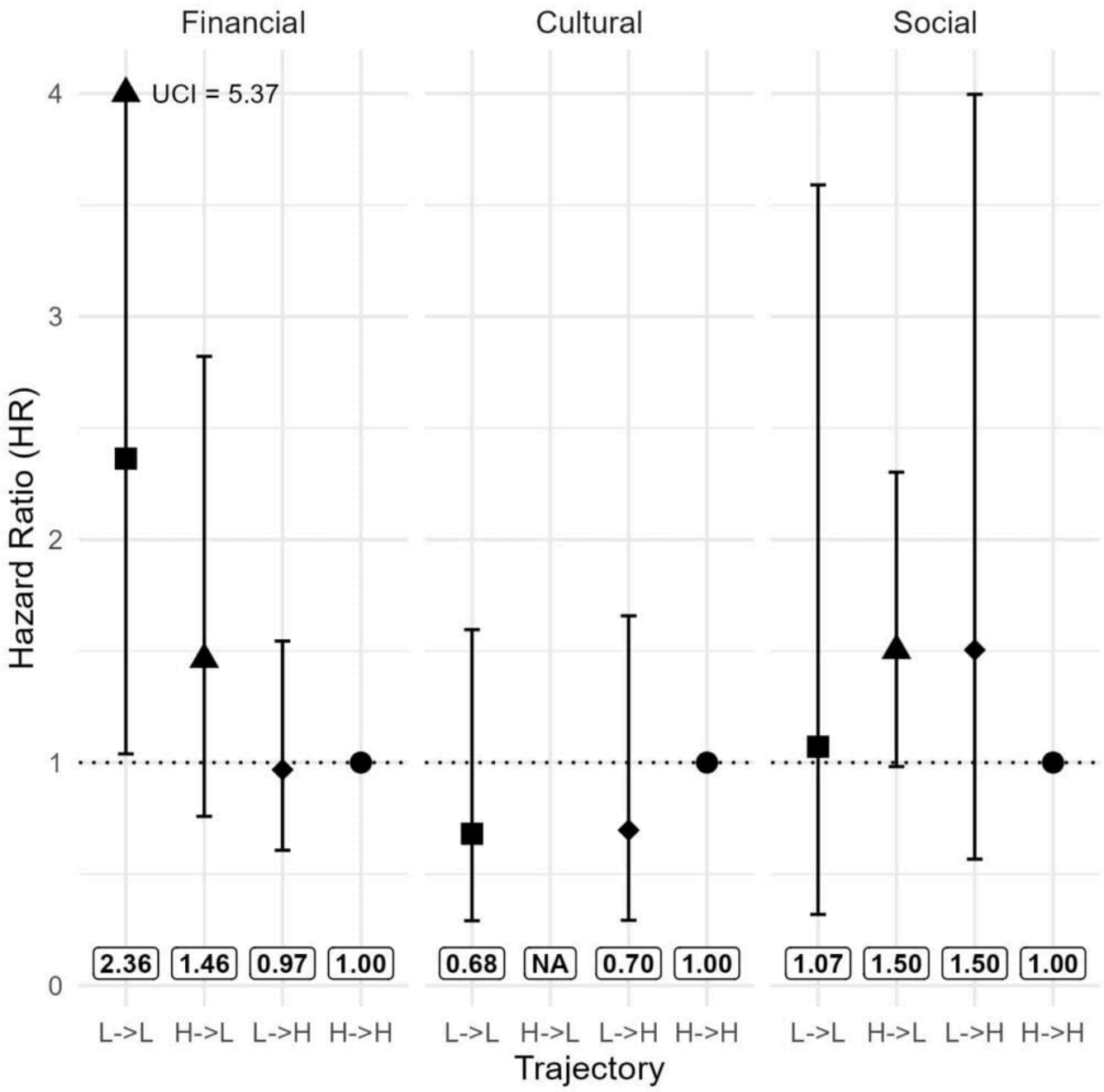
The impact of life course socioeconomic status on incident dementia among the oldest-old in the LifeAfter90 Study Hilary L. Colbeth* Hilary Colbeth Rachel L. Peterson Kristen M. George Alexander Ivan B. Posis Rifat B. Alam Paola Gilsanz Dan M. Mungas Maria M. Corrada Rachel A. Whitmer

Background Low socioeconomic status (SES) in early and late life is associated with lower late-life cognition among the oldest-old. Less is known about life course trajectories of SES in association with dementia risk among diverse populations over 90 years.

Methods This prospective cohort from the LifeAfter90 Study (2018-2022) included 430 participants (mean age=92.1±2.2 years; 24% Asian; 19% Black; 19% LatinX; 7% Multiracial/Other; 30% White). Participants with only mild cognitive impairment were excluded. Childhood and late-life SES were self-reported across three domains: financial, cultural, and social capital, based on Bourdieu's forms of capital. Financial capital is an economic indicator based on income, cultural capital reflects education-based generational gains, and social capital indicates access to resources from social networks. We estimated subdistribution risks in the presence of the competing risk of death for dementia incidence by each domain, adjusting for age, gender, and race/ethnicity. We then examined if associations differed by either childhood residence outside the United States or birth in a Stroke Belt state.

Results We observed 94 incident dementia cases. Participants with consistently low or high to low trajectories had an increased risk of dementia compared to those with consistently high financial capital (Figure 1). Those with mixed social capital trajectories had an increased risk of dementia compared to those consistently high. There was no evidence of an association between cultural capital trajectories and increased dementia incidence. There were no differences by childhood residence or birth state in the associations of financial (p-interaction=0.19), cultural (p=0.99), or social capital (p=0.28) with dementia incidence.

Conclusions Lower financial capital in early and late life is associated with greater incident dementia risk among adults aged 90+, regardless of US childhood residence or birth in the Stoke Belt.


Financial
Cultural
Social
UCI = 5.37
Hazard Ratio (HR)
4
3
2
1
0
2.36
1.46
0.97
1.00
0.68
NA
0.70
1.00
1.07
1.50
1.50
1.00
L->L
H->L
L->H
H->H
Trajectory

Aging

Lifecourse Socioeconomic Position and Cognitive Function: Leveraging Intergenerational Data from the Framingham Heart Study Ruijia Chen* Ruijia Chen Chang Su Phillip Hwang Maria Glymour Andrew Stokes

Background: Parental socioeconomic position (SES) is linked to cognitive function, but many studies relied on offspring-reported parental SES, which is prone to recall bias, and used models inappropriately adjusted for potential mediators across life stages. Using multigenerational data from the Framingham Heart Study (FHS), we fitted marginal structural models to assess the associations of lifecourse SES with cognitive function and decline.

Method: Data are from the 1992-2018 FHS Offspring Cohort, with parental SES derived from the Original Cohort. Own and parental education were assessed by the highest level of education achieved; occupation was based on either current or most-recent pre-retirement occupation. Parental and own education and occupation were classified into high, medium, and low categories (see **Figure 1** note for detailed grouping criteria).Executive function, language, and memory were used as outcomes in linear mixed-effects models with random intercepts. Inverse probability weights were used to account for treatment-confounder feedback loop and loss to follow-up.

Results: Among 1,550 participants (mean age: 60.4 years, SD = 9.7; 52% women), cognitive function showed a strong gradient with own education, more than with parental education. For example, participants with high parental and own education scored 1.00 SD (95% CI: 0.86, 1.15) higher executive function than those with low parental and own education. Those with high parental and medium own education scored 0.51 SD higher (95% CI: 0.29, 0.73), while high parental and low own education showed weaker associations (0.21 [95% CI: -0.27, 0.70]). Occupational gradients were less pronounced. Neither parental nor participants' own SES was associated with cognitive decline over an average of 9.5 years of follow-up.

Conclusions: Both parental and own education contributed to cognitive health in later life, with participants' own education playing a more important direct role than parental education.

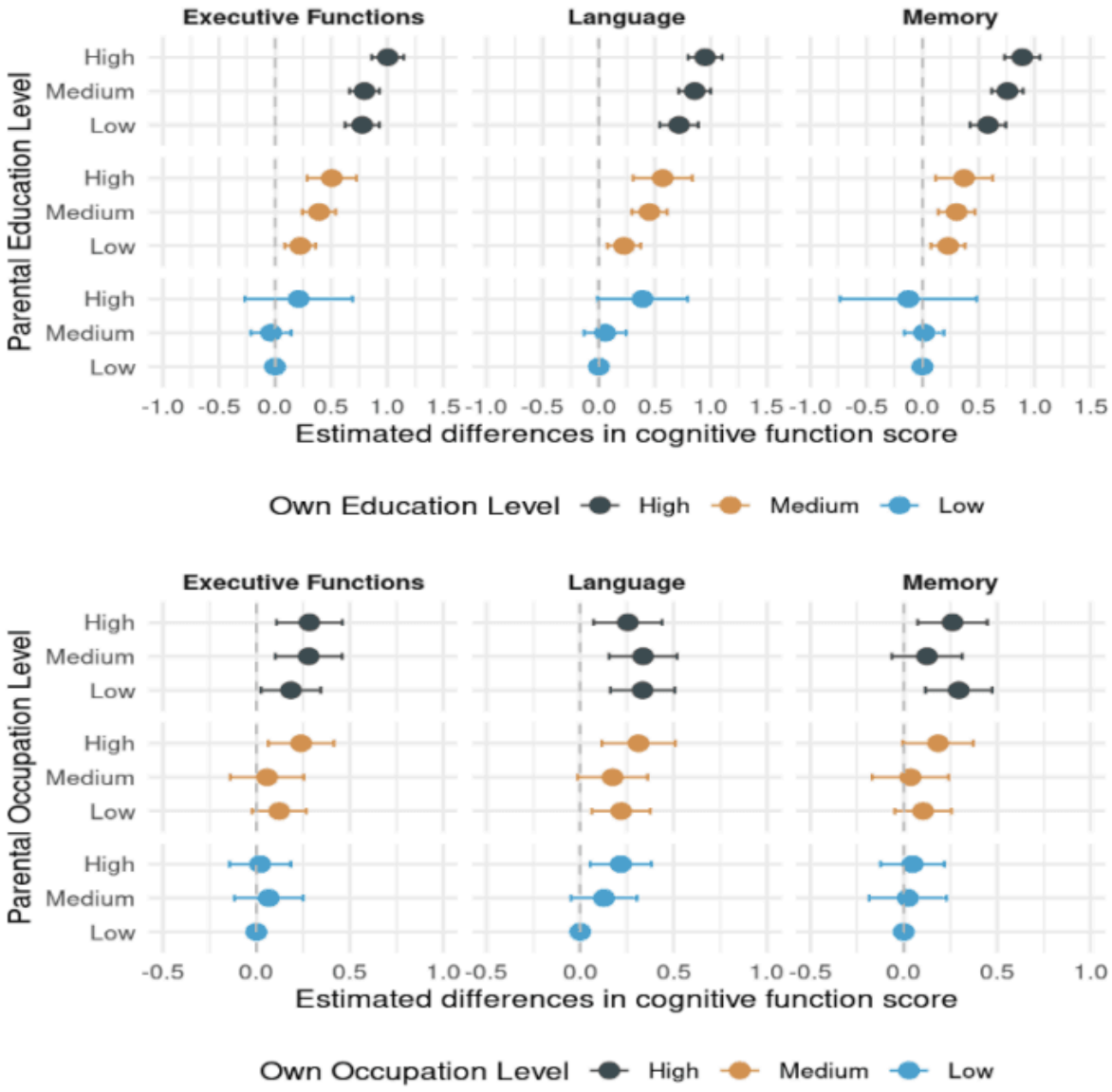


Figure 1. Estimated differences in level of cognitive function by lifecourse education and occupation status from the Framingham Heart Study (n=1,550). Panels in the top row display differences based on parental and own education levels, while panels in the bottom row display differences based on parental and own occupational prestige. Colors indicate own education or occupation levels (high, medium, low). Error bars represent 95% confidence intervals. The x-axis shows the estimated differences in cognitive function scores, and the y-axis represents parental socioeconomic levels. Father's education was grouped into three levels: "low" includes individuals with less than high school education; "medium" includes those who completed high school or some college; and "high" includes individuals with a college degree or higher. Offspring education was categorized as: "low" includes individuals with less than high school or high school degree; "medium" includes those with some college education; and "high" includes those with a college degree or higher. Occupational prestige scores were derived from the 1989 General Social Survey, which assigned scores to various occupations based on their prestige. We categorized parental and own occupation prestige into three levels (low, medium, and high) based on their distribution percentiles (33rd and 67th percentiles).

Aging

Identifying Medicare provider characteristics associated with timely dementia diagnosis

Bryan James* Joya Bhattacharyya Annie Chen Yi Chen Francine Grodstein Bryan D. James Ziwei Song Emma K. Stapp Ali Moghtaderi Melinda Power

Background: Late or missed diagnosis of dementia is common. Research in other areas of healthcare has shown that patient-provider concordance can influence patient-provider interactions above the influence of patient characteristics alone. Increased specialization and decreasing patient-provider relationships may also contribute, given clinical recognition of cognitive decline is needed for dementia diagnosis. We aim to identify provider characteristics associated with timely dementia diagnosis.

Methods: We used data from 5 harmonized cohorts from the Rush Alzheimer's Disease Center (RADC), linked Medicare fee-for-service claims data, and the National Plan and Provider Enumeration System (NPPES) database. In this preliminary work, we examined whether provider gender, provider specialty, or patient-provider gender concordance were associated with timely dementia diagnosis among those with cohort-determined dementia using univariate logistic regression.

Results: In our preliminary analysis, we identified 516 participants with cohort-determined dementia; 385 received a timely diagnosis of dementia and 131 received a late diagnosis in the healthcare setting, determined via linkage to Medicare claims. We did not find any significant associations between provider characteristics and timely diagnosis: male provider gender (OR: 0.81, 95% CI: 0.54, 1.21); patient-provider gender concordance (OR: 1.07, 95% CI: 0.71, 1.61); or specialty of primary care (OR: 0.84, 95% CI: 0.56, 1.25), gerontology (OR: 0.76, 95% CI: 0.23, 2.51), cardiology (OR: 0.80, 95% CI: 0.37, 1.73), and radiology (OR: 1.11, 95% CI: 0.49, 2.52).

Discussion: The provider characteristics investigated in this preliminary analysis do not appear to be central to timely dementia diagnosis, although these findings may change when explored in a larger sample. Expanded analyses will include additional provider characteristics and adjustment for patient characteristics known to be associated with timely diagnosis of dementia.

Aging

Adverse Childhood Experiences and social isolation in older adults : JAGES 2016-2019 Anna Kosaka* Anna Kosaka Maho Haseda Kosuke Inoue Marisa Nishio Katsunori Kondo Naoki Kondo

Introduction
Social isolation adversely impacts physical and mental health. Adverse Childhood Experiences (ACEs), potentially traumatic experiences before the age of 18, may predispose individuals to social isolation in later life, whereas longitudinal studies exploring this association remain limited. This study examined the link between ACEs and social isolation among older adults in Japan.

Methods
We used data from the Japan Gerontological Evaluation Study (JAGES) in 2016 and 2019, including functionally independent individuals aged 65 and older not socially isolated in 2016. Social isolation was measured via the Social Isolation Index, with scores of three or more indicating isolation. ACEs were assessed using an eight-item questionnaire, with four or more ACEs categorized as high exposure. Multivariable modified Poisson regression was used to estimate risk ratios (RR), adjusting for demographic, socioeconomic, and health factors. We conducted subgroup analysis by sex and age and analyzed the association of each ACE item and social isolation.

Results
Among 8,358 study participants (mean age, 73.2 years; female, 40.9%), 528 (6.3%) reported ACEs ≥4 in 2016 and 579 (6.9%) became social isolation in 2019. High ACEs exposure was associated with an increased risk of social isolation (RR=1.55, 95% CI=1.19–2.00). The associations were stronger among females (RR=2.14, 95% CI=1.45–3.15) than males (RR=1.06, 95% CI=0.67-1.69; P for Interaction=0.004), and adults aged 65-75 years old (RR=1.95, 95%CI=1.39-2.73) than those aged 75-years old(RR=1.05, 95%CI=1.39-2.73; P for interaction=0.003). Among the ACE items, physical abuse (RR=2.11, 95% CI=1.27–3.52) was most associated with social isolation.

Conclusion
ACEs were associated with social isolation, particularly among female and adults aged 65-75 years old. These findings suggest that the prevention of social isolation in later life should start from childhood, preventing ACEs.

Aging

Social Isolation and Risk of Dementia: Do Race-Ethnicity and Gender Matter? Zhiyong Lin*
Zhiyong Lin

Social isolation has emerged as a significant psychosocial determinant of dementia risk in older adults. However, limited research has examined how this association varies across racial-ethnic groups and by gender. To address this knowledge gap, we leveraged longitudinal data from the Health and Retirement Study (HRS) (2000–2016) to investigate the relationship between social isolation and incident dementia among non-Hispanic White, non-Hispanic Black, and Hispanic adults aged 65 years and older. Additionally, we assessed potential gender heterogeneity within each racial-ethnic group. Using survival analyses, we observed that social isolation was associated with an increased hazard of dementia among non-Hispanic White and Black individuals, independent of gender. However, no statistically significant association was detected among Hispanic older adults. Stratified analyses further revealed that socially isolated Black adults exhibited the highest dementia risk across all subgroups, highlighting the compounded vulnerability of this population. Gender disparities in dementia risk were evident only among older adults who were not socially isolated. Notably, as levels of social isolation increased, the dementia risk converged for men and women, indicating that social isolation may act as a risk equalizer across genders. Mediation analyses identified socioeconomic resources (e.g., income, education) and health-related factors (e.g., comorbidities, depressive symptoms) as significant pathways linking social isolation to dementia risk among non-Hispanic White and Black adults. These findings suggest that the observed associations are partially explained by structural inequities and cumulative health disadvantages, which exacerbate the impact of social isolation on cognitive decline. Our results underscore the critical role of social isolation as a modifiable risk factor for dementia and emphasize the need for public health strategies targeting vulnerable populations. Culturally tailored interventions to reduce social isolation and promote social engagement, particularly among non-Hispanic Black older adults, may serve as effective mechanisms for mitigating dementia risk and addressing health disparities.

Aging

The mediating effects of depressive symptoms in the association between subjective and objective cognitive decline: Findings from LifeAfter90 and STAR Nancy X Chen* Nancy Chen Kristen George Paola Gilsanz Sarah Tomaszewski Farias Rachel Peterson Maria Corrada Rachel A Whitmer

We investigated whether depression mediates the association between subjective and objective cognitive decline in ethno-racially diverse older adults.

LifeAfter90 (LA90) and Study of Health Aging in African Americans (STAR) are ongoing cohort studies of cognitive aging in participants aged 90+ (LA90) and 50+ (STAR). Verbal episodic memory (VEM) and executive function (EF) were assessed using the Spanish and English Neuropsychological Assessment Scales (SENAS) every 6 months (up to 8 times) for LA90 and 16 months (up to 3 times) for STAR. Subjective cognitive decline was measured using the Everyday Cognition (ECog), with responses (1="Better or no change" to 4="Consistently much worse") averaged across 12 items. Depression was assessed by the 8-item Adult PROMIS Depression short form. The sample included participants without baseline depression. Participants were defined as having onset depression if symptoms developed at a later visit or as never having depression if they did not. Linear mixed models with random intercepts and slopes estimated total and direct effects of ECog on VEM and EF at baseline and over time, adjusting for baseline age, sex, race/ethnicity, education, cohort, interview mode (in-person/phone), and depression (direct effect models only).

Participants' (n=475) baseline mean age was 83±13 years, 65% women, 16% Asian, 53% Black, 8% Latino, 18% White, and 32% had onset depression. For the total effect, greater ECog was associated with faster decline in VEM and EF (bTE-VEM=-0.10, 95%CI -0.19,-0.01; bTE-EF=-0.08, 95%CI -0.15,-0.01). Models of the direct effects showed attenuation of the associations between ECog and cognitive decline (bDE-VEM=-0.08, 95%CI -0.17,0.01; bTE-EF=-0.06, 95%CI -0.13,0.01).

Adults with greater (worse) ECog had faster decline in VEM and EF. However, the attenuation of these effects in the direct effect models suggests that onset of depression partially mediates the relationship between subjective and objective cognitive decline.

Table. Linear mixed models estimating total and direct effects of the Everyday Cognition (ECog) score on verbal episodic memory (VEM) and executive function (EF), adjusting for baseline age, sex, education, cohort, interview mode (in-person or phone), in the harmonized analytic sample of *LifeAfter90* and STAR.

	Coefficient	95% Confidence Interval
Outcome: Verbal episodic memory		
Total effect model		
ECog score	-0.22	-0.51, 0.07
ECog score * Time	-0.10	-0.19, -0.01
Direct effect model		
ECog score	-0.22	-0.51, 0.07
ECog score * Time	-0.08	-0.17, 0.01
Onset of depressive symptoms	-0.01	-0.19, 0.16
Onset of depressive symptoms * Time	-0.08	-0.14, -0.03
Outcome: Executive function		
Total effect model		
ECog score	-0.16	-0.43, 0.11
ECog score * Time	-0.08	-0.15, -0.01
Direct effect model		
ECog score	-0.15	-0.42, 0.12
ECog score * Time	-0.06	-0.13, 0.01
Onset of depressive symptoms	-0.04	-0.21, 0.12
Onset of depressive symptoms * Time	-0.07	-0.11, -0.02

Aging

Association Between Consuming Food Prepared Away from Home and Epigenetic Age Acceleration among Older Adults Jeffrey Liu* Jeffrey Liu Tuo Lan

Background: Healthy aging is a growing public health challenge. Evidence suggests that food prepared away from home (FAFH) is associated with higher mortality risk, but its relationship with aging remains unclear. The objective of this study was to examine the association between FAFH consumption and rapid epigenetic age acceleration (EAA) in older adults using nationally representative data from the National Health and Nutrition Examination Survey (NHANES).

Methods: This cross-sectional study included 1,838 adults aged 60 years and older from NHANES 1999-2002. EAA was defined as the difference between Levine epigenetic age (DNAmPhenoAge) and chronological age, with the top quintile indicating rapid EAA. We categorized FAFH frequency into four levels (<1, 1, 2, ≥3 times/week) and evaluated the association between FAFH consumption and rapid EAA using multivariable logistic regression.

Results: The mean (SE) chronological age was 70.3 years (0.2), and the mean Levine epigenetic age was 59.7 years (0.3). 39.7% had FAFH <1 time/week, 21.4% once/week, 16.4% twice/week, and 22.5% ≥3 times/week. Individuals with frequent FAFH consumption were more likely to be male, non-Hispanic White, and have higher education and income. After adjusting for age group, sex, race/ethnicity, education, poverty-income ratio, smoking status, alcohol use, physical activity, body mass index, and healthy eating index, frequent consumption of FAFH was associated with increased odds of experiencing rapid EAA. Compared to consuming FAFH <1 time/week, OR was 1.77 (95% CI: 1.17-2.96) for once/week and 1.86 (95% CI: 1.09-2.88) for twice/week. No statistically significant association was observed for ≥3 times/week (OR = 1.31, 95% CI: 0.77-2.24).

Conclusions: The findings of this study suggest that FAFH consumption is associated with rapid EAA in older adults. Public health efforts addressing the health risks of FAFH could serve as an effective strategy to support healthy aging in this population.

Aging

Assessing Multidimensional Health in Older Adults: Insights from Wave 8 of the Survey of Health, Aging and Retirement in Europe (SHARE) Naiki Kondo* Amparo Oliver Tayzar Tun Naiki Kondo José Manuel Tomás

Background
Epidemiology specializes in counting health events among individuals. Since the World Health Organization's 1948 definition of health, epidemiology has advanced in measuring physical and mental well-being and is also working to assess social well-being. The recent aging of the population has expanded the understanding of health, suggesting the need for a broader concept beyond these three axes. This study aims to contribute to future epidemiological research by applying psychometric methods to clarify, in a data-driven way, additional potential dimensions of health and their associations with one another, and each dimension's contribution to overall health.
Methodology
Data from SHARE Wave 8, comprising 46,317 participants aged 50 and older (M = 71.3, SD = 9.34, 57.4% females), was analyzed. A structural equation model (SEM) with a second-order factor was estimated based on 34 theoretical and statistically relevant variables based on theoretical and CFA results.
Result
The final model identified health in older adults as a composite of multiple dimensions with these standardized coefficients: physical strength(0.76), cognitive health (0.68), mental wellbeing (0.76), social wellbeing (0.72), financial wellbeing (0.47), clinical symptoms (-0.88), and functional difficulties (-0.74).The model fit indices were 2(389)=53606.8, p<0.001; RMSEA=0.054, 90%CI [0.054, 0.055]; CFI=0.894; SRMR=0.048.
Discussion
This study confirms the multi-dimensional nature of health among older adults, highlighting the importance of often overlooked social and financial dimensions. However, reliance on available SHARE data restricts exploration of other potential dimensions. Multidisciplinary epidemiological studies are needed to refine comprehensive health measurements for aging societies.
Keywords: measurement of health; interdisciplinary approach; aging, SHARE survey

Aging

The effect measure modification of stroke belt birth states on brain biomarkers and cognitive decline Yi Lor* Yi Lor Kristen M. George Rachel L. Peterson Alexander Ivan B. Posis Batool Rizvi Paola Gilsanz Rachel A. Whitmer

The Stroke Belt is an area in the US with high prevalence of stroke and stroke-related mortality. Stroke belt birth (SBB) is associated with worse cognition and a higher risk of dementia, yet less is known about cognitive changes in relation to neuroimaging markers of brain health among those with SBB. We examined whether SBB moderates the association of brain biomarkers and cognitive decline in Black participants.

We used data of older adults who received 3T MRI from two harmonized cohorts, KHANDLE and STAR. Multivariable linear mixed-effect models were used to test the associations of parietal cortical volumes and log white matter hyperintensity (WMH) volumes with executive function (EF) and verbal episodic memory (VEM) over 3 waves (mean 2.5 years). We assessed moderation by testing a three-way interaction (biomarkers-by-time-by-SBB) and comparing estimates from SBB-stratified models.

Of the 295 participants (mean age=68.6; SD=7.7), increased parietal cortex volumes were associated with better EF and VEM, and greater WMH was associated with worse VEM. SBB was associated with worse EF and VEM. The interaction of time, WMH, and SBB was significant (p=0.04) for VEM. Participants born in the Stroke Belt with ≤mean WMH had lower baseline cognition, but cognitive change over time was similar to those not born in the Stroke Belt (Figure 1; C, D). Those with SBB that had WMH 1 SD above the mean and those with SBB that had parietal cortex volumes 1 SD below the mean had consistently lower cognition over time than those with no SBB.

SBB and biomarkers were associated with cognition, but not decline. SBB moderated the associations of WMH and cognition such that participants with SBB who had worse brain health also had worse cognition and cognitive change while those with better brain health had similar changes to participants without SBB. Participants that were not born in the Stroke Belt may have more cognitive resilience compared to participants that were born there.

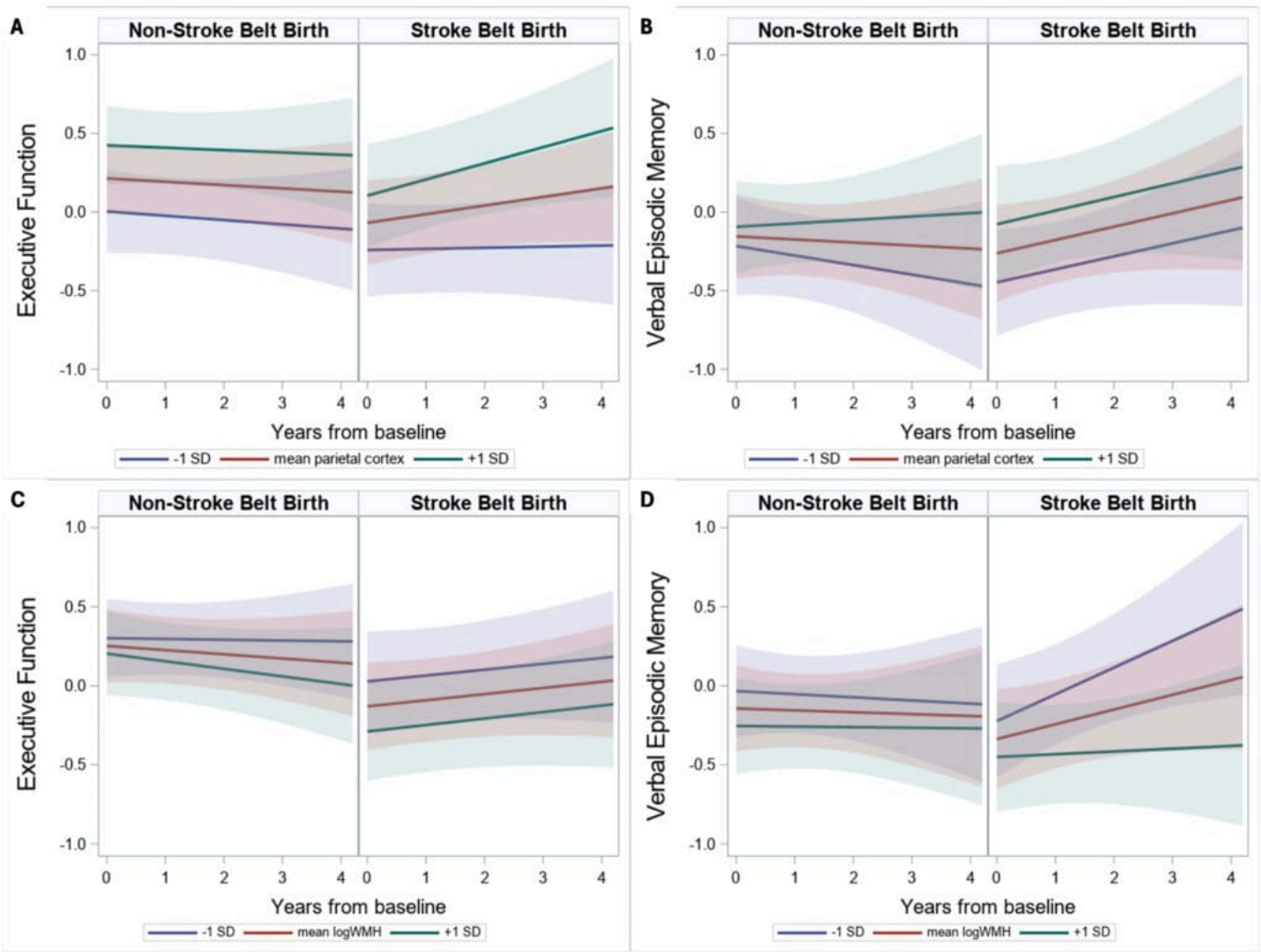


Figure 1 : The association of brain biomarkers on cognitive decline among those with stroke belt birth

A: Executive function and parietal cortex volumes by stroke belt birth, B: Verbal episodic memory and parietal cortex by stroke belt birth, C: Executive function and log white matter hyperintensities by stroke belt birth, D: Verbal episodic memory and log white matter hyperintensities by stroke belt birth. Red line indicates mean biomarkers volumes with green or blue line representing ±1 standard deviation from the mean. All models were adjusted for practice effects, interview mode, age at scan, sex, and parental education. A three-way interaction terms of years from baseline, brain biomarkers and stroke belt birth were included in all models.

Aging

Longitudinal Analysis on the Impact of Generation and Age of Immigration on Later Life Cognitive Performance in KHANDLE Shelli Vodovozov* Shelli Vodovozov Rachel Peterson Adina Zeki Al Hazzouri Oanh L. Meyer Claire C. Meunier Rachel A. Whitmer Anna M. Pederson Scott Zimmerman Maria M. Glymour

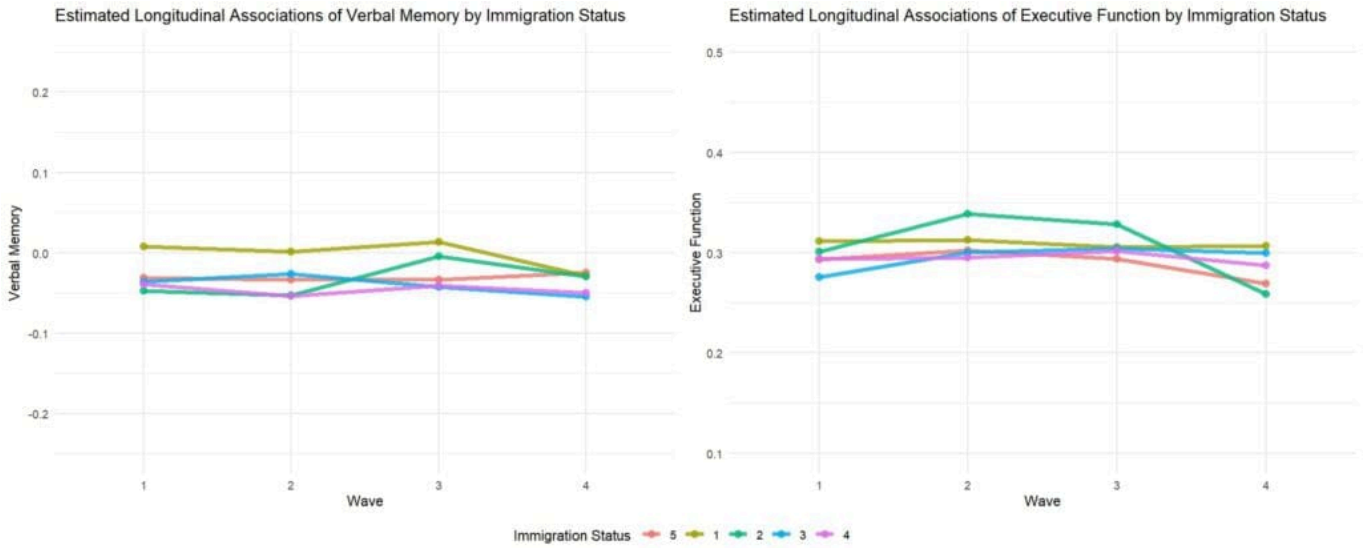
Introduction: Given the heterogeneity in lived experiences and educational quality among the growing immigrant population in the US, understanding the impact of generational status and age at immigration on cognitive aging is critical.

Methods: The Kaiser Healthy Aging and Diverse Life Experiences (KHANDLE) cohort is a diverse cohort of community-dwelling older adults in Northern California (n=1,885). Generational status was constructed using data on country of birth, age at immigration, and parental immigrant status as: first-generation who immigrated in adulthood (>18, n=301); first-generation who immigrated in adolescence (14-18, n=41); first-generation who immigrated in childhood (<14, n=66); second-generation (n=503); and third-generation or greater (n=974). Outcomes included level and change in verbal episodic memory and executive function, assessed at up to 4 waves approximately 18 months apart and Z-scored using baseline. Associations were evaluated using linear mixed effects models adjusted for baseline age, gender, race/ethnicity, education, parental education, and income.

Results: Compared to third-generation or greater participants (ref), immigration in adulthood was associated with lower verbal memory (β = -0.19; 95% CI: -0.30, -0.08) and executive function (β = -0.47; 95% CI: -0.56, -0.38); immigration in adolescence was associated with lower executive function (β = -0.37; 95% CI: -0.57, -0.18). Second-generation status was associated with slightly lower executive function (β = -0.08; 95% CI: -0.16, -0.02).

We found no significant differences in cognitive change across the immigration status categories.

Conclusions: Generational status and age at immigration were associated with later-life cognitive outcomes, a pattern that may reflect the experiences of immigration, the selection into immigration, or measurement challenges. There were no differences in rate of cognitive decline with age, although the sample was small.


Estimated Longitudinal Associations of Verbal Memory by Immigration Status
Verbal Memory
0.2
0.1
0.0
-0.1
-0.2
1
2
3
4
Wave
Estimated Longitudinal Associations of Executive Function by Immigration Status
Executive Function
0.5
0.4
0.3
0.2
0.1
1
2
3
4
Wave
Immigration Status
5
1
2
3
4

Aging

Agreement Between Fingerstick Blood Glucose and Continuous Glucose Monitor Measurements Among Long-Term Care Facility Residents Marzan A. Khan* Marzan Khan Medha N. Munshi Christine Slyne Nina R. Joyce Andrew R. Zullo

Background: Long-term care facility (LTCF) residents with comorbid diabetes and Alzheimer's Disease and Related Dementia (ADRD) are at high risk of hypoglycemia. Continuous glucose monitoring (CGM) is the gold-standard for detecting hypoglycemia including asymptomatic hypoglycemia and involves measuring interstitial glucose at 5-minute intervals over 10-14 days. Observational studies using electronic health record (EHR) data containing fingerstick blood glucose (FBG) measures could help to identify ways to reduce hypoglycemia risk, but we first need to understand the validity of such data.

Objective: To validate EHR-based FBG measures against gold-standard CGM measures of hypoglycemia.

Methods: We studied 2 cohorts in parallel. In the first, we analyzed linked CGM data and Long-Term Care Data Cooperative EHR-based FBG data on residents with comorbid diabetes and ADRD collected in 2023. In the second, we analyzed linked CGM and EHR-based FBG data obtained directly from LTCFs between 2022 and 2023. In both, we defined hypoglycemia as glucose levels < 70 mg/dl and assessed the sensitivity and specificity of FBG versus CGM measures to detect hypoglycemia. The unit of analysis was each pair of contemporaneous FBG-CGM measures.

Results: In the first cohort, 2 White, female residents with a mean (standard deviation [SD]) age of 81[12.7] years generated 25 daily hypoglycemia measurements. The sensitivity and specificity were 14% and 100%, respectively, for FBG-measured hypoglycemia. The second cohort included 40 residents (mean [SD] age 68 [11] years, 45% females, 60% White race) who generated 424 daily measurements of hypoglycemia. The sensitivity and specificity were 13%, and 100%, respectively.

Conclusion: EHR FBG measures of hypoglycemia had high specificity but low sensitivity among LTCF residents. Researchers and healthcare providers should assume hypoglycemia is measured with error in EHRs and account for this in their work.

Aging

Nine-year frailty transitions in older cancer survivors in the National Health and Aging Trends Study (NHATS) Allison Musty* Allison Musty Kathryn Callahan Heidi Klepin Amresh Hanchate Jennifer Gabbard Charles Semelka Emilie D Duchesneau

Background

Older cancer survivors are at risk of frailty. Most research focuses on frailty transitions around cancer diagnosis and treatment; transitions during survivorship are understudied. We described longitudinal frailty transitions in older cancer survivors.

Methods

Using Rounds 1-9 (2011-2019) of NHATS, a nationally representative cohort of adults 65+, we analyzed 1303 older adults with a self-reported cancer history. Frailty was assessed annually using two measures common in research: (1) the frailty phenotype (robust: 0, prefrail: 1-2, and frail: 3-5 of the following symptoms: exhaustion, low physical activity, shrinking, weakness, slowness) and (2) a 40-item deficit accumulation frailty index (FI; robust: <0.15, prefrail: 0.15-0.24, frail: ≥0.25). Multistate Markov models estimated 1-year probabilities of transitioning across frailty states and death, pooling all rounds. Multiple imputation and inverse probability weights accounted for missing data and attrition.

Results

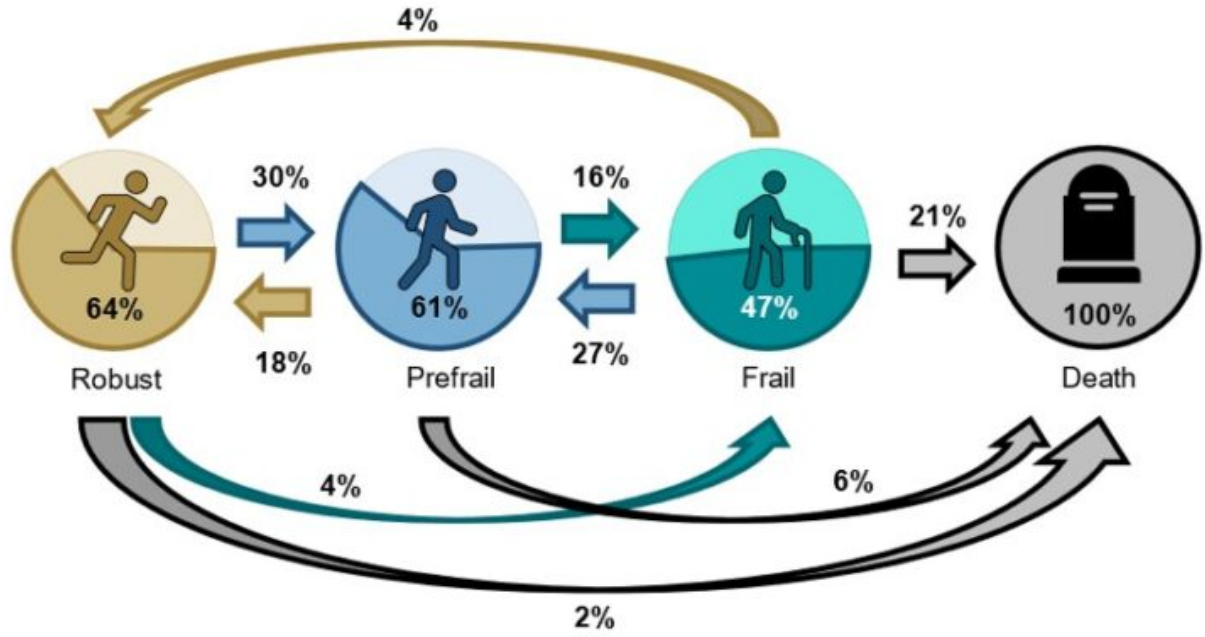
In Round 1, 35% were robust, 47% prefrail, and 18% frail by the frailty phenotype vs. 37%, 25%, and 38% by the FI. Transition probabilities differed by frailty measure (**Figure**). For both measures, prefrail and frail individuals had a higher one-year probability of death than robust individuals. Using the frailty phenotype (**panel A**), transitions between adjacent states (e.g., robust to prefrail) were common, with greater probabilities of improvement (e.g., frail to prefrail: 27%) compared to the FI (e.g., frail to prefrail: 9%). The FI (**panel B**) showed fewer transitions across frailty states and more stability for frail individuals.

Conclusions

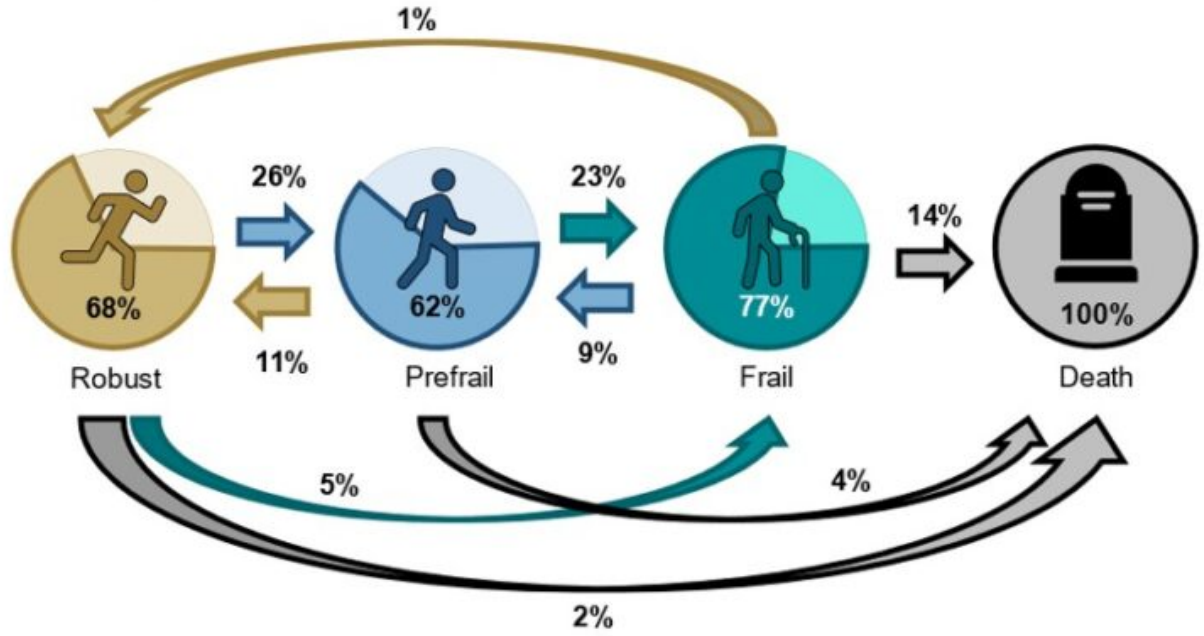
Frailty is dynamic in older cancer survivors and transitions vary by frailty measure. Frailer individuals face elevated mortality risks compared to robust individuals. These findings highlight the importance of frailty measurement selection and the need for targeted interventions to address frailty progression and improve outcomes in this population.

Markov model depicting frailty transitions in cancer survivors in NHATS

A. Frailty phenotype



B. Frailty deficit accumulation index



Arrows represent the 1-year probability of transitioning from one frailty state to the other from the Markov multistate model, pooling across all nine years of data; percentages in pie charts represent the 1-year probability of remaining in the same frailty state.

Aging

The Relationship Between Fall History and Early-Onset Dementia: A 10-Year Prospective Cohort Study Yu-Kai Lin* Yu-Kai Lin Wan-Yu Lin Siang-Chen Chen

Introduction: The prevalence of falls among older adults is increasing as the population ages. While previous studies have focused primarily on the physiological health effects, such as trauma, fractures, and sprains, fewer have examined the psychological effects of falls. The aim of our study is to explore the causal relationship between fall experiences and the risk of developing early-onset dementia among community-dwelling older adults.

Methods: A prospective cohort study is conducted using health examination data of older adults in Taipei City from 2013 to 2022. The study includes individuals aged 65 and above who have no cognitive impairment or dementia at baseline and are followed until the end of the study. Falls is assessed by asking the participants about the number of falls they experienced in the past six months, while early dementia is identified using the Ascertain Dementia (AD-8) scale. Cox regression hazard model is adopted to examine the causal risk of early dementia associated with different frequencies of falls.

Results: The results indicate that, compared to older adults without history of falls in the past half year, the risk of developing early dementia increases with the frequency of falls. Older people who report falling once or twice in the past six months have 1.54-fold (95% CI: 1.29-1.84) and 2.23-fold (95% CI: 1.51-3.29) higher risk of developing early dementia, respectively, compared to those without fall history. Furthermore, the elevated risk is particularly significant among females, singles, individuals with older age, lower education level, and no regular exercise habit.

Discussion: Falls and dementia are both critical health concerns among the older population, with both physical and psychological consequences that should not be overlooked. It is important for governments and healthcare institutions to enhance efforts in promoting fall prevention strategies and raising awareness among older adults and their primary caregivers.

Aging

The effects of family caregiving and cash transfers on probable depression among older adults in the Survey of Health, Ageing and Retirement in Europe (SHARE): simulation using parametric g-formula Sherry Hou* Sherry Hou Jee Won Park M. Maria Glymour Arijit Nandi

When the intensity of caregiving exceeds the capacity of the caregivers, caregivers may experience poorer mental health outcomes. Traditional regression methods cannot account for time-varying confounding or simulate effects of hypothetical interventions. Our goal was to estimate the effect of caregiving on probable depression and how cash transfers, as a hypothetical intervention, could modify that relationship.

Using 7 waves (2004-2012) of SHARE, a cohort study of adults age 50+, we used parametric g-formula to estimate the prevalence of depression (defined as 4+ symptoms on the EURO-D depression scale) under the following simulated scenarios: if all participants, at all waves, were to provide daily, less-than-daily, or no caregiving, with and without a cash transfer of 12,000 €/year in household income. We accounted for time-fixed (gender, number of children, country, and education) and time-varying (age, employment, marital status, income, physical limitations, psychiatric drugs, and receiving help) covariates, and 95% confidence intervals were bootstrapped.

Among 36,359 participants, the average follow-up time was 2.9 waves or 4.8 years. If everyone provided daily caregiving consecutively for one, two, or three waves after baseline, the depression prevalence would be 4.8% [2.5%, 7.3%], 3.1% [0.4%, 6.4%], and 2.8% [-3.5%, 9.3%] higher than if everyone were noncaregivers. If everyone were daily caregivers receiving cash transfer of 12,000 €/year, the depression prevalence would be 0.2% [>-0.1%, 0.6%], 0.3% [-0.8%, <0.1%], and 0.3% [-1.1%, 0.4%] lower than daily caregivers without cash transfer.

Our results found that daily caregiving increased the prevalence of depression. Additional income did not mitigate the effect of daily caregiving on depression. While the g-formula simulation offered insight to how hypothetical cash transfer may affect caregiver mental health, future research using quasi-experimental methods is needed for more robust causal analysis.

Aging

Healthcare utilization and morbidity preceding a dementia diagnosis. The Atherosclerosis Risk in Communities (ARIC) Study. Meng Pan* Meng Pan David Knopman Michele Johnson-Funk Priya Palta Anna Kucharska-Newton

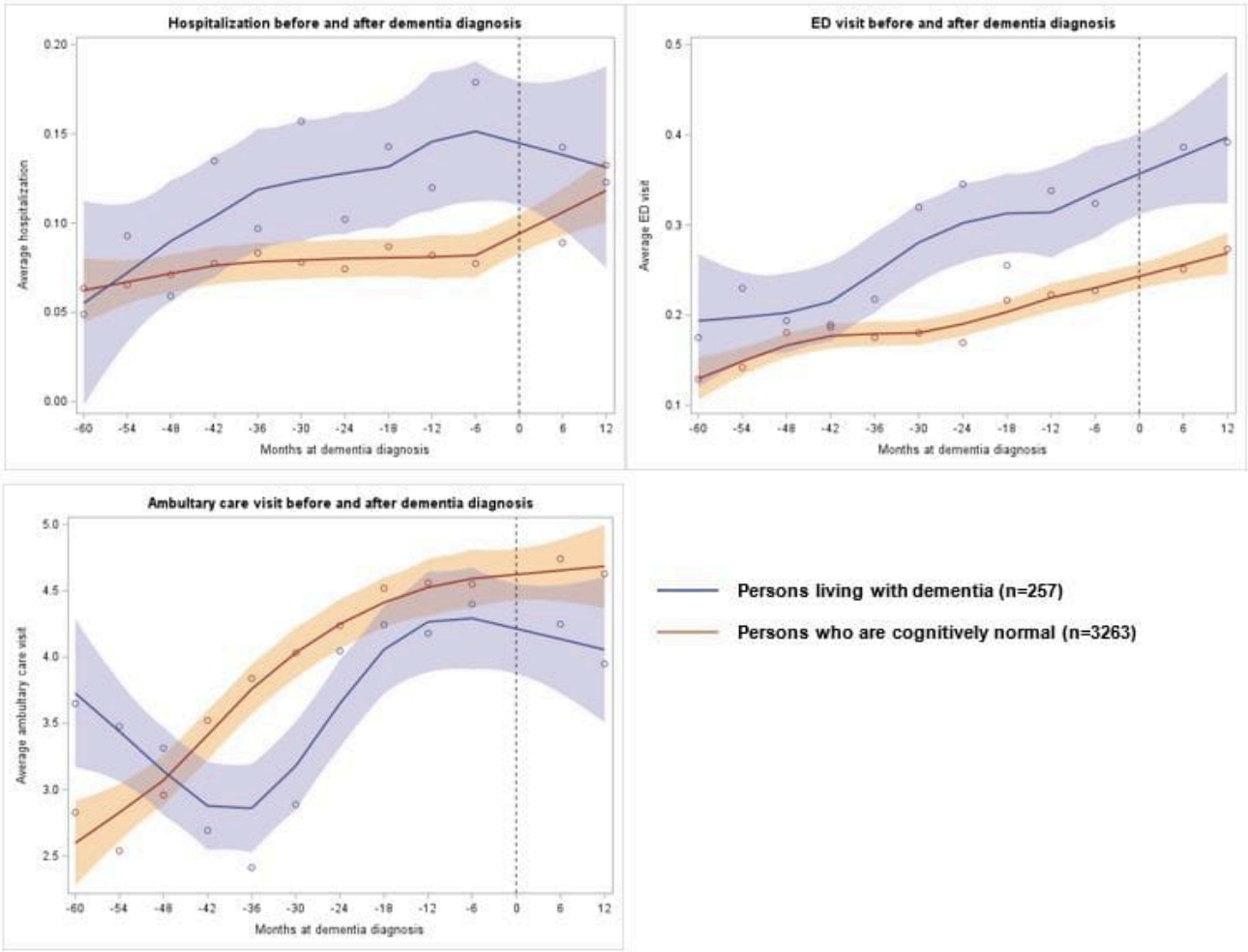
Objectives: To compare healthcare utilization among persons living with dementia (PLWD) and those cognitively normal.

Methods: Within a retrospective cohort of ARIC Visit 6 (2016-2017) participants with continuous Medicare fee-for-service enrollment (2011-2018), Poisson regression was used to compare longitudinal trends in inpatient, Emergency Department (ED), and ambulatory care use in the 5 years prior to and 1 year following a comprehensive syndromic . Inverse probability weights were used to balance groups of participants with and without dementia on baseline age, race, sex, education, and prevalent comorbidities [diabetes, congestive heart failure (CHF), stroke, and coronary heart disease]. Principal discharge diagnosis codes were used to assess the prevalence of Centers for Medicare & Medicaid Services pre-defined chronic conditions associated with each healthcare visit.

Results: Among 3,932 eligible participants at ARIC visit 6 (median age 79 years old, 325 (8.3%) with incident dementia), 59% were women and 24% were Black. During 5 years prior to a dementia diagnosis, participants with, as compared to those without dementia, had on average greater utilization of inpatient (0.11 vs 0.08 hospitalizations) and ED services (0.26 vs 0.18 visits) but lower ambulatory care use (3.53 vs 3.76 visits). (Figure) The most frequent principal diagnoses for inpatient visits occurring within 6 months prior to the diagnosis were CHF (6.4%), ischemic heart disease (5.8%), and stroke/transient ischemic attack (5.8%) among participants with dementia, and rheumatoid arthritis/osteoarthritis (8.8%), CHF (4.3%), and chronic kidney disease (4.1%) among participants without dementia.

Conclusion: Inpatient and ED utilization were on average greater among PLWD as compared to those cognitively normal, while the ambulatory care utilization were on average lower among PLWD.

Figure. Trends of healthcare utilization in the 5 years prior to and 1 year following incident dementia classification* (time=0) among covariates-balanced persons living with dementia and those cognitively normal**



* Incident dementia was classified based on the cognitive assessment at ARIC Visit 6, visit date was used as index date.
** Two groups were balanced on baseline age, race, sex, education, and prevalent comorbidities (diabetes, congestive heart failure, stroke, and coronary heart disease) using Inverse probability weights (IPW). The total patients in the IPW analysis (n=3520) were less than the eligible patients (n=3923) due to some patients were missing balanced covariates and were excluded from the analysis.

Behavior

Unpicking causal relationships between grip strength and cardiorespiratory fitness: a bidirectional Mendelian randomisation study Snehal M Pinto Pereira* Snehal Pinto Pereira Tom Norris Rachel Cooper Victoria Garfield Mark Hamer

Objectives: Understanding the dominant direction of association between cardiorespiratory fitness (CRF) and grip strength could help refine physical activity recommendations. We performed a Mendelian Randomization (MR) analysis to elucidate the bidirectional relationship between CRF and grip strength (GS).

Methods: Using an inverse-variance weighted (IVW) MR framework, we estimated the strength of the GS (exposure)-CRF (outcome) association using genome wide association summary data. When examining CRF (exposure)-GS (outcome), the CRF genetic instrument was related to individual-level GS phenotypic data in 367,693 UK Biobank participants. Several sensitivity analyses were performed (e.g., MR-Egger, MR-weighted median estimator and MR-PRESSO) and both measures were scaled by body weight (w).

Results: When examining associations in the direction GS-to-CRF, a 1-unit increase in GSw (i.e., GS/weight) was associated with 1.70ml/kg/min (95% confidence interval (CI): 1.14,2.27) higher CRFw (IVW model). This finding persisted across most sensitivity analyses. In the reverse direction, there was no evidence supporting an effect of CRFw on GSw, e.g., a 1-unit increase in CRFw led to a 0.00kg/kg (95% CI: -0.01,0.02) higher GSw (IVW model).

Conclusion: Our finding of a dominant direction of association from greater GS to higher CRF is relevant when considering how to promote physical activity guidelines. For example, placing too much emphasis on improving/maintaining CRF is unlikely to result in maximum benefits for other fundamental components of physical fitness, particularly muscle strength.

Behavior

Unsupervised Machine Learning Identifies Hidden Movement Behavior Patterns Linked to Metabolic Syndrome in Multiracial/Ethnic College Students: The 24h-MESYN Study Marcus Vinicius Nascimento Ferreira* Marcus Vinicius Nascimento Ferreira Antonio Gibran de Almeida Cardoso Augusto César F. De Moraes Marcia Ferreira Sales Ethan T. Hunt Gabriela Berg Tiago Almeida de Oliveira Francisco Leonardo Torres-Leal Heráclito Barbosa de Carvalho Shirley Cunha Feuerstein

Aim: We used unsupervised machine learning to identify 24-hour movement behavior patterns in multiracial/ethnic college students and examined their associations with metabolic syndrome.

Methods: Our sample included 518 students (60.1% aged ≤20 years; 68.7% female; 72.0% non-White) from two Brazilian cities (Gini indices ≤0.56). We analyzed self-reported 24-hour movement behaviors, standardized as minutes/day, and assessed guideline adherence. Metabolic syndrome, the outcome, was evaluated in 375 students based on three of five risk factors: high abdominal circumference, blood pressure, triglycerides, fasting glucose, or low HDL. Clusters were identified using unsupervised methods (Calinski-Harabasz index and k-median) and described with compositional data analysis (CoDA). Associations between clusters and outcomes were examined using multilevel logistic regression, adjusted for biological sex, age, residence, work status, and degree program and shift.

Results: We found 56.6% met physical activity guidelines (60 min/day until 17, >30 min/day for ≥18), 43.8% met sedentary behavior guidelines (<2 h/day until 17, <8 h/day for ≥18), and 39.2% met sleep duration guidelines (8–10 h/night until 17, 7–9 h/night for ≥18), with a metabolic syndrome prevalence of 24.5%. Unsupervised modeling identified four behavior clusters, but only cluster #4 (22.2% of participants, with daily distribution of 4.7%±9.5 for physical activity, 60.0%±14.5 for sedentary behavior, and 35.3%±14.2 for sleep) was associated with the outcome in bivariate analysis ($\chi^2 = 3.97$; $p = 0.046$). In adjusted models, no significant associations were found for meeting physical activity (OR: 1.61 [95% CI: 0.86–2.99]), sedentary behavior (OR: 1.40 [95% CI: 0.76–2.58]), or sleep duration (OR: 0.90 [95% CI: 0.49–1.65]) guidelines, while cluster #4 was significant (OR: 2.35 [95% CI: 1.07–5.15]).

Conclusions: Unsupervised machine learning offers a sensitivity alternative for assessing 24-hour movement behaviors, revealing hidden risk patterns associated with metabolic syndrome.

Big Data/Machine Learning/AI

Machine Learning Models for Predicting Prescription Opioid Misuse Among U.S. High School Students: Links with Selected Risky Health Behaviors Asef Raiyan Hoque* Asef Raiyan Hoque Liling Li

Introduction:

Prescription opioid misuse among adolescents in the U.S. is an emerging public health concern. The objective of this study was to develop machine learning models to predict prescription opioid misuse among U.S. high school students using socio-demographic and selected behavioral risk factors.

Methods:

This study analyzed cross-sectional data from the Youth Risk Behavior Surveillance System (YRBSS), a nationally representative dataset of U.S. high school students in grades 9-12. Machine learning models were developed using complete case analysis, with a total of n = 11,492 students meeting inclusion criteria. The outcome variable prescription opioid misuse was defined using reported lifetime misuse. Selected risky health behaviors identified from previous studies were included as predictors. Nine machine learning models were tested, including neural network, logistic regression, linear support vector machine (SVM), radial basis function SVM, random forest, naïve bayes, polynomial SVM, decision tree, and extreme gradient boosting (XGBoost).

Result:

All predictive models achieved high test accuracy (85.8% – 94.3%). Five out of nine classifiers had high test AUC ranging between 79.1% – 89.6%. Random Forest was the best predictive model, with both highest accuracy (94.3%) and AUC value (89.6%). From the Random Forest model, the three most important socio-demographic predictors were age, race, and grade. Most important risky health behaviors by variable importance were lifetime ecstasy use, lifetime methamphetamine use, and current marijuana use, respectively.

Discussion:

The findings showed the importance of socio-demographic factors and risky health behaviors in predicting prescription opioid misuse. Machine learning techniques can be a promising tool for identifying at-risk individuals, enabling more targeted prevention efforts. Future research is needed to explore additional risky health behaviors and consider longitudinal datasets to improve model performance.

Big Data/Machine Learning/AI

Feasibility of smartphone-based digital phenotyping in the 3E cohort of emerging adults

Julianna C. Hsing* Julianna Hsing Lucia E. Calderon Lindsay T. Hoyt Alison K. Cohen Mathew V. Kiang

Background. Epidemiological research often relies on self-reported behavioral data, which can be prone to recall bias, low granularity, and participant fatigue. Digital phenotyping—using smartphone sensor data to capture human activity—offers a low-burden alternative for capturing objective near-real-time behavioral data, but the feasibility of such methods remains understudied in vulnerable populations. This study presents preliminary findings from an ongoing cohort study of emerging adults (aged 18-24) from two public Hispanic-Serving Institutions to assess the acceptability of smartphone data collection.

Methods. A customized smartphone app collected passive sensor data (e.g., GPS, accelerometer) and self-reported nightly survey data over a 9-day period. Participants responded to smartphone feasibility questions related to comfort, awareness, and behavioral changes due to smartphone data collection on a 5-point Likert scale.

Results. From September 2023 to December 2024, 318 participants were enrolled in a smartphone substudy from a larger cohort study of 871 college students. The majority of students identified as Latine (35%) or Asian (31%) and 55% identified as female. High-density, passive smartphone data collection resulted in 2.1 million GPS observations, 1.5 million accelerometer observations, and 9.1 million activity observations across 6,338 participant-days. 76% of participants reported being comfortable with having their personal data collected via smartphones, 78% did not consider smartphone data collection to be burdensome, and only 3% felt it altered their actual behavior.

Conclusion. Digital phenotyping from user-owned smartphones may provide a feasible method for collecting high-frequency, high-resolution behavioral data in socioeconomically and demographically diverse samples, typically underrepresented in traditional data collection methods. Future directions include evaluating agreement and missingness between smartphone and self-reported data.

Big Data/Machine Learning/AI

Investigating Factors Driving Frequent Online Medical Record Access Among U.S. Adults Using Machine Learning: Analysis of the HINTS Survey Ransome Eke* Ransome Eke Joedrecka Brown Speights Shermeeka Hogans-Mathews

Introduction
The integration of online medical records (OMRs) into healthcare systems has significantly improved patient access to personal health information and communication with providers. However, disparities in the frequency of OMR use persist, driven by demographic, socioeconomic, and health-related factors. Identifying predictors of frequent OMR access is critical for addressing these inequities and improving patient engagement. This study analyzes data from the 2022 Health Information National Trends Survey (HINTS) to explore factors influencing frequent OMR access among U.S. adults.

Methodology
Data were derived from the 2022 HINTS survey, a nationally representative dataset examining public engagement with health information. The study included U.S. adults who reported accessing their OMRs at least once in the past 12 months. Variables such as age, gender, income, education, chronic conditions, healthcare utilization, and provider communication were assessed as potential predictors. Lasso regression was used to identify significant predictors of frequent OMR access, defined as logging in three or more times annually. Logistic regression further evaluated these predictors. Weighted analyses ensured the representativeness of the U.S. adult population.

Results
Among 2,234 respondents (weighted N = 91,439,558), 77% were frequent users of OMRs, accessing them three or more times annually. Frequent OMR use was associated with accessing records through both apps and websites (β = 0.39) or apps only (β = 0.07), as well as finding OMRs easy to understand (β = 0.23). Frequent users were more likely to be female, disabled, and Asian compared to non-Hispanic whites. Less frequent users, defined as those logging in fewer than three times annually, were more likely to include non-Hispanic Blacks (β = -0.20), those not encouraged by a healthcare provider to access OMRs (β = -0.20), individuals using only websites (β = -0.19), younger adults under 50 years, and those who found OMRs difficult to understand.

Conclusion
Ease of use, access platform preferences, provider encouragement, and demographic factors influence frequent OMR access. Targeted interventions to address barriers among underrepresented groups, such as Non-Hispanic Blacks and younger adults, are essential to ensuring equitable engagement with digital health tools.

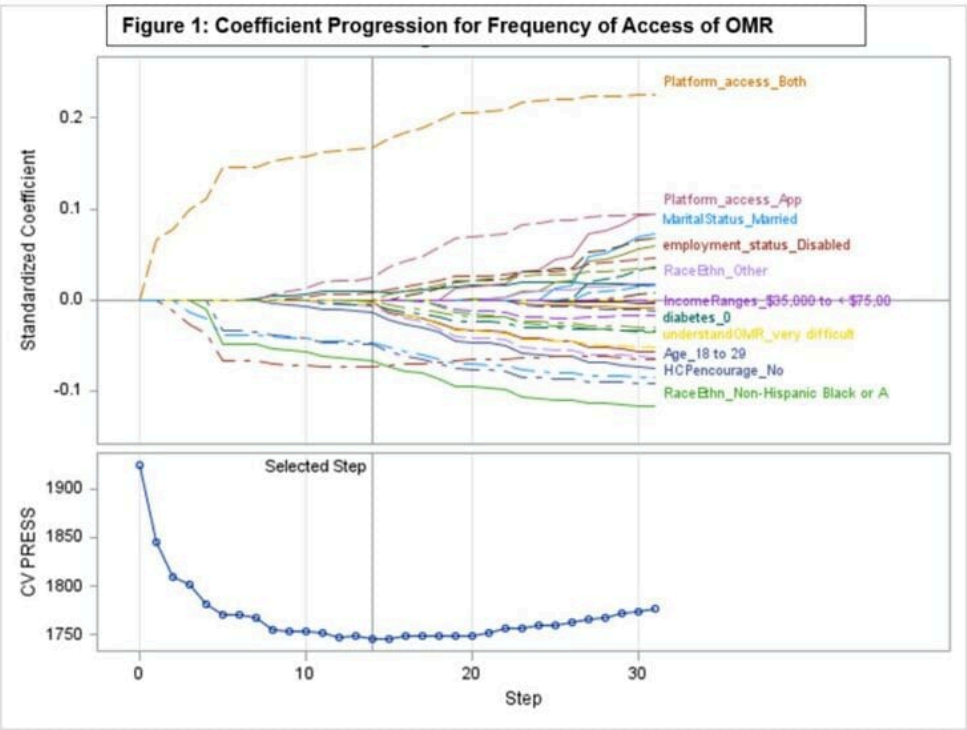


Figure 1: Coefficient Progression for Frequency of Access of OMR
Standardized Coefficient
0.2
0.1
0.0
-0.1
Platform_access_Both
Platform_access_App
MaritalStatus_Married
employment_status_Disabled
RaceEthn_Other
IncomeRanges_$35,000 to < $75,00
diabetes_0
understandOMR_very difficult
Age_18 to 29
HCPencourage_No
RaceEthn_Non-Hispanic Black or A
Selected Step
CV PRESS
1900
1850
1800
1750
0
10
20
30
Step

Big Data/Machine Learning/AI

Trend in incidence rates of Iron deficiency anemia in Inflammatory bowel disease patients: a 14-year descriptive study in Taiwan Yi-Hsuan Lin* Yi-Hsuan Lin

Background: Inflammatory bowel disease (IBD) is a chronic inflammatory disease that occurs in the digestive tract. In the past, the prevalence and incidence of IBD were relatively high in Western countries, and it was generally thought to be due to the western dietary habits and urban industrialization. Long-term damage to the intestinal mucosa not only reduces the absorption of iron, but also increases the risk of anemia due to bleeding from ulcers and the inhibition of red blood cell production. Studies show that 74% of IBD patients suffer from Iron deficiency anemia (IDA). However, research on the long-term trends of the relationship between IBD and the risk of IDA in Taiwan is limited.

Aim: Using a large-scale, population-based national database to examine the incidence of IDA with IBD, and analyze the demographic characteristics of the cohort generation.

Methods: We conducted a descriptive study using Taiwan's National Health Insurance Research Database (NHIRD), identifying about 66,383 new cases of IBD from 2000 to 2013. The study analyzes the distribution of basic demographic characteristics including age, gender, and number of medical visits.

Results: About 901 cases IDA with IBD were diagnosed, as we could see the incidence rate was 41.9 among females and 12.2 among males, which females were higher than males. Overall, the total incidence rate increased from 3.1 to 27.9 in the past 14 years. We grouped the age of patients into five categories, which the incidence rate of IDA with IBD was 16.7 in 20-30 age group, 22.4in 30-40 age group, 20.1 in 40-50 age group, 10.2 in 50-60 age group and 19.5 in ≥60 age group, and discovered that the increase in incidence rates was mostly concentrated in the 30-40 age group. Also, the average number of IBD medical visits was 3.52. The incidence rate of IDA was 12.8, 16.0, and 22.7 by 1-2 visits, 3-4visits and >5 visits for IBD, respectively, which as the number of IBD medical visits increased, the incidence rate of IDA also increased.

Conclusion: The incidence rate of IDA with IBD has steadily increased in Taiwan in the past 14 years. Our finding suggests that there may be a potential relationship between IBD and IDA, and we can focus on the inferential research to assess this correlation in the future.

Trend in incidence rates of Iron deficiency anemia in Inflammatory bowel disease patients: a 14-year descriptive study in Taiwan

Yi-Hsuan Lin[1], Chien-An Sun[2], Yu-Ching Chou[1*]

1 School of Public Health, National Defense Medical Center, Taipei, 2Department of Public Health, College of Medicine, Fu-Jen Catholic University, New Taipei City, Taiwan
*Corresponding author: trishow@mail.ndmctsgh.edu.tw

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Keywords: Inflammatory bowel disease (IBD), Iron deficiency anemia (IDA), National Health Insurance Research Database (NHIRD)

LATEBREAKER

Big Data/Machine Learning/AI

Spatial variability in the association of ambient PM2.5 exposure with child undernutrition in Sub-Saharan Africa A. Kofi Amegah* A. Kofi Amegah Patrick Attey-Yeboah Paul Kwame Adjorlolo Justice M.K. Aheto John Molitor Eric S. Coker

Background and Objective: Studies have associated ambient PM2.5 expsoure with child undernutrition. The exposure-response relationships, however, vary significantly within and between countries and geographical regions, and yet has not investigated. We therefore investigated spatial variability in the association of prenatal and postnatal PM2.5 exposure with childhood undernutrition in sub-Saharan African (SSA) countries to better tailor intervention strategies.

Material and Methods: We integrated data on child undernutrition from Demographic and Health Surveys (DHS) conducted in countries between 1998 and 2022 with high resolution satellite-derived geospatial PM2.5 exposures to create a dataset for our analysis. The dataset included 490,250 children under-five in 33 SSA countries. The exposure metrics was computed using weighted averages during the prenatal and postnatal periods with adjustment for geographic coordinate displacement via urban and rural buffers. We used a spatial random coefficient model set in a Bayesian framework (Integrated Nested Laplace Approximations [INLA] and Stochastic Partial Differential Equation [SPDE]) to model the spatially varying relationships controlling for individual- and area-level confounders assembled from the DHS data.

Results: Prenatal and postnatal PM2.5 exposure was associated with 4.6% and 4.2% increased odds of stunting (AOR = 1.046, 95%CI: 1.039, 1.053 and 1.042, 95%CI: 1.035, 1.049, respectively), and 4.4% and 2.8% increased odds of wasting (AOR = 1.044, 95%CI: 1.0363, 1.052 and 1.028, 95%CI: 1.020, 1.036, respectively). Prenatal PM2.5 exposure was associated with 3.1% increased odds of underweight (AOR = 1.031, 95%CI: 1.021, 1.0412). Postnatal PM2.5 exposure showed no significant association with underweight. The observed associations varied significantly within and between the SSA sub-regions and countries, with West Africa recording the highest exposure health effects followed by East Africa.

Conclusion: The association of ambient PM2.5 exposure with child undernutrition varied within and between SSA countries, and calls for targeted interventions to help address the pervasive child undernutrition problem in the SSA region.

Big Data/Machine Learning/AI

Differential Diagnosis of Bacterial Meningitis Using Machine Learning Models Audêncio Victor* Audêncio Victor Diego Augusto Medeiros Santos Pamella Cristina de Carvalho Lucas Telma Regina Marques Pinto Carvalhanas

Introduction: Meningitis, an inflammatory condition affecting the membranes surrounding the brain and spinal cord, can be caused by various agents. Bacterial meningitis is particularly severe due to its association with high morbidity and mortality. This study aims to explore the application of machine learning (ML) models to aid in the differential diagnosis of bacterial meningitis, utilizing data from SINAN (Brazil's Notifiable Diseases Information System) outbreak database in the State of São Paulo, Brazil.

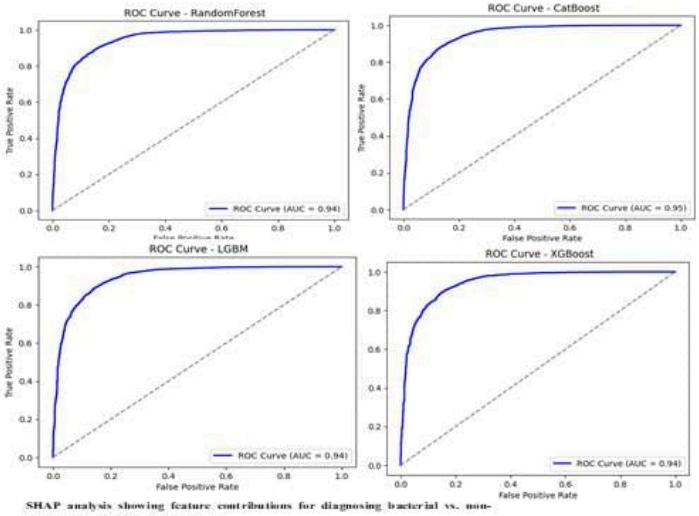
Methods: Data were collected from the SINAN database, including demographic variables, clinical symptoms, and cerebrospinal fluid analyses. Five ML models were applied: Random Forest, LightGBM, XGBoost, CatBoost, and AdaBoost, to classify meningitis cases into bacterial, fungal, viral, and other types. Models were evaluated based on metrics such as AUC-ROC, accuracy, precision, recall, F1-score, and MCC.

Results: The CatBoost model demonstrated superior performance, achieving an AUC-ROC of 0.95 in binary classification (bacterial vs. non-bacterial) and 0.85 in multiclass classification (Neisseria meningitidis, Streptococcus pneumoniae, and Haemophilus influenzae). XGBoost and LightGBM also showed promising results, with AUC-ROC scores of 0.94 and 0.92, respectively, in binary classification. The CatBoost model further exhibited high sensitivity (1.00) and reasonable specificity, emphasizing its applicability in rapid and accurate meningitis diagnosis. SHAP analysis identified variables such as leukocyte count and presence of petechiae as influential predictors.

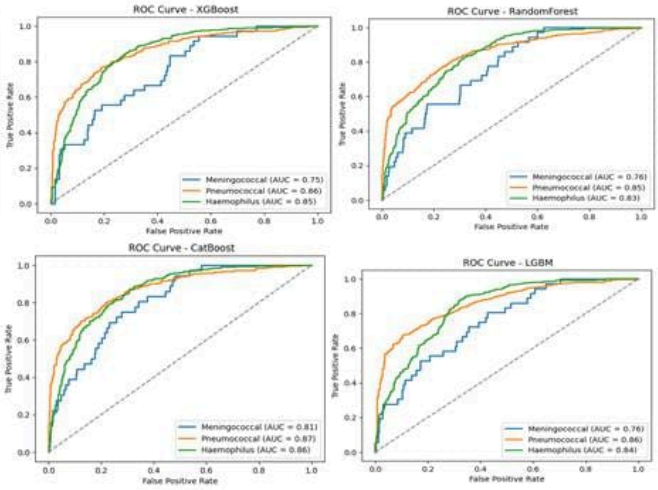
Conclusion: ML algorithms, particularly CatBoost, XGBoost, and LightGBM, proved highly effective for the differential diagnosis of meningitis, providing a valuable tool for the rapid identification of meningitis types and bacterial serogroups. These techniques can be integrated into public health protocols to enhance outbreak responses and optimize patient treatment.

Keywords: Meningitis, Machine Learning, Differential Diagnosis, SINAN (Notifiable Diseases Information System), Surveillance, Epidemiology.

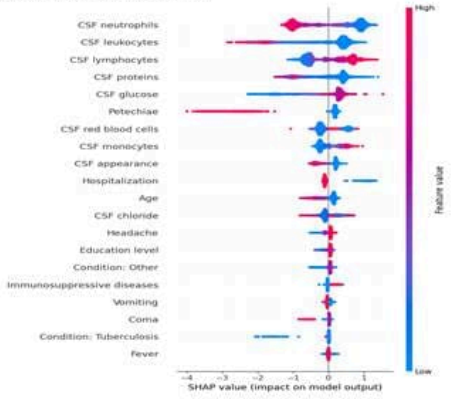
Predictive performance of algorithms for binary classification of bacterial vs. non-bacterial meningitis (AUC-ROC).



Predictive performance of algorithms for multiclass classification by serogroup of bacterial meningitis (AUC-ROC).



SHAP analysis showing feature contributions for diagnosing bacterial vs. non-bacterial meningitis using CatBoost.



Performance metrics of best algorithms for binary classification of bacterial vs. non-bacterial meningitis with hyperparameter tuning.

Model	AUC-ROC	Accuracy	Recall	Specificity	Precision	F1	MCC
RandomForest	0,94	0,71	1,00	0,09	0,71	0,83	0,25
XGBoost	0,94	0,74	1,00	0,17	0,73	0,84	0,35
CatBoost	0,95	0,72	1,00	0,10	0,71	0,83	0,27
LGBM	0,94	0,72	1,00	0,11	0,71	0,83	0,28

Performance metrics of best algorithms for multiclass classification by serogroup of bacterial meningitis with hyperparameter tuning.

Model	AUC-ROC	Accuracy	Recall	Specificity	Precision	F1	MCC
RandomForest	0,82	0,71	1,00	0,16	0,35	0,48	0,48
XGBoost	0,82	0,76	1,00	0,10	0,34	0,47	0,52
CatBoost	0,85	0,76	1,00	0,20	0,36	0,49	0,53
LGBM	0,82	0,69	1,00	0,14	0,35	0,48	0,47

Big Data/Machine Learning/AI

Two-Step Pragmatic Subgroup Discovery for Heterogeneous Treatment Effects Analyses: Novel Framework Toward Enhanced Interpretability Toshiaki Komura* Toshiaki Komura Falco J. Bargagli-Stoffi Koichiro Shiba Kosuke Inoue

Background:

Effect heterogeneity analyses using causal machine learning algorithms have gained popularity in recent years. However, the interpretation of estimated individualized effects requires caution because insights from these data-driven approach might not be presented in a way that a human audience can reasonably understand. Thus, a **practical framework** that integrates advanced machine learning methods and decision-making remains critically needed to achieve effective scientific communication and implementation.

Development:

We introduce a 2-step framework to identify characteristics associated with substantial effect heterogeneity in a format human audiences can reasonably understand (**Figure**). The proposed framework applies distinct sets of covariates for i) estimation of individualized effects and ii) the discovery of subgroups that show effect heterogeneity based on highly interpretable if-then rules. By referring to existing metrics of interpretability, we describe how each step contributes to leveraging a theoretical advantage of machine learning models while creating an interpretable and practically relevant framework.

Application:

We applied the pragmatic subgroup discovery framework for the Look AHEAD trial to assess practically relevant, detailed, and comprehensive insights into the effect heterogeneities of intense lifestyle intervention for individuals with diabetes on cardiovascular mortality. Our analysis identified i) individuals with a history of cardiovascular disease and coronary artery bypass graft had the least benefit from the intervention (outcome risk [95% CI] = 17.67pp [-26.81, -8.54]), while ii) individuals with no history of CVD and age <60 received the highest benefit (outcome risk [95% CI] = -1.77pp [-1.28, 4.83]).

Conclusions:

The proposed framework can help researchers to discover insights into effect heterogeneity and present the results with enhanced interpretability. Our heterogeneous effects discovery approach could be a generic strategy to ensure effective implementation and scientific communication when applying machine learning algorithms in applied causal inference contexts.

Step1:
CATE Estimation

Machine learning algorithms to estimate "individualized effects"

$$E\left[Y_i^{A=1} - Y_i^{A=0} \middle| X_i = x_i\right]$$

Y: outcome, A: treatment, X: covariates, and i: individual

[Aim]
- Explore the underlying data structure

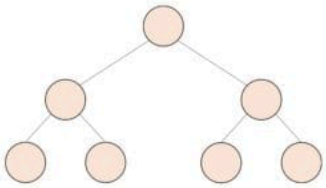
[Covariates]
- Covariates in any format; researchers might decide to perform feature engineering.

[Metrics of Interpretability]
- Predictive accuracy

Reduction of Data complexity

Step2
Subgroup Identification

Classification and regression trees to identify the subgroups with HTE



[Aim]
- Identify subgroup with effect heterogeneity

[Covariates]
- Select and modify covariates for the practical interpretation/decision-making

[Metrics of Interpretability]
- Descriptive accuracy
- Relevancy

Big Data/Machine Learning/AI

Predicting Ischemic Heart Disease Risk Using Family Health Histories from Electronic Healthcare Records Amani F. Hamad* Amani Hamad Joykrishna Sarkar Linda Ejlskov Oleguer Plana-Ripoll Lisa M. Lix

Objectives: Family health histories may improve the prediction of diseases, including ischemic heart disease (IHD). We tested whether parental disease histories from population-based administrative healthcare databases improved IHD risk prediction in two regions: province of Manitoba (MB) in Canada, and Denmark (DNK).

Methods: A retrospective cohort study of individuals 40 years old with linkages to ≥1 parent between 1974 and 2022 in MB and 1978 and 2023 in DNK. Incident IHD diagnoses and predictors were identified from inpatient and outpatient records. Predictors were selected using LASSO logistic regression models with 10-fold cross-validation. The base model included demographics and parental IHD history. Subsequent models included individuals' and their parents' disease histories (130 chronic conditions). Models were evaluated using area under the receiver operating characteristic curve (AUC) and prediction error.

Results: The cohort comprised 118,868 individuals in MB and 774,845 individuals in DNK. 2.5% and 1.5% had an IHD diagnosis during 10-year follow-up in MB and DNK cohorts, respectively. In MB, the base model had an AUC of 63.8%, 95% confidence interval (CI) 60.8-66.9. AUC improved after including individuals' diseases (69.7%, 95% CI 66.7-72.6); but not after including parental diseases (67.2%, 95% CI 63.0-71.4). Similar trends were observed in the DNK cohort. All models had minimal prediction error, with Brier scores between 0.01 and 0.03. In both regions, individuals' sex, and diabetes mellitus and hypertension diagnoses were the most important predictors; diagnoses of migraines, substance use disorders, gastritis and ulcers were also important. The most important parental predictors in MB and DNK were diabetes mellitus and IHD diagnoses, respectively.

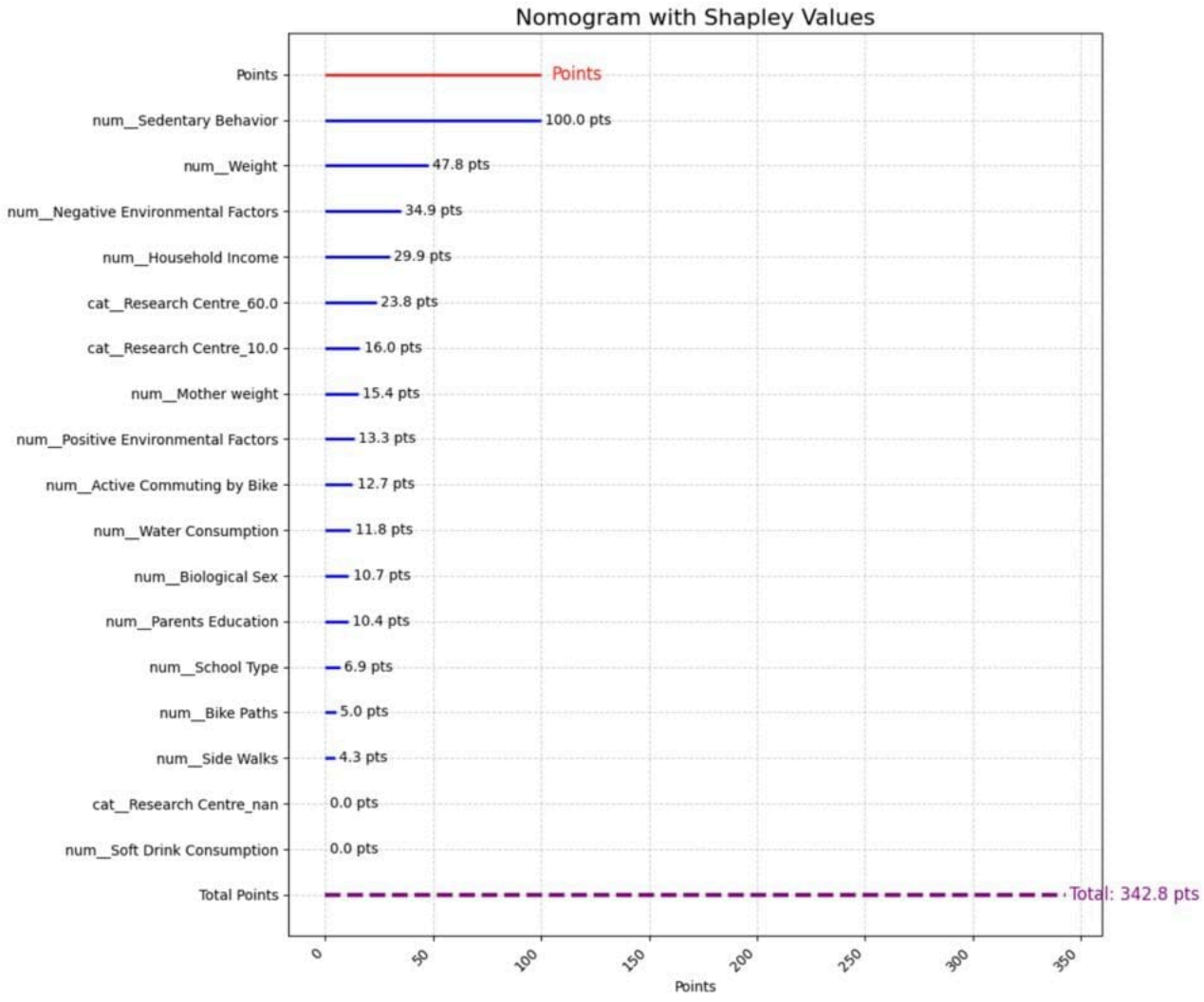
Conclusions: Disease histories of individuals, but not of their parents, improved IHD risk prediction. Several important predictors were identified that could further improve IHD risk prediction models.

Big Data/Machine Learning/AI

CARDIOVASCULAR HEALTH PREDICTION IN CHILDREN USING MACHINE LEARNING

Tiago Almeida de Oliveira* Tiago Almeida de Oliveira Mateus Silva Rocha Keisyanne De Araujo-Moura Marcus Vinícius Nascimento-Ferreira Augusto César Ferreira De Moraes

Aim: To develop and validate risk scores for predicting cardiovascular health in children using Machine Learning algorithms based on extrinsic and intrinsic variables. **Methods:** The SAYCARE study, a cross-sectional, multicenter, school-based study conducted in São Paulo and Fortaleza, Brazil, including 462 children aged 5 to 8 years. The primary outcome was cardiovascular health (CVH), which includes eight cardiovascular health components: healthy diet, participation in physical activity, avoidance of nicotine, restorative sleep, healthy weight, and healthy levels of blood lipids, glycated blood hemoglobin, and blood pressure. Each metric has a scoring algorithm ranging from 0 to 100 points, allowing the generation of a composite cardiovascular health score that varies from 0 to 100 points. Potential predictors were based on sociodemographic, maternal, environmental, and behavioral factors and nutritional status. The data were split 70/30, with the CVH variable transformed into a binary outcome: 1 (high CVH) and 0 (lower CVH). Three Machine Learning algorithms (Random Forest, XGBoost, and LightGBM) were optimized via GridSearch with 5-fold cross-validation. Precision, Recall, F1 Score, AUC, and the Precision-Recall curve were assessed. Variable importance was interpreted using Shapley Values, which also informed a nomogram. **Results:** The outcome is imbalanced with prevalence of 1 (high CVH) in 32.47% of cases and 0 (lower CVH) in 67.53%. Despite this imbalance the Random Forest model excelled in predicting cardiovascular conditions in the binary scenario, achieving an AUC of 0.88, precision of 0.85, recall of 0.77, F1-Score of 0.79, and a Precision-Recall curve area of 0.78, highlighting its robustness and clinical applicability. The most influential variables are: Sedentary Behavior, Weight, Negative Environmental Factors, and Household Income. These variables underscore the interplay between individual and environmental contributors to cardiovascular risk. A nomogram was developed to translate these contributions into a visual scale, effectively illustrating each variable’s relative importance. **Conclusion:** The Random Forest model demonstrated the best performance to predict cardiovascular health in children, and environmental factors and lifestyle behaviors are most important.


Nomogram with Shapley Values
Points
num__Sedentary Behavior
num__Weight
num__Negative Environmental Factors
num__Household Income
cat__Research Centre_60.0
cat__Research Centre_10.0
num__Mother weight
num__Positive Environmental Factors
num__Active Commuting by Bike
num__Water Consumption
num__Biological Sex
num__Parents Education
num__School Type
num__Bike Paths
num__Side Walks
cat__Research Centre_nan
num__Soft Drink Consumption
Total Points
Points
100.0 pts
47.8 pts
34.9 pts
29.9 pts
23.8 pts
16.0 pts
15.4 pts
13.3 pts
12.7 pts
11.8 pts
10.7 pts
10.4 pts
6.9 pts
5.0 pts
4.3 pts
0.0 pts
0.0 pts
Total: 342.8 pts
0
50
100
150
200
250
300
350
Points

Big Data/Machine Learning/AI

Understanding AI use in epidemiology education: attitudes, predictors, and implications

Teresa M. Janevic* John B. Wetmore Natalie A. Boychuk Marco Thimm-Kaiser Teresa M. Janevic

Artificial intelligence (AI) is transforming education, yet little is known about AI use among epidemiology students or its impact on learning.

We anonymously surveyed 109 master's students enrolled in a coding-intensive epidemiology course based on the Modern Epidemiology textbook. We used multinomial logistic regression to estimate the relationship between attitudes toward AI, measured by the validated AI Attitude Scale (AIAS), and AI use frequency. We also used linear regression to estimate the relationship between AI use frequency and perceived learning gains, measured by the Student Assessment of Their Learning Gains (SALG) instrument. Both models adjusted for age, sex, race-ethnicity, language spoken at home, and nativity.

Among students, 28% used AI infrequently ("never/rarely"), 39% occasionally ("sometimes"), and 33% frequently ("often/always"). ChatGPT was the most used resource (84%), followed by Grammarly (17%). Students primarily used AI to understand concepts (71%), write SAS code (49%), and improve writing quality (40%). Regression modeling (50%), survival analysis (47%), sources of bias (44%), and interaction (44%) were the most common topics for which AI was used. Students largely regarded AI as helpful (67%).

For every one-unit increase in a student's AIAS score, their odds of frequent compared to infrequent AI use increased by 80% (OR=1.8, 95% CI: 1.4–2.4); however, attitudes did not predict occasional use (OR=1.1, 95% CI: 0.9–1.4) after adjustment. When comparing infrequent and occasional AI users to frequent users, there was no meaningful difference in perceived learning gains (β=0.1, 95% CI: -0.1–0.2).

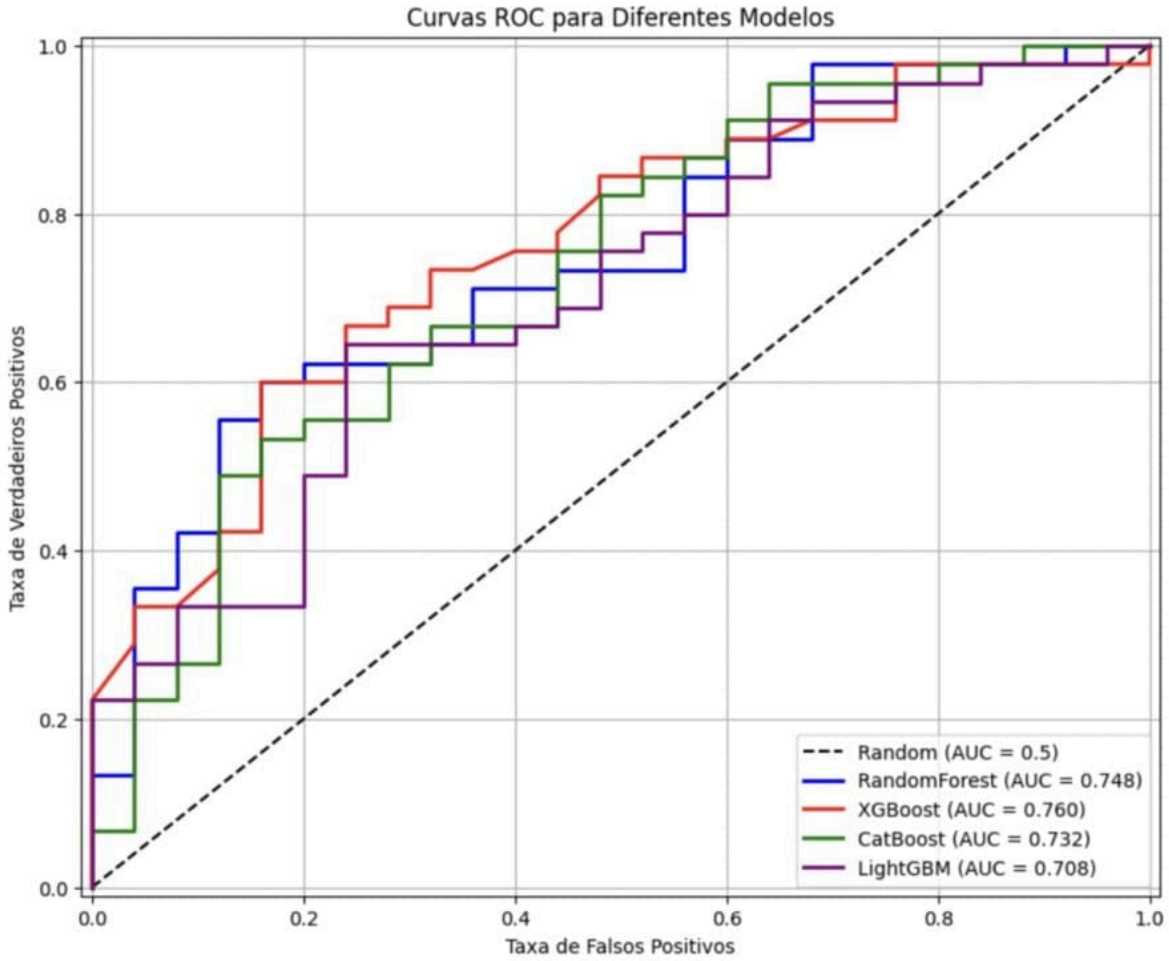
Positive attitudes toward AI predict frequent use, but AI use frequency does not correlate with perceived learning gains. These findings highlight the frequency and types of AI use among epidemiology graduate students. Future research should explore applications of AI that optimize student learning and achievement.

Big Data/Machine Learning/AI

Machine Learning Algorithms to Predict Subclinical Small Vessel Brain Lesions based on cardiovascular health: Insights from the ELSA-Brasil study Carine Savalli* Marianna Leite Carine Savalli Arão O Belitardo Carlos Leandro S dos Prazeres Paulo A Lotufo Itamar S Santos Isabela Benseñor Claudia C Leite Maria CG Otaduy Adriana B Conforto Alexandre Chiavegatto Alessandra C Goulart

Neuroimaging markers of cerebral small-vessel disease (CSVD) are associated with an increased risk of cognitive decline, stroke, and death. We applied machine learning (ML) methods to assess whether lower adherence to the “Life’s Essential 8” proposed by the American Heart Association (LE8: diet, physical activity, nicotine exposure, BMI, blood lipids, blood glucose, blood pressure, and sleep) can predict CSVD on 3T brain magnetic resonance imaging (3T-MRI) in the ELSA-Brasil study, a prospective cohort. Among 233 participants (66.1±9.2 years, 59% women), cardiovascular health information from the three study waves (2008 to 2019) and a 3T-MRI (2022-2024) were considered. Variables included were: LE8 adherence (1-3; higher=better), LE8 trajectory change from Wave 1 (2008-2010) to Wave 3 (2017-2019), and demographics at baseline (age, income, education, race, and marital status). MRI binary outcomes (yes/no) were the individual components of the CSVD score (lacunes-LAC, enlarged perivascular spaces-EPS, white matter hyperintensities-WMH, and microhemorrhages and calcifications-MH/C). Four ML algorithms (Random Forest, XGBoost, LightGBM, and CatBoost) were trained for each outcome (70%/30% as training/testing), with hyperparameter tuning via a repeated 5-fold cross-validation. The performance was evaluated using AUC-ROC. The contribution of variables to the prediction was accessed by the SHAP (Shapley Additive exPlanations). Frequencies of CSVD were: LAC, 11.6%; WMH, 28.3%; MH/C, 12.1%; EPS, 64.8%. The predictive performance for EPS was good (AUC=0.760), variables that most contributed to this prediction were age, blood lipids in Wave 3, and improved sleep from Wave 1 to 3. The performance was moderate for WMH (AUC=0.693) and MH/C (AUC=0.615) and, poor for LAC (AUC=0.492). ML showed a modest predictive capacity for CSVD. XGBoost for EPS was the most promising model, but these preliminary findings highlight the need for larger datasets to improve prediction accuracy.

Enlarged Perivascular Spaces - EPS



Cancer

HPV vaccination beliefs and cancer screening among sexual and gender minorities: Potential cancer prevention opportunities from community engagement Geetanjali Datta* Geetanjali Datta Marvin Langston Dong Hee Kim So Yung Choi Laurel Finster Marc Goodman A. Barbara Moscicki Melissa Bondy Michelle Khan Robert Haile Zul Surani

Background: HPV vaccination and cancer screening remain underutilized among members of sexual and gender minority (SGM) communities. Engaging SGM people through PRIDE events could provide a valuable opportunity for implementing targeted interventions. However, little is known about the prevalence of cancer-related beliefs and screening uptake among PRIDE attendees. **Methods:** Community Outreach and Engagement coordinators administered questionnaires during 5 PRIDE events throughout Southern California from 2022-2023 among individuals over 18 years old who reside in Los Angeles County (N=790). Separate analyses were conducted for each outcome. To be inclusive of most ages for which HPV vaccination can be recommended, we included responses from individuals <50 yrs for assessment of HPV vaccination beliefs(N=492). In-line with recommendations, we calculated the prevalence of lifetime screening uptake for colorectal (among all age 50-75, N=75), cervical (among those assigned female at birth with a cervix age 24-65, N=257), and breast (among those assigned female at birth age 50-74, N=27) cancer. Separate analyses were conducted for each outcome. **Results:** Twelve percent of respondents answered “no“ and 19% answered “I don’t know“ to the question, “Do you think the HPV vaccine is effective in reducing the risk of cervical cancer?“ Fifteen percent of those who met screening criteria reported never having been screened for cervical, 7% for breast, and 15% for colorectal cancer (CRC). **Conclusion:** Lifetime breast and CRC screening uptake among respondents were comparable to or higher than the US average, though rates for cervical cancer screening were below national estimates. Furthermore, over 30% of respondents were either unaware or were unconvinced of the cervical cancer prevention benefits of HPV vaccination. PRIDE events could serve as an effective venue to implement interventions aimed at increasing knowledge and uptake of HPV vaccination and cervical cancer screening.

Cancer

Food Environment Index and Pancreatic Cancer Survival in North Carolina Shenghui Wu*
Shenghui Wu Leilani Tseng Yanning Liu

Background: Exploring the potential role of the food environment on cancer survival could facilitate prevention and control approaches to improve cancer survivorship. This study examined the associations between food environment index (FEI) and survival for pancreatic cancer in North Carolina.
Methods: This retrospective cohort study included 30,361 patients diagnosed with overall cancer from January 1, 2000 to December 31, 2022 from the North Carolina Cancer Central Registry. The individual-level demographic, tumor, and treatment information were provided by the North Carolina Cancer Central Registry. FEI and other county-level exposures were obtained from the County Health Rankings & Roadmaps databases. The county-level food environment index is an indicator of access to healthy foods (0 is worst, 10 is best). Cox regression was used to calculate hazard ratios (HRs) and 95% confidence intervals (CIs) for the associations between FEI and cancer survival after adjusting for individual-level and county-level covariates.
Results: Higher levels of FEI were associated with a statistically significant better survival for colorectal cancer (fully adjusted HR for every score increase=0.98, 95% CI 0.96, 0.995; P <0.0001; adjusted HR for the 3rd tertile vs. 1st tertile = 0.94, 95% CI 0.89, 0.99).
Conclusion: These results suggest that a healthy food environment, as measured by FEI, may be a protective factor for pancreatic cancer survival in North Carolina. To improve pancreatic cancer survival, further strategies to improve food environment at the county level are warranted.

Cancer

Urinary Heavy Metal Mixtures and Colorectal Cancer Incidence: Pilot Results from the Louisville Environmental Assessments Pilot Study (LEAPS) in Colorectal Cancer

Olufunmilayo Babarinde* Olufunmilayo Babarinde Sandy Kavalukas Lu Cai Jianxiang Xu Allie Jin Adhikari Jeevan Daniel Riggs Jeremy Gaskins Kira Taylor Kathy Baumgartner Natalie DuPre

Introduction

Epidemiologic evidence on the association between carcinogenic metal exposures, individual or mixtures, and the risk of colorectal cancer (CRC) is scarce.

Objective

To examine the individual and joint associations between urinary arsenic (As), cadmium (Cd), antimony (Sb), and thallium (Tl) exposures and the odds of CRC incidence in an area with a high CRC incidence and metal-emitting industries.

Methods

In an ongoing case-control study, eligible consented participants included CRC cases diagnosed and receiving surgical treatment and controls screening negative for CRC. Participants provided biospecimens and completed a detailed questionnaire. Urinary metals were measured using inductively coupled plasma mass spectrometry (ICP-MS) in 41 CRC cases and 84 controls and creatinine normalized. The incidence odds ratio (OR) and 95% confidence interval (CI) of CRC were estimated using multivariable logistic regression modeling metal exposures as continuous with a log transformation and binary variables based on the median value of controls. Bayesian Kernel machine regression (BKMR) was used to assess the association between metal mixtures and the odds of CRC. Models were adjusted for age at diagnosis, gender, family history of CRC, and urinary cotinine indicating smoking status.

Results

Median concentrations of metals were higher among cases than controls for As (3.62±9.4 vs. 2.8±3.2ng/mg creatinine), Cd (0.43±0.6 vs. 0.29±0.6ng/mg creatinine), Sb (0.13±0.2 vs. 0.10±0.09ng/mg creatinine), and not Tl (0.11±0.2 vs. 0.15±0.5ng/mg creatinine). A one-unit increase in the natural log of urinary Cd was associated with 90% higher odds of CRC (Adjusted OR: 1.90, 95%CI: 1.12, 3.21); and those with Cd levels above the median had 3.0 times higher odds of CRC (95%CI: 1.2, 7.50) compared to those below the median. In the BKMR modeling, the association between the metal mixture and CRC risk was not statistically significant. However, the posterior inclusion probabilities (PIP) show that Cd is the most commonly included in the mixture for predicting CRC risk (PIP=0.802).

Conclusion

Higher urinary Cd was associated with higher incidence odds of CRC independent of urinary cotinine. Our study findings suggest that interventions mitigating Cd exposure may be beneficial in reducing CRC risk.

Cancer

Cancer Prevalence Across Ethnicity-Education-Deprivation Subgroups: An Intersectional Analysis Vladimir Jolidon* Vladimir Jolidon Bernadette WA van der Linden Stefano Tancredi Andrew Bell Daniel Holman

Background: Identifying variation in cancer prevalence across population subgroups is critical for public health. Previous research has shown that cancer prevalence is lower among non-White ethnic groups compared to White ethnic groups in England. However, these studies relied on broad ethnic categories and overlooked the intersection of ethnicity and socioeconomic position. The present study examines cancer prevalence across more specific ethnicity-education-deprivation subgroups from an intersectional perspective.

Methods: Data from the UK Biobank, a prospective cohort study, included 267,803 women and 223,864 men aged 40-69 years old at baseline. The outcome was all cancer prevalence, excluding non-melanoma skin cancer. Multilevel analysis of individual heterogeneity and discriminatory accuracy (MAIHDA) was conducted, nesting individuals within 42 subgroups based on seven ethnic groups, three education levels (low, middle, high), and two deprivation levels (low, high), stratified by sex and adjusted for age.

Results: Overall, cancer prevalence was 14.6% among women and 16.3% among men. As in prior studies, cancer prevalence was generally lower in Non-White groups. However, ethnicity-education-deprivation subgroup analysis highlighted key differences. Among men, Black subgroups had the highest cancer prevalence, especially in groups with lower education and higher deprivation levels. Among women, cancer prevalence was highest among Irish and British subgroups with lower education and higher deprivation levels. MAIHDA models revealed that between-group differences were additive rather than multiplicative.

Conclusions: This study highlights disparities in cancer prevalence across intersectional subgroups, revealing patterns that are often masked by ethnicity-only analyses using broad categories. Identifying subgroups at higher risk of cancer can inform targeted interventions to address inequities in cancer prevention and care.

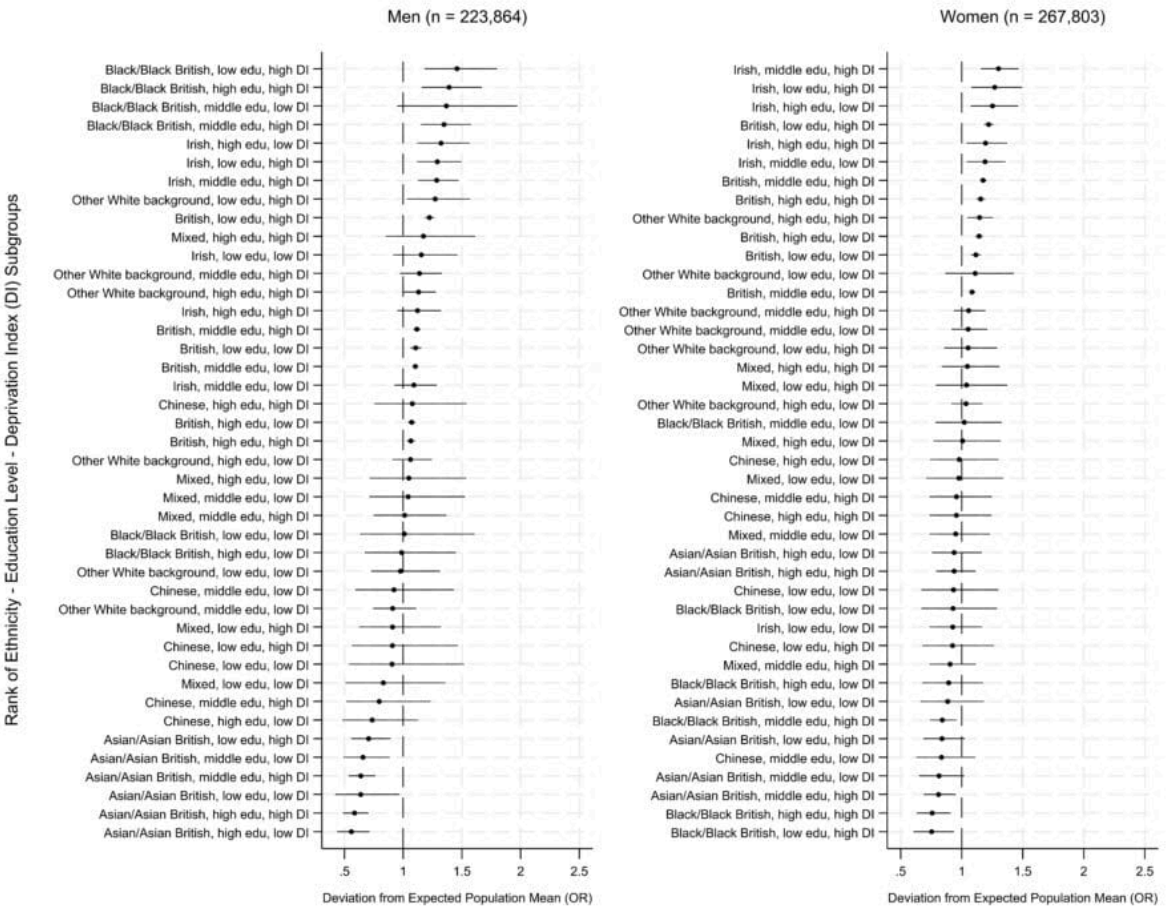


Figure 1. All-cancer prevalence across ethnicity-education-deprivation subgroups, deviation from expected population mean (OR)

Note: edu = Education level; DI = Deprivation Index; OR = odds ratio

Cancer

Disparities in oropharyngeal cancer survival outcomes between individuals living with and without HIV Amelia Nichols* Amelia Nichols Vivian Vo Jessica Islam Jesse Qualliotine Brittney L. Dickey

Human Papillomavirus (HPV) is the primary etiologic agent responsible for the majority of oropharyngeal cancer (OPC) cases in the United States. People with HIV (PWH) face an elevated risk for HPV infection and HPV-associated malignancies. However, the impact of HIV status on survival following a diagnosis of HPV-OPC remains unknown. The objective of this study was to explore differences in HPV-OPC survival among people living with and without HIV (PWoH).

Data from the National Cancer Database (NCDB) was used to identify patients diagnosed with oropharyngeal cancer (ICD-0-3 codes: C01.9, C02.4, C05.1, C052, C09.0-9.1, C09.8-9.9, C10.0-10.4, C10.8-10.9, C14.2) with a positive result for HPV-DNA to a high-risk type. PWH were identified using ICD9 (04200 to 04499, 07953, and V08) and ICD10 (B20 to B24, R75, Z21, B97.35) codes. Demographics (sex, age, race), cancer stage, and treatment receipt was descriptively compared by HIV status. Kaplan Meier curves assessed survival time after cancer diagnosis by HIV status and treatment received (surgery, radiation, chemotherapy, and immunotherapy).

There were 146,539 individuals identified with HPV-OPC of which 163 were living with HIV and 24,401 without HIV. Significant differences were observed between the two groups in demographics, stage, and treatment received ($p < 0.0001$). PWoH experienced better overall survival than PWH ($p < 0.0001$). Additionally, stratification by treatment type revealed that PWH had worse survival outcomes across all modalities including surgery, radiation, chemotherapy, and immunotherapy ($p < 0.0001$).

HIV status is associated with significant disparities in survival among individuals with HPV-OPC. Those with HIV have worse overall survival and after stratifying by cancer treatment type. These findings underscore the need for further research to better understand the underlying factors driving these disparities and to develop interventions aimed at improving survival in this vulnerable population.

Cancer

Plasma metabolomic profiles associated with breastfeeding history and subsequent ovarian cancer risk Jennifer Mongiovi* Jennifer Mongiovi Julian Avila Pacheco Nan Lin Mary K. Townsend Britton Trabert Nicolas Wentzensen Nicole Prince Jessica A. Lasky-Su A. Heather Eliassen Clary B. Clish Shelley S. Tworoger Oana A. Zeleznik Naoko Sasamoto

Breastfeeding may reduce risk of epithelial ovarian cancer (EOC), but the biological mechanisms remain unclear. We identified plasma metabolites associated with breastfeeding history and explored their relationships with EOC.

Data included 606 plasma metabolites from 9,904 parous women in the Nurses' Health Studies (NHS/NHSII). Associations between breastfeeding (≤6 months, >6 to <12 months, ≥12 months) and metabolite levels were assessed using multivariable linear regression and replicated in 663 participants from the Vitamin D Antenatal Asthma Reduction Trial (VDAART). Metabolite set enrichment analysis (MSEA) identified metabolite classes associated with breastfeeding. False discovery rate (FDR) correction addressed multiple testing. To examine the relationship between breastfeeding-related metabolites and EOC, we used a metabolite-based breastfeeding score (MBS) previously derived and replicated among 4,349 NHS/NHSII and 2,088 Women's Health Initiative participants. The MBS included 6 metabolites (3 triglycerides, cotinine, N-acetyltryptophan, hippurate). Multivariable linear regression and meta-analysis were used to assess the association of the MBS with EOC risk in 436 NHS/NHSII and 412 Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial participants.

We observed positive associations for 12 metabolites with breastfeeding ≥12 months (FDR<0.05; C24:1 ceramide, C14:0 cholesteryl ester, indole-3-proprionate, threitol, uracil, organic acids, phosphatidylethanolamines) and negative associations for threonine and myristoleic acid. Similar associations were observed in the VDAART cohort for all available metabolites except serine. MSEA revealed positive associations with phosphatidylcholines and phosphatidylethanolamines. Comparing the highest quartile of MBS to the lowest, we observed 43% lower odds of EOC (OR: 0.57; 95% CI: 0.33-0.99).

These findings suggest that breastfeeding influences metabolic pathways long-term, potentially reducing EOC risk.

Cancer

Temporal patterns of uterine and ovarian cancer incidence rates in Utah after correcting for gynecologic surgeries Britton Trabert* Britton Trabert Claire E. Dunlap Jennifer A. Doherty Jessica N. Sanders Lori M. Gawron Robert L. Dood Britton Trabert

Background: Registry-based gynecologic cancer incidence rates may underestimate disease burden since the denominator includes individuals who have undergone hysterectomy or bilateral salpingo-oophorectomy (BSO), which dramatically reduce susceptibility to uterine or ovarian cancer, respectively.

Methods: Gynecologic surgical procedures (2000-2018) were identified in the Utah Population Database (UPDB) using ICD-9/-10 and CPT codes. Procedures were categorized as any hysterectomy (with/without BSO) or any BSO. Prevalence estimates were derived using standard formula, where duration was defined as the median age at the procedure for each 5-year category subtracted from Utah's female life expectancy (82.1 years). Uncorrected uterine and ovarian (including fallopian tube and primary peritoneal) cancer rates for Utah were obtained from SEER for the same period. To estimate corrected annual cancer rates, we subtracted prevalent surgical procedures from the age-specific denominators for Utah and recalculated rates. All rates were age-adjusted using the US 2000 standard population. Annual percent change (APC) was calculated using linear regression.

Results: Hysterectomy and BSO incidence rates decreased over time (Figure). Uncorrected uterine cancer incidence rates fluctuated between 22.4 and 26.4 cases per 100,000 from 2000-2018. After adjustment of the denominator to account for individuals no longer at risk due to hysterectomy, corrected rates showed a declining trend from 51.4 in 2000 to 32.6 in 2018 (APC -2.1%, 95%CI 3.4 to -0.7%). Uncorrected ovarian cancer rates were 14.9 per 100,000 in 2000 and 11.9 in 2018. Corrected ovarian cancer incidence rates decreased over time from 22.5 in 2000 to 12.9 in 2018 (-2.5%, -3.4 to -1.6%).

Conclusion: The differences in magnitude between the uncorrected and corrected incidence rates for ovarian and uterine cancer in Utah highlight the importance of refining population denominators to exclude individuals no longer at risk.

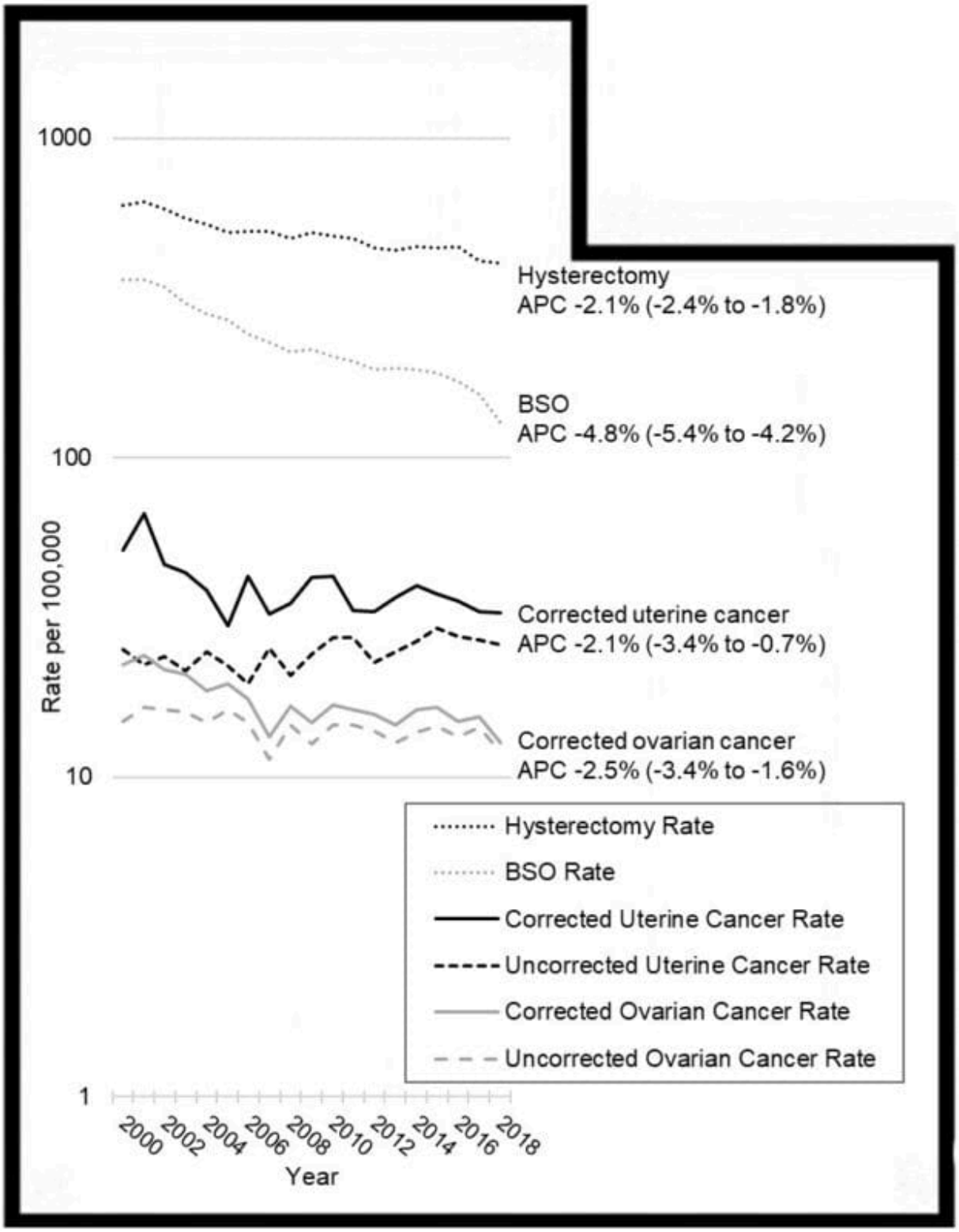


Figure. Temporal trends of age-adjusted incidence rates for gynecologic surgical procedures (hysterectomy and bilateral salpingo-oophorectomy (BSO), *dotted lines*) and gynecologic cancer (uterine and ovarian), both uncorrected for *(dashed lines)* and corrected for *(solid lines)* the prevalence of gynecologic organ removal, in Utah between 2000 and 2018. All rates were age-adjusted to the US 2000 standard population and reported per 100,000 person-years. Annual percent change (APC) in trends for gynecologic surgeries and surgery-corrected gynecologic cancer rates was calculated using linear regression of the natural log-transformed annual rate by calendar year.

Cancer

The Association Between Working with Poultry and Esophageal Cancer Mortality; A Case-cohort Study Christina Joshua* Christina Joshua Leanna Delhey Benjamin C. Amick Jaimi L Allen Wendy N. Nembhard Robert Delongchamp

Background. While research suggests poultry industry workers have an increased risk of cancer mortality, little is known about the risk of esophageal cancer mortality. We investigated the association between working with poultry and esophageal cancer mortality while concurrently investigating other occupational and non-occupational risk factors amongst poultry industry workers. **Methods**. We conducted a case-cohort analysis from a cohort of unionized workers in the United States (N=46,816) and conducted follow-up for mortality from 1950-2019 with the National Death Index. Cases were those who died of esophageal cancer and a sub-cohort was randomly selected (N=2,666) for further analysis. We interviewed participants and relatives about their work and personal life. We conducted multivariable Cox proportional hazards regression to estimate the hazard of esophageal cancer mortality due to working with poultry among the full cohort and weighted regression for the sub-cohort and those interviewed. We conducted exploratory analyses to estimate hazard ratios (HR) and 95% confidence intervals (CI) for each interview question, adjusted for confounders, and computed a false discovery rate (FDR). **Results**. In the full and sub-cohort, working in a poultry plant was associated with an increased hazard of esophageal cancer mortality (HR=1.62, 95% CI=1.05, 2.50; HR=1.65, 95% CI=1.03, 2.65, respectively). Among responders, working in a poultry plant appeared to decrease risk of esophageal cancer mortality (HR=0.67; 95% CI=0.34, 1.35). **Conclusions**. Working in poultry plants may increase the risk of death from esophageal cancer, but further research is needed to validate these findings and explore potential mechanisms.

Cancer

Temporal changes in modifiable risk factors of breast cancer in the Generations Study

Isobel Jackson* Isobel Jackson Alicia Heath Michael Jones Montse Garcia-Closas Amy Berrington de González Marc Gunter

Background: Several established breast cancer risk factors are modifiable and exposure may change over the life course. Understanding temporal changes in these risk factors is crucial to inform breast cancer prevention strategies. However, most cohorts rely on single exposure measurements and longitudinal data assessing long-term exposure patterns are scarce.

Methods: Using the Generations Study, a prospective cohort of >113,700 UK women aged ≥16 years, we investigated changes in self-reported alcohol intake, smoking, body mass index (BMI) and physical activity (PA). We analyzed changes in risk factors between baseline and follow-ups at 6.2 and 14.3 years after study entry. Within-person changes were calculated comparing follow-up to baseline exposure measurements overall and stratified by birth cohort. Predictors of exposure change were analyzed using logistic and linear regression for binary and continuous changes, respectively, adjusting for baseline age and exposure.

Results: Changes in risk factors were modest overall. At each round, most women reported current drinking, non-smoking, high PA and healthy BMIs, with minimal changes in observed values across rounds. Over a median follow-up of 14.3 years, participants' BMI and total PA increased by a median of 0.5 kg/m2 (interquartile range [IQR]:-0.9, 2.2) and 1.4 MET-h/week (IQR:-14.3, 18.5), respectively, while alcohol intake and smoking intensity decreased by a median of 2.4 g/day (IQR:-9.6, 3.3) and 9 cigarettes/day (IQR:-15.0, -3.1), respectively, among current/former drinkers or smokers at follow-up. Exposure patterns were heterogeneous across birth cohorts. Factors associated with exposure changes included socioeconomic status and education.

Conclusion: Although exposure change varied by birth cohort, modifiable risk factors of breast cancer appear relatively stable over time. For these risk factors, a single baseline measurement may be sufficient to capture medium to long term exposures for risk assessment.

Cancer

The Mediating Effect of Socioeconomic Status and Persistent Poverty on Pediatric Cancer Mortality in the USA Josiane Kabayundo* Josiane Kabayundo Apu Das Krishtee Napit Emma Hymel Shinobu Watanabe-Galloway

Background: Existing evidence among adults demonstrates that socioeconomic (SE) factors play a critical role in racial/ethnic disparities in cancer mortality. However, research examining the interplay between SE factors and race/ethnicity in pediatric cancer mortality is limited. **Objective:** Evaluate the mediating effect of socioeconomic status (SES) and persistent poverty in racial/ethnic mortality of childhood cancer. **Methods:** The 2006-2020 SEER Research plus specialized data with census tract attributes were used. Cases of age 0-19 years were included. Race/ethnicity was categorized as Non-Hispanic White, Non-Hispanic Asian, Non-Hispanic American Indian/ Alaska Native, Non-Hispanic Black, and Hispanic. Cause-specific Cox-proportional hazard models were used to examine the association of race/ethnicity with cancer mortality, adjusting for covariates. The proportional hazard assumptions were tested using Schoenfeld residuals. A mediation analysis was performed using R4.1.3 mediation package. We performed separate analyses for each mediator. The total, direct, and indirect effects were estimated using the hazard ratio scale and percentage mediated and 95% CIs calculated from 100 bootstraps resampling. **Results:** 96, 665 cases were included. Using White as a reference, the risk of cancer death was higher among Black (aHR:1.53; 95% CI: 1.45-1.62), Hispanic (aHR:1.17; 95% CI: 1.12-1.22) and PI (aHR: 1.24; 95% CI:1.15-1.33). The proportion mediated by SES was 13.5% (11.7% – 15.1%) for Blacks and 29.3% (26.8 % – 29.5%) for Hispanics. The proportion mediated by persistent poverty was 6% (4.7% – 6.8%) for Blacks, 13% (11.3% – 14%) for Hispanics, and 1% (0.75% -1.1%) for Asians. **Conclusion:** SES and persistent poverty significantly contributed to disparities, with variations across racial/ethnic groups and cancer types. Addressing these intersecting factors requires multi-level interventions targeting systemic inequities and barriers in clinical care and individual level.

Cancer

Prenatal pesticide exposure and neuroblastoma – A statewide case-control study in California Darcy Van Deventer* Darcy Van Devebter Beate Ritz Myles Cockburn Julia E. Heck

Background: Previous studies investigating neuroblastoma risk and parental pesticide exposure have mixed findings but there is evidence of associations between maternal occupational and residential pesticide exposure and neuroblastoma. No previous studies have investigated the relationship between neuroblastoma risk and ambient residential exposures to specific pesticides.

Objective: To evaluate associations between childhood neuroblastoma and prenatal exposure to specific pesticides through residential proximity to agricultural pesticide applications.

Methods: We identified neuroblastoma cases from the California Cancer Registry and cancer-free controls from birth certificates. Analyses were restricted to those living in rural areas and born between 1998–2016, resulting in 141 cases and 155,226 controls. Probable and possible carcinogens were selected from the Environmental Protection Agency's classifications and pesticide use was collected from the California Department of Pesticide Regulation's Pesticide Use Reporting system and linked to land-use surveys. Exposures for subjects were assessed using a 4000m buffer around the geocoded residential addresses at birth. We used a distance decay model and defined exposure as exposure during pregnancy above the median pounds for each pesticide. Odds ratios were calculated using unconditional logistic regression models adjusted for maternal age, SES, race/ethnicity, and birth year as well as hierarchical regression models co-adjusted for other pesticides.

Results: We observed an elevated risk of neuroblastoma with exposure to the pesticide class n-methyl carbamate (aOR: 1.47; 95% CI: 0.98-2.21). In our hierarchal models, we observed elevated risks of neuroblastoma with exposure to penoxsulam (aOR: 1.58; 95% CI: 1.03-2.44) and flonicamid (aOR: 1.57; 95% CI: 1.09-2.26).

Conclusion: Our findings suggest that ambient exposure to certain pesticides or pesticide classes during pregnancy may increase the risk of neuroblastoma.

Cancer

Pre-diagnostic circulating carotenoids and lethal breast cancer risk: a novel approach for precision prevention Cheng Peng* Cheng Peng Boyang Chai A. Heather Eliassen Bernard A. Rosner

Background: Identifying pre-diagnostic modifiable factors that are associated with lethal breast cancer risk may provide targeted prevention strategies to those who are most likely to develop fatal disease. We sought to examine whether circulating carotenoid levels are associated with lower risk of lethal breast cancer.

Methods: This study included 6,071 Nurses' Health Studies participants who were cancer-free at the time of carotenoid measure and followed over 20 years, during which 2,910 incident breast cancer cases arose, and 249 cases had recurrence or died due to breast cancer. Plasma carotenoids (α-carotene, β-carotene, β-cryptoxanthin, lutein/zeaxanthin, and lycopene) were assayed using high-performance liquid chromatography and total carotenoid was calculated as the sum of individual carotenoids. Based on a multi-state model which combined separate estimates for breast cancer incidence and recurrence/mortality due to breast cancer among cases, we estimated the probability of transitioning from disease-free to developing breast cancer to breast cancer recurrence/death over a 20-year period. We performed stratified analyses by menopausal status, smoking, and body mass index, assessed at blood draw.

Results: Comparing to the lowest quintile (Q1), women in the highest quintiles (Q5) of β-carotene and total carotenoids had a 30% and a 38% lower risk of lethal breast cancer (β-carotene: HR=0.70, 95% CI: 0.52-0.94; total carotenoid: HR=0.62, 95% CI: 0.46-0.85). However, there was significant heterogeneity by menopausal status and smoking, with stronger inverse associations observed for women who were postmenopausal (total carotenoid: Q5 vs. Q1 HR=0.53) or reported ever smoking (total carotenoid: Q5 vs. Q1 HR=0.50). Associations between other carotenoids and lethal breast cancer risk were in general not significant.

Conclusion: Our findings suggest that circulating carotenoids may present a novel primary prevention strategy targeting the lethal form of breast cancer.

Figure 1. Postmenopausal circulating carotenoid levels and breast cancer incidence, recurrence/mortality and lethal breast cancer risk over 20 years follow-up in NHS and NHS2.

(1) Incidence analysis: Fine-Gray competing risk model with time since blood draw as the time scale;
(2) Recurrence analysis: Fine-Gray competing risk model with time since diagnosis as the time scale;
(3) Two-stage analysis: probability of transitioning from disease-free to developing breast cancer to recurrence/death due to breast cancer

	Incidence (n=3244; breast cancer case=1530)					
Circulating Carotenoids	HR(95%CI)_q1	HR(95%CI)_q2	HR(95%CI)_q3	HR(95%CI)_q4	HR(95%CI)_q5	Ptrend
Alpha_carotene	ref	0.86 (0.73-1.02)	1.05 (0.89-1.23)	0.95 (0.81-1.12)	0.93 (0.79-1.10)	0.80
Beta_carotene	ref	1.02 (0.87-1.19)	1.06 (0.90-1.25)	0.96 (0.82-1.14)	0.96 (0.81-1.13)	0.40
Beta_cryptoxanthin	ref	1.12 (0.95-1.32)	1.15 (0.98-1.36)	1.03 (0.87-1.22)	1.01 (0.85-1.20)	0.50
Lycopene	ref	0.97 (0.83-1.14)	0.99 (0.85-1.16)	0.86 (0.73-1.01)	0.96 (0.82-1.13)	0.38
Lutein/zeaxanthin	ref	0.91 (0.77-1.07)	1.03 (0.88-1.21)	0.93 (0.79-1.09)	0.95 (0.80-1.12)	0.69
Total_carotenoid	ref	0.93 (0.79-1.09)	0.98 (0.83-1.15)	0.90 (0.76-1.06)	0.91 (0.77-1.07)	0.27
	Mortality (breast cancer case=1528; recurrence/death due to breast cancer=144)					
Circulating Carotenoids	HR(95%CI)_q1	HR(95%CI)_q2	HR(95%CI)_q3	HR(95%CI)_q4	HR(95%CI)_q5	Ptrend
Alpha_carotene	ref	1.23 (0.71-2.14)	1.23 (0.72-2.11)	0.90 (0.51-1.59)	0.95 (0.51-1.78)	0.46
Beta_carotene	ref	0.81 (0.48-1.37)	1.14 (0.68-1.91)	0.61 (0.34-1.09)	0.63 (0.35-1.13)	0.07
Beta_cryptoxanthin	ref	0.79 (0.46-1.34)	0.71 (0.42-1.22)	1.12 (0.67-1.87)	0.72 (0.40-1.28)	0.60
Lycopene	ref	0.89 (0.52-1.55)	0.85 (0.50-1.43)	1.34 (0.79-2.28)	1.04 (0.61-1.78)	0.52
Lutein/zeaxanthin	ref	0.88 (0.51-1.50)	0.88 (0.53-1.47)	0.64 (0.36-1.16)	1.02 (0.58-1.81)	1.00
Total_carotenoid	ref	0.51 (0.28-0.92)	1.09 (0.67-1.78)	1.08 (0.64-1.81)	0.51 (0.28-0.94)	0.19
	Two-stage (n=3244, breast cancer case=1528; recurrence/death due to breast cancer=144)					
Circulating Carotenoids	HR(95%CI)_q1	HR(95%CI)_q2	HR(95%CI)_q3	HR(95%CI)_q4	HR(95%CI)_q5	Ptrend
Alpha_carotene	ref	1.07 (0.75-1.51)	1.24 (0.89-1.74)	0.88 (0.62-1.26)	0.91 (0.62-1.34)	0.28
Beta_carotene	ref	0.85 (0.61-1.18)	1.17 (0.85-1.61)	0.64 (0.45-0.92)	0.66 (0.46-0.94)	0.01
Beta_cryptoxanthin	ref	0.88 (0.63-1.25)	0.83 (0.59-1.17)	1.13 (0.81-1.58)	0.75 (0.52-1.09)	0.34
Lycopene	ref	0.88 (0.62-1.26)	0.86 (0.61-1.20)	1.15 (0.82-1.63)	1.01 (0.71-1.42)	0.58
Lutein/zeaxanthin	ref	0.83 (0.58-1.17)	0.92 (0.66-1.27)	0.64 (0.44-0.94)	0.98 (0.68-1.42)	0.89
Total_carotenoid	ref	0.53 (0.37-0.77)	1.06 (0.78-1.44)	0.98 (0.71-1.36)	0.53 (0.36-0.77)	0.03

LATEBREAKER

Cancer

Illuminating Cancer Risk: Light at Night as a Potential Contributor to Hormone-Related Cancers Yong Zhu* Yong Zhu Yidan Meng Yaya Guo Kinsey Garofalo Yong-Moon Park

Background: Light at Night (LAN) is a circadian disruptor that affects multiple physical and biological functions and has a potential association with cancer risk. This study tested whether there is an association between LAN and cancer incidence, particularly hormone-related cancers, using data from the Northeastern United States (U.S.).

Methods: We used county-level data from all seven Northeastern U.S. states. Linear regression and spatial analyses were conducted to assess the association between LAN and cancer incidence, adjusting for multiple neighborhood level confounding factors.

Results: We found significant positive associations between LAN and hormone-related cancer rates, including breast ($p = 0.007$), prostate ($p = 0.022$), Non-Hodgkin Lymphoma ($p = 0.049$), and thyroid cancer ($p < 0.001$). We also found a consistent trend of an inverse association between LAN and colon cancer, with significant results at the 0.05 level across the study area.

Conclusions: Our findings suggest that exposure to ambient LAN may increase the risk of several hormone-related cancers. Additionally, poverty and race/ethnicity may play important roles in this association. Further research is needed to explore the mechanisms behind these relationships.

LATEBREAKER

Cancer

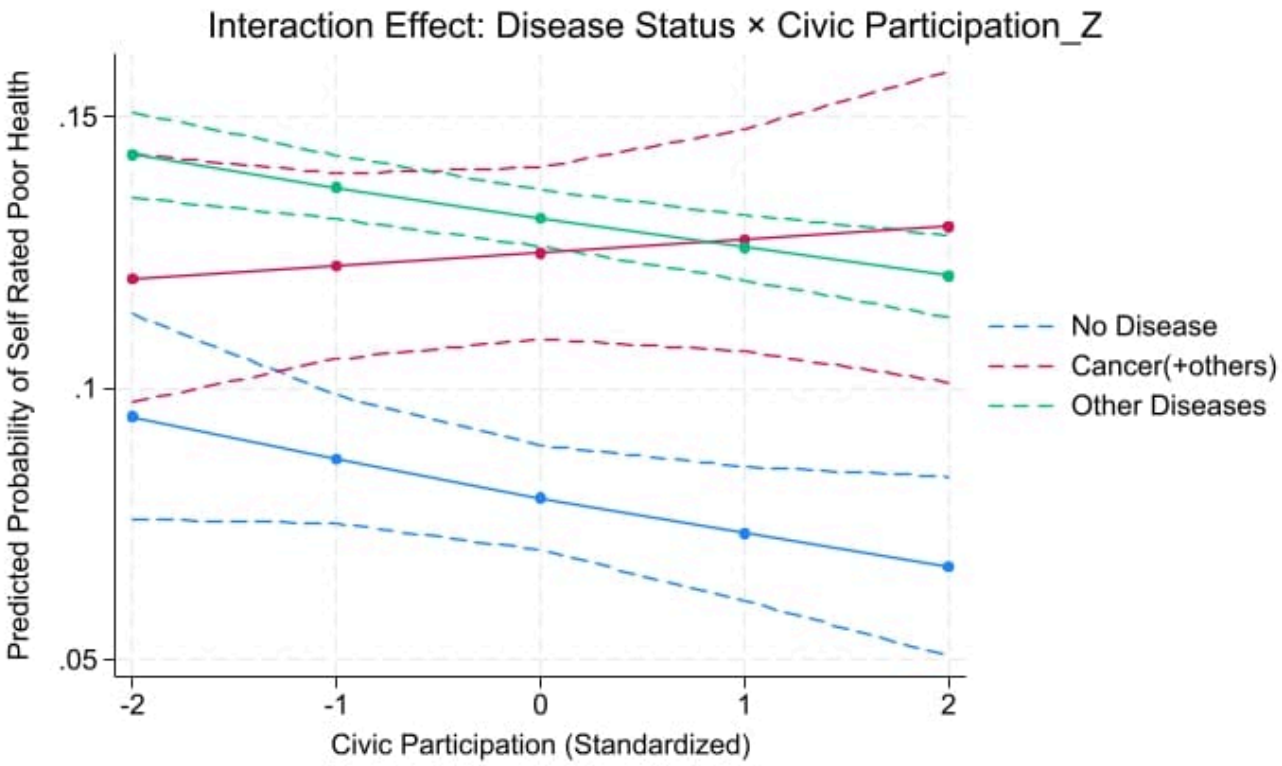
Community-Level Social Capital and Well-Being Among Older Adults in Japan: Effect Modification by Cancer and Other Chronic Diseases Kaori Suga* Kaori Suga Maho Haseda Yuri Ito Ichiro Kawachi Naoki Kondo

Background
Cancer treatment and its side effects often disrupt social activities in older adults. Community-level social capital (CSC) helps prevent social isolation and promote health, but its effects on older adults with cancer are still not well studied. This study examined the associations between CSC scores and well-being among older adults in Japan, comparing those with cancer or other chronic diseases to those without them.

Methods
We analyzed panel data from the Japan Gerontological Evaluation Study, including 32,702 functionally independent, community-dwelling adults aged ≥65 years across three waves (2013, 2016, and 2019). School-district CSC, the exposure variable from the 2016 wave, was assessed using three components: civic participation, social cohesion, and reciprocity. Outcomes from the 2019 wave included self-rated health, depressive symptoms, happiness, and social isolation. Multilevel analyses were performed using a modified Poisson regression model to estimate adjusted prevalence ratios (PRs) with 95% CIs.

Results
The mean age of participants was 72.1 years (SD = 5.0), and 52.0% were women. Among the participants, 18.2% had no disease, 3.1% had cancer, and 78.7% had other diseases. . Community-level civic participation, defined as the average level of group participation within a community, was inversely associated with poor self-rated health (PR = 0.92, 95% CI: 0.84–1.00). This association was observed in the no-disease and other-disease groups but showed a trend in the opposite direction among those with cancer (p for interaction = 0.064). No clear effect modification by cancer status was observed for other CSC components or outcomes.

Conclusion
Our findings did not provide evidence that CSC positively influenced well-being in older adults with cancer. To identify community characteristics that enhance the well-being in this population, it is necessary to explore their needs for living in their local environment.


Interaction Effect: Disease Status × Civic Participation_Z
Predicted Probability of Self Rated Poor Health
.15
.1
.05
-2
-1
0
1
2
Civic Participation (Standardized)
No Disease
Cancer(+others)
Other Diseases

LATEBREAKER

Cancer

Improving Cancer Surveillance: Estimating Hysterectomy-Corrected EC Mortality and Disparities in the US (2003-2020) Emma Joo* Emma Joo Lauren McCullough Jeffrey M. Switchenko Larissa Weirich Maret L. Maliniak

Background: At present, endometrial cancer (EC) mortality rates in the Surveillance, Epidemiology, and End Results (SEER) program do not adjust for hysterectomy prevalence, including women in the denominator who are not at risk of EC. Hysterectomy is the most common non-obstetric surgery among US women, with Black women and women in the South having some of the highest rates. To address this gap, we examined trends in hysterectomy-corrected EC mortality rates in the US by state among non-Hispanic Black (NHB) and non-Hispanic White (NHW) women.

Methods: We extracted EC mortality rates from SEER and corrected using hysterectomy prevalences from the Behavioral Risk Factor Surveillance System (BRFSS) for 2003–2020, stratified by state and 10-year age groups for NHW and NHB women over 50 years of age, pooled over 3-year intervals to stabilize rates by state. Corrected rates were age-standardized using the 2000 US standard population. For disparities by state, we calculated NHB:NHW rate ratios (RRs) by time interval and used Joinpoint regression to calculate average annual percent changes (AAPCs). We excluded states with insufficient data to examine trends across both races; 19 states were included in our analysis.

Results: The hysterectomy-corrected EC mortality rates ranged from 15.2 per 100,000 (Mississippi, NHW, 2006-2008) to 72.2 per 100,000 (South Carolina, NHB, 2018-2020). NHB women had greater EC mortality rates than NHW women across all states (range in NHB:NHW RR: 1.5 in Ohio, 2012-2014 to 3.4 in Alabama, 2012-2015). When examining the AAPCs (Figure 1), every state except Alabama saw increases in EC mortality between 2003 and 2020 for both NHB and NHW. AAPCs were larger for NHB than NHW women in 12 states, whereas the AAPC was larger for NHW women in 6 states.

Conclusions: Our results using hysterectomy-corrected population-based surveillance data show that EC mortality is increasing for nearly all states in our analysis, with NHB women disproportionately impacted.

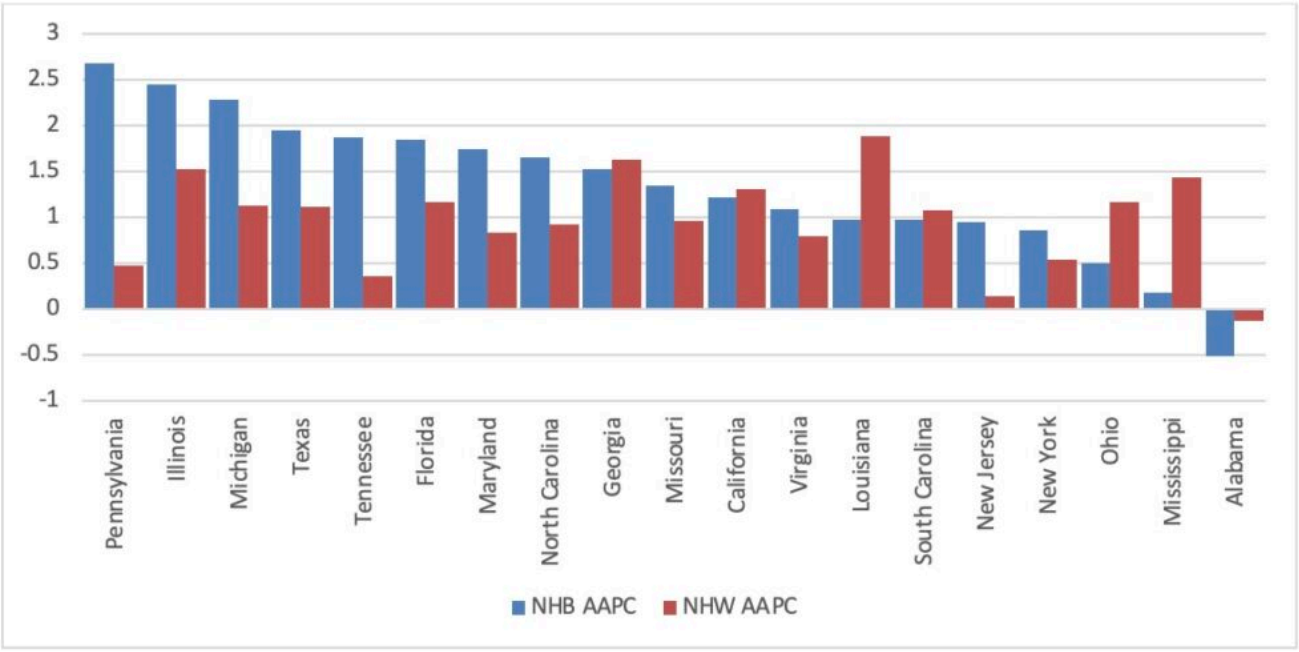


Figure 1: Average Annual Percentage Change of Hysterectomy-Corrected and Age Standardized Endometrial Cancer Mortality Rates by Race and State between 2003-2020.

LATEBREAKER

Cancer

Social and Intersectional Inequalities in Emergency Presentation (EP) of Cancer among Older Adults in the US Yuelin He* Yuelin He Sarah E Soppe Sharon Peacock Hinton Ellis C Dillon Megan A Mullins Nicholas Pettit Matthew Thompson Matthew Barclay Allison W Kurian Sandi L Pruitt Georgios Lyratzopoulos Caroline A Thompson

Background: Emergency presentation (EP) of cancer, a diagnostic episode involving an unplanned emergency inpatient stay (EP-IP) or outpatient Emergency Department visit (EP-OP), is estimated to be highly prevalent and associated with poorer cancer outcomes. Limited evidence exists on systematic differences in EP prevalence by social determinants, which may indicate structural barriers to timely diagnosis and cancer care delivery.

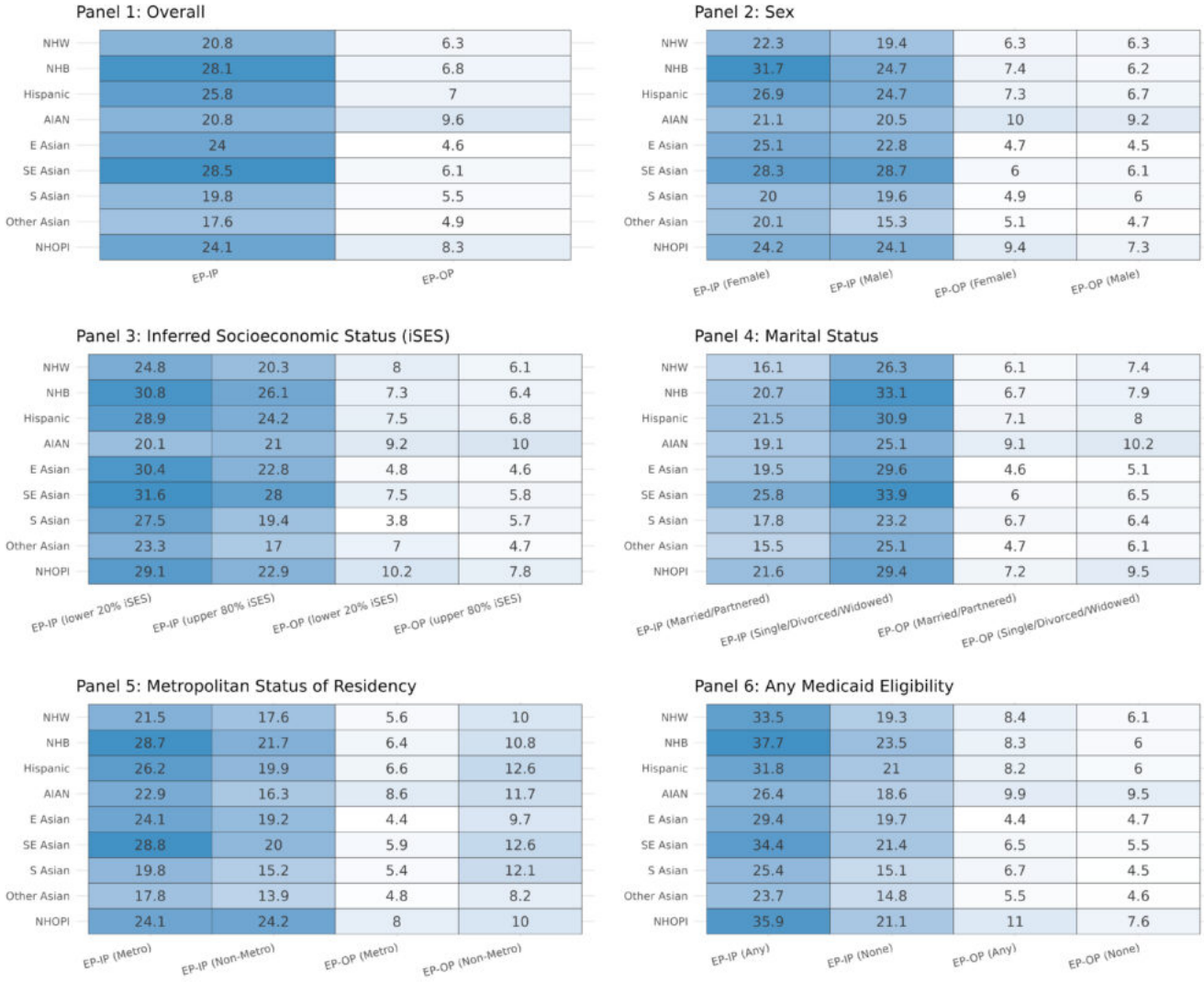
Methods: Based on analyses of 920,761 beneficiaries aged 66+ in SEER-Medicare (2008-2017), we described inequalities in EP by race/ethnicity and other social disadvantage measures across 16 cancer sites. With dichotomized EP, we calculated Prevalence Ratios for unordered or binary measures, and Relative Concentration Index (RCI) to quantify the extent to which EP is concentrated among each ordinal measure. With a 3-level classification (EP-IP, EP-OP, vs. non-EP), we examined the joint distribution of EP prevalence by race/ethnicity and each binarized measure.

Results: With 21.8% EP-IPs and 6.4% EP-OPs overall, most racial/ethnic minoritized groups had higher prevalence than non-Hispanic whites. A downward gradient in EP was observed with higher inferred socioeconomic status [RCI=-0.075 (95% CI: -0.077, -0.073)] and lower degree of urbanization [RCI=-0.008 (95% CI: -0.010, -0.006)]. Across racial/ethnic groups, similar patterns emerged: except among some Asian subgroups and AIANs, higher prevalence of EP-IP and EP-OP were seen in those who had Medicaid eligibility (with large contrast in EP-IP prevalence), or were female, at lower socioeconomic status, and single/divorced/widowed; metropolitan residents had higher EP-IP but lower EP-OP prevalence than non-metropolitan counterparts.

Conclusion: EPs were disproportionately concentrated among socially disadvantaged individuals, with joint effects of race/ethnicity and other measures on EP. Identifying EP disparities may facilitate targeted interventions to improve cancer health equity in the US.

Figure 1. Prevalence of EP-IP and EP-OP Overall and Comparing Binarized Social Disadvantage Measures (%), Stratified by Race/Ethnicity

Abbreviations: Non-Hispanic White (NHW), Non-Hispanic Black (NHB), American Indian and Alaska Native (AIAN), East Asian (E Asian), Southeast Asian (SE Asian), South Asian (S Asian), NHOPI (Native Hawaiian or Other Pacific Islander).



LATEBREAKER

Cancer

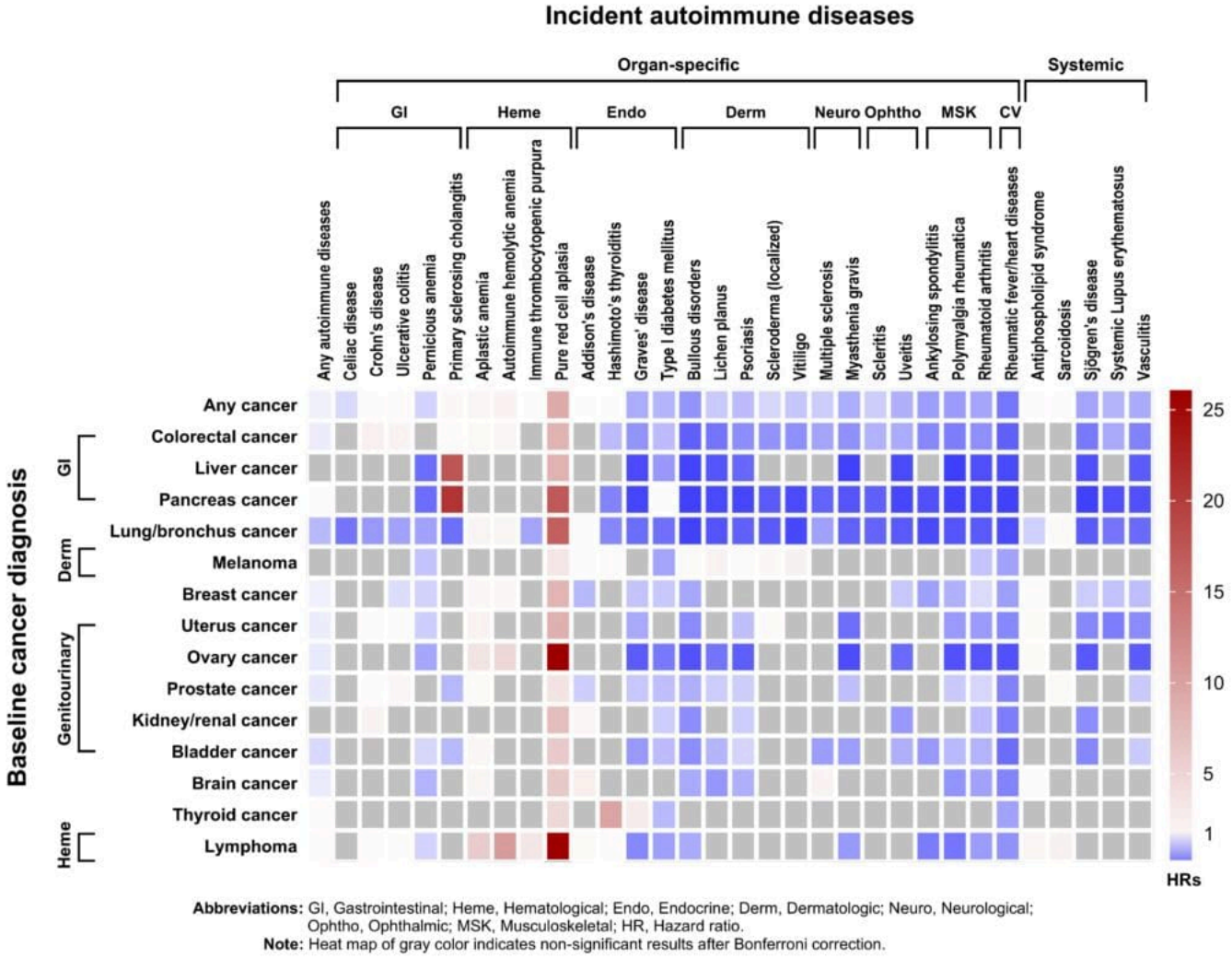
Association between Cancer and Incident Autoimmune Diseases among Older Adult Population in the U.S. Dongwon Yoon* Dongwon Yoon Minkyo Song

BACKGROUND: Prior studies on autoimmunity in cancer patients have mainly focused on the effects of immunotherapy, but evidence on cancer itself and autoimmune diseases remains limited and conflicting.

METHODS: We conducted a retrospective cohort study using SEER–Medicare data, matching cancer patients 1:1 with noncancer Medicare beneficiaries by age, sex, index year, and coverage. Patients with pre-existing autoimmune diseases were excluded. The primary outcome was any autoimmune disease, with secondary outcomes assessing 31 specific autoimmune diseases. Cox regression with robust variance estimators estimated hazard ratios (HRs) and 95% confidence intervals (CIs), applying Bonferroni corrections. We also analyzed 14 common cancers.

RESULTS: Among 2,780,580 matched pairs (mean age: 77.1 years, 49.2% female, median follow-up: 5.8 years for cancer), cancer was modestly associated with lower risk of any autoimmune disease (HR: 0.95, 95% CI: 0.94–0.96), with decreased risks in 20 of 31 autoimmune diseases. Among the 14 cancer–31 autoimmune disease associations, 65 were positive, 174 inverse, 195 non-significant. Organ-specific patterns of increased risk of autoimmune diseases were observed: colorectal cancer-Crohn’s disease/ulcerative colitis (HR, 95% CI; 2.22, 2.07-2.37; 2.01; 1.92-2.11); liver/pancreatic cancers-primary sclerosing cholangitis (17.4, 14.7–20.5; 20.7, 18.7–23.0), thyroid cancer-Hashimoto’s thyroiditis/Graves’ disease (9.78, 8.23–11.6; 2.84, 2.51–3.23), melanoma-dermatologic and lymphoma-hematological autoimmune disease (HR range 1.33–2.11; 3.21–26.2). Notably, pure red cell aplasia had increased risk across all cancers (HR range 3.19–26.1).

CONCLUSIONS: We observed a predominantly inverse association between cancer and autoimmune diseases, with organ-specific patterns, suggesting distinct immunologic mechanisms. Cancer treatments may influence these associations, warranting cautious interpretation given potential informative censoring and detection bias.



Abbreviations: GI, Gastrointestinal; Heme, Hematological; Endo, Endocrine; Derm, Dermatologic; Neuro, Neurological; Ophtho, Ophthalmic; MSK, Musculoskeletal; HR, Hazard ratio.
Note: Heat map of gray color indicates non-significant results after Bonferroni correction.

Cancer

Approaches to Assessing Prognostic Biomarkers: An example with the Proliferation Marker Ki-67 in Prostate Cancer. Sinead Flanagan* Sinead Flanagan Hannah E. Guard Michelangelo Fiorentino Richard Flavin Zhike Lin Jane B. Vaselkiv Pati Soule Lia DePaula Oliveira Adrianna A Mendes Tamara L. Lotan Massimo Loda Stephen P. Finn Lorelei A. Mucci Konrad H. Stopsack

Background: A subset of localized prostate cancer metastasizes despite curative surgery, underscoring the need for improved prognostication. Using the proliferation marker Ki-67, we evaluated methodological strategies for assessing prognostic utility.

Methods: Prostate cancer patients (N=910 diagnosed 1983-2004) from two prospective cohorts were followed for lethal disease (distant metastases or prostate cancer-specific death) up to 2020. Tumor tissue microarrays were immunostained for Ki-67, quantified as positive nuclei per tumor cell count and categorized as 0%, >0 to <1%, ≥1 to <5% and ≥ 5%. Discrimination was evaluated with time-varying area-under-the-curve (tAUC) using a risks-based ("cumulative/dynamic") approach and compared to a usual hazards-based ("incident-dynamic") overall AUC (Harrell's c).

Results: The majority of tumors (82%) had Ki-67 expression of <1%, while 3% had high Ki-67 expression (≥5%). Among 888 men without metastasis at diagnosis, 97 lethal events occurred over 32 years of follow-up. Compared to no Ki-67 expression, high Ki-67 expression (≥5%) was associated with greater rates of lethality (hazard ratio 3.9, 95% confidence interval (CI) 1.4-11), adjusted for age at diagnosis and Gleason score, a standard-of-care prognostic marker. The tAUC for Ki-67 expression to discriminate the 5-year risk of lethal disease was 0.66 (95% CI 0.56, 0.76), higher than its overall AUC across follow-up of 0.60 (95% CI 0.55, 0.65). Throughout follow-up, from 5 to 25 years, the tAUCs for the combination of Ki-67 positivity and Gleason score for assessing the risk of lethal disease (0.74 to 0.73) were comparable to those of Gleason score alone (0.71 to 0.72).

Conclusions: Risks-based (cumulative/dynamic) tAUC evaluation of the Ki-67 biomarker highlighted its potential to inform prognostication in the early years after prostate cancer surgery, but less so later during follow-up. These time trends would not be apparent with hazards-based overall AUC modeling.

Cancer

Cancer-Specific Standardized Incidence Ratio in a Cohort of Health Screening Participants in Korea Sun Ha* Sun Ha Jee Keum Ji Jung Da Hye Kang

Background: Prospective cohorts composed of the general population visiting health screening centers are sometimes utilized in epidemiological research. However, studies comparing cancer-specific incidence risks in these cohorts with those of a stable general population are rare. This study analyzed whether cancer risks among individuals visiting health screening centers in Korea differ from those of the overall Korean population.

Methods: The Korean Cancer Prevention Study-II (KCPS-II) is a prospective cohort established between 2004 and 2013, comprising 159,844 participants who visited 18 health screening centers nationwide for routine health examinations. Cancer incidence among the participants was identified annually from 2004 to 2021 through linkage with the National Cancer Center's cancer registry database. Standardized Incidence Ratios (SIRs) with 95% confidence intervals (CIs) were calculated for the cohort, and SIRs were further analyzed by sex and age group.

Results: The mean age of the participants was 41.28 years (standard deviation, 10.36 years), with an average follow-up duration of 13.5 years (2,087,619 person-years). A total of 11,278 cancer cases (7.3%) were identified. The overall cancer risk in the cohort was similar to that of the general population, with an SIR of 98.9 (95% CI, 97.1–100.7). By sex, the SIR was higher in females (110.9; 95% CI, 107.9–114.1) and lower in males (91.0; 95% CI, 88.8–93.3). Among age groups, SIRs were above 100 for all age groups between 20 and 49 years but declined to 100 or below in participants aged 50 years and older. For thyroid cancer, the SIR was 123.9 (95% CI, 118.9–129.1), with a higher value in males (182.6; 95% CI, 171.4–194.6) than in females (100.5; 95% CI, 95.2–106.0). Age-specific analysis revealed that SIRs were above 100 for participants younger than 60 years but fell below 100 for those aged 60 years or older.

Conclusion: The overall cancer incidence risk in the cohort established with health screening participants was similar to that of the general population. However, differences in SIRs were observed for specific cancers, including thyroid cancer.

This study was supported by BasgenBio, the National Cancer Center (HA21C0142), and the Korea Health Industry Development Institute (HI20C0517).

Cancer

Ingested nitrate and nitrite and incidence of thyroid cancer in the Agricultural Health Study Dazhe Chen* Dazhe Chen Christine G. Parks Laura E. Beane Freeman Jonathan N. Hofmann Rashmi Sinha Maya Spaur Jessica M. Madrigal Mary H. Ward Dale P. Sandler

Background: Nitrate and nitrite ingestion is associated with increased risk for some cancers, possibly via the endogenous formation of carcinogenic N-nitroso compounds. However, evidence on thyroid cancer (TC) is limited. We examined the associations of water nitrate and dietary nitrate and nitrite intakes with incident TC in the Agricultural Health Study. We also stratified analyses by sex, given the predominance of TC in women, and by vitamin C, an inhibitor of endogenous nitrosation.

Methods: We determined the primary drinking water source for participants at enrollment (1993-1997). For public water supply users with historical measurement data (N=14,779), we computed average nitrate concentrations in drinking water. For private well users (N=44,896), we developed random forest model estimates of nitrate concentrations based on well location, nitrogen inputs, and other predictors. Dietary nitrate and nitrite were assessed among the 29,371 participants who completed a diet history questionnaire at the first follow-up (1999-2003). Incident TC cases between study enrollment or first follow-up and 2021 were identified by linkage with Iowa and North Carolina cancer registries. We estimated adjusted hazard ratios (HRs) and 95%CI for associations of tertiles (T) of exposure with incident TC overall and in strata of sex and vitamin C intake from foods and supplements.

Results: We identified 192 TC cases (77 for dietary analyses). Water nitrate and dietary nitrate/nitrite were not associated with TC overall. We found a positive association between water nitrate and TC in women (N=25,356; T2 vs. T1 HR: 1.37, 95%CI: 0.86, 2.21; T3 vs. T1 HR: 1.44, 95%CI: 0.91, 2.26) but not men. We also found elevated HRs (>1.50) in upper tertiles of water nitrate and dietary nitrite exposures in those with vitamin C <median, although exposure-response trends were not monotonic.

Conclusion: Water nitrate and dietary nitrite intakes may increase the incidence of TC among women.

Cancer

Lung Cancer Survival in Texas: Analyzing Histological Subtypes and Sociodemographic Influences Dalila Coimbra* Dalila Caroline do Amaral Coimbra Natalie Archer Paige Miller

Introduction
Lung cancer represents a significant public health challenge in Texas. In 2022, 13,482 new cases were reported. It remains the leading cause of cancer mortality in the state, with a poor survival rate of approximately 24%. Despite advancements, disparities persist across different histologic subtypes and demographic factors.

Methods
This study analyzed survival trends for 175,540 patients from the Texas Cancer Registry aged 20 years and older diagnosed with lung cancer between 2007 and 2020, followed through 2021. We examined survival rates stratified by sex, race, geographic region, insurance status, and lung cancer histological subtype. Statistical analyses included 5-year observed and relative cancer survival using SEER*Stat, survival trend analysis using JPSurv, and Cox proportional hazards survival regression model using SAS.

Results
Lung cancer 5-year relative survival (RS) was 22.1% (Annual Average Change [AAC]=0.64). Non-Small Cell Lung Carcinoma (NSCLC) adenocarcinoma had a RS of 29.2% (AAC=0.82), while NSCLC squamous RS was only 20.2% (AAC=0.43). Women had higher RS (25.7%) than men (18.8%). Racial disparities were evident; non-Hispanic blacks had the lowest RS (20.4%). Geographic analysis revealed the lowest RS rates in North Texas (16.9%) and the highest in South Texas, near San Antonio (34.7%). Uninsured patients had a RS of 21.6% (AAC=0.84) and privately insured 29.9% (AAC=1.35). Cox regression indicated that histological type, race/ethnicity, year of diagnosis, sex, cancer stage at diagnosis, and insurance type significantly affected survival ($p<0.05$).

Discussion
Findings highlight significant differences in lung cancer survival based on several demographic and socioeconomic factors. These results emphasize the need for targeted interventions and policies to improve access to care and address social determinants.

Conclusion
This study underscores the multifaceted nature of lung cancer survival in Texas, necessitating a comprehensive approach.

Cardiovascular

Association of Coronary Heart Disease and Stroke with Adverse Social Determinants of Health and Health-Related Social Needs Among US Adults Aged ≥18 Years Guixiang Zhao*
Guixiang Zhao Machell Town Jing Fang Fatima Coronado Paul Eke

Background: Social determinants of health (SDOH) and individual-based health-related social needs (HRSN) have emerged as non-medical factors that influence people's health. We examined the associations of coronary heart disease (CHD) and stroke with adverse SDOH and HRSN measures among US adults.

Methods: SDOH/HRSN data collected through the Behavioral Risk Factor Surveillance System in 2022 were analyzed to measure life satisfaction, social and emotional support, loneliness, employment stability, food security, housing stability, transportation access, utilities security, mental stress, and cost barrier for needed medical care. Weighted prevalences for history of CHD and stroke were estimated by individual or cumulative SDOH/HRSN measures, and the associations were assessed by conducting log-linear regression analyses with adjustment for potential confounders.

Results: The prevalences of CHD and stroke were significantly higher among adults with most adverse SDOH and HRSN compared to those without. After adjustment for demographic characteristics and traditional cardiovascular risk factors, the adjusted relative prevalences for CHD and stroke remained significantly higher for adults with most adverse SDOH and HRSN compared to those without. The relative increases ranged from 13% for CHD and 14% for stroke among those lacking social and emotional support, to 64% and 78%, respectively, for those lacking reliable transportation. The adjusted prevalences of CHD and stroke were linearly and positively associated with the SDOH/HRSN composite score.

Conclusions: The prevalences of CHD and stroke were significantly higher among adults with underlying contributing factors to health inequities. Reducing CHD and stroke calls for an integrated approach that addresses disparities in SDOH and HRSN, along with medical therapy and lifestyle modifications.

Cardiovascular

Longitudinal patterns of cardiovascular-kidney-metabolic syndrome in adolescents: Assessments of transition dynamics and clinical determinants Pei-Wen Wu* Pei-Wen Wu Yu-Ting Chin Sharon Tsai Wei-Ting Lin Chien-Hung Lee

Background: Cardiovascular-kidney-metabolic (CKM) syndrome, arising from the intricate interplay of metabolic risk factors, chronic kidney disease, and cardiovascular conditions, is a progressive disorder that can begin in early life. Changes in CKM risk factors during adolescence may impact the development of early stages of CKM syndrome. This follow-up study investigated the conversion of CKM structure among adolescents and evaluated the determinants of CKM transition. **Methods**: A representative cohort of 1,638 adolescents, recruited from three areas with varying economic levels, was evaluated for CKM syndrome and followed for 2.5 years to determine the transition of CKM stages. Multinomial logistic regression was used to assess the association between changes in cardiovascular risk factors and CKM conversion. **Results**: At baseline, the prevalence of CKM stages 0, 1, and 2 was 53.8%, 27.7%, and 18.5%, respectively. After 2.5 years, the incidences of stages 1 and 2 were 5.5% and 4.7%. Among adolescents with CKM stage 1 at baseline, 25.3% remitted to stage 0, 49.0% persisted, and 25.7% progressed to stage 2. For those with CKM stage 2, 27.5% remitted to stage 0, 25.5% to stage 1, and 47.1% persisted. Controlling for covariates, a 1-unit increase in body mass index (BMI) and hemoglobin A1c (HbA1c) was associated with 1.45- and 2.43-fold risks of incident CKM stage 1, respectively. Additionally, a 1-unit elevation in systolic blood pressure and triglycerides correlated with 1.08- and 1.03-fold risks of incident CKM stage 2. Reduced BMI and HbA1c levels were linked to remission from stage 1, while decreased fasting blood sugar was associated with remission from stage 2. **Conclusion**: This study highlights the dynamics of CKM progression and remission in adolescents, emphasizing the roles of BMI and HbA1c in influencing disease stages. Effective management of these factors may enhance remission rates and improve outcomes in CKM.

Cardiovascular

Effect of replacing sedentary behavior with physical activity on the risk of atrial fibrillation: the REGARDS study Linzi Li* Linzi Li Amit Shah Yi-An Ko Dayna A. Johnson Yan V. Sun Emily B. Levitan Virginia J. Howard Suzanne E. Judd Elsayed Z. Soliman Alvaro Alonso

Background

Prolonged sedentarism has been identified as a distinct cardiovascular risk factor separate from physical activity (PA), but its impact on atrial fibrillation (AF) risk when replaced with PA is unclear.

Methods

We studied 5777 participants in the REGARDS cohort, excluding those with prevalent AF, missing data on AF incidence, and missing accelerometry. Sedentary behavior (SB) and PA were objectively measured via accelerometry between May 2009 and January 2013. Incident AF was identified during follow-up visit through electrocardiograms and by self-reported medical history between May 2013 to December 2016. SB was assessed as sedentary time per day and as a percentage of accelerometer wear time (excluding sleep). PA was categorized into light (LPA) and moderate to vigorous (MVPA), as well as the corresponding percentages of total wear time. Using logistic regressions, we applied isotemporal substitution to examine the effect of replacing 30-minute sedentary time or 1% of sedentary time per day with equivalent durations or percentages of each type of PA on AF risk, adjusting for demographic, clinical, and behavioral covariates.

Results

The study sample had an average age of 63 (SD 8.3) years, with 55% females, 45% males, 31% and 69% Black and White adults. On average, participants engaged in 686.5 (SD 116.1), 193 (SD 76.9), and 14.1 (SD 18.0) minutes of SB, LPA, and MVPA per day, with 486 AF cases identified. Substituting 30-min SB per day with MVPA was associated with decreased odds of AF (OR 0.79, 95% CI 0.62, 1.00) after adjustment for covariates, whereas LPA showed no association. Similarly, replacing 1% of sedentary time with MVPA was linked to decreased odds of AF (OR 0.93, 95% CI 0.87–1.00), but no association was observed for LPA.

Conclusion

Replacing SB with PA with moderate or higher intensity may decrease AF risk. These findings highlight the potential benefits of reducing sedentarism to lower AF burden, warranting validation in future studies.

Cardiovascular

Cost-Effectiveness Analysis of Statins, Berberine and Their Combined Use for Primary Prevention of Cardiovascular Disease Yuanqing Xia* Yuanqing Xia Jie V. Zhao Kathy Leung

Background: Statins are the cornerstone treatment for the primary prevention of cardiovascular disease (CVD), but intolerance and side effects can hinder adherence. Berberine, with promising lipid-lowering effects and good tolerance, presents a potential alternative for statin-intolerant patients. To estimate and compare the cost-effectiveness of statins, berberine, and their combined use for primary CVD prevention.

Methods: The Scottish CVD Policy Model was used to predict long-term health and cost outcomes in Scottish adults aged 40 years or older without pre-existing CVD. Intervention and cost inputs were sourced from published literature and health service cost data. The primary outcome measure was the lifetime incremental cost-effectiveness ratio (ICER), evaluated as cost per quality-adjusted life year (QALY) gained. The intervention strategies of no intervention, atorvastatin 20 mg per day ("statins"), berberine 1000 mg per day ("berberine"), simvastatin 20 mg plus berberine 1500 mg per day ("combined intervention 1") and simvastatin 20 mg plus berberine 900 mg per day ("combined intervention 2") were analyzed for individuals with ASSIGN risk scores ≥20% and ≥10%.

Results: All intervention strategies were cost-effective (statins: ICER £1,260.7/QALY, 95%CI: £-2,528.6/QALY ~ £2,305.5/QALY; berberine: ICER £6,192.4/QALY, 95%CI: £4,655.7/QALY ~ £11,387.0/QALY; combined intervention 1: ICER £5,506.5/QALY, 95%CI: £4,506.8/QALY ~ £10,732.0/QALY; combined intervention 2: ICER £3,846.4/QALY, 95%CI: £3,107.0/QALY ~ £5,270.1/QALY), compared to no intervention, at the threshold of ICER of £20,000 per QALY. Compared to statins, berberine was less cost-effective, but the combined interventions remained cost-effective (£10,198.6/QALY [95%CI: £6,740.4/QALY ~ £58,473.3/QALY]; £6,362.8/QALY [95%CI: £5,187.7/QALY ~ £12,499.2/QALY]) at the threshold of £20,000/QALY. Notably, when using drug costs from China (reflecting lower berberine prices), berberine and the combined interventions were preferable to statins alone.

Conclusions: Statins, berberine, and combined interventions are all cost-effective options for primary CVD prevention. Berberine could be considered a valuable alternative or complementary therapy, particularly if its price decreases below that of statins.

Cardiovascular

Relationship Between Body Mass Index and ADP MA (Maximum Amplitude) in Deep Vein Arterialization Patients Using TEG-PM Isabella Ferlini Cieri* Isabella Ferlini Cieri Adriana A. Rodriguez Alvarez1 Mounika Boya Leela Morená Shiv Sureshchandra Patel Andrea Nurko Anahita Dua

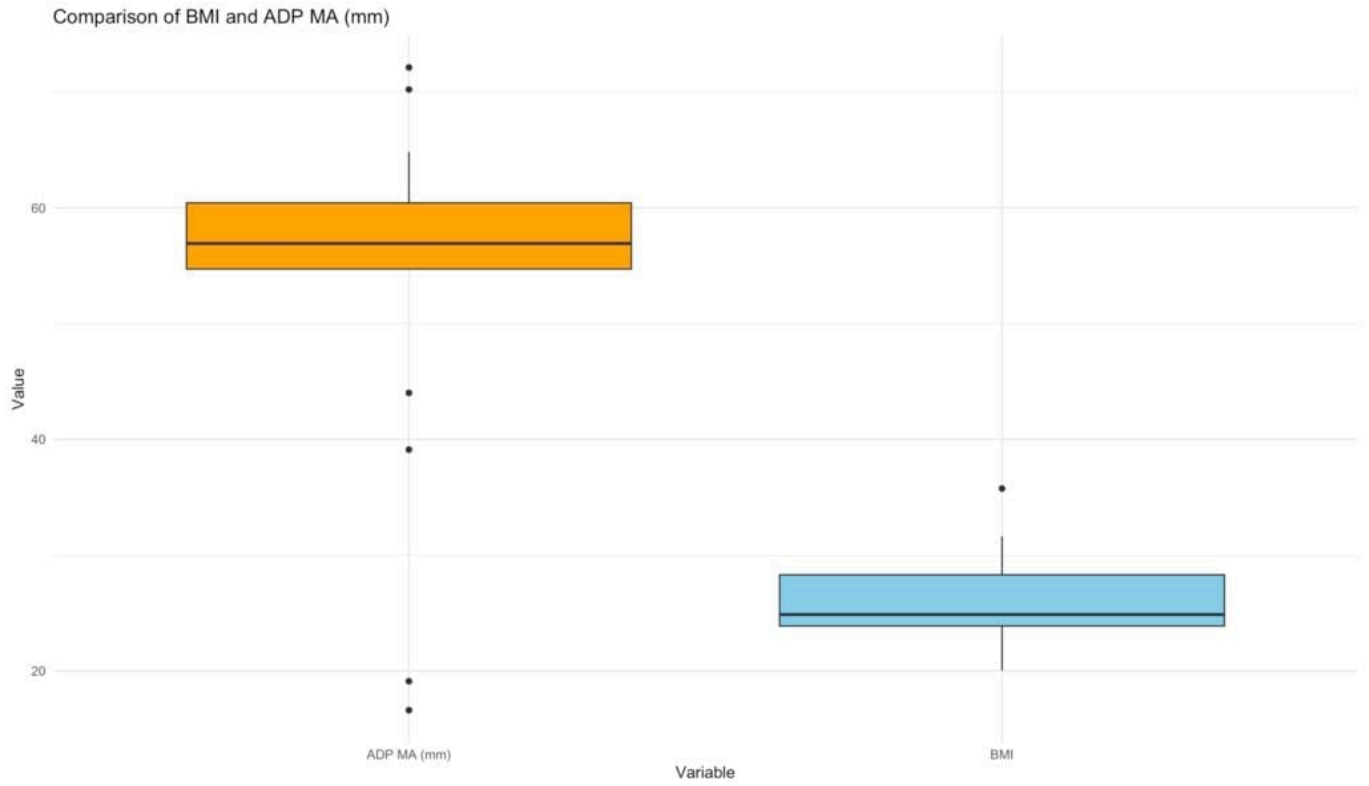
Background: Deep vein arterialization (DVA) represents an innovative therapeutic approach for patients with no-option critical limb-threatening ischemia and peripheral arterial disease (PAD). Understanding the complex relationship between patient characteristics and platelet function is crucial for optimizing procedural outcomes and reducing complications. Adenosine diphosphate maximum amplitude (ADP MA) measured by thromboelastography with platelet mapping (TEG-PM) is a key parameter that reflects the degree of platelet aggregation in response to ADP stimulation, providing valuable information about platelet reactivity. This study investigates the correlation between body mass index (BMI) and platelet function as measured by TEG-PM.

Methods: In a prospective single-center study of DVA patients (2020-2024), we conducted a detailed analysis of the correlation between BMI and ADP MA from TEG-PM measurements. Comprehensive descriptive statistics and Mann-Whitney test were performed to characterize the relationship between these parameters.

Results: Among 17 patients undergoing DVA procedures, BMI measurements (median 24.86 kg/m^2, IQR 23.09-28.40) and ADP MA values (median 56.90 mm, IQR 49.35-61.45) demonstrated significant variation. Statistical analysis revealed a strong and significant relationship between these parameters ($p<0.001$). The BMI measurements exhibited notably less variability (SD: 4.075) compared to ADP MA measurements (SD: 15.42), suggesting complex and multifaceted interactions between body mass and platelet function in this specialized patient population.

Conclusion: Our analysis reveals a significant relationship between BMI and TEG-PM parameters in DVA patients, potentially influencing perioperative assessment strategies. Further investigation in larger cohorts is warranted to validate these findings.

Keywords: Deep vein arterialization, thromboelastography, platelet mapping, body mass index, peripheral artery disease.


Comparison of BMI and ADP MA (mm)
60
40
20
Value
ADP MA (mm)
BMI
Variable

Cardiovascular

Association of Neighborhood Deprivation and Carotid Intima-Media Thickness in the Bogalusa Heart Study Cohort Jenilee Cueto* Jenilee Cueto Eunsun Gill Ileana De-Anda Duran Lydia Bazzano Alexander Kimbrough Shakira Suglia Maeve Wallace Emily Harville Kirsten Dorans

Introduction: Neighborhood deprivation, a measure of socioeconomic status, has been linked to cardiovascular and cardiometabolic diseases. The impact of neighborhood deprivation in rural areas and its association with subclinical cardiovascular disease is unclear.

Objective: To evaluate the association of neighborhood deprivation and carotid intima-media thickness (CIMT) among adults participating in the Bogalusa Heart Study (BHS).

Methods: Neighborhood deprivation was defined using the Area Deprivation Index (ADI), a factor-based deprivation index using 16 poverty, education, housing, and employment factors, and divided into quintiles. Two far-wall carotid intima-media measurements were obtained and averaged. Composite-CIMT was defined as the average of the segmental maximum CIMT. Participants with complete data (n=1104 after exclusions for missing data) were assessed for the association of their most recent ADI and CIMT in adulthood (measured 2013-2016) using linear regression, adjusting for age, sex, race, blood pressure, lipids, body mass index, smoking, alcohol use, employment, and education.

Results: The median age of the BHS cohort was 49 years (IQR 8.4). Fifty-eight percent were female, 36% were Black, and mean BMI was 31.3±7.7 kg/m2. Median CIMT was 0.87 (IQR 0.31). In the unadjusted model, mean CIMT significantly differed by ADI quintile (p=0.03). CIMT in the 4th quintile was 5% (95% CI -1 to 11%) higher compared to CIMT in the first quintile (p=0.07). In adjusted analyses, there was no association between ADI and CIMT and test for trend did not demonstrate linearity (p=0.4). Adjusted analyses stratified by age and race were also not significant.

Conclusion: There was no association between neighborhood deprivation and CIMT measured in midlife. Future research is needed to study the association of early-life ADI with CIMT and other markers of CVD risk.

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Cardiovascular

Racial and sex disparities in the association between stressful life events and cardiovascular disease Ugochinyere Vivian Ukah* Ugochinyere Vivian Ukah Nkasiobi Nwobi

Background: Racial disparities exist in the incidence of cardiovascular disease (CVD) with black women having a higher risk of CVD, compared with other racial groups. Stressful life event (SLE) is a risk factor for cardiovascular disease CVD. However, whether racial and sex difference exist in the relationship between SLEs and CVD risk is understudied.

Methods: We analyzed the US Go dataset, which integrates three harmonized cohorts of participants from the United States enrolled between 1948 and 2002: the Multi-Ethnic Study of Atherosclerosis (MESA), the Cardiovascular Health Study (CHS), and the Women's Health Initiative (WHI). SLEs were derived from study-specific questionnaires that captured the occurrence of traumatic events in the past year, such as the death of a loved one, divorce, and financial difficulties. We analyzed SLEs as a continuous stress variable, with a range of 0–1. We used Cox proportional hazards models to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for the association between SLEs and incident CVD or CVD-related mortality, adjusting for confounders. Participants were then stratified by race (White, Black) and sex (male, female).

Results: A total of 82,721 participants were included. The overall mean stress level was higher among Black participants (0.21 ± 0.18) compared to White participants (0.15 ± 0.13). SLEs were associated with an increased risk of CVD (HR 1.95, 95%CI 1.70–2.23). The association was similar across racial groups, with HRs of 1.88 (95%CI 1.39–2.54) for Black participants and 1.86 (95% CI 1.59–2.17) for White participants. Among females, SLEs were strongly associated with CVD risk (HR 2.35, 95%CI 2.01–2.75), and for both Black HR: 2.27 (1.56–3.31) and White (HR 2.14, 95%CI 1.80–2.54) females. In contrast, no associations were found among males (HR 1.13, 95%CI 0.86–1.50).

Conclusions: In our study, Black individuals were more likely to experience higher SLEs compared to White individuals and the risk of CVD was higher among females experiencing more SLEs. Our findings suggest that race and sex may contribute to a disproportionate risk of cardiovascular CVD among Black populations.

Cardiovascular

Association Between State-Level Policies and Stroke Mortality Kerri S Ivey* Kerri Ivey Gidarell Bryant Elizabeth Heitman Caroline Compretta Benjamin H Walker

Introduction: Despite the status of stroke as a top cause of death in the United States, notable state-level variations in stroke mortality are not well understood. Our study examines the impact of state policy, sociodemographic composition, and access to care on US stroke mortality from 2000-2019.

Methods: We merged annual state-level stroke mortality rates (per 100,000) from the National Center for Health Statistics from 2000 to 2019 with annual data on state-level policy variables. State policy variables included minimum wage, earned income tax credit, total number of economic and labor preemption laws, maximum monthly allotment of Food Stamp/SNAP benefits for 2-person family, an index of Medicaid generosity (including income eligibility, administrative burden, immigrant benefits, and Medicaid benefits), paid sick leave policies, tobacco tax, beer and wine tax, and total number of opioid-related laws. A linear fixed-effects regression was used to examine the association between state-level policies and stroke mortality.

Results: Our preliminary results show that increases in the following variables were associated with reductions in stroke mortality: state tobacco taxes (B = -3.13; 95% CI = -4.59, -1.67), total number of opioid-related laws (B = -1.28; 95% CI = -1.86, -.70), maximum monthly allotment of Food Stamp/SNAP benefits (B = -0.11; 95% CI = -0.14, -0.08), Medicaid generosity (B = -0.19; 95% CI = -0.37, -0.01), and the total number of economic and labor pre-emption laws (B = -1.24; 95% CI = -1.82, -0.67).

Conclusion: These results suggest the state-level policy context is associated with stroke mortality rates which underscores the potential for upstream economic and health policies to address geographic differences in stroke mortality. Additional analyses will explore the role of state sociodemographics and access to care variables to better understand these associations.

Cardiovascular

Agreement between parent and adolescent report of adolescent cardiovascular health behaviors: The Young Hearts Study Rachel Zmora* Rachel Zmora Yaojie Wang Lucia Catherine Petito Aashima Chopra Darci Phillips Ileah Rios Amy Yu Amanda M Perak Donald M Lloyd-Jones Sarah De Ferranti Holly Gooding Stephen Daniels Darwin Raymond Labarthe Matthew M. Davis Marc Brian Rosenman Rashmi Narayan Mark Pletcher Francis Alenghat Rupali Gandhi Cheryl Lefaiver Amanda Luff Huma Khan Brad Appelhans Karen Lui Rachel Caskey Norrina Allen

Background

Accurate assessment of cardiovascular health (CVH) behaviors among adolescents is critical to the study of the early origins of cardiovascular disease. However, the agreement between parents and adolescents when reporting CVH behaviors is poorly understood.

Methods

We compared self and parent reports of CVH behaviors among adolescent-parent dyads in the Young Hearts study, an ongoing diverse pediatric cohort study based in Chicago, IL. Adolescents aged 12-17 and their parents responded to identical questions about diet, physical activity, sleep, and screen utilization of the adolescent. As identical reporting is highly implausible and these variables are skewed, we examined the adolescent-parent agreement falling within the lowest quartile for each CVH behavior using Kappa statistics. The thresholds for the lowest quartile were defined within adolescents and parents, respectively.

Results

Of 589 included adolescents, 55.7% were female and 54.5% were non-Hispanic White, with an average age of 14.8 (SD 1.71) years. Agreement within adolescent-parent dyads varied by CVH behavior but overall was low (kappa range 0.282 – 0.565). Agreement was highest for infrequent weekly family dinners (kappa = 0.565, adolescent Q1 = 3, parent Q1 = 2). Agreement was lowest for daily average hours of sleep among those most lacking sleep (kappa = 0.282, adolescent Q1 = 7.9, parent Q1 = 8.3). Agreement was also low for low levels of screentime (daily average kappa = 0.290) and low levels of weekly physical activity (kappa = 0.297).

Conclusion

Agreement between parents and adolescents regarding adolescent CVH behaviors ranged from poor to moderate, suggesting that misclassification within low or high-risk categories may occur. This work emphasizes the need for improved approaches to self-report of CVH behaviors as well as objective assessment of CVH behaviors among adolescents.

CVH Behaviors	Adolescent Q1	Parent Q1	kappa	95% CI
Physical Activity, Sleep, & Screen Time				
Physical activity, weekly	3	3	0.297	0.211, 0.382
Sleep, daily average	7.9	8.3	0.282	0.197, 0.367
Screentime, daily average	3	2	0.290	0.215, 0.373
Screentime, chatting	0.5	0.5	0.369	0.292, 0.445
Screentime, games	0.5	0.5	0.424	0.348, 0.500
Screentime, tv	0.5	0.5	0.395	0.314, 0.476
Diet				
Fruit, servings	2	2	0.518	0.444, 0.592
Veggies, servings	2	2	0.491	0.420, 0.561
Soda, frequency	2	2	0.444	0.371, 0.518
Fast food, frequency	2	2	0.500	0.430, 0.570
Salty foods, frequency	3	3	0.380	0.304, 0.456
Sweets, frequency	3	3	0.405	0.330, 0.480
Snacks, frequency	2	2	0.385	0.308, 0.462
Family Behaviors				
Meals at home, weekly	3	3	0.461	0.315, 0.607
Dinner with family, weekly	4	4	0.565	0.495, 0.636
Dinner with screen, weekly	0	0	0.553	0.486, 0.621
Q1 = Lowest quartile				

LATEBREAKER

Cardiovascular

The Moderating Role of Physical Activity on the Association Between Waist Circumference and Heart Failure: The Jackson Heart Study Garrett Jordan* Garrett Jordan Benjamin Walker Abigail Gamble Elizabeth Heitman Michael Hall Wondwosen Yimer

Introduction: Heart failure (HF) affects 6.2 million adults in the United States, posing a significant public health challenge. Waist circumference (WC) is a known risk factor for HF, while moderate-to-vigorous physical activity (MVPA) may mitigate this risk. This study examined the association of WC with incident HF hospitalization (HFH) and whether MVPA moderates this relationship in the Jackson Heart Study (JHS).

Methods: Our preliminary analysis used JHS data to examine the association of WC (continuous, cm) and incidence of HFH. Self-reported MVPA was categorized as poor (0 minutes/week), intermediate (1-149 minutes/week), and ideal (150 minutes/week). Descriptive statistics were used for demographic characteristics and distributions of WC, MVPA, and covariates (e.g. sedentary behavior, diabetes). Cox proportional hazards models were used to examine the association between WC and the incidence of HFH and whether this association was moderated by MVPA.

Results: Among 3,397 participants (median follow-up: 12.0 years), 280 HFH events occurred. The median WC was 103 cm (IQR: 96–111 cm) for men and 98 cm (IQR: 89–106 cm) for women. Higher WC was associated with increased HFH risk (hazard ratio [HR] per cm = 1.013, 95% CI: 1.005, 1.023). MVPA was not independently associated with HFH after adjustment for covariates. Interaction terms for intermediate (HR = 1.01, 95% CI: 0.99, 1.03) and ideal MVPA levels (HR = 1.01, 95% CI: 0.99, 1.04) with WC suggest no effect modification.

Conclusions: Higher WC is associated with increased HFH risk, independent of MVPA. MVPA alone may not sufficiently mitigate HF risk, particularly among individuals with abdominal obesity. Additional analyses will explore restricted cubic splines for WC and time-varying covariates to better understand these relationships.

LATEBREAKER

Cardiovascular

Sexual violence and risk of hypertension in the Black Women's Health Study Lulu Zhang* Lulu Zhang Sarah M. Rothbard Alexandra Hillcoat Shakira F. Suglia Julie R. Palmer Yvette C. Cozier Karestan C. Koenen Rebecca B. Lawn

Hypertension (HTN) is a significant public health concern in the U.S., accounting for one-third of incident cardiovascular disease in Black adults. Prior work has provided evidence of an association of sexual violence with an increased risk of HTN in women. Although Black women experience a greater burden of both sexual violence and HTN than their White counterparts, the association between the two in Black women remains less clear. We investigated whether exposure to sexual violence predicted incident HTN over 14 years of follow-up using data from the Black Women's Health Study. Our sample included 22,213 women with no history of HTN as of 2005, when questions on sexual violence history were asked. Participants' mean age in 2005 was 45.8 years (SD = 9.4 years). Sexual violence history was defined as a binary variable capturing any reported experience of assault or seeing someone expose their genitals in childhood, adolescence, or adulthood. In 2005, 9,383 (42.2%) participants reported a history of sexual violence. Women who self-reported physician-diagnosed HTN with the use of either antihypertensive medications or diuretics on a biennial questionnaire were considered an incident case in the year of diagnosis. Between 2005 and 2019, there were 9,052 (40.8%) incident cases of HTN. Results from Cox proportional hazards models, stratified by age and study period and adjusted for parental education, parental history of heart attack, and parental history of stroke, revealed no clear association between any sexual violence history and HTN (Hazard Ratio: 0.99; 95% CI [0.95, 1.04]). In subsequent analyses, we will investigate whether this association varies according to the timing of sexual violence or across key sociodemographic factors.

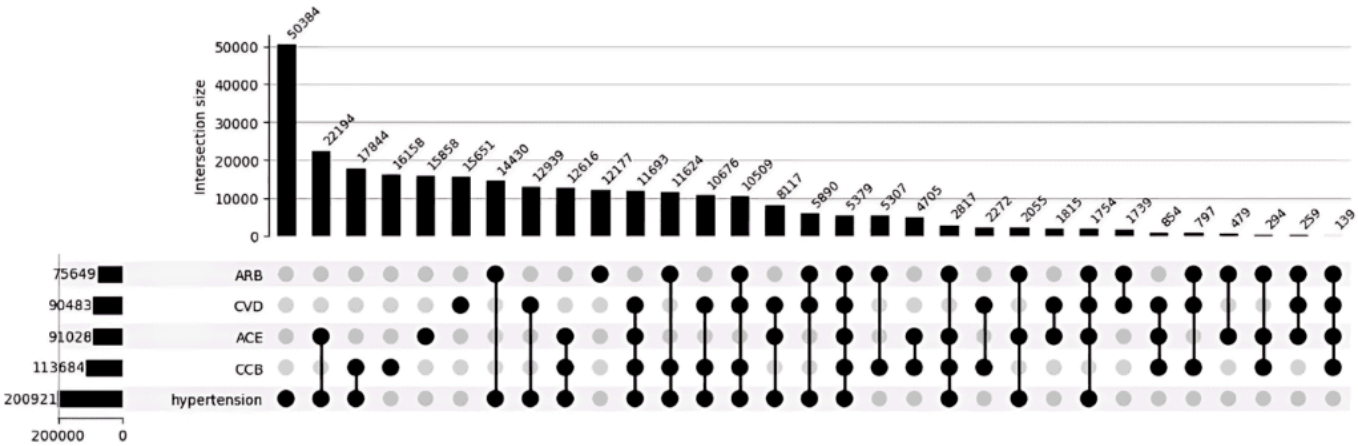
LATEBREAKER

Cardiovascular

Analyzing clinical trajectories of patients with hypertension and/or cardiovascular disease diagnoses and/or antihypertensive drug prescriptions using data from electronic health records Vaishnavi Jahagirdar* Vaishnavi Jahagirdar Marie-Laure Charpignon Mike Hogarth

Hypertension (HTN) is a leading global health concern, affecting ~1.28 billion adults and contributing to 702800+ annual deaths as the primary risk factor for cardiovascular disease (CVD). While established treatment guidelines recommending ACE inhibitors (ACEi), Angiotensin receptor blockers (ARB), and Calcium channel blockers (CCB) as first-line therapies, real-world prescription patterns and their clinical impacts remain insufficiently explored. This study analyzes patient trajectories by characterizing prescription and disease sequences in electronic health records (EHR) using graph representations.

Using the University of California San Diego EHR, we analyzed a cohort of 279425 people with at least one diagnosis of HTN/CVD/ACEi/ARB/CCB prescription. Overall, 72% had a history of HTN, and 32% had a history of CVD. First, we considered the unordered set of diseases and drug prescriptions (eg, HTN and CVD and ACEi) that ever appeared in each patient's EHR. We identified 31 unique patient groups. Some prominent results are- Patients with HTN only (18%), with HTN and CVD only (4%), with HTN and CVD with at least a drug prescription (19%). In contrast, patients with only CVD diagnosis accounted for 5%. Next, we analyzed the time-ordered sequence of events (e.g., HTN diagnosis followed by CVD diagnosis) and whether prescriptions occurred on the same date. Overall, 993 unique sequences ranging in length from 1 to 5 were identified. The most common two-event sequence was an ACEi prescription followed by an HTN diagnosis, while the most common three-event sequence was CVD, HTN (on the same date), followed by a CCB prescription. Ongoing work focuses on calibrating a multistate model to accurately estimate transition rates between events, enabling a deeper understanding of event progression. Future research will investigate sex-specific patterns and the comparative effectiveness of different HTN treatment strategies on CVD risk mitigation.



LATEBREAKER

Causal Inference

Association of polygenic risk score for habitual alcohol intake with all-cause mortality

Yingxi Chen* Yingxi Chen Xiaoyu Wang Haoyu Zhang Christian Abnet

Background

Genomically predicted behaviors may provide novel insight into factors that influence mortality risk with minimal concerns about confounding. We aimed to investigate the association between the polygenic risk score (PRS) for habitual alcohol intake and all-cause mortality.

Method

We constructed a PRS for lifetime habitual alcohol intake using published single-nucleotide variants associated with Alcohol Use Disorder Identification Test-Consumption score from 274,424 subjects in a multi-ancestry Million Veteran Program, and applied it to 108,796 participants from the Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial. Participants had detailed baseline data and up to 28 years of follow-up. We used Cox regression models with age as the time scale to evaluate the association between PRS and all-cause mortality. Additionally, we used linear regression to examine the correlation between PRS and self-reported alcohol consumption to inform the predictive power of the score. Analysis was conducted in R version 4.3.1.

Results

The PRS showed a significant correlation with self-reported alcohol consumption, with each one-standard-deviation increase in PRS associated with an additional 0.80g increase in self-reported daily pure alcohol consumption (beta=0.80, 95%CI=0.59-1.01, p=4.4×10–14). Additionally, we found that a one-standard-deviation increase in PRS was associated with a 4% higher risk of all-cause mortality (Hazard Ratio=1.04, 95%CI=1.03-1.05, p=5.0 ×10–13). The mortality risk increased by 6% when comparing the highest and lowest PRS quartiles (HR=1.06, 95%CI=1.03–1.08, p=1.3 ×10–4).

Conclusion

A higher genetic predisposition to habitual alcohol intake, as captured by PRS, is significantly associated with increased all-cause mortality in the PLCO study, supporting a potential causal link between genomically predicted alcohol consumption and mortality risk.

Causal Inference

Frailty and adverse surgical outcomes: exploring the mediating pathway through Enhanced Recovery After Surgery protocols Sophia Fuller* Sophia Fuller Anlan Cao Sidney Le Elizabeth Cespedes Feliciano

Complications of surgery in frail adults are common and costly; perioperative care pathways such as Enhanced Recovery After Surgery (ERAS) protocols are designed to improve outcomes for patients after surgery. However, adherence to ERAS protocols is low and the extent to which achievement of ERAS milestones, such as early ambulation, can improve outcomes for frail patients is unclear. Causal mediation analysis can help clarify whether additional interventions should be mounted to support these patients in adhering to ERAS protocols. A cohort of 11,115 patients who had abdominal surgery between 2015 and 2020 at Kaiser Permanente were evaluated using the Hospital Frailty Risk Score and categorized as frail or non-frail. We modeled the causal relationship between frailty and 30-day morbidity, defined as mortality and major surgical complications, mediated by early ambulation. Among the 23% of patients classified as frail, 42% achieved ambulation within 12 hours of surgery compared to 65% of non-frail patients. We found that, had all patients been frail, morbidity would have been 15.3% (95%CI: 13.4% to 17.2%) higher than had all patients been non-frail. Most of the total effect is explained by the direct effect of frailty on 30-day morbidity (13.8%; 95%CI: 11.9% to 15.7%), however, the average causal mediation effect among frail and non-frail patients differed slightly. Had all patients been frail, there is a slight decrease in morbidity (-1.9%; 95%CI: -2.4% to -1.5%) if patients had been set to achieve early ambulation under what it would have been for non-frail patients than for frail patients. If all patients had been set to non-frail, this decrease is 1.1% (95%CI: -1.4% to -0.01%). This indicates a small benefit to patients, with more improvement among frail patients, of early ambulation. Using a causal mediation framework, we were able to quantify the relationship between frailty, early ambulation, and morbidity to understand additional benefit to frail patients.

Causal Inference

Survivorship as a source of confounding, selection bias and effect modification C Mary Schooling* C Mary Schooling Yang Guoyi

Background: Survivorship, i.e., the state or condition of being a survivor, is a source of confounding, selection bias and effect modification that is often overlooked. Here, we describe how it can occur and when it can be averted.

Methods: Directed acyclic graphs were used to illustrate how survivorship could cause confounding and selection bias. Selection diagrams were used to illustrate how survivorship could cause effect modification by factors such as age or health status.

Results: Survivorship can be a confounder that biases towards favouring the exposure when exposure allocation starts or changes after recruitment. Survivorship can be a source of type 1 selection bias that attenuates or reverses estimates, when the exposure and the outcome, or the exposure and a competing risk of the outcome, affect survivorship before recruitment. Survivorship can be a source of type 2 selection bias when survivorship is an effect modifier. Confounding and selection bias by survivorship can largely be averted by ensuring exposure allocation is determined at recruitment. Given, survivorship is usually most relevant to older or sicker groups, bias from survivorship may be evident as associations which attenuate or reverse with advancing age or poorer health status.

Conclusions: Confounding by survivorship should be considered when exposure allocation starts or changes after recruitment. Type 1 selection bias from survivorship should be considered when the exposure starts before recruitment, and type 2 selection bias when survivorship is an effect modifier. Given, long-term exposures are often of interest, and confounding as well as selection bias are difficult to address, study designs less open to these biases might be preferable.

Causal Inference

The use of Mendelian randomization to explore the causal consequences of childhood maltreatment: consideration of assumptions and challenges Ka Kei Sum* Ka Kei Sum Amanda Hughes Alexandra Havdahl Laura Howe

Mendelian randomization (MR) uses genetic variants as instrumental variables to enhance causal inference. Studies have identified genetic variants related to childhood maltreatment, but interpreting the effects of these variants or assessing the plausibility of MR assumptions is complex. We aim to investigate the feasibility of applying MR to complex social traits using the association between childhood maltreatment and mental health and behavioral outcomes as an example. We explore four potential key concerns: confounding by population phenomena, horizontal pleiotropy, reverse causality, and selection. For each concern, we demonstrate scenarios where MR studies of childhood maltreatment may be biased using DAGs and critical appraisal of previous MR analyses. For confounding by population phenomena, we further perform within-family genetic analyses in 42,101 parent-offspring trios from the Norwegian Mother, Father and Child Cohort Study (MoBa) to address bias due to family-level processes. Our results showed same-trait shrinkage (11% attenuation of the association between children's polygenic risk scores of childhood maltreatment (PRSCM) and mothers' report of children's physical abuse) but not cross-trait shrinkage (children's PRSCM and children's mental health and behavioral outcomes) after adjusting for parental PRSCM. The lack of cross-trait shrinkage suggests that genetic variants related to child maltreatment may be capturing other child-level phenotypes, after adjusting for family-level processes. Mothers' PRSCM were also associated with mothers' own maltreatment experiences in childhood and adulthood with similar magnitudes, suggesting these genetic effects are not specific to childhood maltreatment. Due to the complexity involved in the causal chain of childhood maltreatment, the interpretation of MR studies for childhood maltreatment is challenging. Other causal approaches should be considered for observational studies of complex social traits.

Causal Inference

Paraquat exposure and Parkinson's Disease: A meta-analysis stratifying by decade of publication, study design, and adjustment for history of head injury Tony Cappello* Tony Cappello Alex Riordan Elizabeth Best Hannah Mazzotta

We conducted a preliminary literature review and meta-analysis of studies that examined the risk of Parkinson's Disease among persons exposed to paraquat, including residential and occupational settings. Our systematic literature search in PubMed identified 25 published papers that were considered for meta-analyses. Pooled risk estimates or meta-relative risks (meta-RR) were calculated using random effects models, stratifying by overall risk, decade of publication, study design, and adjustment for history of head injury. The overall preliminary meta-RR for Parkinson's disease was 1.37 (95% CI: 1.21-1.66). For the decade of publication, meta-RRs were only elevated at a level of statistical significance for the earliest decade (1990s) compared to the later decades (2000s, 2010s, and 2020s), reflective of study quality improvement over time. For study design, meta-RRs were only elevated at a level of statistical significance for case-control studies, compared to cohort studies which did not reach statistical significance. When adjusted for history of head injury, the meta-RR was 1.22 (95% CI: 0.74- 2.02) and did not reach a level of statistical significance. Based on this analysis, there is consistent evidence to suggest that exposure to paraquat is not associated with an increased risk of Parkinson's Disease.

COVID-19 Pandemic

Freezing data to increase efficiency within the COVID-19 program in Tennessee. Magdalena Dorvil-Joanem* Chaitra Subramanya Jennifer Jain Sarah Waldo Vanessa Davis Kelly Squires Jane Yackley

BACKGROUND: The COVID-19 program's continuously increasing data needs for both public dissemination and internal usage lead to a significant surge in data processing in SAS, affecting its performance and causing low resource errors. Long processing times also negatively impacted the staff who run these codes. Therefore, program staff implemented a data freeze for the years 2020 and 2021 to reduce staff and resource burden and to preserve data integrity, with the added benefit of reproducibility.
METHODS: All reported cases of COVID-19 in Tennessee are recorded in the National Electronic Disease Surveillance System (NEDSS) Base System (NBS). Tables and linelists summarizing years 2020 and 2021 by cases, hospitalizations, deaths, and labs were frozen using SAS. Three codes were utilized to separate and later merge the large dataset. The first code froze 2020 and 2021 data for cases, deaths, hospitalizations, and labs, and exported output tables and linelists. The second exported the data from 2022-current. The third merged the frozen 2020 and 2021 data with the 2022-current data. The final exports were stored on a secure server.
RESULTS: Efficiency concerns were mitigated following the data freeze, which substantially decreased the volume of data requiring processing. The program's completion time dropped from 2.5 hours to 1.2 hours, reducing staff time spent running codes.
CONCLUSIONS: Freezing COVID-19 data by year reduced the burden on both technical and human resources and improved the program's efficiency.

COVID-19 Pandemic

The impact of SARS-CoV-2 on fatigue and quality of life: prevalence of post COVID-19 condition in a Dutch population-based serosurveillance cohort in the first year of the pandemic. Cheyenne van Hagen* Cheyenne van Hagen Elizabeth N. Mutubuki Siméon de Bruijn Eric R.A. Vos Gerco den Hartog Fiona R.M. van der Klis Cees C. van den Wijngaard Hester E. de Melker Albert Jan van Hoek

We studied Post COVID-19 Condition (PCC) by investigating health-related quality of life (HRQoL) and fatigue in the general Dutch population in the early phase of the pandemic, including symptomatic and asymptomatic infections.

Participants aged ≥15 years were selected from the February 2021 round of the nationwide seroepidemiological PIENTER Corona cohort study. We assessed associations between the time since serologically-identified SARS-CoV-2 infection and four outcome measures: health utility (Short-Form 6 Dimensions), mental health and physical health (Short Form Health Survey 12) and fatigue (Checklist Individual Strength subscale fatigue). Per outcome, cutoff points were selected at each 5% increment (5-75%) along the cumulative distribution of those uninfected. At each cutoff, multivariable logistic regression models (score below cutoff yes/no) were fitted adjusted for infection history, age, sex, education level, comorbidities, COVID-19 vaccination, and restriction intensity.

At the cutoff of the lowest 15th percentile among uninfected, an example of the lower ends of cumulative distributions, significant differences between uninfected (n=4,614) and infected ≤4 months ago (n=368) were observed for health utility (OR [95%CI]: 1.6 [1.2-2.2]), physical health (1.7 [1.3-2.3]) and fatigue (1.6 [1.2-2.0]), but not for mental health (1.2 [0.9-1.6]) (Figure 1). There were no significant differences between uninfected and infected >4 months ago (n=345) for all outcomes at any cutoff, with post-hoc analysis showing a power to detect prevalence differences as low as 7.5%.

In the first year of the pandemic, individuals with a SARS-CoV-2 infection ≤4 months ago reported poor health utility and physical health, and more severe fatigue compared to those uninfected. Interestingly, differences in HRQoL and fatigue remained below the detection limit for those infected >4 months ago, suggesting a lower population PCC prevalence than currently found in literature for this period.

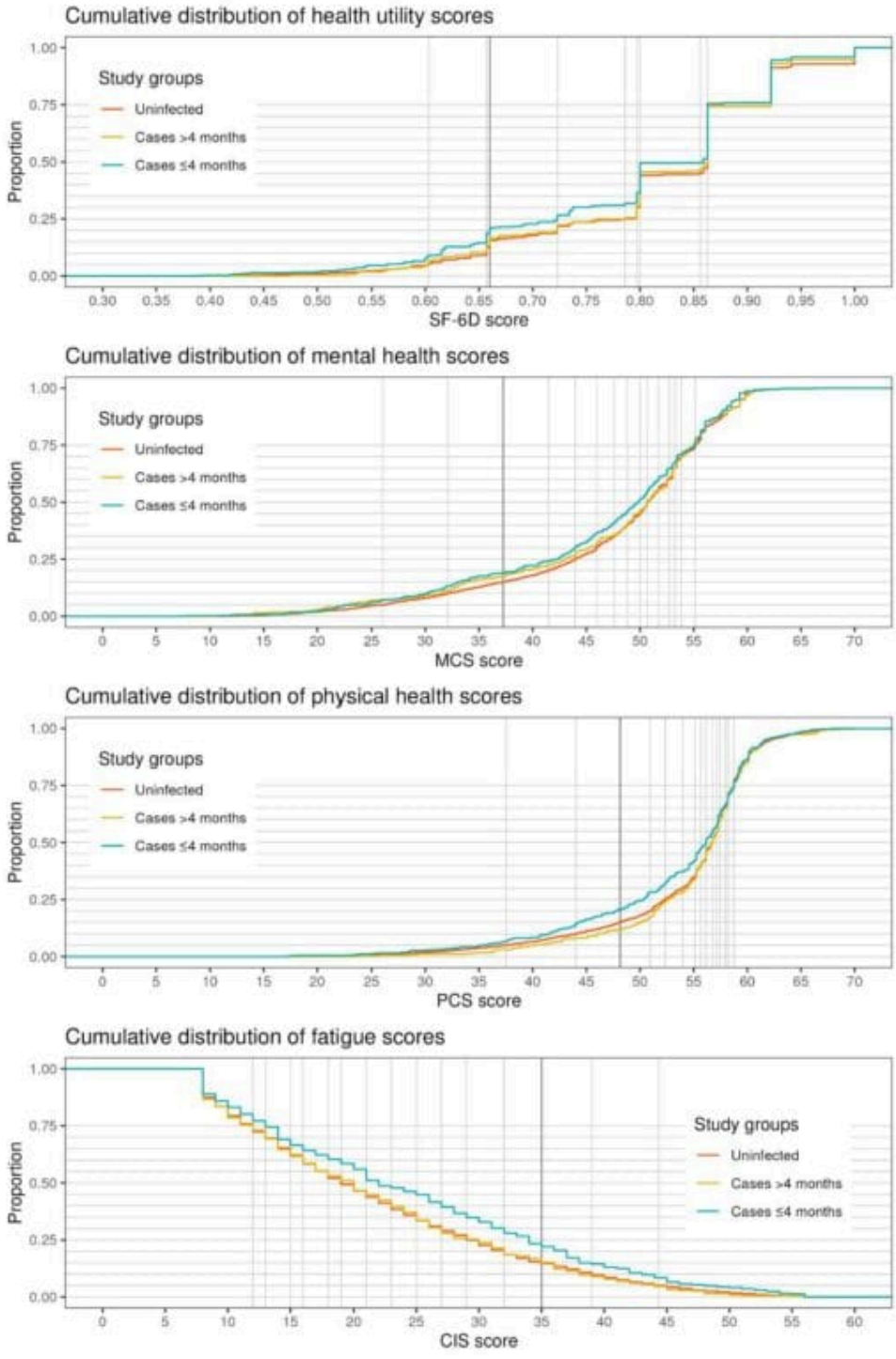


Figure 1: Cumulative distributions of outcomes (health utility, mental health, physical health and fatigue) per study group. Each 5% increment (5-75%) along the cumulative distribution of the uninfected is marked with a grey bar. The 15% point of the distribution is marked with a dark grey bar. Since higher CIS scores indicate worse outcomes (as opposed to SF-6D, MCS and PCS scores), the cumulative distribution of the CIS scale was inverted for comparability.

COVID-19 Pandemic

Nirmatrelvir-ritonavir (Paxlovid) Initiation Timing and Completion During Acute COVID-19

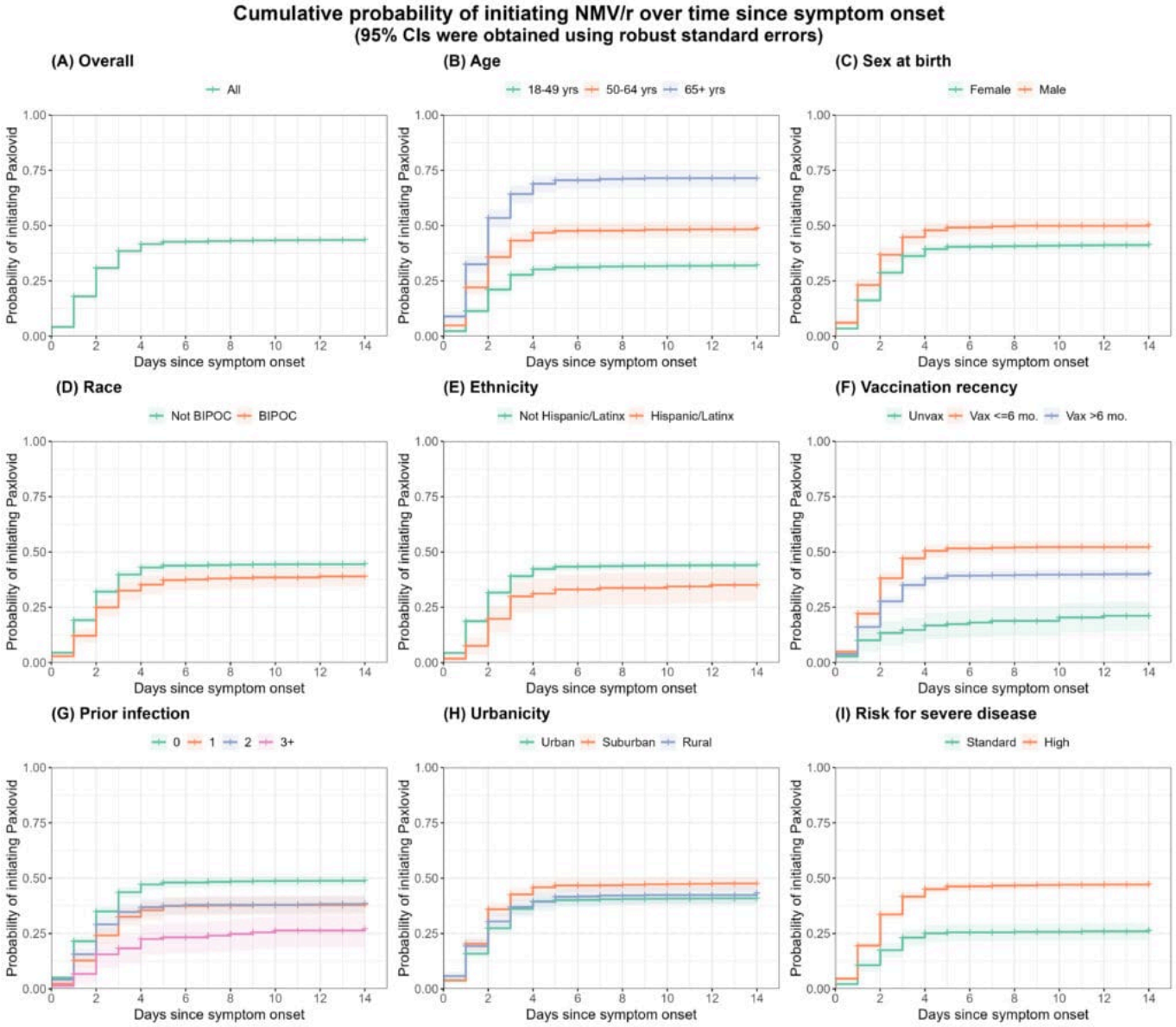
Ning Zhang* Ning Zhang Jessie K. Edwards Katie R. Mollan Stephen R. Cole Justin Lessler Bonnie E. Shook-Sa William A. Fischer David A. Wohl

Background The oral antiviral Nirmatrelvir-ritonavir (Paxlovid, NMV/r) is effective in treating COVID-19 when initiated within 5 days of symptom onset and continued for 5 days in high-risk individuals, but the real-world timing of NMV/r initiation and discontinuation have not been well described.

Methods Within a large prospective, observational study of people in North Carolina with acute COVID-19, we characterized patterns in NMV/r use among symptomatic individuals who tested positive for SARS-CoV-2 within 7 days of study entry between October 2022 and March 2024. We presented the probability of initiating NMV/r from 0 to 14 days after symptom onset and the probability of remaining on NMV/r at 0 to 6 days after initiation, using inverse probability censoring weighted Kaplan-Meier curves. Analyses were conducted overall and stratified by age, sex at birth, self-reported race, ethnicity, vaccination recency, prior infection(s), residential urbanicity, and risk for progression to severe disease. The average time to NMV/r initiation and discontinuation were reported by individual characteristics.

Results Among 3,141 symptomatic participants, the median age was 47 (IQR: 35, 61); 39% received their last SARS-CoV-2 vaccine within the prior 6 months, and 57% were experiencing their first known infection. The estimated probability of initiating NMV/r within 5 days of symptom onset was 0.43 (95% CI: 0.41, 0.44). Participants less likely to initiate NMV/r within 5 days included those who were younger (<65 years of age), female, non-white, Hispanic/Latinx, unvaccinated, or had 3+ prior infections (Figure). Among the 1,243 NMV/r recipients, 7.9% did not complete treatment, and the estimated probability of taking >6 days to finish the full course was 0.10 (95% CI: 0.08, 0.12). The probability of premature discontinuation was similar across groups defined by baseline covariates.

Conclusions Unvaccinated and historically marginalized groups were associated with lower NMV/r use.


Cumulative probability of initiating NMV/r over time since symptom onset
(95% CIs were obtained using robust standard errors)
(A) Overall
All
(B) Age
18-49 yrs
50-64 yrs
65+ yrs
(C) Sex at birth
Female
Male
(D) Race
Not BIPOC
BIPOC
(E) Ethnicity
Not Hispanic/Latinx
Hispanic/Latinx
(F) Vaccination recency
Unvax
Vax <=6 mo.
Vax >6 mo.
(G) Prior infection
0
1
2
3+
(H) Urbanicity
Urban
Suburban
Rural
(I) Risk for severe disease
Standard
High
Probability of initiating Paxlovid
Days since symptom onset

LATEBREAKER

COVID-19 Pandemic

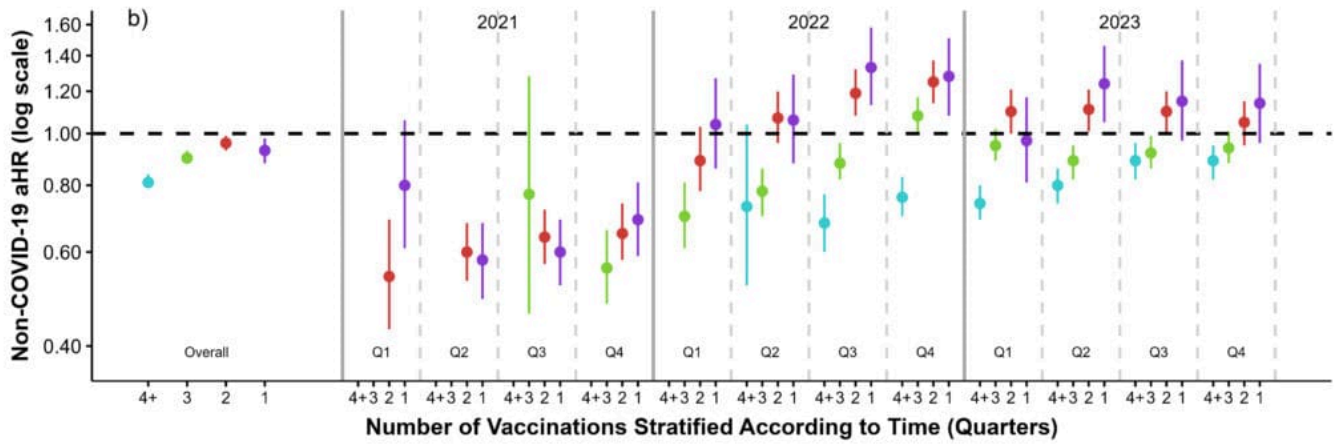
Estimates of underlying health biases in SARS-CoV-2 vaccination recipients: a nationwide study in previously-infected adults Uwe Riedmann* Uwe Riedmann Alena Chalupka Lukas Richter Dirk Werber Martin Sprenger Peter Willeit Marc Rijksen Julia Lodron Tracy Beth Høeg John PA Ioannidis Stefan Pilz

Background: Observational studies may over- or under-estimate SARS-CoV-2 vaccine effectiveness (VE) depending on whether healthier (i.e. healthy vaccine effect (HVE)) or more ill individuals are preferentially vaccinated. To evaluate this issue, we compared non-COVID-19, all-cause, cancer and COVID-19 mortality in vaccinated versus unvaccinated individuals.

Methods: This is a nationwide retrospective observational study in the entire adult population in Austria with previously documented SARS-CoV-2 infection with a follow-up from 2021 to 2023. Cox regression analyses were used to calculate hazard ratios (HRs) according to the number of SARS-CoV-2 vaccinations. We also performed matched analyses, where on each day, newly vaccinated individuals were matched with unvaccinated individuals based on age, sex and nursing home residency.

Results: Overall, 4,324,485 individuals (median age (IQR): 46 (33-59) years; 52.56% female) were eligible and 2.23 non-COVID-19 deaths occurred per 100,000 person days. Group differences in non-COVID-19 mortality risk were most prominent in the early periods (e.g., in Q4 2021, adjusted HRs (95% CI) in vaccinated versus unvaccinated were 0.69 (0.59 – 0.81), 0.65 (0.58 – 0.74), and 0.56 (0.48 – 0.66) for 1-, 2-, and 3-vaccinations, respectively) and decreased thereafter. Matched analyses for the first two weeks after vaccination showed HRs below 0.5 for vaccinated versus unvaccinated individuals irrespective of vaccination numbers. Similar findings were retrieved for non-COVID-19, all-cause, and cancer deaths. Overall, COVID-19 deaths were significantly reduced in vaccinated individuals.

Conclusions: HVE for SARS-CoV-2 vaccines was strong early after vaccination and diminished over time. HVE should be considered when estimating VE.



LATEBREAKER

COVID-19 Pandemic

COVID-19 and new-onset autoimmune mediated gastrointestinal illness: a database cohort study conducted in England Michael Hawkings* Michael Hawkings Dan Hungerford Iain Buchan Alex Elliot David Hughes

Since the emergence of SARS-CoV-2 in 2019, there is growing interest in whether individuals previously infected are at an increased risk of autoimmune disease, including coeliac disease (CD) and inflammatory bowel disease (IBD). We conducted a database cohort study using routinely collected healthcare data in England to investigate the associations between COVID-19 illness and incident CD and IBD. Patients with a COVID-19 test result between 01 March 2020 – 01 March 2022 were eligible, with test-negative patients allocated to a control cohort and follow up data available to 30 September 2024. Our primary outcomes were a diagnosis of CD and IBD, and we also explored vaccination as a time-varying covariate in addition to hospitalisation. We developed a propensity score model including the variables of smoking status, comorbidity score, ethnicity and deprivation index. This was used to weigh participants in a multivariate Cox model, with age and sex being explored within the model. 702,926 participants were included, with 463,178 and 237,352 being allocated to our test-negative and positive cohorts respectively. Preliminary results identified an increased risk for incident IBD in hospitalised COVID-19 patients when adjusted for age (aHR 14.29 [95% CI: 4.33 – 47.15]), however did not observe any effect for CD (aHR 4.41 [95% CI: 0.44 – 43.84]). We did not identify any association between SARS-CoV-2 exposure and incident CD (aHR 0.977 [95% CI: 0.821-1.162]) or incident IBD (aHR 1.037 [95% CI: 0.903-1.190]) in cases not requiring hospital admission. We also identified a protective effect against incident IBD in SARS-CoV-2 vaccinated patients, with a modest dose-response effect (first dose aHR 0.772 [95% CI: 0.657-0.907]; second dose aHR 0.770 [95% CI: 0.642-0.924]; and third dose aHR 0.702 [95% CI: 0.534-0.922]). Our study shows promise for SARS-CoV-2 vaccination modulating the inflammation hypothesised to trigger IBD.

COVID-19 Pandemic

Factors associated with changes in perceived importance of COVID-19 vaccination: Insights from a longitudinal survey in Japan Shuko Takahashi* Shuko Takahashi Satoru Kanda Haruki Shimoda Kozo Tanno Masaru Nohara

Background: There has been no study on the predictors of changes in people's perceived importance of COVID-19 vaccination. This study aimed to identify factors associated with the changes in vaccination perception during the late phase of the COVID-19 pandemic in Japan.

Methods: Serial cross-sectional data were collected via online surveys of residents in Iwate Prefecture in October in 2021 (baseline) and December in 2023 (follow-up survey, n=4,091). Respondents rated the perceived importance of vaccination through self-reported questions, which were categorized into high or low levels in each survey. Based on changes in levels of perception, four trajectories were defined: remaining at a high level, decreasing to a low level, improving to a high level, or persisting at a low level. Logistic regression models were used to identify factors associated with these trajectories.

Results: Of those with a high perceived importance of vaccination at baseline, 31.6% shifted to the low-level group at follow-up. In contrast, 85.3% of those in the low-level group at baseline remained in this category. Individuals who contracted COVID-19 after the baseline survey were significantly more likely to show a decreased perception of vaccination importance (OR [CI], 1.40 [1.15–1.71]; P <0.001). Additionally, while individuals with a history of long COVID tended to be persistent low-level group (OR, 0.20 [0.04–1.01]), those currently experiencing long COVID symptoms were strongly associated with persistence in the low-level group (OR, 10.79 [1.21–96.14]).

Conclusion: Policymakers should carefully design vaccination programs, taking into account evolving COVID-19 dynamics and the ongoing impacts of long COVID.

COVID-19 Pandemic

The Relationship Between Disordered Eating Behaviors and the Pandemic Among Undergraduate Students: A Systematic Review Bridget Murphy Hussain* Bridget Hussain Meredith Hannigan Aletha Huckins Mackenzie Gordon Danielle Conklin Audrey Beauvais

Background: Undergraduate students are vulnerable to social, emotional, physical, and financial stressors that increase risk for disordered eating behaviors. The impact of the COVID-19 pandemic on disordered eating is not fully understood, particularly as campuses reconcile the long-term impacts on students who may have missed critical developmental milestones due to the pandemic. This study sought to review observational studies evaluating disordered eating among undergraduate students during and after the pandemic.

Methods: Seven databases were searched through August 2024. Observational studies that included terms to capture disordered eating (bulimia nervosa, anorexia nervosa, and binge eating disorder) and COVID-19 (coronavirus) among undergraduates in the United States were reviewed. The search strategy was developed with an interdisciplinary team and conducted by two authors.

Results: Of 20 articles that evaluated the effects of COVID-19 on disordered eating, seven met inclusion criteria. All studies were cross-sectional, with four including data from repeated surveys among different groups. Overall, studies found a higher prevalence of anxiety and depression reported among students during COVID-19 than pre-pandemic, which was associated with more disordered eating behaviors, particularly higher caloric intake characteristic of binge eating disorder and bulimia nervosa. Studies reported the mediating effects of social media use and impact of perceived social connectivity.

Conclusions: Studies suggest a relationship between COVID-19 and disordered eating patterns, which is worsened by higher social media use, lower tolerance of uncertainty, and maladaptive stress management during the pandemic. Individuals who were undergraduate students during the pandemic and impacted by these behavioral coping mechanisms should be followed longitudinally and monitored for increased risk for long-term morbidity and mortality associated with eating disorders.

COVID-19 Pandemic

Small Area Estimation of County-Level COVID-19 Cases by Incorporating Social Determinants of Health and Spatial Correlation Kathryn Shea* Kathryn Shea J. Sunil Rao Lorena Garcia Lorena Garcia Jiming Jiang

Background: In April 2020, COVID-19 became a nationally notifiable condition, and jurisdictions were asked to report cases to the CDC, though some did not report through the entire public health emergency. Even for reported cases, accuracy can be improved by "borrowing strength" via statistical models. Small area estimation (SAE) is a potentially valuable statistical approach for more accurate estimation in areas where cases were underreported or unreported. Despite its potential, SAE has only been sparsely used in the context of infectious diseases. **Objective**: This research aims to understand the efficacy of SAE methods in estimating COVID-19 cases using auxiliary information, such as social determinants of health (SDoH) and spatial correlation, to provide robust case estimates for all counties in the contiguous US. **Methods**: COVID-19 case data are sourced from the February 2023 release of the CDC COVID-19 Case Surveillance Restricted Access Detailed Data, containing over 95 million reported cases in the US and territories from 2020 to 2023. SDoH data are sourced from the Agency for Health Research and Quality Social Determinants of Health Database which compiles county-level administrative data from several federal sources for all five SDoH domains. Specifically, we focus on cases in 2021 and 2022 in the contiguous US, using Poisson mixed effect models with population offset to model the case counts in each year. **Results**: Preliminary results suggest that several candidate SDoH variables are significantly associated with the case count outcome but are correlated with each other. We use elastic net regularization to identify variable clusters and select a final model. Residual autocorrelation is indicated by Global Moran's I ($p = 0.00167$) with a 500km distance band from county centroids. **Conclusion**: These results suggest that SDoH and spatial correlation contain valuable auxiliary information for SAE models to estimate COVID-19 cases in counties in the contiguous US.

Diabetes

Association between exposure to air pollution and acute complications of diabetes Wei-Ting Chen* Wei-Ting Chen Tsu-Hsuan Weng Yi-Ting Wu Daphne-Yih Ng Ya-Ching Tsao Kai-Min Yu Tzy-Shiuan Fu Fu-Huang Lin

Background: Long-term exposure to air pollution has been shown to impair endothelial function and trigger oxidative stress, leading to insulin resistance and glucose metabolism disorders. Acute diabetes complications, such as hyperglycemic hyperosmolar state (HHS), ketoacidosis (DKA), hypoglycemia, and diabetic coma, have a 10-20% mortality rate if untreated. This study aims to examine the relationship between air pollution and acute diabetes complications in Taiwan.

Method: This study employed a case-crossover study design to analyze air pollutant monitoring data from the Taiwan Environmental Protection Agency (TEPA) with data from patients hospitalized with acute complications of diabetes between 2016 and 2020. The day of admission (Lag 0) was designated as the case day, and the days 1-3 before the case day (Lag 1-3) were designated as the control days. The data were stratified by gender, age, region, and season to analyze the effect of air pollutant concentrations on the risk of patients with acute complications of diabetes mellitus by logistic regression.

Results: The total number of cases in this study was 5,420, with an average age of 69.86 years, and 54.3% were male. Among females, exposure to CO and NO2 increased the risk of HHS by 36.8% (OR=1.368) and 1.3%. Exposure to SO2 increased the risk of DKA by 79%, and exposure to NO2 increased the risk of hypoglycemia by 3.3%. Among the elderly aged 65 years or older, exposure to CO and NO2 increased the risk of HHS 50.1% and 1.5%, and exposure to NO2 increased the risk of hypoglycemia by 2%. When the study was stratified by season, it was observed that exposure to NO2 during springtime in Taipei increased the risk of HHS by 1.1%. Exposure to NO2 and PM2.5 increased the risk of diabetic coma by 4.5% and 1.3%, respectively.

Conclusion: CO and NO2 increase the risk of HHS, and SO2 raises the risk of DKA. CO, NO2, and PM2.5 are linked to diabetic coma, with women and the elderly most vulnerable.

Diabetes

Association between fertility situation and diabetes among women in Taiwan Yi-Ting Wu* Yi-Ting Wu Jyun-Rong Wu Wei-Ting Chen Daphne-Yih Ng Ya-Ching Tsao Kai-Min Yu Tzy-Shiuan Fu Fu-Huang Lin

[illegible]

[illegible]

[illegible] 55 [illegible]SPSS[illegible]25.0[illegible]

[illegible] 24,079 [illegible] 2.07 [illegible] 1.40 [illegible] (95% CI=0.98-1.99)[illegible] 2.76 [illegible] 1.53 [illegible] 25 [illegible] 5 [illegible]OR = 1.81[illegible]95% CI = 1.04-3.15[illegible]

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Diabetes

Alcohol use among Veterans with type 2 diabetes who do and do not receive GLP-1 analogs

Kirsha S Gordon, PhD* Kirsha Gordon Alissa Chen, MD Cynthia A Brandt, MD James Dziura, PhD Robin M Masheb, PhD Lori Bastian, MD William C Becker, MD

Background

Glucagon like peptide-1 receptor agonists (GLPs) have demonstrated benefit in the treatment of type 2 diabetes (DM2) and obesity. Emerging data suggest an association between use of this class of agents and decreased urges for and consumption of alcohol. The purpose of this cross-sectional observational study is to examine the association between GLPs and alcohol use among a large US sample of patients in care with DM2.

Methods

Data from the Veterans Health Administration's Corporate Data Warehouse, a national repository that contains clinical, administrative, pharmacy, and financial information was accessed through the VA Informatics and Computing Infrastructure for fiscal years 2017-2023. Veterans with DM2 (based on ICD-10 E11) were identified and their GLP receipt status (yes/no) and alcohol use (based on AUDIT-C scores, ranging from 0-12) ascertained. A negative binomial (NB) model, adjusted for demographic and clinical factors, was used to assess the relationship between receipt of GLPs and alcohol use.

Results

There were 2,142,992 patients with DM2 in care from 2017-2023 of which 12% received GLPs. Those receiving GLPs were younger (<65 years older; 50% vs. 68%), more likely to be female (8% vs. 4%) and obese (85% vs. 63%), and less likely to be Black (18% vs. 20%), compared to those not receiving GLPs. Those receiving GLPs had a lower proportion of alcohol use disorder (7% vs. 8%). In NB models, receipt of GLPs was associated with lower AUDIT-C score (prevalence ratio (95% CI)=0.781 (0.776, 0.786)). Factors associated with higher AUDIT-C score were male sex, PTSD, and substance use.

Conclusions

In a nationwide sample of patients with DM2, those receiving GLPs had 22% lower AUDIT-C score. Further work is needed to assess the association of GLP receipt on alcohol use over time.

Diabetes

Social factors and diabetes follow-up visits after screening in Japan: a cohort study based on the JPHC-NEXT study Miho Hara* Miho Hara Atsushi Goto Kouichi Tamura Yuki Arakawa Tanno Kozo Nobuyuki Takanashi Kazumasa Yamagishi Isao Muraki Nobufumi Yasuda Isao Saito Koutatsu Maruyama Kazuhiko Arima Ayuko Takatani Rieko Kanehara Mariko Hanafusa Taiki Yamaji Motoki Iwasaki Manami Inoue Shoichiro Tsugane Norie Sawada

Objective:
Two-thirds of the patients who were positive for diabetes after screening in Japan missed follow-up visits for diabetes care. We aimed to assess the association between social factors, known to influence physician visits, and diabetes follow-up visits after screening in this population.
Methods:
We conducted a cohort study of adults who were newly found to test positive for diabetes through screening (fasting blood glucose≥126mg/dL or HbA1c≥6.5%), using data on social factors, diabetes-related information, and health screening from a population-based study conducted in seven regions of Japan (2011-2021) and a claims database. A follow-up visit for diabetes care was defined as a consultation with a physician within 6 months of screening. A modified least-squares regression approach was performed to estimate the association between each social factor (education, occupation, income, marital status, and social support) and diabetes follow-up visits, adjusting for gender, age, region, family history of diabetes, and year of health screening.
Results:
Of the 1,965 patients who were positive for diabetes, 885 (45.0%) attended follow-up visits. Education, occupation, income, and marital status were not statistically significantly associated with follow-up visit attendance. However, people with low social support had a lower follow-up rate compared to those with medium to very-high social support (adjusted rates: 40% [95% CI:36–44] for the low social support group; 48% [44–53] for medium; 48% [42–53] for high; 45% [41–48] for very-high). The rate difference between the low social support group and the combined non-low social support groups was 6.6% [1.5–11.7].
Conclusion:
In this population-based cohort study in Japan, factors such as education, occupation, or income appear to have a limited impact on follow-up visits. However, social support may be important for increasing the rate of follow-up visits among those who were positive for diabetes through screening.

Diversity and Inclusion

An Intersectional Perspective on Promoting Diversity and Inclusion: Reasons for Differential Impacts of COVID-19 on Productivity among a Sample of Epidemiologists and Public Health Professionals Lindsay Fernandez-Rhodes* Lindsay Fernandez-Rhodes Brooke S. Staley Nour Makarem David S. Fink Luther-King O. Fasehun Cara L. Frankenfeld

Epidemiologists and other public health professionals from marginalized backgrounds may experience a disparate impact of large-scale (public health) events, such as the COVID-19 pandemic or any future pandemics. Although the differential impact of COVID-19 pandemic on healthcare workers of diverse identities has been documented, the impact on productivity of epidemiologists has not. Using the Society for Epidemiologic Research (SER) 2021 Diversity & Inclusion Survey of members and affiliates (participants in past SER research-focused programming), we applied an intersectional approach to model how individual- and interpersonal-level characteristics are associated with specific reasons for reporting negative impacts on productivity during the COVID-19 pandemic (personal physical/mental health concerns, responsibilities to others at work and dependent care responsibilities/mental health). Of 943 respondents in our sample, 52% indicated being less productive due to the COVID-19 pandemic, specifically due to their own health (72.2%), increased work (61.1%) or dependent care responsibilities/mental health (49.9%). The **Figure** illustrates the intersectional identities that patterned specific reasons for decreased productivity. For example, women in non-academic positions were more likely than men to report impacts due to their personal health (OR=4.7, 95% CI: 1.4-16.2), but this gender effect reversed for trainees (OR=0.2, 95% CI: 0.1-1.0). In English-speaking households, individuals ≥35 years were more likely than those <35 years to report impacts due to increased dependent care responsibilities/mental health (OR=5.2, 95% CI: 2.1-12.4), but again this effect was reversed in households speaking other languages (OR=0.7, 95% CI: 0.2-3.2). We conclude that future research and advocacy should work to address the perceived stressors and objective harms of large-scale public health events on productivity and advancement and to better advance diversity and inclusion efforts.

Figure

Figure. Heatmaps of the estimated lnOR for stratified analyses of each covariate and the lnodds of decreased productivity due to specific reasons (column headers) during COVID-19 as compared to due other reasons for decreased productivity, the Society for Epidemiologic Research Diversity & Inclusion Survey, 2021.

Impacts on self (mental or physical health)

	Women	Men	No Caregiving	Caregiving Responsibilities	English at home	Other Language at home	Country of Residence Same as Country of Birth	Country of Residence Different as County of Birth	Academic Non-Student	Graduate Student, Postdoc	Non-Academic
>=35 years (ref=<35 years)	**-0.71**	-2.13	**-1.06**	-0.58	**-1.01**	-0.36	**-0.99**	-0.53	**-1.53**	0.15	-1.08
Women (ref=Men)			0.31	-0.06	0.41	-0.33	0.02	0.43	0.26	**-1.70**	**1.55**
Non-Hispanic Asian or South Asian (ref=Non-Hispanic White)	-0.31	0.44	-0.12	-0.05	-0.24	0.00	-0.14	0.01	0.19	-0.27	0.38
All other race/ethnic groups* (ref=Non-Hispanic White)	0.31	0.94	0.52	0.32	0.46	0.42	0.67	0.02	**1.17**	-0.85	0.63
Gay or Lesbian, Bisexual, Pan, Queer, Questioning, or Asexual* (ref=Heterosexual)	0.87	1.26	0.86	1.37	**1.14**	0.18	**0.86**	1.69	0.89	1.79	0.91
First generation student (ref=Not)	-0.10	-1.04	-0.38	-0.50	-0.25	-0.69	-0.46	-0.45	**-1.01**	-0.22	0.26
0 or 1 full-time earners (ref=2+ full-time earners)	0.30	-0.31	-0.05	0.34	0.03	0.38	0.19	0.15	-0.07	0.25	0.85
Financial barriers to attending meeting (ref=None)	**0.80**	0.92	**1.43**	0.36	**1.15**	0.14	**0.70**	0.85	0.25	**1.20**	1.41
Household with dependents needing supervision (ref=None)	-0.53	-0.19			-0.11	**-1.14**	-0.19	-0.56	-0.21	**-1.14**	-0.59
Language other than English spoken at home (ref=English)	-0.62	0.09	0.12	-0.55			-0.45	0.19	-0.68	0.20	-0.07
Country of residence different than country of birth (ref=Same)	0.49	-0.42	0.13	0.17	0.10	0.09			0.35	-0.39	0.37
Graduate student and postdoctoral researcher (ref=Academic, non-student)	0.13	1.33	0.38	0.33	0.26	0.93	0.63	-0.05			
Non-academic setting (ref=Academic, non-student)	0.23	-0.61	0.03	-0.10	-0.25	0.58	-0.16	0.17			

Increased responsibilities to others at work

	Women	Men	No Caregiving	Caregiving Responsibilities	English at home	Other Language at home	Country of Residence Same as Country of Birth	Country of Residence Different as County of Birth	Academic Non-Student	Graduate Student, Postdoc	Non-Academic
>=35 years (ref=<35 years)	0.42	-1.12	0.53	-0.22	0.39	-0.59	**0.64**	**-1.27**	0.43	-0.26	1.14
Women (ref=Men)			0.04	-0.63	0.07	-0.43	0.13	-0.68	0.15	-0.46	-0.24
Non-Hispanic Asian or South Asian (ref=Non-Hispanic White)	0.36	1.10	0.12	**1.80**	0.50	0.89	0.38	0.43	0.65	0.09	1.66
All other race/ethnic groups* (ref=Non-Hispanic White)	-0.05	0.95	0.35	0.09	-0.14	0.99	0.27	0.01	0.18	0.54	-0.12
Gay or Lesbian, Bisexual, Pan, Queer, Questioning, or Asexual* (ref=Heterosexual)	0.20	1.01	0.51	0.67	0.28	**1.42**	0.50	0.15	0.00	0.51	1.39
First generation student (ref=Not)	0.24	0.44	0.50	-0.27	0.52	0.21	0.61	-0.11	0.27	0.59	-0.13
0 or 1 full-time earners (ref=2+ full-time earners)	-0.26	-0.46	**-0.63**	0.61	-0.01	**-0.86**	-0.16	-0.47	0.12	-0.46	-0.57
Financial barriers to attending meeting (ref=None)	0.00	0.11	-0.08	0.08	0.14	-0.37	0.03	-0.34	0.04	0.03	-0.34
Household with dependents needing supervision (ref=None)	0.13	**1.28**			0.44	0.54	0.33	0.84	**0.80**	-0.54	0.57
Language other than English spoken at home (ref=English)	0.25	-0.16	0.39	0.21			0.47	-0.25	-0.32	**0.85**	-0.11
Country of residence different than country of birth (ref=Same)	-0.37	-0.03	-0.28	-0.24	0.02	**-0.90**			0.10	-0.35	-0.27
Graduate student and postdoctoral researcher (ref=Academic, non-student)	**-1.36**	**-1.75**	-0.67	**-2.58**	**-1.55**	**-1.16**	**-1.21**	**-1.85**			
Non-academic setting (ref=Academic, non-student)	**-1.09**	-0.67	**-0.95**	**-1.26**	**-0.96**	-1.05	**-1.03**	**-1.25**			

Increased responsibilities due to dependent care and mental health

	Women	Men	No Caregiving	Caregiving Responsibilities	English at home	Other Language at home	Country of Residence Same as Country of Birth	Country of Residence Different as County of Birth	Academic Non-Student	Graduate Student, Postdoc	Non-Academic
>=35 years (ref=<35 years)	**0.99**	1.41	**0.93**	0.71	**1.64**	-0.34	**1.04**	0.64	**2.47**	0.29	1.27
Women (ref=Men)			0.66	0.62	**1.04**	0.34	0.63	0.65	**1.25**	0.23	0.43
Non-Hispanic Asian or South Asian (ref=Non-Hispanic White)	-1.15	-0.52	-0.92	**-2.00**	0.15	**-1.92**	**-1.56**	-0.59	**-2.02**	-0.90	0.73
All other race/ethnic groups* (ref=Non-Hispanic White)	-0.27	**1.90**	**0.84**	-1.28	0.54	0.12	0.11	0.67	-0.29	0.64	1.35
Gay or Lesbian, Bisexual, Pan, Queer, Questioning, or Asexual* (ref=Heterosexual)	0.59	-0.15	0.28	-	0.52	0.32	0.47	0.26	-0.42	**1.13**	1.09
First generation student (ref=Not)	-0.36	0.33	0.16	-0.71	0.17	-0.25	0.37	-1.09	-0.25	0.38	-0.23
0 or 1 full-time earners (ref=2+ full-time earners)	**-1.07**	-0.43	-0.65	-1.05	**-0.83**	-0.84	**-0.91**	-0.64	**-1.24**	**-1.03**	0.67
Financial barriers to attending meeting (ref=None)	-0.06	-0.05	0.09	-0.49	-0.29	0.13	-0.19	0.75	0.32	-0.01	-0.57
Household with dependents needing supervision (ref=None)	**3.72**	**3.98**			**4.07**	**3.57**	**3.64**	**4.44**	**4.05**	**3.91**	**4.76**
Language other than English spoken at home (ref=English)	0.10	-1.08	0.26	-0.74			0.04	-0.49	**-1.30**	0.80	0.34
Country of residence different than country of birth (ref=Same)	0.56	-0.23	-0.12	**1.42**	0.33	0.19			0.44	-0.05	0.58
Graduate student and postdoctoral researcher (ref=Academic, non-student)	0.15	1.83	0.17	1.13	0.13	1.04	0.30	0.76			
Non-academic setting (ref=Academic, non-student)	-0.59	0.21	-0.89	0.42	**-1.15**	0.96	-0.71	0.80			

*Combined due to small sample size. Bolded lnOR signifies p-values<0.05.

Environment/Climate Change

Health Impacts of Tijuana River Pollution: Preliminary Results from A Community-Based Survey on Environmental and Public Health Challenges Yu Ni* Yu Ni Penelope Quintana Eyal Oren Eunha Ho Nicolas Lopez-Galvez Miguel Angel Zavala Perez Linda Lara-Jacobo Kai-Chung Cheng Jade Johnson Yaritza Benitez Elora Shakoor Laura Magaña Shannon McBride Lauren Bonneval Paula Stigler Granados

Background: Raw sewage and industrial pollution from Tijuana, Mexico flow north via the Tijuana River into the estuary in southern San Diego County, CA, creating a longstanding transboundary pollution crisis. The situation has significantly worsened in 2024, with residents reporting unbearable odors and major health concerns.

Methods: A bilingual (Spanish/English) rapid response survey was launched online to evaluate the pollution's impact on community wellbeing. Individuals living and working near the estuary were recruited through outreach to community organizations, flyer distribution in targeted locations, and social media. The survey captured environmental perceptions and health symptoms across several domains. We fitted Poisson regressions to estimate the pollution-health symptom associations, controlling for sociodemographic and lifestyle factors.

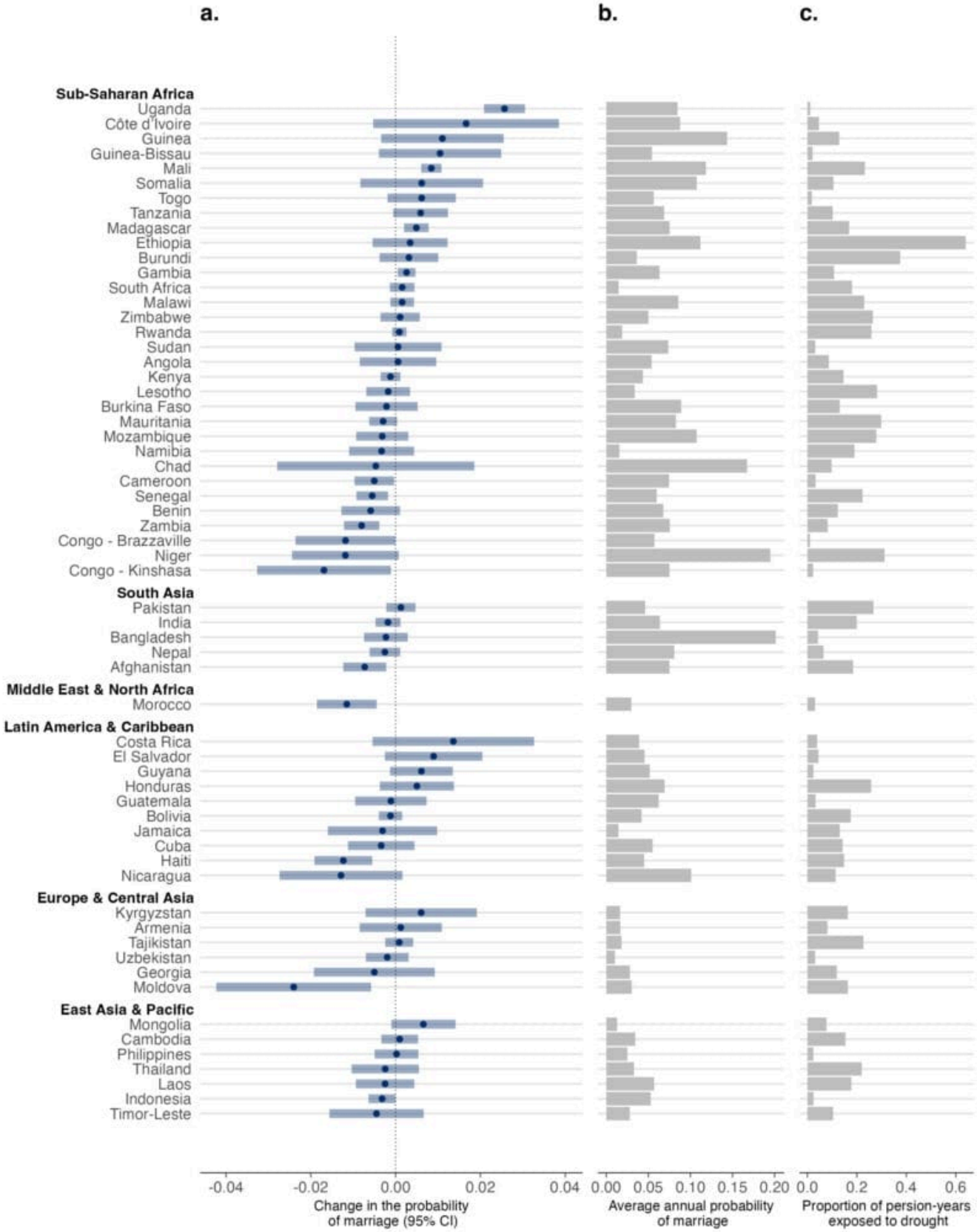
Results: Since Oct 2024, 304 participants (40% Hispanic) have completed the survey. Three-quarters reported upper respiratory symptoms in the past two weeks, and 47% experienced diarrhea. Other common symptoms included allergic reactions (69%), headaches (77%), and trouble sleeping (64%). Most participants (78%) rated air quality as unhealthy, very unhealthy, or hazardous, and 23% reported severe odors daily. Compared to those perceiving neighborhood air quality as good or moderate, participants who rated it as unhealthy, very unhealthy, or hazardous were more likely to report various health issues – prevalence ratios (PR) of 1.2-1.5 for upper respiratory symptoms, 1.5-1.8 for allergic reactions, 2.6-3.0 for diarrhea, and 3.4-3.9 for trouble sleeping. Strong odors were associated with headaches (PR: 1.4–1.6) and loss of appetite (PR: 2.4–4.7).

Conclusion: The survey results underscore the severity of the sewage crisis. Follow-up surveys aiming to track changes over time are underway. Immediate action is needed to reduce sewage flows and improve living environment for affected environmental justice communities.

Environment/Climate Change

The effect of drought on the rate of child marriage in 61 countries Anna Palmer* Anna Palmer Jill Baumgartner Alissa Koski

Extreme weather events, such as droughts, have the potential to affect the rate of child marriage by creating or exacerbating economic hardship, including by lowering household income, increasing unemployment, and intensifying food insecurity. In this study, we analyze over 12 million person-years of nationally representative data across 61 countries to estimate the effect of 218 major drought events occurring between 1980 and 2018 on the rate of child marriage. We employ a recently developed difference-in-differences study design estimated via a flexible linear model which controls for national-level trends and subnational characteristics, allows for staggered exposure to drought, and allows for heterogeneous treatment effects across sub-national regions and time. We find that the rate of child marriage remained relatively unchanged during drought events in most countries. However, our study identifies several countries where the rate of child marriage increased (e.g. Uganda, Mali) and decreased (e.g. Haiti, Democratic Republic of the Congo) in response to droughts. Our findings challenge the prevailing narrative that droughts consistently contribute to increasing child marriage and suggest the effect of droughts on child marriage is highly context-dependent.


a.
b.
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Sub-Saharan Africa
Uganda
Côte d'Ivoire
Guinea
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Mali
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Togo
Tanzania
Madagascar
Ethiopia
Burundi
Gambia
South Africa
Malawi
Zimbabwe
Rwanda
Sudan
Angola
Kenya
Lesotho
Burkina Faso
Mauritania
Mozambique
Namibia
Chad
Cameroon
Senegal
Benin
Zambia
Congo - Brazzaville
Niger
Congo - Kinshasa
South Asia
Pakistan
India
Bangladesh
Nepal
Afghanistan
Middle East & North Africa
Morocco
Latin America & Caribbean
Costa Rica
El Salvador
Guyana
Honduras
Guatemala
Bolivia
Jamaica
Cuba
Haiti
Nicaragua
Europe & Central Asia
Kyrgyzstan
Armenia
Tajikistan
Uzbekistan
Georgia
Moldova
East Asia & Pacific
Mongolia
Cambodia
Philippines
Thailand
Laos
Indonesia
Timor-Leste
-0.04
-0.02
0.00
0.02
0.04
Change in the probability of marriage (95% CI)
0.00
0.05
0.10
0.15
0.20
Average annual probability of marriage
0.0
0.2
0.4
0.6
Proportion of persion-years exposed to drought

Environment/Climate Change

Residential radon exposure and birth weight Meghan Angley* Meghan Angley Yijia Zhang Uma Reddy Ka Kahe

Objective: Radon is the major source of background radiation exposure in the U.S. Only one other study has examined residential radon and birth weight, despite the fact that ionizing radiation exposure during pregnancy is known to cause fetal growth restriction.

Methods: We used data from the Nulliparous Pregnancy Outcomes Study: Monitoring Mothers-To-Be (nuMoM2b), a multi-center prospective cohort study of women. Estimates of residential radon exposure in pCi/L at the county level were developed by the Lawrence Berkeley National Laboratory and linked to participants by maternal address. Birth weight (BW) was collected via chart abstraction. BW was converted to z-scores for gestational age and infant sex using the INTERGROWTH-21st standards. Linear mixed models included random effects for study center and adjusted for maternal age, BMI, smoking, education, percent of the federal poverty level, season of conception and average PM2.5 levels during pregnancy. We also examined interaction by maternal smoking status in the 3 months prior to pregnancy.

Results: We excluded participants whose pregnancies ended prior to 20 weeks gestation and implausible birth weight values. Of the 6,278 women with non-missing data included in the analysis, the median county-level radon concentration was 1.6 pCi/L (IQR: 0.9-2.8). After adjustment for confounders, radon was not associated with BW z-scores (-0.02 [95% CI: -0.05, 0.02]). However, radon was associated with lower BW z-scores among women who smoked ≥20 cigarettes/day (-0.16 [95% CI: -0.33, 0.01] and those who smoked 0 – <20 cigarettes/day (-0.06 [95% CI: -0.13, 0.01]), but not those who did not smoke prior to pregnancy (0.00 [95% CI: -0.04, 0.03]).

Conclusions: Radon was found to be associated with lower birthweight among women who smoked prior to pregnancy. Next steps include obtaining radon measurements at a more granular level and examining how residential radon exposure affects trajectories of fetal growth.

Environment/Climate Change

Examining Interaction on an Additive Scale between Short-Term Ambient Air Pollution Exposure and Cardiovascular Disease for Risk of Adverse COVID-19 Outcomes Sneha Kannoth* Sneha Kannoth Pam Factor-Litvak Stephen S. Morse Earle C. Chambers Kristen M. Rappazzo Cong Zhang Sandra S. Albrecht Alexander Azan Min Qian Perry E. Sheffield Azure Thompson Jennifer A. Woo Baidal Stephanie Lovinsky-Desir Jeanette A. Stingone

Introduction

Research suggests a link between short-term particulate matter (PM2.5) exposure and adverse COVID-19 outcomes. Cardiovascular disease (CVD), a COVID-19 risk factor, may increase vulnerability to the effects of short-term PM2.5. We assessed whether short-term PM2.5 and CVD interact to induce greater risk of adverse COVID-19 outcomes.

Methods

We used NYC COVID-19 hospitalization records (Mar-Dec 2020; N=15361). Short-term PM2.5 was a 7-day residential ZIP Code average before hospital admission, using EPA Community Multi-Scale Air Quality modeled data. CVD was defined using 15 common cardiovascular conditions, such as atrial fibrillation, cerebrovascular disease, myocardial infarction, etc. We estimated the relative excess risk of interaction (RERI) between short-term PM2.5 and CVD on adverse COVID-19. We used targeted maximum likelihood estimation (TMLE) to assess the average treatment effect (ATE) of short-term PM2.5 on adverse COVID-19, among those with and without CVD. Modified Poisson regression estimated the risk of acute respiratory distress syndrome, pneumonia, ventilation, and dialysis and Cox regression estimated the risk of fatality and discharge, adjusting for age, sex, smoking, and environmental vulnerability.

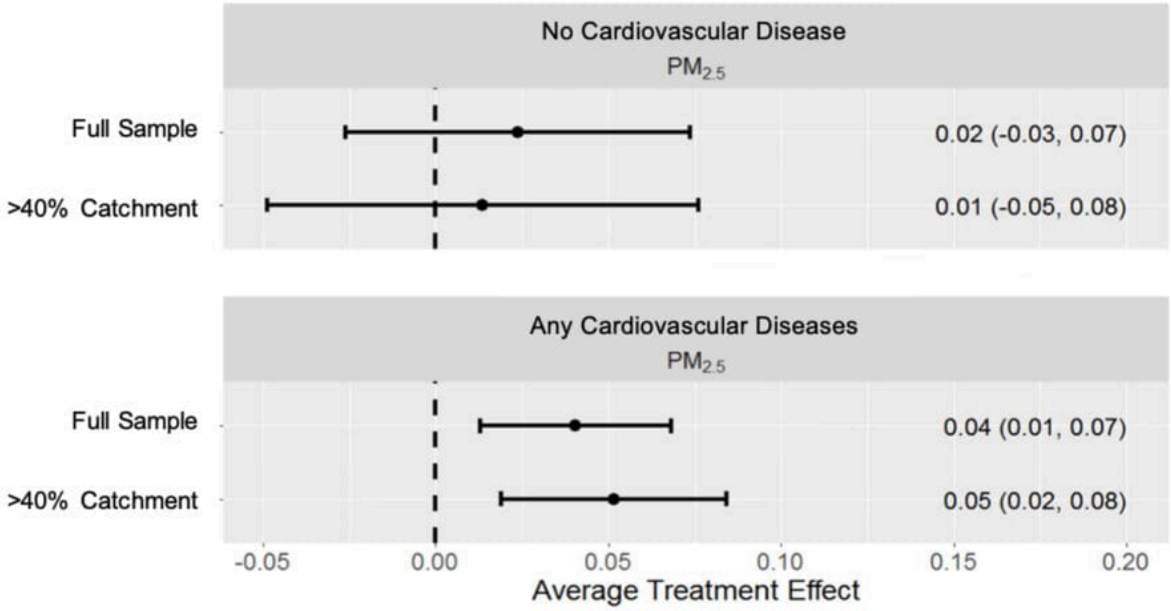
Results

We observed synergistic interaction between short-term PM2.5 and CVD for pneumonia risk from July to Dec 2020 (e.g., myocardial infarction (RERI:0.30; 95%CI:0.05-0.55), atrial fibrillation (RERI:0.23; 95%CI:0.05-0.40)). TMLE analyses suggest that short-term PM2.5 increased risk of pneumonia only among those with CVD (ATE:0.04, 95%CI:0.01-0.07; Fig1).

Discussion

Short-term PM2.5 interacts with CVD to induce greater risk of COVID-19 pneumonia in the latter half of 2020, which had higher short-term PM2.5 variability. TMLE analyses suggest short-term air pollution reductions targeted towards those with greater health vulnerability (i.e., greater cardiovascular burden) may reduce incidence of acute respiratory infections, such as pneumonia.

Fig1. Assessing average treatment effect of short-term $PM_{2.5}$ exposure on COVID-19 pneumonia risk, using targeted maximum likelihood estimation analyses (among subpopulations with no cardiovascular disease or any cardiovascular diseases) from July to December 2020[1-2]



[1] Short-term $PM_{2.5}$ [24 hr-avg] exposure (7-day average prior to hospital admission date) assigned dichotomously, as in the uppermost quartile [10.25 $\mu g/m^3$, 17.98 $\mu g/m^3$] or the lower three quartiles [4.34 $\mu g/m^3$, 10.24 $\mu g/m^3$]

[2] Abbreviations and Definitions: Full Sample – main study analysis including the full sample (N=15361); >40% Catchment – sensitivity analysis restricting to a subset of ZIP Codes within the hospitals' primary catchment areas (N=9918); $PM_{2.5}$ – Particulate Matter; $\mu g/m^3$ – micrograms per cubic meter

Environment/Climate Change

Ambient air pollution and mortality in older breast cancer patients Yaguang Wei* Yaguang Wei Edgar Castro Kanhua Yin Min Zhang Hannah Thompson Joel Schwartz

Importance: Air pollution is likely associated with increased breast cancer mortality due to its carcinogenic properties and the increased sensitivity of patients to environmental stressors. However, robust and large-scale evidence remains limited.

Objective: To evaluate associations between annual exposures to fine particulate matter (PM2.5), warm-season ozone, and nitrogen dioxide (NO2), three major regulated air pollutants, and mortality in a large cohort of senior breast cancer patients following diagnosis.

Design, Setting, and Participants: An open cohort constructed using SEER-Medicare data, including Medicare beneficiaries aged ≥65 years with primary diagnosis of breast cancer between 2000–2016.

Exposures: Spatio-temporal estimates of annual PM2.5, warm-season ozone, and NO2 were obtained using hybrid models at 1-km^2 grid resolution across the contiguous US. The estimates were aggregated and linked to patients' residential ZIP codes as proxy exposure measures.

Main Outcome: A three-pollutant Cox proportional hazard model was fitted to estimate the hazard rate of mortality per unit increase in exposures, adjusting for demographics, cancer stage, treatments, marital status, comorbidities, meteorological conditions, and neighborhood characteristics.

Results: Among 593,333 patients included in the study, a 1-μg/m^3 increase in annual PM2.5, 1-part-per-billion (ppb) increase in warm-season ozone, and 1-ppb increase in NO2 were associated with hazard ratios of 1.0053 (95% CI: 1.0031–1.0075), 1.0023 (95% CI: 1.0015–1.0032), and 1.0020 (95% CI: 1.0012–1.0027) for mortality, respectively. The effects were larger at low exposure levels. Younger patients, patients diagnosed at later stages, and those who received chemotherapy or radiation were more susceptible to the effects.

Conclusions: Our findings on chronic effects of air pollution on breast cancer mortality suggests that improving air quality would help mitigate the significant and escalating disease burden.

Environment/Climate Change

Interaction between social deprivation and air pollution on mortality in hexagonal France: A nationwide analysis, 2018-19. Tom Fischer* Tom Fischer Stéphanie Vandentorren Ludovic Cépré Andrew C. Stokes Geneviève Chêne

Introduction: Air pollution and social deprivation independently contribute to premature mortality. This analysis explored whether social deprivation modifies the relationship between air pollution and mortality during the period immediately preceding the COVID pandemic in hexagonal France.

Methods: A cross-sectional ecological analysis was conducted at the municipal level in hexagonal France to evaluate the associations between NO_2, PM_{10} and $PM_{2.5}$ average concentrations (2009-19) and mortality (2018-19), focusing on overall and premature deaths (<75 and <65 years). Three generalized negative binomial models were developed, with interaction terms for air pollution and the French Deprivation Index, as well as for longitude and latitude to adjust for spatial autocorrelation. Results are reported as Relative Rates (RR) with 95% CI for a 1 SD increase in exposure. Data were sourced from open-access repositories, including INERIS, INSEE, and CépiDc.

Results: 1,044,055 deaths were included (322,588 <75 years, 163,773 <65 years) across 34,172 municipalities (0–7,285 deaths). Higher exposure to NO_2, PM_{10}, and $PM_{2.5}$ was associated with elevated risk of premature mortality (<75 years: RR = 1.010 (1.006-1.015); 1.019 (1.013-1.024); 1.007 (1.001-1.013); <65 years: RR = 1.012 (1.006-1.018); 1.020 (1.013-1.027); 1.008 (1.000-1.016)). NO_2 and PM_{10} were associated with overall mortality (RR = 1.012 (1.002-1.018); 1.012 (1.008-1.016)). Social deprivation was also associated with mortality, with higher RR ranging from 1.059 (1.059-1.063) to 1.167 (1.160-1.174). Interaction analyses showed that social deprivation amplified NO_2 and PM_{10} effects on overall mortality, and $PM_{2.5}$ on <75 years mortality, with no significant interactions for <65 years mortality.

Conclusion: This analysis confirms that social deprivation amplifies the health risks of air pollution in hexagonal France and highlights the need for targeted interventions in disadvantaged areas to reduce health inequalities.

Environment/Climate Change

County-level radon and offspring wheezing and asthma Yijia Zhang* Yijia Zhang Elizabeth F Minsky Meghan Angley Shai Bejerano Brian J Smith Erin M Bell Diane L Putnick Edwina H Yeung Ka Kahe

Background The health risks of radon exposure beyond lung cancer are understudied. Maternal radon exposure, along with tobacco smoke, may be connected to offspring respiratory health.

Methods Upstate KIDS, a population-based prospective cohort consists of more than 5000 pregnancies from 57 counties in New York (excluding NYC). County-level radon exposure was measured by Lawrence Berkeley National Laboratory (LBL), categorized into ≥ 2 and <2 picocuries per liter (pCi/L), and linked to participants. Data on child wheeze was obtained from questionnaires completed around 4, 8, 12, 18, 24, 30, and 36 months of age and “persistent wheeze” defined as “yes” on two or more questionnaires. Asthma was defined as any maternal report of physician-diagnosed asthma or prescription of asthma medication or inhaler and assessed at two time points: up to 36 months and 7–9 years. Multivariable mixed-effects logistic regression was used to calculate adjusted odds ratios (aOR) and 95% confidence intervals (CI).

Results Maternal age averaged 30.7 years, and most were non-Hispanic White (80.0%). The median radon concentration is 1.29 pCi/L. Largely due to attrition, sample sizes for the analysis of wheezing, asthma up to 36 months, and asthma at 7–9 years were 5,683; 3,714; and 1,963, respectively. Radon was positively but not significantly associated with persistent wheeze (aOR = 1.25, 95% CI: 0.36–4.36). When stratifying by maternal smoking, the association remained in the same direction among never-smokers, but not smokers. The associations were also non-significant for both asthma outcomes.

Conclusions The ecological nature of the exposure assessment, limited variability in radon levels, and insufficient statistical power may have contributed to the observed non-significant associations between radon exposure and child asthma. However, these findings do not rule out a potential association. Future studies employing individual-level radon measurements and larger sample sizes are needed.

Environment/Climate Change

Trajectories of prenatal phthalate exposure and associations with gestational weight gain and infant birthweight – Findings from an Ethnically Diverse U.S. Pregnancy Cohort (2010-2015). Shabnaz Siddiq* Shabnaz Siddiq Jeanette A. Stingone Andrew Rundle John Meeker Virginia Rauh Susannah Leisher Pam Factor-Litvak

Background:
We assessed trajectories of prenatal phthalate metabolites (PthM) and their associations with gestational weight gain (GWG) and birthweight in a diverse U.S. sample.

Methods:
We analyzed 951 controls (without pregnancy complications) from a nested matched case control study embedded in the Nulliparous Mothers to Be Study who provided 1-3 urine samples (total n=2723) throughout pregnancy. Eleven PthM were investigated. Maternal weight was recorded prospectively once per trimester, and birthweight (in grams) was recorded at delivery. We applied latent class growth analysis (LCGA) to identify trajectories of PthM exposure and estimated associations with total GWG and infant birthweight, adjusting for confounders Analyses were stratified by maternal BMI, race/ethnicity, and infant sex.

Results:
We identified stable trajectories for high-molecular-weight and low-molecular-weight phthalates, while replacement PthM showed temporal changes throughout pregnancy, reflecting distinct exposure patterns. Higher Monobenzyl phthalate (MBzP) trajectories which indicated increases in the second or third trimester were associated with lower total GWG compared to low-exposure trajectory (i.e 2.5-4.0 lb decrease). Stronger associations were found in obese compared to non-obese women, in non-Hispanic Black women and Hispanic women compared to Non-Hispanic White women, and women delivering female compared to male infants. Higher Mono-isobutyl phthalate (MiBP) trajectories were associated with lower infant birthweight (i.e. 87 gram decrease), with stronger effects observed among underweight/normal weight women, Hispanic women, and women carrying female infants.

Conclusions:
Higher MBZP and MiBP trajectories were associated with lower GWG and infant birthweight. While most infants were born within the healthy birthweight range, these findings suggest certain PthM trajectories could affect maternal and fetal health

Environment/Climate Change

Mediation of immunological markers in the association between per- and polyfluorinated substances (PFAS) and respiratory outcomes among Inuit adults Amira Aker* Amira Aker Melanie Lemire Pierre Ayotte

Objective: Per- and polyfluorinated substances (PFAS) are stable and bioaccumulative compounds. They are detected at high concentrations in the Arctic compared to the general Canadian population and have been associated with changes to the immune system in other populations and animal models. Our objective was to examine the mediating effect of immune markers on the relationship between PFAS and respiratory outcomes among Inuit adults of Nunavik.

Materials and Methods: The study included 1322 participants of the Qanuilirpitaa? 2017 Inuit Health Survey. Factor analyses were used to identify latent immunological profiles based on cytokine concentrations. Structural equation models assessed individual PFAS against the ratio of the forced expiratory volume to the lung forced vital capacity (FEV1/FVC), and the mediating effect of a Th2 response (driven by IL4, IL5, and IL13), a Th1 response (driven by IFN-γ, TNF-β, IL6, and IL1-β), and immune-related proteins (periostin, YKL40, and adiponectin).

Results: All PFAS congeners were associated with a 7-13% increase in periostin; associations with strongest with PFNA and PFOA. PFHxS and PFOS were associated with a 7-8% decrease in YKL40. YKL40 levels significantly mediated the relationship between PFOA, PFDA, PFUnDA, and PFOS and FEV1/FVC. Evidence of mediation by a Th2 response and periostin was also observed, but varied by PFAS congener.

Conclusion: There was evidence of changes in immune biomarkers by PFAS contributing to respiratory outcomes. This adds evidence to the biological mechanism of PFAS leading to adverse human health effects.

LATEBREAKER

Environment/Climate Change

Associations of persistent organic pollutants with coronary heart disease in Hispanic/Latino adults: The Hispanic Community Health Study/Study of Latinos (HCHS/SOL) Mariam Oladosu* Mariam Oladosu Victoria Persky Robert M Sargis Martha Daviglus Jianwen Cai Chibuzor Abasilim Robert Kaplan Gregory A Talavera Humberto Prada Sally Feels Mary E Turyk

Background: Coronary heart disease (CHD) has been linked to persistent organic pollutants (POPs) exposure. However, studies examining CHD in association with POP exposure in US Hispanic/Latino adults are limited.

Methods: We studied a subsample of 1,146 men and 1,187 women without diabetes at enrollment (2008 – 2011) from the HCHS/SOL, a multi-site prospective cohort study of diverse Hispanic/Latino adults in the US. Prevalent CHD at enrollment was defined as self-reported physician-diagnosed angina, myocardial infarction, bypass, angioplasty, stent placement, or evidence of electrocardiographic abnormalities indicative of CHD. POPs, such as organochlorine pesticides, brominated flame retardants, and polychlorinated biphenyls (PCBs), were measured in stored fasting serum samples by gas chromatography isotope dilution high-resolution mass spectrometry. Sex-stratified multivariable logistic regression models were used to estimate odds ratios (ORs) and 95% confidence intervals (95%CIs) for the associations between POPs levels and prevalent CHD. Effect modification by glycemic status and hypertension was also explored.

Results: In men, each doubling in levels of β-Hexachlorocyclohexane (β-HCCH; OR: 1.43, 95% CI: 1.11–1.90) and hexachlorobenzene (HCB; OR: 1.58, 95% CI: 1.09–2.28) was associated with higher odds of CHD. A doubling in levels of 2,2-bis(4-chlorophenyl)-1,1-dichloroethene (p'p-DDE; OR: 1.46, 95% CI: 1.09, 1.96) was associated with higher odds of CHD only in hypertensive men. In women, no statistically significant associations were observed overall, but a doubling in levels of total PCBs was associated with a two-fold increase in CHD (∑PCBs; OR: 1.98: 95% CI: 1.18, 3.31) in normoglycemic women.

Conclusions: Specific POPs, including β-HCCH, HCB and DDE, and PCBs, are associated with the prevalence of CHD among Hispanic/Latino adults and particularly among men. Further studies are needed to confirm these findings and elucidate the underlying mechanisms.

LATEBREAKER

Environment/Climate Change

Prenatal per- and polyfluoroalkyl substance exposure in relation to maternal prenatal and postpartum anxiety and depression Claire Nurse* Claire Nurse Emily Barrett Sally Thurston Kannan Kurunthachalam Jessica Brunner Richard K. Miller Thomas G. O'Connor Susan W. Groth

Objective: Per- and polyfluoroalkyl substances (PFAS), are ubiquitous, endocrine-disrupting synthetic chemicals. Considering the importance of hormones to mental health and the small literature linking PFAS exposure to depressive symptoms, we examined gestational PFAS exposure in relation to maternal anxiety and depression both pre- and postnatally.

Materials and Methods: Using LC-MS/MS, we measured five PFAS species in second trimester serum samples from participants in the UPSIDE-ECHO cohort (Rochester, NY; n=283). In each trimester and at 6 and 12 months postpartum, participants reported on symptoms of depression (Edinburgh Postnatal Depression Scale; EPDS) and anxiety (Penn State Worry Questionnaire; PSWQ), with higher scores indicating more affective symptoms. In covariate-adjusted linear regression models, we examined log-transformed PFAS concentrations in relation to average prenatal and average postnatal depression and anxiety scores, imputing missing data using MICE.

Results: Approximately 85% of PFAS in the sample were above the limit of detection (0.02 ng/mL). Median prenatal and postnatal scores for EPDS were 5.0 and 5.3 respectively, while PSWQ scores were 42 and 45 respectively. In our primary models, associations between PFAS and prenatal EPDS scores tended to be positive, with the strongest result observed for PFOS (β=0.22, 95% CI: 0.07, 0.38). No significant associations between PFAS and prenatal PSWQ scores were observed. In complete case models, PFNA was associated with lower postpartum EPDS (β=-0.133, 95% CI: -0.26, -0.004) and PSWQ scores (β= -0.071, 95% CI: -0.13, -0.015).

Conclusion: These preliminary findings suggest that PFAS exposures impact maternal perinatal affective symptoms. Further studies are needed to investigate potential causal mechanisms, including altered hormone profiles.

LATEBREAKER

Environment/Climate Change

Wildfire PM2.5 exposure and emergency department utilization in the first year of life Tona Pitt* Tona Pitt Anais Teyton Tarik Benmarhnia

Exposure to wildfire fine particulate matter (PM2.5) is associated with poor health outcomes across the life course. As wildfires increase in frequency and severity, it is important to understand the health impacts of wildfire-specific PM2.5, especially during critical periods such as during gestation and in the first year of life. This study aims to examine the association of pre- and post-natal wildfire-specific PM2.5 exposure on emergency department (ED) visits in the first year of life.

The population-based Study of Outcomes in Mothers and Infants (SOMI) cohort was used, consisting of all live singleton births in California from 2014 to 2017. Exposure data are wildfire-attributable PM2.5 measured at the zip code level and based on an ensemble model. Health outcomes of interest include the first respiratory-specific and, separately, cardiovascular-specific ED visit in the 12 months after birth. We consider the week-specific, cumulative, and lagged association of wildfire PM2.5 exposure pre and postnatally on all-cause and cause-specific ED visit, using a combination of pooled logistic regression and distributed lag non-liner models, while adjusting on a priori identified covariates.

As this study is in progress, we provide descriptive statistics, with adjusted estimates anticipated. The sample consists of 1,586,719 infants with 518,007 (33%) presenting at ED in the 12 months after birth. Approximately 49% of the infants were female, and 85% of mothers had at least a high school education, 49% were Hispanic, and 45% used Medi-Cal insurance. Of the 3,897,784 zip code days in this study, 447,154 (11.5%) had wildfire PM2.5 smoke exposure over 0 µg/m3.

We anticipate that findings will identify associations of immediate and lagged effects of wildfire PM2.5 on early life ED utilization. The findings can help identify key windows of susceptibility and provide guidance on reducing the wildfire-specific exposure risks to this vulnerable subpopulation.

LATEBREAKER

Environment/Climate Change

Evaluating objective and subjective measures of neighborhood stress and vulnerability in relation to placental metals concentrations in a U.S. pregnancy cohort. Megan Hansel* Megan Hansel Sean A. Stratton Alyssa Juenke Anushka Pande Carolyn W. Kinkade Catherine S. Yount Pamela Ohman-Strickland Cathleen Doherty Brian Buckley Jessica Brunner Richard K. Miller Thomas G. O'Connor Emily S. Barrett Zorimar Rivera-Núñez

Given that social and environmental exposures may co-occur and impact perinatal outcomes, we examined neighborhood stress and social vulnerability in relation to placental metals concentrations. The UPSIDE study recruited pregnant participants (n=242). In the third trimester, participants reported on neighborhood stressors using the City Stress Inventory which has two subscales: neighborhood disorder (e.g., vacant buildings) and violence (personal experiences of violence). Neighborhood disorder was considered as quartiles (Q) and exposure to violence was considered binary (any/none). Participant addresses were linked to the CDC's Social Vulnerability Index (SVI), which contains four themes (socioeconomic status, household composition and disability, minority status and language, housing type and transportation) and overall SVI. Each tract receives a U.S.-wide percentile ranking (expressed as a fraction from 0-1, higher values indicating greater vulnerability). SVI measures were categorized as low, medium [M], and high. Placental lead, arsenic, cadmium, chromium, and manganese at delivery were analyzed by ICP-MS. We fitted adjusted linear regression models examining neighborhood stress and SVI measures in relation to each log-transformed metal. Results are reported as percentage difference (%Δ) in metals concentrations. Most participants (73%) reported ≥1 exposure to neighborhood disorder, 24% reported exposure to violence, and the mean overall SVI was 0.4±0.3. Compared to the lowest neighborhood disorder category, higher disorder was associated with higher cadmium (Q2:%Δ= 25.5, 95%CI: 0.3,57.1). Positive associations were observed for minority status and language with cadmium (M:%Δ= 26.4, 95%CI: 2.9,55.1) and housing type and transportation with chromium (M:%Δ= 27.1, 95%CI: 1.3,59.6) compared to the lowest tertile. Aspects of neighborhood stress and social vulnerability are associated with placental metals concentrations with implications for perinatal health.

Environment/Climate Change

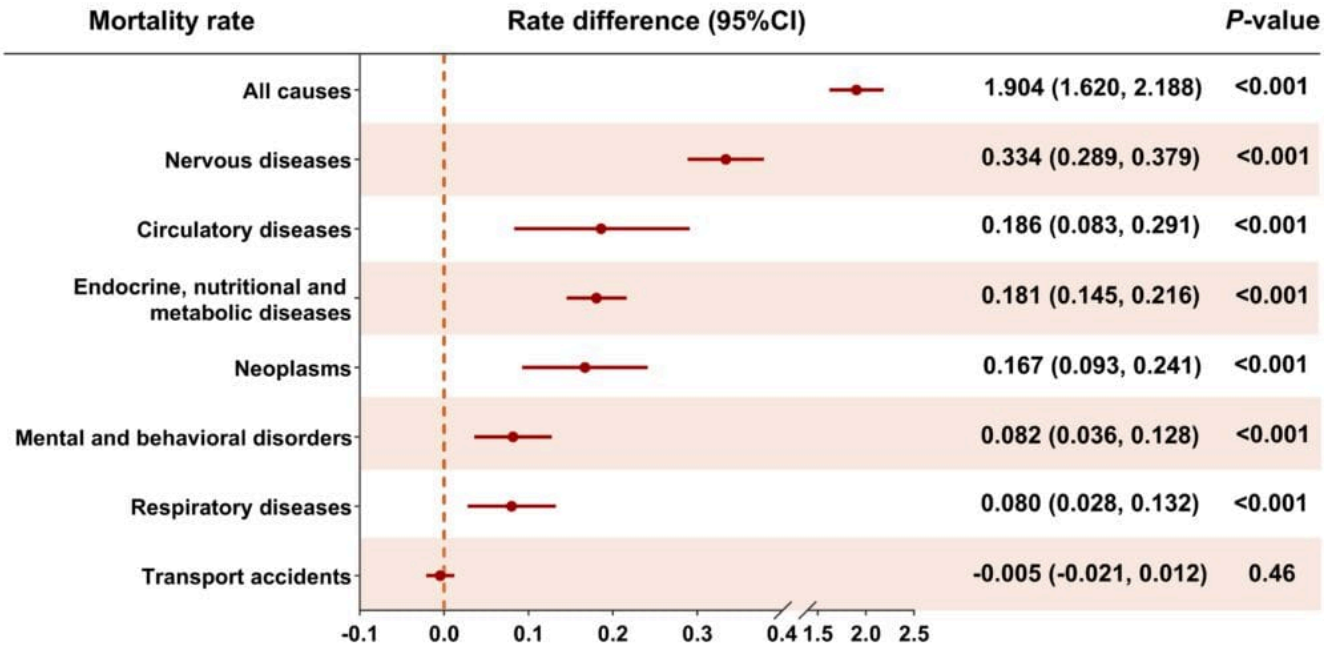
Wildfire smoke PM2.5 and mortality rate in the contiguous United States: a causal modeling study Yaguang Wei* Yaguang Wei Min Zhang Edgar Castro Alexandra Shtein Adjani A. Peralta Mahdieh Danesh Yazdi Xiao Wu Joel D. Schwartz

Background: Smoke PM2.5 has emerged as a significant environmental hazard in the US, driven by increasing wildfire activities due to climate change. However, the causal relationship between chronic exposure to smoke PM2.5 and mortality remains particularly scarce.

Methods: The annual all-cause mortality for 3068 counties in the contiguous US, along with cause-specific death records for circulatory diseases, nervous diseases, neoplasms, respiratory diseases, endocrine, nutritional and metabolic diseases, and mental and behavioral disorders, were collected from US Centers for Disease Control and Prevention from 2006 to 2020. Concentrations of smoke PM2.5 were estimated using spatio-temporal models at a 10 km2 resolution. We used a doubly robust method, incorporating flexible generalized propensity score estimation strategies while relaxing the distributional assumption for exposure, to estimate additive effects of annual exposure to smoke PM2.5 on mortality. Transport accident mortality was used as a negative outcome control to test the assumption of no unmeasured confounding.

Results: Each 0.1-unit increase in smoke PM2.5 was associated with increased all-cause mortality rate (rate difference: 1.904, 95% CI: 1.620 to 2.188 per 100,000 persons) and increased mortality for all cause-specific outcomes, with nervous diseases being most susceptible. This translated to approximately 5,594 attributable all-cause deaths per year. The exposure-response curve for all-cause mortality showed no evidence of “safe” threshold. There was no evidence of the association between smoke PM2.5 and the negative outcome control. Effects were greater in communities with a higher percentage of population under 65 years old, in more rural areas, and during periods of lower temperatures in summer and winter.

Conclusions: Our study provided robust evidence for the chronic effect of smoke PM2.5 on mortality, underscoring the urgent need to mitigate the escalating burden of wildfires.


Mortality rate
Rate difference (95%CI)
P-value
All causes
1.904 (1.620, 2.188)
<0.001
Nervous diseases
0.334 (0.289, 0.379)
<0.001
Circulatory diseases
0.186 (0.083, 0.291)
<0.001
Endocrine, nutritional and metabolic diseases
0.181 (0.145, 0.216)
<0.001
Neoplasms
0.167 (0.093, 0.241)
<0.001
Mental and behavioral disorders
0.082 (0.036, 0.128)
<0.001
Respiratory diseases
0.080 (0.028, 0.132)
<0.001
Transport accidents
-0.005 (-0.021, 0.012)
0.46
-0.1
0.0
0.1
0.2
0.3
0.4
1.5
2.0
2.5

Environment/Climate Change

A difference-in-differences analysis evaluating the impact of a clean heating policy on inflammatory biomarkers among rural Beijing adults Wenlu Yuan* Wenlu Yuan Kaibing Xue Talia Sternbach Xiaoying Li Collin Brehmer Xiang Zhang Ellison Carter Brian Robinson Christopher Barrington-Leigh Guofeng Shen Sam Harper Jill Baumgartner Shu Tao Yuanxun Zhang

Populations with high blood inflammatory biomarkers face greater risk of chronic illness and premature death. Outdoor and indoor PM2.5 are known contributors to elevated levels of these biomarkers. Coal has been commonly used for residential space heating in northern China, substantially contributing to indoor and outdoor PM2.5. In 2016, Beijing implemented the Clean Heating Policy (CHP), to switch homes from coal to electric heating and improve air quality. We leveraged the natural experiment from the CHP's staggered rollout across rural Beijing villages and applied a Difference-in-Differences (DiD) approach to estimate its impact on blood inflammatory biomarkers (IL-6, TNF-α, CRP).

We enrolled participants >40yrs from 50 villages that were eligible for, but not yet treated by, the CHP in Beijing during winter 2018-19. By winter 2019-20, 10 villages had joined the CHP. Sociodemographic data was collected via home visits and blood samples were taken in village clinics by trained nurses during both winters. IL-6, TNF-α, and CRP concentrations were measured using automated enzyme-linked immunosorbent assay. We used generalized linear models with Gamma distribution and a log link to estimate CHP impacts. Dummy variables for treatment exposure, post-treatment period, and their interaction were used to implement the DiD design. Standard errors were clustered at the village level.

A total of 982 participants were included. We did not find strong evidence that the CHP affected IL-6, TNF-α, or CRP among the treated (ATT). We observed stronger ATTs among males for TNF-α (2.5pg/mL, 95%CI: 0.9, 4.1) and CRP (0.9mg/L, 95%CI: 0.1, 1.7), which were different from females (TNF-α: $p<0.05$, CRP: $p<0.01$). Our study suggests the CHP increased inflammation in male residents, despite no overall effect. The findings highlight the need for future studies to understand the mechanisms through which the CHP affected inflammation and guide similar policies in the future.

Environment/Climate Change

Oil and Gas Development and Adverse Birth Outcomes: A Conceptual Framework, Literature Review, and Bias Analysis Marijke Rowse* Marijke Rowse Cassandra Clark Julia Bond Kaylin Vrkljan Erin Polka Erin Campbell Amelia Wesselink Amira Aker Mary Willis

Background: An estimated 17.6 million Americans reside within 1.6 km of active oil and gas development. Many studies have examined associations between oil and gas development (OGD) and adverse reproductive health outcomes. However, the strengths and weaknesses of this literature need further examination to improve future research. Building upon a recent systematic review (Aker et al. 2024), we identified the biases and gaps in the existing research, analyzed the potential influence of unmeasured confounding by income, and suggested potential research avenues for future studies.

Methods: Building on the previous review by Aker et al., we identified 18 epidemiologic studies of oil and gas development exposure and adverse birth outcomes. We extracted measures of association (e.g., risk ratios, odds ratios, hazard ratios) for the relation between OGD and specific birth outcomes from each study. For each study, we evaluated for pre-identified sources of bias that are common in reproductive health research (e.g., live birth bias). We will use quantitative bias analysis (QBA) to evaluate the potential impact of unmeasured confounding by socioeconomic status on the published associations.

Results: Among the 18 included studies, 83.3% relied on vital statistic records as their primary data source which can introduce misclassification and selection bias. The most common endpoints were birth weight (77.8% of studies), preterm birth (72.2%), and small-for-gestational-age (55.6%). QBA will help disentangle to what extent unmeasured confounding from income may be a key source of bias in this association.

Conclusion: Our detailed review of existing literature on the association between oil and gas development and birth outcomes highlights important sources of bias that should be considered when interpreting the results, including points of expansion for future research.

Environment/Climate Change

Residential Greenness and Cognitive Decline in a Community-Based Cohort Anna M. Staddon* Anna Staddon Tara E. Jenson Francine Grodstein Lisa L. Barnes Melissa Lamar Gregory A. Wellenius Jennifer Weuve Marcia Pescador Jimenez

Objective: Greenness may promote cognitive health by reducing stress and air pollution exposure, and/or supporting exercise and social connection. However, research on the association between greenness and cognitive decline in diverse populations is limited.

Methods: We studied 2761 participants from the Rush Alzheimer's Disease Research Center Memory and Aging Project, Minority and Aging Research Study, and Latino Core (enrollment began in 1997, 2004, and 2016, respectively, with ongoing follow-up). We estimated residential greenness using the Normalized Difference Vegetation Index (NDVI) at 30m resolution, a satellite-based greenness indicator at baseline and follow-up. At each wave, we assessed global cognitive function as a composite z-score combining five cognitive domains (visuospatial ability, semantic memory, working memory, perceptual speed, and episodic memory). We used mixed models to examine the association of cumulative average greenness with cognitive function and rate of cognitive decline over each year, adjusted for age, sex, race/ethnicity, education, and personal income at baseline and age 40.

Results: Mean baseline age was 77.7 (SD 7.8). In fully adjusted models, higher NDVI interquartile range (IQR) was associated with higher baseline global cognitive score (0.08; 95% CI: 0.05, 0.11; p-value: <0.0001) and slower cognitive decline (mean difference: -0.01 per year; 95% CI: -0.01, 0.00; p-value: <0.0001). Associations between NDVI and cognitive function differed for White and Black participants (0.04; 95% CI: 0.00, 0.09; p-value: 0.05, and 0.05; 95% CI: -0.02, 0.11; p-value: 0.14, respectively), while cognitive decline results were similar across White and Black participants (0.00; 95% CI: 0.00, 0.01; p-value: 0.08).

Conclusion. Residential greenness may be positively associated with baseline global cognitive function and a slower rate of cognitive decline among older adults.

Environment/Climate Change

Associations between residential proximity to oil and gas development and adverse birth outcomes in a North American preconception cohort Erin Campbell* Erin Campbell Kaylin Vrkljan Martha Koenig Dmitrii Krivorotko Jordan Kuiper Nicole Deziel Jonathan Buonocore Amelia Wesselink Lauren Wise Mary Willis

Background: Despite widespread calls for decarbonization, the oil and gas industry continues to expand in the U.S. A growing body of literature reports associations between living near oil and gas development and higher risk of adverse birth outcomes. However, no study explored these associations using a prospective cohort study with primary data collection.

Methods: We used data from U.S. participants enrolled in Pregnancy Study Online (PRESTO), a prospective North American preconception cohort study of self-identified female participants attempting conception without fertility treatment. Among participants whose pregnancy progressed beyond 20 weeks, we obtained birth outcome data from self-administered questionnaires. We created a measure of small vulnerable newborn (SVN) status, a validated clinically relevant composite of low birthweight, preterm, and small-for gestational-age. Using participants' geocoded addresses, we calculated residential proximity measures to the nearest active oil and gas development site at conception. To evaluate the association between residential proximity to oil and gas development and risk of SVN, we used Cox proportional hazard models to estimate age-adjusted hazard ratios (HRs) and 95% CIs, with gestational weeks as the timescale.

Results: Among 5,373 participants in the analytic sample, 17.4% (n=932) gave birth to a newborn categorized as SVN, and 10.5% (n=562) resided within 5km of active oil and gas development. We found that residence within 5km of active oil and gas development was associated with an age-adjusted HR of 1.16 (95% CI: 0.94, 1.43), compared to residence greater than 10km from active oil and gas development. Associations were similar magnitude among components of SVN (e.g., low birthweight, preterm, and small-for gestational-age).

Conclusion: Although results were imprecise, our preliminary models indicate that closer residential proximity to oil and gas development is associated with slightly higher risk of SVN.

Environment/Climate Change

The long-term Particulate Matter2.5 Exposure and Prevalent Depression Symptoms in the Environmental Health Study for Western New York (EHS4WNY) Matthew Bonner* Matthew Bonner Tammy Milillo Meng Wang Lina Mu Laurene Tumiel Berhalter James Olson

Purpose: We investigated long-term, low-level exposure to ambient PM2.5 and the prevalence of depression symptom in a general population cohort exposed to industrial pollution.

Methods: EHS4WNY is a prospective cohort study started in 2018 when we began enrolling 13,306 individuals aged 18+years who resided in three communities in Erie County, NY. We ascertained information about demographics, residential history, smoking and secondhand smoke exposure, personal medical history, and self-reported symptoms of depression (CES-D-10), using mailed and internet-based self-administered questionnaires. Daily ambient PM2.5 predictions were interpolated to each residential baseline address, aggregated over 17 years from 2000 to 2016, and dichotomized the exposure variable at the 3rd quartile (10.27 ug/m3; IQR = 0.32). We calculated prevalence ratios (PRs) and 95% CIs using Poisson regression, adjusting for age, pack-years of smoking, income, and biological sex.

Results: 2,225 participants scored greater than 10 on the CES-D-10, reflecting a prevalence of 23.5% (95% CI = 22.6-24.36%) for mild or significant depressive symptoms. Long-term average PM2.5 exposure greater than 10.27 ug/m3 was positively associated with prevalent depression symptoms (PRadjusted = 1.16; 95% CI = 1.03-1.30). The association was slightly stronger when the analysis was restricted to never smokers, although less precise (PRadjusted = 1.22; 95% CI = 1.04-1.44).

Conclusion: Overall, long-term exposure to relatively low levels of PM2.5 was associated with the prevalence depression symptoms. Given the use of prevalence, these results are prone to prevalence-incidence bias, among other threats to validity. Nonetheless, they are consistent with the extant literature, setting the stage to investigate such associations using incident symptoms of depression.

Environment/Climate Change

Examining the relationship between high ambient temperatures and reproductive hormone levels in healthy premenopausal women: BioCycle study Kaniz Rabeya* Kaniz Rabeya Neil J. Perkins Lindsey M. Russo Pauline Mendola Timothy P. Canty Karen C. Schliep Nidhi Manchikanti Carrie J. Nobles

Background: Rising temperatures due to climate change have been linked to adverse reproductive health outcomes. While hormones play a critical role in reproductive health, the impact of high ambient temperature on hormone levels has been underexplored. We examined the relationship between ambient temperature and reproductive hormones in healthy premenopausal women.

Method: A prospective cohort study (BioCycle, 2005–2007) enrolled 250 regularly menstruating women (18-44 years) for two menstrual cycles from Buffalo, NY. Daily ambient temperature was averaged across the week (1-7 days) before menses, week (1-7 days) after menses, and 2nd week (8-14 days) after menses. Estradiol (E2), follicle-stimulating hormone (FSH), luteinizing hormone (LH), and progesterone (P4) were measured in serum at 8 time points during the menstrual cycle, including menstruation, mid-follicular phase, and LH/FSH surge. Generalized linear mixed models estimated the association between temperature and hormones overall, by season, and for temperature thresholds ≥ 22°C vs. 85th percentile) adjusting for season, age, and PM2.5.

Result: While we observed a trend of increasing E2 with increasing temperature, E2 decreased above higher temperature thresholds. For example, a 1°C increase in temperature one week before menses was associated with 0.26 pg/mL (95% CI, 0.04, 0.49) higher E2 at menstruation. Conversely, exposure to temperatures ≥ 22°C vs. < 22°C was associated with -13.74 pg/mL (95% CI, -25.66, -1.82) lower E2 at menstruation. The association between E2 and temperature was similar in the mid-follicular phase and LH/FSH surge. Additionally, we observed lower LH and FSH at LH/FSH surge and lower P4 at menses with higher temperatures.

Conclusion: Exposure to high ambient temperatures was associated with consistently lower E2 and modest reductions in LH, FSH, and P4, indicating reproductive hormones may play a role in the impact of high temperatures on women’s reproductive health.

Environment/Climate Change

Investigating associations among perfluoroalkyl and polyfluoroalkyl substances (PFAS) levels and demographic characteristics within the Extremely Low Gestational Age Newborns (ELGAN) cohort. Kristina Stuckey* Kristina Stuckey Cailee Harrington Lauren Eaves T. Michael O'Shea Rebecca Fry

Perfluoroalkyl and polyfluoroalkyl substances (PFAS) are present throughout the environment and accumulate within water, food, and humans. PFAS exposure is associated with higher serum cholesterol, decreased immune function, higher risk of preeclampsia, and lower birth weight. Understanding demographic and social variables associated with higher exposure to PFAS can inform interventions for decreasing exposure. In this study, we investigated associations between socioeconomic and demographic variables and 4 PFAS: perfluorooctanesulfonic acid (PFOS), perfluorooctanoic acid (PFOA), perfluorononanoic acid (PFNA), and perfluorohexanesulfonic acid (PFHxS) among 161 mothers who delivered babies in the Extremely Low Gestational Age Newborns (ELGAN) cohort from 2002-04. PFAS exposure was quantified in maternal blood spots taken during a perinatal window. Demographic variables include insurance type, use of food stamps, marital status, educational status, smoking during pregnancy, and hospital of birth, based on medical records and self-report. We also derived the Centers for Disease Control and Prevention's Social Vulnerability Index (SVI) total percentile, based on reported residence during pregnancy. We assessed differences in PFAS exposure, both dichotomized and continuous, by key demographic variables using Wilcox and Kruskal-Wallis tests. A linear regression model was used to assess the relationship of SVI and PFAS exposure. Use of food stamps was associated with lower levels of PFOA (group mean 0.4428571 ng/ml and 0.1818182 ng/ml) and PFNA (0.471 ng/ml and 0.227 ng/ml) exposure. Increased social vulnerability was associated with lower PFNA exposure (Beta= 0.136, p-value= 0.096). Levels of all 4 PFAS differed based on the hospital of birth. Future analysis will include the incorporation of occupation data as well as investigate potential interactions of these variables.

Environment/Climate Change

Association Between Long-Term Methylmercury Exposure from Fish Consumption and Frailty and Cognition in Older Women Edwin van Wijngaarden* EDWIN VAN WIJNGAARDEN Gary Myers Matthew Rand Conrad Shamlaye Emelyn Shroff JJ Strain Alison Yeates Emeir McSorley Maria Mulhern Sally Thurston

Background: Methylmercury (MeHg) exposure from fish consumption has been associated with neurotoxic effects, yet its long-term impact on physical and cognitive function in older adults is unclear. We examined the relationship between MeHg and measures of frailty and cognition in a cohort of middle-aged to older women in a high fish-eating population.

Methods: This study included 609 women (mean age: 58 years, range: 45-77 years), originally recruited in 1990 as part of the Seychelles Child Development Study and re-enrolled in 2013 and 2021. In 2021, frailty was assessed using the Short Physical Performance Battery (SPPB) and hand grip strength (using dynamometry), while cognition was measured with the St. Louis University Mental Status (SLUMS) exam. MeHg exposure was determined as total Hg in hair samples. Fish consumption data was collected in 2013 and 2021. Mean hair Hg (averaged over all three time points) was examined in relation to frailty and cognition outcomes using linear regression adjusted for age, education, occupational status, smoking, alcohol use, waist to hip ratio, parity, marital status, KBIT (a measure of intelligence), and fish intake (averaged over the two time points). We also examined the interaction between fish intake and categories of estimated average Hg, fatty fish percent, and maternal age.

Results: Mean hair Hg concentrations were 6.8 ppm (1990), 6.7 ppm (2013), and 7.3 ppm (2021). Mean fish consumption was 10.3 and 9.8 fish dishes/week in 2013 and 2021, respectively. Hair Hg was not associated with SPPB scores (β = 0.002, 95% CI: -0.032, 0.036), hand grip strength (β = -0.012, 95% CI: -0.149, 0.125), or SLUMS scores (β = -0.026, 95% CI: -0.136, 0.084). Fish intake was not associated with frailty and cognition measures, and the fish intake associations were not significantly different across average Hg, fatty fish, or age categories.

Discussion: These findings suggest that dietary MeHg exposure at observed levels does not affect frailty or cognition in older women. Further cohort follow-up is needed to confirm this. Future research should explore potential modifiers such as dietary nutrient intake or genetic susceptibility.

Environment/Climate Change

Prenatal exposure to Organophosphate Ester Flame Retardant and Child Cognition at Age 4-6 years: The Environmental influences on Child Health Outcomes (ECHO) Cohort Akhgar Ghassabian* Akhgar Ghassabian Taylor Etzel Jennifer L. Ames Thomas G. O'Connor Jessie P Buckley Sarvenaz Shahin Julie B. Herbstman Emily S Barrett Donghai Liang Lisa A. Croen Rebecca J. Schmidt Lesliam Quiros-Alcala Susan L Schantz Kristen Lyall Giehae Choi Courtney Carignan Tracey J. Woodruff Rachel Morello-Frosch Claudia Buss Kurunthachalam Kannan Deborah H. Bennet

Despite experimental evidence showing developmental neurotoxicity of organophosphate esters (OPEs) flame retardants and plasticizers, epidemiological data are sparse. We examined associations between prenatal exposure to OPEs and child cognition and tested if associations differed by child sex.

We used data from 831 mother-child pairs from 3 sites in the Environmental influences on Child Health Outcomes Cohort with data on gestational urinary OPE metabolites and child cognition (pregnancies 2009-2019). We used 9 dilution-standardized OPE biomarkers modeled as log2-transformed for detection>75%, categorical (high, low, or non-detect) for detection 50-75%, or detect/non-detect binary variables for detection<50%. Children's cognition was measured using the Wechsler Preschool and Primary Scale of Intelligence or Wechsler Intelligence Scale for Children at mean age 5.7 years (SD=0.7). We examined associations of OPE biomarkers with age- and sex-standardized cognition scores using linear regression with generalized estimating equations to account for clustering within cohorts. We tested for effect measure modification by sex.

The OPE biomarkers with the highest detection rates were: diphenyl phosphate (DPHP) (96.4%), the composite of dibutyl phosphate and di-isobutyl phosphate (85.7%), and bis(1,3-dichloro-2-propyl) phosphate (81.8%). A unit increase in log2(DPHP) was associated with a 0.46 point lower cognition score (95%CI: -0.90, -0.02). Detectable concentrations for bis(1-chloro-2-propyl) phosphate (BCPP) and bis(2-methylphenyl) phosphate (BMPP) (vs. non-detectable levels) were associated with higher cognition scores in males only (β=4.02, 95%CI: 1.25, 6.79 and 3.26, 95%CI: 0.34, 6.17, respectively). No other associations with other OPEs were observed.

Prenatal exposures to DPHP, a widely detected OPE, may be associated with slightly lower child cognitive functioning. Findings with less detected OPEs, i.e., BMPP and BCPP, in males need further investigation.

Environment/Climate Change

Associations of Objective Indoor Temperature and Parent-Reported Thermal Discomfort with Sleep Health Outcomes in an Urban Sample of School-aged Children Taylor Robinson*
Taylor Robinson Jarvis Chen Gary Adamkiewicz Susan Redline

Objectives:

Thermoregulatory mechanisms influence sleep, with optimal sleep occurring at temperatures of 65-68°F. Rising global temperatures and indoor temperatures may contribute to insufficient sleep in vulnerable populations, contributing to health disparities. This study examined the association between objective indoor temperature measurements and parent-reported temperature concerns with sleep outcomes in children.

Methods:

The study sample included children aged 6-12 years, from predominantly low-income neighborhoods in Boston, enrolled in the Environmental Assessment of Sleep Youth (EASY) study. Both objective (temperature and actigraphy) and subjective (parent-reported thermal discomfort) measures were included to capture distinct but overlapping dimensions of how temperature influences sleep, acknowledging that subjective experiences may reflect nuanced interactions between environmental conditions and individual perceptions. Parents reported how often it was, “too hot to sleep at night,” with responses categorized as Never, Once in a while, and Often. Indoor temperatures were recorded in the main living areas continuously over 7-days using Environmental Multipollutant Monitoring Assembly devices. Sleep impairment and sleep disturbance were measured using the pediatric Patient-Reported Outcome Measurement Information System (PROMIS) surveys. Sleep efficiency and sleep duration were assessed using wrist actigraphy data collected over 7 nights.

Results:

Among the 329 children studied, 24.3% of parents reported it was “often” too hot for their child to sleep. In adjusted linear regression models, these children had 4.8-point higher sleep disturbance score and 5.4-point higher sleep impairment score compared to children whose parents never reported it being too hot. Objective nighttime temperatures were not significantly associated with these sleep outcomes or actigraphy-based measures in multilevel models.

Conclusions:

Thermal discomfort was linked to poor sleep quality and increased sleep-related impairment in children from low income neighborhoods. Device-based temperature and actigraphy measurements did not identify significant associations, possibly due to limited sampling periods.

LATEBREAKER

Genetics

Angiopoietin-like protein 3 inhibition and kidney function: multi-ancestry Mendelian randomization analyses Guoyi Yang* Guoyi Yang

Background: Serum angiopoietin-like protein 3 (ANGPTL3) is associated with nephrotic syndrome. We hypothesized that ANGPTL3 inhibition improves kidney function through enhancing lipoprotein lipase (LPL) and endothelial lipase.

Methods: We conducted drug-target Mendelian randomization (MR) analyses to assess the associations of genetically proxied ANGPTL3 inhibition, LPL enhancement, and endothelial lipase enhancement with estimated glomerular filtration rate based on serum creatinine (eGFRcrea) and chronic kidney disease (CKD) risk. We compared these associations with the associations for ANGPTL4 inhibition, ANGPTL8 inhibition, and hepatic lipase enhancement. We used data from the largest publicly available genome-wide association study of eGFRcrea (N = 1,785,582, 282,852, and 67,943 of European, East Asian, and African ancestry) and from the All of Us, Penn Medicine Biobank, CKDGen Consortium, Million Veteran Program, UK Biobank, FinnGen, and Biobank Japan (total CKD cases = 151,409, 2,117, and 34,872 of European, East Asian, and African ancestry, respectively). We performed ancestry-specific analyses and meta-analyzed MR estimates.

Results: For a 1-standard deviation (SD) decrease in triglycerides, genetically proxied ANGPTL3 inhibition and LPL enhancement were associated with higher eGFRcrea (0.09 [95% confidence interval 0.07 to 0.11] and 0.02 [0.01 to 0.03]) and lower CKD risk (odds ratio 0.82 [0.71, 0.95] and 0.89 [0.83 to 0.95]). For a 1-SD decrease in high-density lipoprotein cholesterol, genetically proxied endothelial lipase enhancement was associated with higher eGFRcrea (0.02 [0.003 to 0.04]) and lower CKD risk (odds ratio 0.93 [0.87 to 1.00]). Genetically proxied ANGPTL4 inhibition was also associated with lower CKD risk (odds ratio 0.80 [95% CI 0.71 to 0.91]) per 1-SD decrease in triglycerides, but ANGPTL 8 inhibition and hepatic lipase enhancement had little association with eGFRcrea or CKD risk.

Conclusions: ANGPTL3 inhibition increases eGFRcrea and reduces CKD risk, partially through enhancing LPL and endothelial lipase.

Genetics

A Novel Method for Summary-data-based Multivariable Mendelian Randomization Ming Ding* Ming Ding Fei Zou

Summary-data-based multivariable Mendelian randomization (MVMR) methods, such as MVMR-Egger, MVMR-IVW, MVMR median-based, and MVMR-PRESSO, assess the causal effects of multiple risk factors on disease. However, accounting for variances in summary statistics related to risk factors remains a challenge. We propose a linear mixed model with measurement error correction (LMM-MEC) that accounts for the variance of summary statistics for both disease outcomes and risk factors. In step I, a linear mixed model is applied to account for the variance in disease summary statistics. Specifically, if heterogeneity is present in disease summary statistics, we treat it as a random effect and adopt an iteratively re-weighted least squares algorithm to estimate causal effects. In step II, we treat the variance in the summary statistics of risk factors as multiple measurement errors and apply a regression calibration method for simultaneous multiple measurement error correction. In a simulation study, when using independent genetic variants as instrumental variables (IV), our method showed comparable performance to existing MVMR methods under conditions of no pleiotropy or balanced pleiotropy with the outcome, and it exhibited higher coverage rates and power under directional pleiotropy (**Figure**). Similar findings were observed when using genetic variants with low to moderate linkage disequilibrium (LD) ($0 < 2 \leq 0.3$) as IVs, although coverage rates reduced for all methods compared to using independent genetic variants as IVs. In the application study, we examined causal associations between correlated cholesterol biomarkers and longevity. By including 739 genetic variants selected based on P values <510-5 from GWAS and allowing for low LD ($2 \leq 0.1$), our method identified that large LDL-c were causally associated with lower likelihood of achieving longevity.

Figure. A simulation study estimating causal associations between positive (X_1), null (X_2), and negative (X_3) risk factors and outcome (Y) under no linkage disequilibrium (ρ^2=0) between genetic variants.

	No pleiotropy with outcome			Balanced pleiotropy, InSIDE satisfied			Directional pleiotropy, InSIDE satisfied		
	k_1=0.1	k_2=0	k_3= -0.1	k_1=0.3	k_2=0	k_3= -0.3	k_1=0.1	k_2=0	k_3= -0.1
	Estimated mean value								
LMM-MEC	0.09	0	-0.09	0.26	0	-0.27	0.09	0	-0.09
MVMR-Egger	0.06	0	-0.09	0.17	0	-0.27	0.06	0.03	-0.06
MVMR IVW	0.09	0	-0.09	0.27	0	-0.27	0.12	0.03	-0.06
MVMR median-based	0.09	0	-0.09	0.27	0	-0.27	0.12	0.03	-0.06
MVMR-PRESSO	0.09	0	-0.09	0.27	0	-0.27	0.12	0.03	-0.06
	Estimated standard error								
LMM-MEC	0.02	0.02	0.02	0.08	0.08	0.08	0.02	0.02	0.02
MVMR-Egger	0.04	0.02	0.02	0.16	0.07	0.07	0.05	0.02	0.02
MVMR IVW	0.02	0.02	0.02	0.07	0.07	0.07	0.02	0.02	0.02
MVMR median-based	0.03	0.03	0.03	0.06	0.06	0.06	0.03	0.03	0.03
MVMR-PRESSO	0.02	0.02	0.02	0.07	0.07	0.07	0.02	0.02	0.02
	Coverage (%)								
LMM-MEC	93	96	92	92	95	93	90	96	91
MVMR-Egger	83	96	92	88	95	92	86	75	55
MVMR IVW	93	97	93	93	95	92	87	75	54
MVMR median-based	96	98	95	77	79	74	88	80	66
MVMR-PRESSO	92	95	92	91	93	91	85	73	52
	Power (%)								
LMM-MEC	100	—	100	93	—	94	99	—	99
MVMR-Egger	28	—	100	18	—	96	24	—	79
MVMR IVW	100	—	100	96	—	96	100	—	77
MVMR median-based	95	—	95	94	—	95	99	—	55
MVMR-PRESSO	100	—	100	94	—	94	100	—	76

Global Health

Intersectional Inequalities in the Context of Rurality on Cognitive Functioning: A MAIHDA Analysis of the Harmonized Cognitive Assessment Protocol Network in Mexico, India, and China L. Paloma Rojas-Saunero* L. Paloma Rojas-Saunero Janette Vazquez Erika Meza Cristina A. F. Román Sneha Sarah Mani Ruijia Chen Yingyan Wu Lindsay Kobayashi Justina Avila-Rieger Elizabeth Rose Mayeda Marcia Pescador Jimenez

INTRODUCTION: There is limited evidence on how living in rural areas intersects with systems of oppression to influence cognitive health, particularly in non-Western countries. Guided by an intersectional framework, we examine how rurality intersects with sexism, ageism, and limited educational access to characterize cognitive performance in India, Mexico, and China.

METHODS: We use data from 3 participating countries of the Harmonized Cognitive Assessment Protocols (HCAPs): Mexico (MEXCog, n=2024; age: 54-104), India (LASI-DAD; n=2319; age: 60-105) and China (CHARLS-HCAP, n=9755; age: 60-108). We created 24 intersectional strata based on residence (rural/urban), sex/gender (women/men), age 75+ (yes/no) and education (no/early; primary; secondary/higher). Cognitive performance was measured cross-nationally with harmonized general cognitive function factor scores and z-scored. We performed a parallel multilevel analysis of individual heterogeneity and discriminatory accuracy (MAIHDA) to calculate the variance in cognitive performance due to intersectional strata. We fitted multilevel linear models with random effects for intersectional strata adjusting for age, and a second model with main effects for rurality, sex/gender, age 75+ and education. We calculated the proportional change in variance (PCV) to estimate the cognitive performance variance explained by the interaction of these social identities after accounting for main effects.

RESULTS: The variance between intersectional strata accounted for 41% of the total variance in cognitive function in MEXCog, 33% in LASI-DAD, and 34% in CHARLS-HCAP. After including main effects, the PCV was 9% in MEXCog, 19% in LASI-DAD and 5% in CHARLS-HCAP. Women ages 75+ in rural areas with no education had lower cognitive performance compared to other strata.

CONCLUSION: These results highlight that cognitive health is shaped by the interaction of multiple social identities, with varying impacts across countries.

Global Health

Assessing the Impact of Household Characteristics on Cholera Risk in Haiti: Insights from the 2016-2017 Demographic and Health Survey Colette Davis* Colette Davis Armelle Delouis

Background: Cholera remains a critical public health challenge in Haiti, influenced by various household characteristics. This study investigats the association between household factors and cholera risk to guide targeted interventions.

Methods: We analyzed data from 10,759 households in the 2016-2017 Demographic and Health Survey (DHS). Key household factors examined included water source type (structured vs. unstructured), sanitation facilities (connected vs. unconnected), handwashing practices (fixed vs. mobile stations), and water treatment measures. Covariates included household size, presence of children under five, urban/rural residence, electricity availability, cooking fuel type, livestock ownership, and wealth index. Chi-square tests and binary logistic regression were employed to assess associations between these factors and cholera risk.

Results: Households with structured water systems (69.3%) had a significantly lower risk of cholera (OR: 0.57, 95% CI: 0.51-0.64). Urban households were more likely to treat water (OR: 1.63, 95% CI: 1.45-1.83). Access to electricity was inversely associated with water treatment practices (OR: 0.57, 95% CI: 0.51-0.64), while using non-fossil fuels increased water treatment likelihood (OR: 1.57, 95% CI: 1.39-1.77). Household size, wealth index, and the presence of children under five were significant covariates. No significant associations were found between household head gender and sanitation practices.

Conclusion: Addressing household factors, particularly improving water and sanitation infrastructure, is crucial for reducing cholera risk in Haiti. These findings provide critical insights for targeted public health strategies to prevent cholera outbreaks in vulnerable communities.

Global Health

Mechanisms of impact of early water, sanitation, hygiene and nutrition interventions on development in middle-childhood: A causal mediation analysis Helen Pitchik* Helen Pitchik Fahmida Tofail Mahbubur Rahman Kara E. Rudolph Jennifer Ahern Peter J. Winch Stephen P. Luby Lia C. H. Fernald

Background

A cluster randomized controlled trial of individual and combined water, sanitation, hygiene (WASH), and nutrition interventions in rural Bangladesh (WASH-B) found improvements in both child diarrhea and child development outcomes at 2 years of age with a recent school-aged follow-up finding sustained impacts on development at 7 years of age. Two similar early WASH interventions in Kenya and Zimbabwe did not find intervention impacts on child development. Identifying the pathways of intervention impacts in Bangladesh will enable the design of future interventions.

Methods

We use data from the baseline, 2-, and 7- year assessments in the WASH-B intervention cohort (n=3,832 at 7 years) to examine mediators of 7-year intervention effects on child development, maternal mental health, and the home environment. We selected mediators based on a review of the literature on modifiable risk factors, data availability, and 2-year intervention impacts. We used targeted maximum likelihood estimation with ensemble machine learning to estimate the interventional direct and indirect effects through the multiple mediators, accounting for post-exposure confounding.

Results

At 2 years of age the potential mediators impacted by the WASH and nutrition interventions include indicators of child health (child 7-day diarrhea prevalence, child growth), caregiver depressive symptoms, and the quality of stimulation in the home. A preliminary analysis of the mediator-outcome associations demonstrates that stimulation at 2 years is associated with 7-year outcomes for social-emotional development, and diarrhea, home stimulation, and caregiver depressive symptoms at 2 years are associated with 7-year full-scale IQ. Results from the interventional indirect and direct effects for each mediator as well as for the combination of mediators will be presented and discussed. This work builds on evidence on key intervention components that contribute to sustained intervention effects in childhood.

Global Health

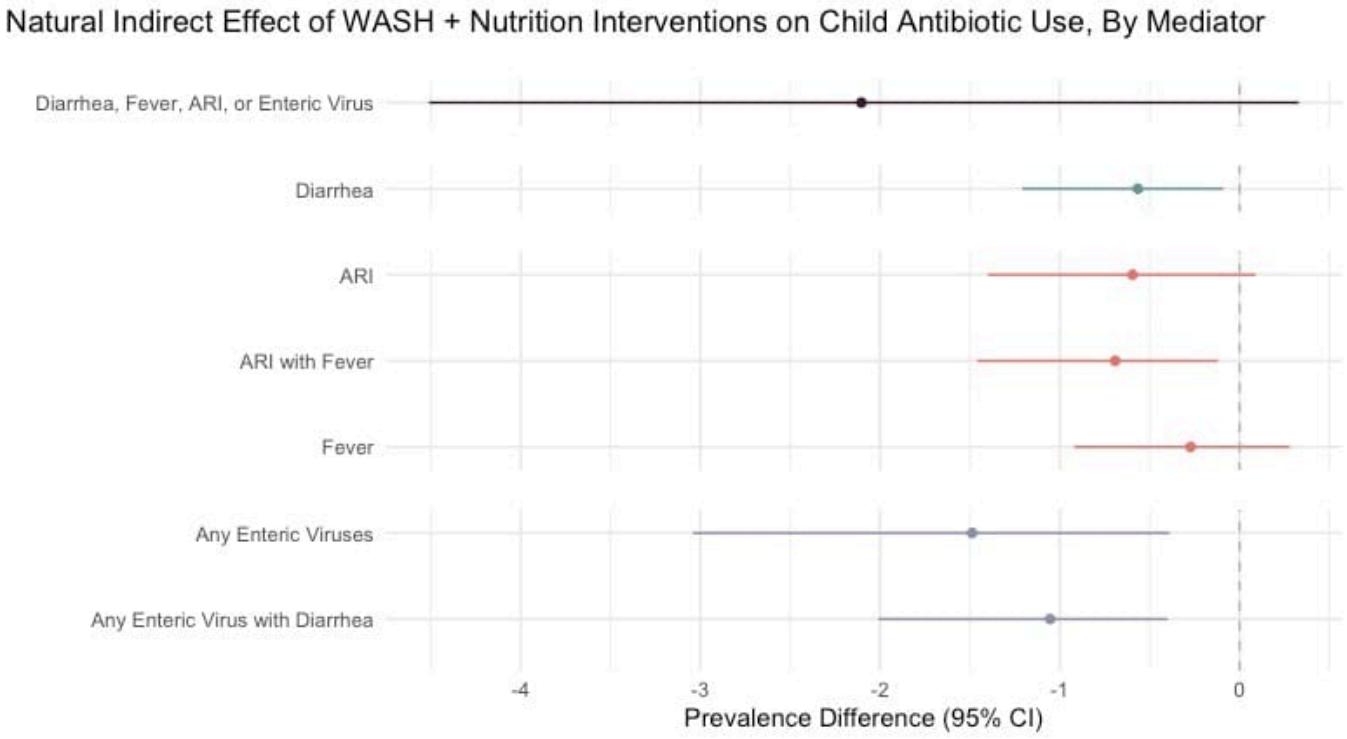
Pathways through which water, sanitation, hygiene, and nutrition interventions reduce antibiotic use in young children: a mediation analysis of a cluster-randomized trial Anna Nguyen* Anna Nguyen Gabby Barratt Heitmann Andrew Mertens Sania Ashraf Md Ziaur Rahman Shahjahan Ali Mahbubur Rahman Benjamin F. Arnold Jessica A. Grembi Audrie Lin Ayse Ercumen Jade Benjamin-Chung

Background: Low-cost water, sanitation, and hygiene (WASH) and nutrition interventions can reduce pediatric antibiotic use, but the mechanism through which interventions reduce antibiotic use has not been investigated.

Methods: We conducted a causal mediation analysis using data from the WASH Benefits Bangladesh cluster-randomized trial (NCT01590095). Among a subsample of children within the WSH, nutrition, nutrition+WSH, and controls arms (N=1,409), we recorded caregiver-reported antibiotic use at ages 14 and 28 months and collected stool at age 14 months. Mediators included caregiver-reported child diarrhea, acute respiratory infection (ARI), and fever; and enteric pathogen carriage in stool measured by qPCR. Models controlled for mediator-outcome confounders.

Results: The receipt of any WASH or nutrition intervention reduced antibiotic use through all pathways in the past month by 5.5 percentage points (95% CI 1.2, 9.9), from 49.5% (95% CI 45.9%, 53.0%) in the control group to 45.0% (95% CI 42.7%, 47.2%) in the pooled intervention group. When separating this effect into different pathways, we found that interventions reduced antibiotic use by 0.6 percentage points (95% CI 0.1, 1.3) through reduced diarrhea, 0.7 percentage points (95% CI 0.1, 1.5) through reduced ARI with fever, and 1.5 percentage points (95% CI 0.4, 3.0) through reduced prevalence of enteric viruses. Interventions reduced antibiotic use through any of these measured mediators (diarrhea, fever, ARI, or enteric viruses) by 2.1 percentage points (95% CI -0.3, 4.5).

Conclusion: WASH and nutrition interventions reduced pediatric antibiotic use through the prevention of enteric and respiratory infections in a rural, low-resource population. Given that many of these infections are caused by viruses or parasites, WASH and nutrition interventions may help reduce inappropriate antibiotic use in similar settings.


Natural Indirect Effect of WASH + Nutrition Interventions on Child Antibiotic Use, By Mediator
Diarrhea, Fever, ARI, or Enteric Virus
Diarrhea
ARI
ARI with Fever
Fever
Any Enteric Viruses
Any Enteric Virus with Diarrhea
-4
-3
-2
-1
0
Prevalence Difference (95% CI)

Global Health

The Impact of Circular Migration on the HIV Care Continuum: A Qualitative Analysis in Northeastern South Africa Maryam Alkhamees* Maryam Alkhamees Rachel Yorlets Linda Ndlovu Maryam Alkhamees Nomi Nkalanga Philasande Accordance Carren Ginsburg Abigail Harrison Mark N Lurie F Xavier Goméz-Olivé

Background

Within-country migration is a well-documented driver of the HIV epidemic in South Africa, as living away from home complicates health care uptake. However, minimal literature gives voice to migrants' first-hand perspectives on how living away from home facilitates or complicates engagement in each step of HIV care.

Methods

Using the frameworks of the HIV care cascade and the three delays model, we conducted semi-structured interviews with migrants living with HIV. In August 2022, a trained fieldworker interviewed 30 participants from The Migration and Health Follow-Up Study, focusing on adults aged 18-40 from Agincourt, Mpumalanga. We used stratified purposive sampling to select participants with a confirmed HIV diagnosis who spent four to five nights away from home per week before the study. After translation and de-identification, one analyst undertook immersion, coding, and thematic synthesis.

Results

Migrants described seeking HIV care in the absence of social support: several explained that making a clinic appointment results in lost revenue, as they have no one to run their business, and numerous participants had never disclosed their HIV status outside their immediate family; one had never disclosed to anyone other than a clinical provider. In reaching care, migrants face the financial barrier of taxi fare, which they must borrow. At the clinic, participants overall said that they were satisfied with the confidentiality and privacy at clinics, although some noted long wait times. Motivation for adherence was unrelated to migration; most cited their own survival, often for children.

Conclusions

Migrants living with HIV faced financial and logistical obstacles in seeking and reaching care, but migration had no negative effect on treatment adherence. We suspect interventions like mobile clinics and medication delivery systems would alleviate the costs associated with HIV care.

LATEBREAKER

Global Health

An innovative and improved study design and matching algorithm for assessment of progression to dementia and early dementia among stroke survivors in population-based cohorts in Europe and the U.S.A Reem Waziry* Reem Waziry et al.

Background. With the AI revolution and translational advances in biomarkers' technology, many cerebrovascular disease survivors will soon become eligible for inclusion in clinical trials on Alzheimer's and Related Dementias (ADRD). Stroke survivors represent a key population at risk. Global collaborative efforts, large sample sizes and improved study designs are critical to allow for rigorous comparative inference from population-based cohorts to cohorts of clinical trials on ADRD.

Objective & Methods. To assess risk of progression to dementia and early dementia following first-ever stroke with a focus on stroke subtype and role of APOE ε4 allele carriership. We developed an improved population-based study design for global ADRD risk and ADRD biomarker assessment in this population. Meta-analysis of prospective population-based studies in Europe and USA (including Three City (France), Framingham Heart Study (USA) and the Rotterdam Study (Netherlands). Methods were harmonized and reproduced in a consistent manner across prospective cohorts in Europe and U.S.A.

Results. Following hemorrhagic stroke compared to stroke-free individuals, the combined hazard ratio was 1.75 (95% CI 0.85, 3.60) after APOE ε4 adjustment compared to 2.23 (95% CI 1.13, 4.43) following ischemic stroke. After excluding early dementia, the risk of dementia following hemorrhagic stroke was 2.49 (95% CI 0.89, 6.94) and 1.74 (95% CI 1.24, 2.43) following ischemic stroke.

Conclusion. Using an innovative and improved study design reproduced in a consistent manner across prospective cohorts in Europe and U.S.A, findings support that after adjustment for APOE4 carriership, risk of dementia remains high following ischemic or hemorrhagic stroke. These observations provide evidence support to optimize stroke survivors' inclusion in future cohorts of clinical trials on ADRD.

LATEBREAKER

Global Health

Tuberculosis (TB) Aftermath non-inferiority trial: phone screening compared to home-based screening post TB Samyra Cox* Samyra Cox Abhay Kadam Shahanara Valawalkar Gayatri Lele Aye Hnin Moe Akshay Gupte Nishi Suryavanshi Emily Kendall Hojoon Sohn Christopher J Hoffmann AL Kakrani Nikhil Gupte MS Barthwal Jonathan E. Golub Vidya Mave

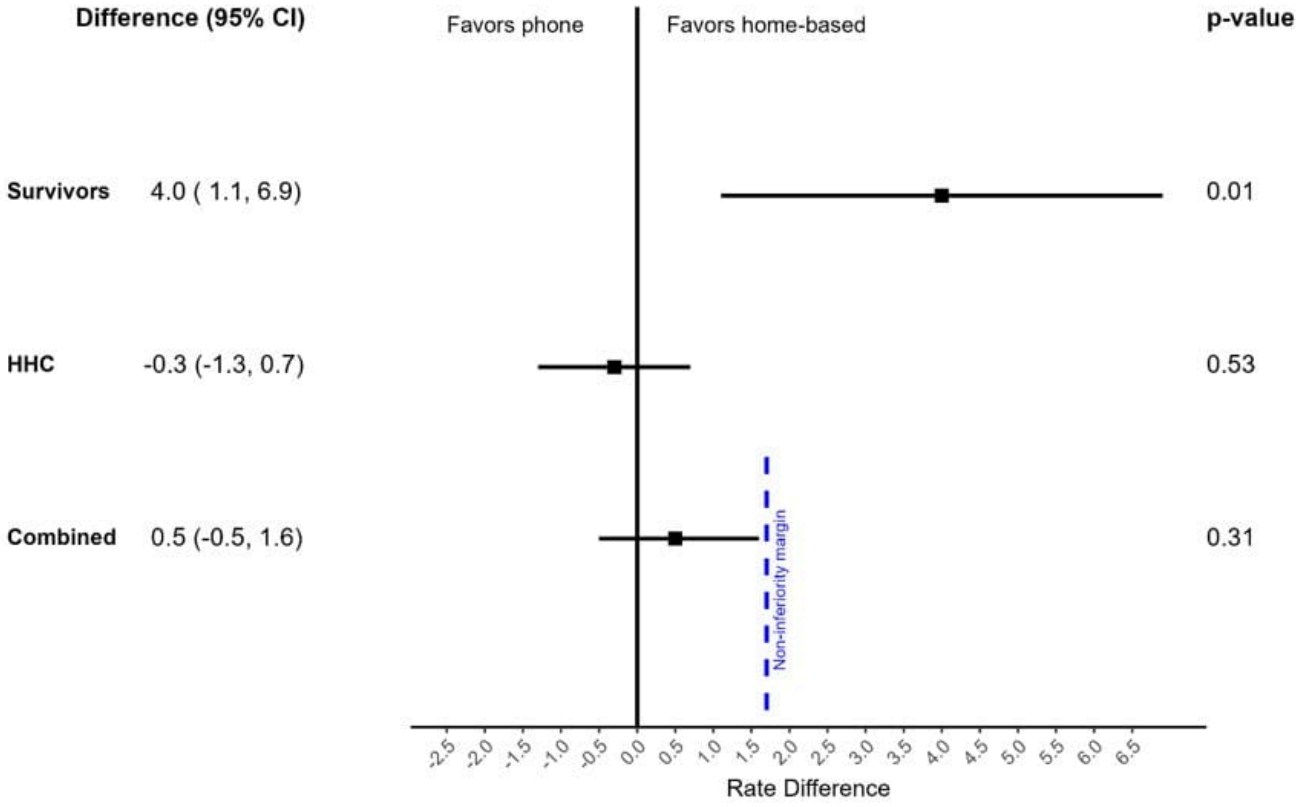
Introduction: Tuberculosis (TB) survivors and their household contacts (HHC) are at elevated risk for TB even after treatment; however, effective strategies for post-TB screening remain untested. We conducted a hybrid effectiveness-implementation trial in India to assess whether phone screening is non-inferior to home-based screening after TB treatment.

Methods: We enrolled TB survivors (>18 years) within 60 days of completing treatment. Participants were randomized to phone or home-based symptom screening at 6- and 12-months post-treatment. HHC were enrolled during follow-up (Jan 2021-Feb 2025). Our primary outcome was rate of TB detection/100 person-years by arm among TB survivors and HHC. Our non-inferiority margin was set a-priori as a rate difference of 1.7. We adjusted for household-level clustering using multilevel Poisson regression. We also compared rates (Wald test) and time to diagnosis (Wilcoxen rank-sum) by arm among TB survivors and HHC separately.

Results: We enrolled 1076 TB survivors (537 phone, 539 home-based) and 1773 HHC (693 phone, 1080 home-based). Seventy-five (7%) TB survivors and 28 (2%) HHC were diagnosed with TB. Phone was non-inferior to home-based screening (rate difference: 0.5/100 person-years [95% CI: -0.5, 1.6]). Among TB survivors, recurrence rate/100 person-years was 4.4 (2.7, 6.0) in phone vs. 8.4 (6.0, 10.8) in home-based (p-value: 0.01). Among HHC, TB rate was 1.3 (0.5, 2.1) in phone vs. 1.0 (0.5, 1.6) in home-based (p-value: 0.53). Among 75 recurrences, 44 (59%) were diagnosed within 6 months; median time to diagnosis was similar by arm (p-value: 0.50).

Conclusions: Risk of TB remains high for households with a TB survivor. Overall, phone was non-inferior to home-based screening for detecting TB after treatment. However, for detecting recurrence, home-based screening was more effective. Countries with a high burden of TB recurrence should consider home-based strategies for post-TB screening to help close the case detection gap.

Figure: Forest plots of difference in rate of TB detection/100 person-years comparing phone screening to home-based screening post TB among TB survivors only, household contacts (HHC) only, and combined (primary outcome)



Global Health

The Influence of Political Determinants on Antenatal Care and Mortality in LMICs Sueny Paloma* Sueny Paloma Lima dos Santos Dr. Zelalem Haile

Antenatal care (ANC) is critical for improving maternal and child health (MCH) outcomes, yet disparities persist, particularly in low- and middle-income countries (LMICs). This study investigates the impact of political determinants—governance, corruption, and gender inequality—on MCH outcomes, including maternal mortality ratio (MMR), neonatal mortality rate (NMR), infant mortality rate (IMR), and under-5 mortality rate (URMR). Using country-level data from the World Bank, Demographic and Health Surveys, WHO, and UNICEF, we analyzed associations between governance indices and MCH outcomes. Negative binomial regression and mediation analysis were performed. The Global Women's Health Index (HGWHI) and Universal Health Coverage (UHC) scores demonstrated significant negative associations with mortality outcomes (coefficients: -0.03 to -0.07, $p < 0.001$), while CCI showed similar trends (coefficients: -0.03 to -0.06, $p < 0.001$). Countries with higher UHC and CCI scores, such as Brazil and Malaysia, exhibited lower mortality rates, whereas lower scores in Afghanistan and Sierra Leone were associated with worse outcomes. The Gini Index, reflecting income inequality, showed weak and non-significant associations with mortality outcomes (coefficients: 0.00 to -0.01, $p = 0.35$). The Gender Inequality Index (GII) and Women's Peace and Security Index (WPS) were critical determinants, with GII positively associated with mortality outcomes (coefficients: 4.44 to 8.02, $p < 0.001$) and WPS negatively associated (coefficients: -3.1 to -4.36, $p < 0.001$). Mediation analysis revealed UHC and CCI partially mediated the relationship between governance factors and IMR, URMR, and MMR, with significant indirect effects (Estimates: -0.0139 to -0.0251, $p < 0.001$). Sobel tests confirmed that the CCI mediated the relationship in NMR models, whereas CPI did not. These findings highlight the importance of governance and gender equity in reducing mortality and improving access to ANC. Policy recommendations include expanding UHC, addressing gender disparities, and implementing anti-corruption measures to improve equitable healthcare for women and children in LMICs.

Global Health

Disentangling the associations between women's decision-making power dynamics and maternal and child health outcomes in 35 sub-Saharan African countries Yun-Jung Eom*
Yun-Jung Eom Rockli Kim

Background: So far, most research has treated women's sole and joint decision-making as having the same nature under the name of women's empowerment. This paper explores the most effective ways women's decision-making power might operate to enhance maternal and child health (MCH) in sub-Saharan Africa (SSA).

Methods: We used most recent data from Demographic and Health Surveys across 35 countries in SSA. Decision-making power dynamics were identified by distinguishing women's sole and joint decision-making. Seven exemplary MCH outcomes were selected: antenatal care contacts, facility deliveries with skilled birth attendants, postnatal care, low birth weight, stunting, full immunization coverage, and child morbidity. A series of logistic regressions were estimated adjusting for covariates with country and survey year fixed effects.

Results: Any decision made by husbands or others consisted of more than half the sample (59.1%), followed by decisions usually made jointly with husbands (32.6%) and decisions made by women alone (8.3%). For all MCH outcomes, decisions made jointly yielded the best health outputs. For example, children whose mothers usually made decisions jointly were 20% (OR=0.80; 95% CIs=0.77-0.83) and 13% (OR=0.77; 95% CI=0.76-0.79) less likely to have one or more morbidities compared to children whose mothers usually made decisions alone and children whose fathers or someone else made any decisions, respectively.

Conclusions: Joint decision-making may reflect more equitable gender beliefs and practices in spousal relationships than women's sole decision-making. Empowering women through interventions that promote mutual respect and shared responsibility among spouses in household decisions is crucial for shifting the gender power balance and improving health and well-being of women and children in SSA.

Table 5. Associations between different scenarios of decision-making power dynamics and maternal healthcare use.

	Maternal healthcare use					
	ANC4+[a]		FD with SBA[a]		Any PNC[a]	
	OR	95% CI	OR	95% CI	OR	95% CI
Scenario 1. Decisions by 'women alone' combined with 'jointly'						
[A] Any by husband or others	ref		ref		ref	
[B] All by women alone or jointly	1.10***	1.07-1.13	1.19***	1.15-1.23	1.15***	1.12-1.18
Scenario 2. Decisions by 'women alone' distinguished from 'jointly'						
[A] Any by husband or others	ref		ref		ref	
[B-1] Usually by women alone	1.02	0.98-1.07	1.13***	1.08-1.19	1.07**	1.02-1.11
[B-2] Usually jointly	1.12***	1.09-1.15	1.21***	1.17-1.25	1.17***	1.14-1.20
[A] Any by husband or others	0.98	0.93-1.01	0.88***	0.84-0.93	0.94**	0.90-0.98
[B-1] Usually by women alone	ref		ref		ref	
[B-2] Usually jointly	1.09***	1.05-1.14	1.07**	1.02-1.12	1.10**	1.05-1.15
Observations	N=207,132					

**p<0.01; ***p<0.001. OR = Odds ratios. CI = confidence intervals.

a. ANC4+ = antenatal care >= 4 times; FD with SBA = facility delivery with skilled birth attendants; any PNC = any postnatal care.

b. Covariates included birth order, women's age, women's education, women's working status, number of children aged <5, type of place of residence, and household wealth. Country and survey year fixed effects are further included.

Table 6. Associations between different scenarios of decision-making power dynamics and child health outcomes.

	Child health							
	Low birth weight		Stunting		Full immunization coverage[a]		Child morbidity[b]	
	OR[c]	95% CI	OR[d]	95% CI	OR[d]	95% CI	OR[d]	95% CI
Scenario 1. Decisions by 'women alone' combined with 'jointly'								
[A] Any decision by husband or others	ref		ref		ref		ref	
[B] All decisions by women alone or	0.91***	0.88-0.95	0.96**	0.94-0.99	1.06**	1.02-1.11	0.81***	0.79-0.83
Scenario 2. Decisions by 'women alone' distinguished from 'jointly'								
[A] Any decision by husband or others	ref		ref		ref		ref	
[B-1] Usually by women alone	0.97	0.91-1.03	1.00	0.96-1.05	0.99	0.92-1.06	0.97	0.94-1.00
[B-2] Usually jointly	0.90***	0.86-0.94	0.95**	0.93-0.98	1.08***	1.04-1.13	0.77***	0.76-0.79
[A] Any decision by husband or others	1.03	0.97-1.10	1.00	0.95-1.04	1.01	0.94-1.09	1.03	1.00-1.07
[B-1] Usually by women alone	ref		ref		ref		ref	
[B-2] Usually jointly	0.93*	0.87-0.99	0.95*	0.91-0.99	1.09*	1.02-1.17	0.80***	0.77-0.83
Observations	N=164,722		N=176,770		N=60,866		N=307,862	

*p<0.05; **p<0.01; ***p<0.001. OR = Odds ratios. CI = confidence intervals.

a. Sample restricted to children aged 12-23 months.

b. Child morbidity is defined as a child suffering from any of the following past two weeks: diarrhea, fever, and acute respiratory infection.

c. Covariates included child sex, birth order, women's age, women's education, women's working status, number of children aged <5, type of place of residence, and household wealth. Country and survey year fixed effects are further included.

d. Covariates included child sex, child age, birth order, women's age, women's education, women's working status, number of children aged <5, type of place of residence, and household wealth. Country and survey year fixed effects are further included.

Global Health

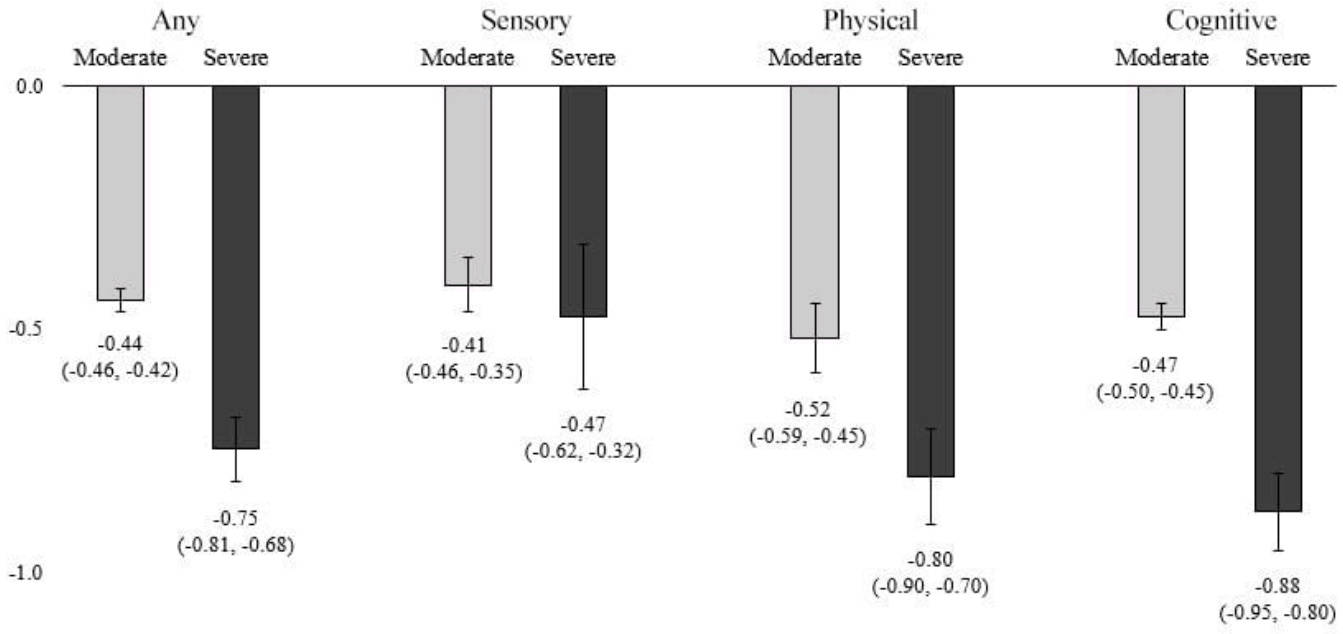
Child's functional difficulties and early childhood development in 22 low- and middle-income countries Hyejun Chi* Hyejun Chi Rockli Kim

Backgrounds: Disability is one of the health components that can compromise the developmental potential of children. However, only few studies have explored how a child's disabilities can affect their early childhood development (ECD) in low- and middle-income countries (LMICs); the existing literature was limited in terms of considering the types and severity of disabilities and their potential moderators.

Methods: Using Multiple Indicator Cluster Surveys from 22 LMICs (2017-2020), we performed three-level random effects linear regressions to assess the association with a child's functional difficulties and the standardized ECD z-score. Difficulties were further categorized into sensory, physical, and cognitive functions and according to their severity. Statistical interaction with functional difficulties and learning-related variables were additionally estimated.

Results: Overall, 6.0% of children reported any functional difficulties (sensory 1.0%; physical 0.9%; cognitive 5.1%). After adjusting for sociodemographic covariates, having any functional difficulties was associated with 0.47 lower ECD z-score (b=-0.47, 95% CI=-0.50, -0.45). Difficulty in sensory, physical, and cognitive functions were also associated with lower ECD z-score (b=-0.42, 95% CI=-0.47, -0.36 for sensory; b=-0.62, 95% CI=-0.67, -0.56 for physical; b=-0.51, 95% CI=-0.53, -0.49 for cognitive). Severe functional difficulties were associated with lower ECD z-score across the categories. We found little statistical interaction between functional difficulties and learning-related variables (interaction p-value>0.05).

Conclusions: Children with functional difficulties showed less optimal developmental status compared to their peers without difficulties. Efforts to improve the ECD of these children should focus on inclusive education and family support programs so that they can be successfully integrated into societies.



Global Health

Ill-defined mortality in Brazil during the COVID-19 pandemic: population study by region and race/ethnicity Doris Duran* Doris Duran Renzo Calderon-Anyosa Jay S. Kaufman

Ill-defined or garbage codes (GC) are uninformative ICD-10 codes in mortality statistics. Smaller GC proportions indicate better data quality. The Global Burden of Disease (GBD) group classified GC into four classes by their health planning impact and redistribution potential. Class 1 is the most critical, as reassignment to a specific cause is difficult (e.g., sepsis), while class 4 is more specific and can be reallocated to disease groups. During COVID-19, with overwhelmed health systems and high excess mortality in Brazil, GC deaths likely varied by region and race/ethnicity.

Aim: To describe GC mortality rates in Brazil by race/ethnicity before and during the COVID-19 pandemic.

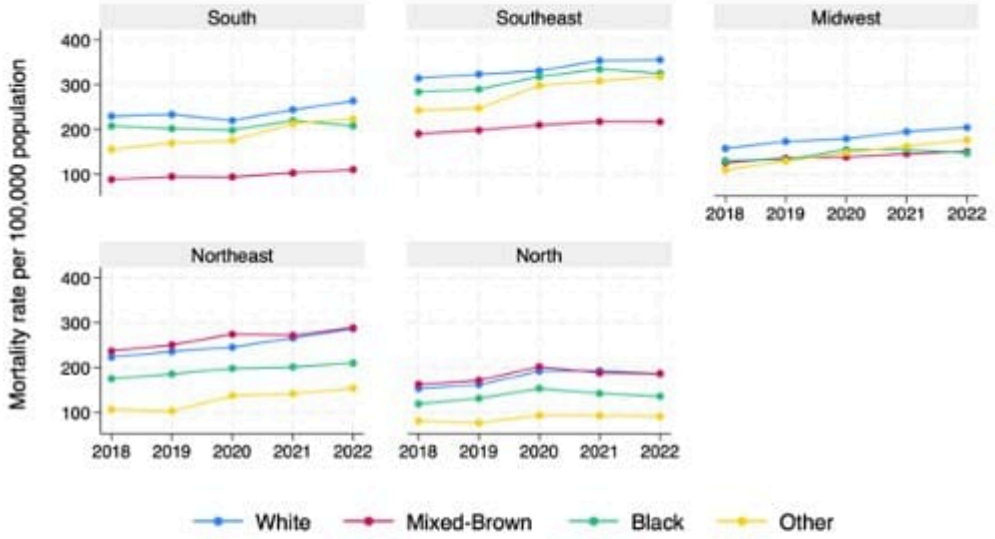
Methods: Mortality data were from vital statistics (SIM Brazil). Population data came from census-based projections. Mortality rates for deaths with a GC code were estimated by region, race/ethnicity, and GBD class from 2018–2022 for ages 25+. Annual percentage changes were calculated by GC class.

Results: There were 7,158,724 deaths during the study. Deaths peaked in 2020–2021. GCs accounted for 35.5% (n=2,514,756) of all deaths. The South had the lowest GC proportion (27%), and the Northeast the highest (39.2%). Blacks had the highest GC proportion (38.8%), Whites the lowest (33.6%). GC mortality in the North was highest among Mixed-Brown individuals; in the South, it was among Whites and Blacks. GC mortality rose during the pandemic for all groups, except in the North region in 2020 (Fig1A). Class 4 GCs made up 39.4% of GC deaths; Class 1, 29.9%. Classes 1–2 increased for all groups until 2021 (Fig1B). Classes 1–3 saw slight improvement in 2022.

Conclusion: GC mortality is high in Brazil, and it increased during COVID-19 particularly for classes 1-2. Northern and Southern regions showed opposing trends for the Mixed-Brown group, Brazil’s second largest race/ethnicity group. GC deaths challenge cause-specific analysis and should be redistributed for accurate assessments by region and race.

Figure 1: Ill-defined mortality rates by race/ethnicity groups and regions in Brazil during 2018-2022

A – Total GC mortality by region



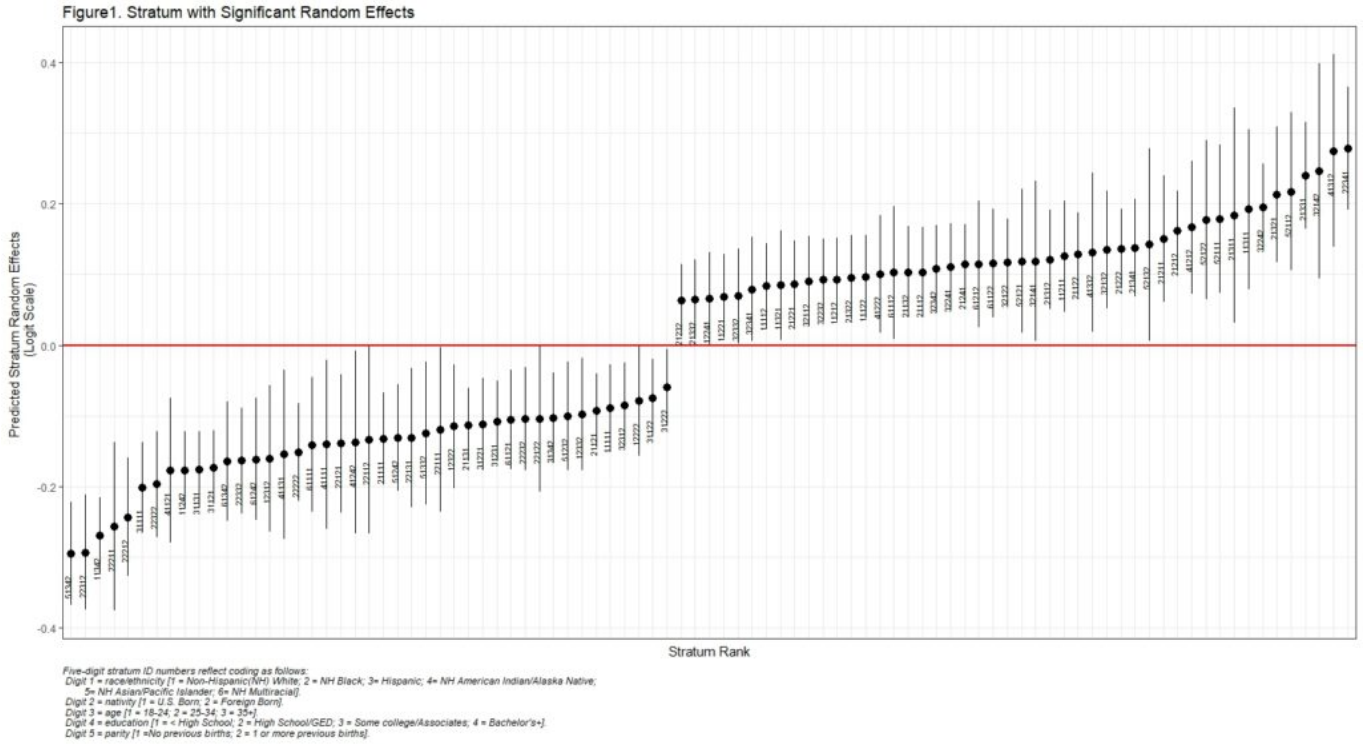
B– GC mortality rates annual percentage change by class and race/ethnicity

BRAZIL	GC-Class 1				GC-Class 3			
	APC 2019	APC 2020	APC 2021	APC 2022	APC 2019	APC 2020	APC 2021	APC 2022
White	5.94	4.71	14.37	-0.85	2.40	22.04	-9.12	-3.93
Mixed-Brown	7.37	11.30	3.67	-1.13	2.09	22.00	-9.98	-0.81
Black	6.86	9.97	7.59	-4.71	-2.09	25.57	-5.66	-4.69
Other	10.93	20.11	5.49	5.92	-0.05	60.11	-14.08	-15.06
	GC-Class 2				GC-Class 4			
	APC 2019	APC 2020	APC 2021	APC 2022	APC 2019	APC 2020	APC 2021	APC 2022
White	2.86	12.40	16.31	-0.61	1.53	-12.27	4.71	11.29
Mixed-Brown	8.03	14.16	6.37	1.10	2.57	-3.30	-1.58	9.65
Black	3.37	15.04	10.92	-3.99	0.32	-1.84	-0.25	5.06
Other	-2.13	37.76	10.10	-0.81	-3.80	-0.35	8.28	8.99

Health Disparities

Intersectional Multilevel (MAIHDA) Analysis of Preterm Birth Disparities in the United States Meredith Cahill* Meredith Cahill Claire Margerison

Preterm birth (PTB) impacts about 10% of U.S. births and is associated with increased morbidity, mortality, and healthcare burdens. Disparities by maternal race/ethnicity, nativity, age, education, and parity suggest that intersectional structural inequities may shape risk. Grounded in an ecosocial framework, we used Intersectional Multilevel Analysis of Individual Heterogeneity and Discriminatory Accuracy to examine PTB disparities across axes of maternal social identity, focusing on group differences, discriminatory accuracy, and interaction effects to deepen understanding of PTB disparities and identify high-risk groups. Using 2018-2019 natality data (n=7,008,531; PTB prevalence=9.9%), we grouped observations into 264 strata defined by maternal race/ethnicity, nativity, age, education, and parity. We used generalized linear mixed-effects models with a binomial-logit link to assess variability in PTB among strata. Predicted probabilities of PTB ranged from 5.2% (95%CI:4.4-6.2) to 28.4% (95%CI:25.5-31.6) and were highest among non-Hispanic (NH) Black, U.S.-born women 35+ years of age with ≤high school education, and lowest among NH-White, foreign-born women <35 with a college degree. Stratum-level differences explained 3.8% of total variation in probability of PTB, with the greatest proportion attributable to education (33.1%), age (24.8%), and race/ethnicity (22.9%). Overall, main effects accounted for 90.7% of variation, with 9.3% attributable to interactions. Significant random effects occurred for 91 of the 264 strata (Figure 1). These findings suggest within-stratum differences drive variations in PTB, but structural factors like educational status and race/ethnicity also contribute to variation. The finding that some variation in PTB is attributable to interaction effects combined with significant random effects in many strata indicates that intersectional inequities in PTB also exist.



Health Disparities

Beyond Borders: The Intersection of Migration, Culture, and Female Sexual Dysfunction

Negin Mirzaei Damabi* Negin Mirzaei Damabi Mumtaz Begum Jodie Avery Salima Meherali Zohra Lassi

Introduction and objectives:

Australia's diverse migrant population necessitates a deeper understanding of migrant health needs, particularly in sexual and reproductive health. Female sexual dysfunction (FSD) significantly impacts quality of life, yet evidence on its prevalence and associated factors among migrant women in Australia is limited. This study aimed to explore FSD prevalence among migrant women from low and middle-income countries (LMICs) residing in Australia, compare FSD prevalence between migrant and Australian-born women, and examine socio-demographic factors associated with FSD in both groups.

Method(s) and sample:

This national survey included reproductive-aged women (N=868), comprising migrant women from LMICs (N=421) and Australian-born women (N=447). Participants were recruited through quota sampling via the Qualtrics online platform. The study employed the Female Sexual Function Index (FSFI) and a demographic questionnaire. Data analysis involved descriptive statistics, chi-square tests, and logistic regression.

Results:

FSFI domain comparisons revealed significant differences between migrant and Australian-born women, migrant women reported significantly better overall sexual function (24.98 ± 7.18 vs. 23.57 ± 0.96, p=0.01). Longer relationships were negatively associated with sexual function, while religious affiliation showed a significant impact on sexual dysfunction compared to no religious affiliation. Logistic regression analysis highlighted those high-income migrants had higher odds of better sexual function (OR: 2.27, 95% CI: 1.10-4.66) compared to low-income migrants. Regarding religion, non-religious Australian showed higher odds (OR: 3.24, 95% CI: 1.12-9.32) compared to religious ones.

Discussion and recommendations / Conclusion:

This pioneering study highlighted the need for tailored interventions considering socioeconomic status and cultural background, providing a foundation for further research on the intersections of migration, culture, and sexual well-being. This study contributes to a more comprehensive understanding of sexual health in Australia's multicultural context, promoting overall well-being and quality of life for all women.

Health Disparities

Allostatic load, racial and economic segregation, and birth outcomes Cynthia Wynn* Cynthia Wynn Beatrice Palazzolo Michael Petriello Gwendolyn S. Norman Nicholas Weil Ananda Sen Sarah S. Comstock Kimberly S. McKee

Objectives: Structural racism may affect birth outcomes through chronic stress. We examined if the Index of Concentration at the Extremes (ICE), a measure of racial and economic segregation, was associated with gestational age at birth and assessed allostatic load (i.e., the physiologic response to chronic stress) as a biosocial mechanism of structural racism.

Methods: Using data from the Michigan Archive for Research on Child Health cohort, part of the National Institutes of Health Environmental Influences on Child Health Outcomes Consortium, we examined a subset with select biomarkers and prenatal records. ICE scores ranged continuously from -1 to 1 (least to most privilege) and were categorized using quintiles. We operationalized allostatic load using eight parameters drawn from inflammatory biomarkers and prenatal records, deriving a sum score, then dichotomized as ≥4 (high) or <4 (low). We assessed, separately and together, the associations between ICE, allostatic load, and the outcome of gestational age at birth, using Generalized Estimating Equations with zip code as the cluster level.

Results: Of the n=389, 46% were Black, 16% of which were preterm compared to 9.6% of non-Black births. Black pregnant people were four times more likely to have an allostatic load score ≥4 (OR=4.1, 95% CI=2.2, 7.5) and had a significant half-week reduction in gestational age at birth (β=-0.6, 95% CI=-1.1, -0.06) compared to non-Blacks. Pregnant people living in the highest ICE quintile had shorter gestational ages at birth compared to the lowest quintile, but the effects were not significant (β=0.34, 95% CI=-0.37, 1.0). ICE was not associated with allostatic load ≥4 (p=0.6).

Conclusion: Although allostatic load was higher among Black pregnant people, we did not find evidence that ICE was associated with allostatic load or gestational age at birth. Other structural racism constructs may drive some of the racial differences in allostatic load and birth outcomes.

Health Disparities

Human papillomavirus vaccination access in adolescents and young adults with and without a disability: A systematic review Melina Albanese* Melina Albanese Jayati Khattar Kathryn Barrett Hasmik Beglaryan Hilary Brown

Individuals with disabilities have lower receipt of several preventive healthcare services, including vaccination. Human papillomavirus (HPV) is a leading cause of cervical cancer and is almost entirely preventable through vaccination. We conducted a synthesis of literature on access to HPV vaccination by disability status among adolescents and young adults (AYA). We followed systematic review methodology and Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Medline, Embase, PsycInfo, CINAHL, and Web of Science Core Collection were searched from database inception to July 9, 2024, using keywords and subject headings for the concepts “disability” and “HPV vaccination.” We included peer-reviewed observational studies published in English comparing HPV vaccination in AYA with and without a disability. Quality was assessed using the Effective Public Health Practice Project tool. A narrative synthesis of the findings was performed. Of 1164 unique records identified, 8 met our inclusion criteria. Studies were mostly cross-sectional surveys (n=4) from the United States (n=3) and examined receipt of 1 or more doses of any HPV vaccine (n=5) or a full series (n=3) among AYA with physical (n=2), sensory (n=1), and developmental (n=3) disabilities, or a composite measure of disability (n=6). Overall, 50% of studies were rated as “weak” quality, 37.5% as “moderate”, and 12.5% as “strong.” Selection bias and failure to adjust for confounding were common reasons for downgrading study quality. Overall, studies found lower access to HPV vaccination in AYA with neurodevelopmental and neurological disabilities but not other disabilities. Findings reflect the need for future studies with population-based designs, validated measures, and good control for confounding. Current literature suggests AYA with neurodevelopmental and neurological disabilities could benefit from public health and clinical strategies to improve HPV vaccination access.

Health Disparities

Bridging the Benefit Gap: Addressing Health Disparities Through Data-Informed Outreach at Link Health Precious Amiewalan, B.S.* Precious Amiewalan Poorvi Mohanakrishnan Vivian Lin Timothy Scheinert, B.S.

Background

Link Health is a Boston-based non-profit connecting low-income families with federal benefits. Poverty has a detrimental impact on well-being, causing toxic stress linked to chronic illness. Unfortunately, $80 billion in benefits go unclaimed annually due to lack of awareness and complex applications. In collaboration with community stakeholders, Link Health bridges this gap, supporting basic needs through streamlined benefit enrollment.

Methods

Link Health employs hybrid outreach via sign-up clinics, online applications, and text-blast messaging. The two-tiered enrollment process involves eligibility screening and application assistance with Patient Navigators. Data is stored in a HIPAA-compliant Dashboard, and applications are processed remotely and submitted to administering agencies. Data from July 2022-December 2024 is evaluated for demographic and eligibility trends, along with uptake in Supplemental Nutrition Assistance Program (SNAP) and Lifeline (a broadband internet discount).

Results

Link Health enrolled 2,996 individuals; 57% identified as Hispanic, 18% White, 17% African American, and 3% Asian; 38% were Spanish speakers. Most individuals qualified via Medicaid (65%) and prior SNAP enrollment (34%). Enrollees were majority aged 30-59 years (59%). Among 121 enrollees in SNAP, 79% were Hispanic; 55% were English-speakers and 38% Spanish-speakers. Lifeline sign-ups totaled 1772; enrollees were 44% Hispanic; 48% were English speakers, and 28% Spanish speakers.

Conclusion

Link Health has created data-driven means to assess community needs, tailoring its approach for Spanish-speaking, low-income adults and partnering with universities and Pathway Programs to recruit bilingual navigators. Educational materials are created with non-English speakers in mind. Programming has grown to address several health determinants, with sign-ups facilitated through a centralized dashboard. To date, Link Health has disbursed $3.4 million into homes.

Health Disparities

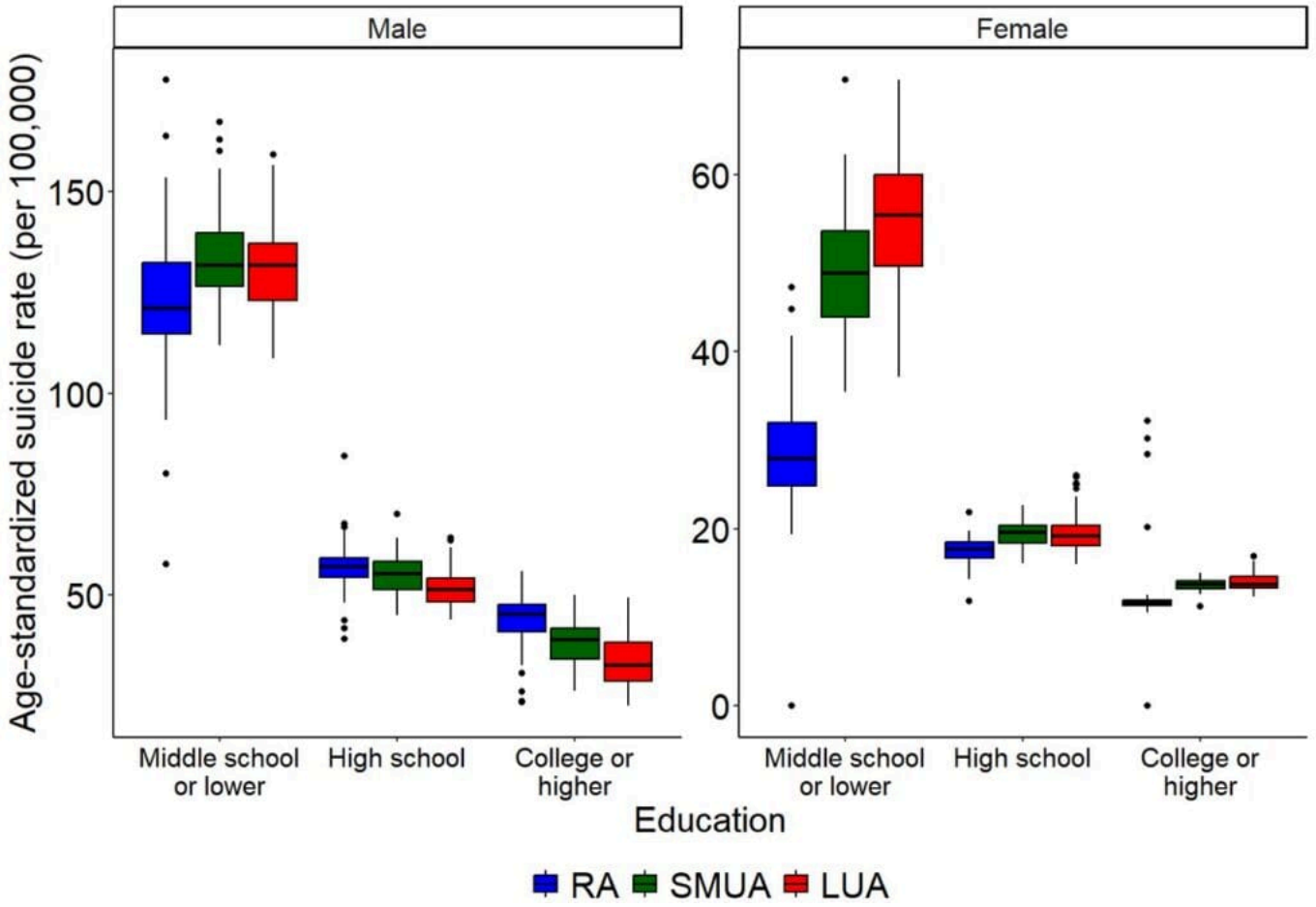
Intersecting urbanity level and educational inequalities in suicide mortality by gender and age group in Korea, 2015-2020: an ecological study Ikhan Kim* Ikhan Kim

Background: Among countries in the Organization for Economic Co-operation and Development, South Korea has one of the highest rates of suicide. This study aims to estimate the suicide rate for each of Korea's 247 districts based on gender, age group, and educational attainment and to determine district-level factors that are associated with the suicide rate.

Methods: To obtain the average number of population and suicide deaths over the period by gender/10 years (30-39,…,80+),/district/education level(middle school or lower, high school, college or higher), we utilized data from South Korea's population censuses undertaken in 2015 and 2020 as well as death statistics data collected between 2013 and 2022. Using the Bayesian spatio-temporal model, the age-standardized suicide death rates by educational attainment for each district were estimated. Ten district-level variables, including 3 material explanations, 2 social capital explanations, 3 social fragmentation explanations, and 2 healthcare services explanations, were used for the education-level stratified spatial regression analysis.

Results: Low-educated people and rural areas had higher suicide death rates for both males and females. When stratified analysis was done by educational attainment, suicide mortality among males and females with middle school education or less was relatively lower in rural areas than in metropolitan and urban areas, in contrast to other levels of education. In females, this tendency was more pronounced. Suicide mortality among low-educated people, particularly females, was more clearly associated with the social support level. This tendency was driven by relatively young age groups.

Discussion: Contrary to other educational levels, suicide mortality was lower in rural than in metropolitan areas for both males and females with middle school education or less. When making efforts to prevent suicide in the local community, policies based on proportional equity that consider socioeconomic position, including education attainment, should be implemented. This study suggests that community social support can protect the suicide mortality in the low-educated population more than other education groups.


Male
Female
Age-standardized suicide rate (per 100,000)
150
100
50
60
40
20
0
Middle school or lower
High school
College or higher
Education
RA
SMUA
LUA

Health Disparities

Association Between Social Risk Factors and Major Adverse Cardiovascular Events and Mortality Among Individuals with Rheumatic Conditions Leah Santacroce* Leah Santacroce Jeong Yee Jing Cui Emily Oakes Hongshu Guan Karen Costenbader Candace Feldman

Background

Individuals with rheumatic conditions are at an increased risk of experiencing cardiovascular events. Social risk factors contribute to inequities in comorbidities and adverse outcomes and may confer higher risk of Major Adverse Cardiovascular Events (MACE) in patients with rheumatic conditions.

Methods

We used data from the nationwide NIH All of Us Research Program (V7) and included adults with ≥ 2 diagnosis codes ≥30 days apart for lupus (SLE), rheumatoid arthritis (RA), and osteoarthritis (OA) 2 years pre-enrollment.

A Social Determinants of Health questionnaire was completed at enrollment. We developed social risk factor indices for economic instability and healthcare access challenges based on needs reported. Discrimination was measured with the Everyday Discrimination Scale.

The primary outcome of MACE included myocardial infarction, stroke, intervention for coronary artery disease, and all-cause mortality. Patients were followed from enrollment until their first event or end of study period.

We used multivariable Cox proportional hazard models to evaluate the associations between each social risk factor index and MACE and mortality, adjusting for age, sex, race, rheumatic disease and Deyo-Charlson Comorbidity index.

Results

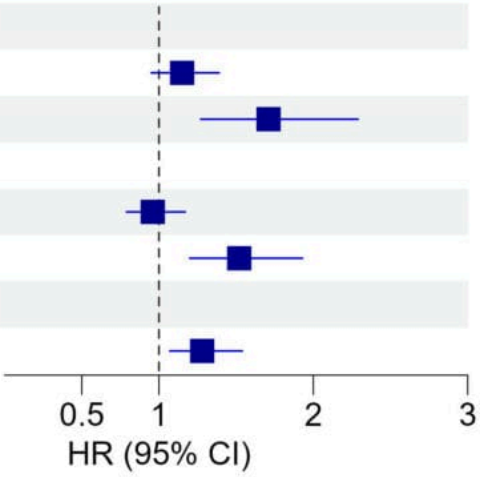
We identified 9,390 patients who met our criteria. There were 637 events, and the mean (SD) follow up time was 2.3 (1.4) years. After adjusting for covariates, individuals with 3+ economic insecurities (HR 1.86, 95% CI 1.86 – 2.43), 3+ healthcare access challenges (HR 1.52, 95% CI 1.20 – 1.93), or experienced discrimination (HR 1.28, 95% CI 1.07 – 1.54) were at higher risk of MACE compared to those without each social risk factor (Figure 1).

Discussion

In this national study, we found that higher burden of social risk factors was strongly associated with increased risk of MACE and mortality among individuals with SLE, RA, and OA. Further studies should determine whether addressing social needs reduces risk of cardiovascular events.

Social Risk Factor Index	N (%)*
Economic Instability (ref = 0)	5636 (60%)
1-2	2871 (31%)
3+	883 (9%)
Healthcare Access Challenges (ref = 0)	3204 (34%)
1-2	3444 (37%)
3+	1679 (18%)
Everyday Discrimination (ref = 0-2)	7027 (75%)
3+	2360 (25%)

*Number and percent of individuals in each social risk factor index category



Health Disparities

Pediatric asthma disparities, school absenteeism, and decreased physical activity among children in Central Texas Emily Hall* Emily Hall Khamron Micheals Sarah Chambliss Darlene Bhavnani Erin Rodriguez Susan Balcer-Whaley Elizabeth Matsui

Background

There are racial and ethnic disparities in pediatric asthma morbidity in the United States. The downstream effects of these disparities are not well understood. To fill this gap, we assessed racial and ethnic differences in asthma-related impacts on physical activity and school attendance among children with persistent asthma in Central Texas, a population with observed racial and ethnic disparities in asthma morbidity.

Methods

We described outcomes by race and ethnicity among children aged 5-17 years enrolled in the cross-sectional Texas Home Assessment of Asthma and Lung Exposures (TexHALE) Study. Data were collected using validated questionnaires.

Results

The majority of the 259 participants were Hispanic (N=145), followed by White (N=59), and Black (N=55). Black and Hispanic participants reported more asthma symptoms, with a mean (SD) of 6.0 (5.5) and 5.2 (5.2) maximum symptoms days respectively in the 2 weeks prior to interview, compared with 3.6 (4.4) days among White participants (p=0.03). 18% and 27% of Hispanic and Black children, respectively, reported missing school due to asthma in the prior 2 weeks vs. 13% of White children (p=0.20). Black and Hispanic children were almost twice as likely to limit physical activity due to asthma in the 2 weeks prior to interview. For example, 46% and 40% respectively reported limited participation in gym class due to asthma vs. 21% of White children (p=0.02). 40% of Black and 43% of Hispanic participants had to limit moderate physical activity because of asthma whereas 19% of White participants did (p=0.01).

Conclusions

Black and Hispanic children were more likely to experience asthma morbidity that impaired their daily activities than White children. Asthma-related reductions in physical activity and increased school absences could have detrimental impacts on health and educational attainment later in life. Further investigation will elucidate factors contributing to these disparities and subsequent impacts.

Health Disparities

Income Inequality and Physical Health in the United States: The Mediating Role of Public Health Funding Kaelan Findlay* Kaelan Findlay Jason Mulimba Were Sze Yan Liu Roman Pabayo

Background: Income inequality has been previously linked to poorer physical health. However, the mechanisms underlying this relationship remain unclear. In this study we examined whether state income inequality is directly associated with physical health, if public health funding mediates this relationship, and whether these associations differ by gender, as suggested by prior research.

Methods: Individual-level data was drawn from the 2023 Behavioral Risk Factor Surveillance System, whereas state-level data were obtained from the 2019 U.S. Census, and the 2020 State Health Access Data Assistance Center. Our sample comprisedof 406,686 adults from 48 states and the District of Columbia. Physical health was measured using self-reported days of poor physical health in the past 30 days. Income inequality was measured using the state-level Gini coefficient, and public health funding was measured using per capita public health funding in each state. The data was analyzed using multilevel path models.

Results: In the full model, higher income inequality was significantly associated with more self-reported days of poor physical health (β = 0.11; 95% CI= 0.01, 0.21). In the stratified analysis, significant findings were observed among men. Higher income inequality was associated with more self-reported days of poor physical health (β = 0.13; 95% CI= 0.13, 0.61). However, public health funding did not significantly mediate this relationship in any of the models.

Conclusion*:* Policymakers should aim to reduce state income inequality, as it may help reduce poor physical health days in American adults, particularly among males, who may be disproportionately affected. More research is needed to identify mechanisms in which income inequality leads to poor physical health.

LATEBREAKER

Health Disparities

Lifetime Discrimination as a Contributor to Black-White Disparities in Actigraphy-Assessed Sleep Duration in the Multi-Ethnic Study of Atherosclerosis (MESA) Kaylin M. White* Kaylin White Shakira F. Suglia Regine Haardoerfer Tené Lewis Ashley I. Naimi Dayna A. Johnson

Sleep is an essential physiologic state and health behavior vital to overall health and a source of physiological and psychological resilience. Racial disparities in sleep duration, where non-Hispanic Black Americans sleep less than non-Hispanic White Americans, are well-documented. However, mechanisms driving these disparities remain unclear, emphasizing the need to examine race salient contributors such as discrimination. This study assessed the contribution of lifetime discrimination to Black-White disparities in sleep duration using the counterfactual disparity measure (CDM) approach in the Multi-Ethnic Study of Atherosclerosis (MESA). The sample included 1,446 participants (57% non-Hispanic White, 43% non-Hispanic Black, aged 54-93 years) from the MESA Sleep Ancillary Study (2010–2013). Lifetime discrimination was assessed using a six-item scale measuring unfair treatment experiences summarized as a score. Sleep duration was measured via 7-day actigraphy. We estimated racial differences in sleep duration using linear regression and applied CDM to estimate the racial difference if lifetime discrimination were eliminated, using inverse probability weights (IPWs) to balance confounders (age, gender, education, income, study site, occupation, and body mass index (BMI). Discrimination was reported by 64% of Black participants versus 41% of Whites. Very short sleep (<6 hours) was more prevalent among Black compared to White participants (44% vs.19%). Lifetime discrimination was associated with shorter sleep duration (β: -8.31, 95% CI: -15.21, -1.42). The racial difference in sleep duration was -47.47 minutes (95% CI: -55.67, -39.27), reduced to -29.25 minutes (95% CI: -52.99, -5.50) when discrimination was eliminated. Using CDM as a method to measure the magnitude of inequity, we found that lifetime discrimination partially explains Black-White disparities in sleep duration in the MESA cohort, highlighting the importance of reducing discrimination to promote sleep equity.

LATEBREAKER

Health Disparities

Sexual Victimization and Gender Identity: A National Study of High School Students in the US, 2023 Anna Holdiman* Anna Holdiman Alex Lao Ruby Charak Dylan Barker Andrew Yockey Dale Mantey

Introduction: Experiencing sexual violence is an adverse childhood experience. Emerging data suggests transgender youth disproportionately experience sexual violence. We investigate differences in sexual violence victimization by gender identity in a nationally representative sample of US high school students.

Methods: We analyzed data from n=15,073 US high school students via the 2023 Youth Risk Behavior Surveillance Survey (YRBSS). Multivariable logistic regressions compared three measures of sexual victimization (lifetime forced sexual intercourse [FSI]; past 12-month any sexual violence; and past 12-month dating sexual violence) by gender identity. We also conducted these analyses stratified by sex assigned at birth. Models controlled for grade, race, ethnicity, and alcohol use.

Results: Transgender youth had significantly greater odds of lifetime FSI (aOR: 3.29), past 12-month sexual violence (aOR: 2.47), and past 12-month dating violence (aOR: 2.01), relative to cisgender youth. Interactions were significant for all three outcomes ($p<0.001$). Among those who identified their sex as male, transgender identity corresponded with greater odds of reporting lifetime FSI (aOR:13.17), past 12-month sexual violence (aOR: 9.24), and past 12-month dating violence (aOR: 9.56). Conversely, among those who identified their sex as female, the odds of any sexual violence victimization outcome were equivalent by gender identity.

Conclusion: Transgender youth, particularly those who identified their sex as male, had significantly higher odds of experiencing sexual violence in their lifetime and within the past year. Prevention measures, as well as trauma-informed treatment, are needed to reduce the incidence and impact of sexual violence among youth.

LATEBREAKER

Health Disparities

Availability of sexual orientation and gender identity (SOGI) data in a cohort of transgender and gender diverse people: An analysis of electronic health records Cynthia N. Ramirez* Cynthia N. Ramirez Kristine Magnusson Wendy Leyden Alexandra Lea Darios Getahun Courtney McCracken Suma Vupputuri Lee Cromwell Timothy Lash Oumaima Kaabi Guneet K. Jasuja Michael J. Silverberg Michael Goodman

Purpose: Electronic health records (EHR) offer a unique opportunity to systematically collect sexual orientation and gender identity (SOGI) data. The objectives of this study were to examine the prevalence and determinants of SOGI reporting in an EHR-based cohort of transgender and gender-diverse (TGD) people.

Methods: In this cohort study, we identified TGD people with and without SOGI documentation enrolled in Kaiser Permanente (KP) Georgia (GA), Mid-Atlantic States (MAS), Northern California (NC) and Southern California (SC) health plans between 01/01/2022-01/01/ 2024. Using log-binomial regression models, we examined the associations of demographic (age, sex assigned at birth, race and ethnicity), study site (KPGA, KPMAS, KPNC, KPSC), socioeconomic (Medicaid coverage, residence in a poverty area), and Charlson comorbidity index associated with SOGI documentation.

Results: Among 23,060 TGD persons included in the analysis, over 70% had SOGI recorded in the EHR. In unadjusted models, SOGI documentation varied by age, sex assigned at birth, race and ethnicity, study site, and socioeconomic and clinical factors. In the multivariable model (Table 1), age was associated with SOGI documentation with prevalence ratios (95% confidence intervals) of 1.21 (1.18-1.24), 1.17 (1.13-1.21), 1.10 (1.06-1.15), and 0.93 (0.88-0.99), for those 21-39, 40-49, 50-59, and ≥60 years, respectively. Other factors associated with SOGI documentation included enrollment in KPNC, higher levels of care utilizations, and male sex assigned at birth. Residence in a poverty area was not associated with SOGI documentation.

Conclusion: This study adds to the growing body of literature that supports efforts to inform care and increase representation of TGD patients in health research. Health systems should prioritize systematic collection of SOGI information in the EHR and emphasize equitability of reporting to reduce disparities.

Table 1. Factors associated with SOGI reporting*

Participant characteristics	% SOGI reporting	PR	95% CI		p
Current age (years)**					
<20	62%	1	Reference		
20-39	75%	1.21	1.18	1.24	<0.01
40-49	72%	1.17	1.13	1.21	<0.01
50-59	67%	1.10	1.06	1.15	<0.01
≥60	57%	0.93	0.88	0.99	0.01
Sex assigned at birth					
Female	72%	1	Reference		
Male	69%	0.98	0.97	1.00	0.03
Race/ethnicity					
Asian	72%	0.98	0.96	1.01	0.16
Black, non-Hispanic	71%	0.98	0.95	1.01	0.23
Hispanic	65%	0.97	0.95	0.99	<0.01
Other, non-Hispanic***	75%	1.02	0.98	1.05	0.37
Unknown	70%	1.00	0.97	1.04	0.83
White, non-Hispanic	73%	1	Reference		
Study site					
Georgia	58%	0.72	0.67	0.77	<0.01
Mid-Atlantic States	79%	0.98	0.96	1.01	0.19
Northern California	79%	1	Reference		
Southern California	58%	0.73	0.71	0.74	<0.01
Medicaid coverage					
No	71%	1	Reference		
Yes	70%	0.98	0.96	1.00	0.01
Care utilization (encounters/year)†					
<10	67%	1	Reference		
10-29.9	71%	1.08	1.06	1.10	<0.01
≥30.00	74%	1.16	1.14	1.19	<0.01
Residence in poverty area§					
No	68%	1	Reference		
Yes	71%	1.00	0.97	1.03	0.99
Charlson comorbidity index					
0	71%	1	Reference		
1	73%	1.00	0.98	1.02	0.70
≥2	65%	0.95	0.92	0.99	0.03

* Includes persons enrolled after 2022
** As of 01/01/2024
*** Includes Native Hawaiians/Pacific Islanders, American Indians/Alaskan Natives, non-Hispanic persons of multiple race categories with particular category unknown, and non-Hispanic persons identified as Other with values that do not fit any other value
† Defined as average annual number of all encounters between 2022 and 2024
§ Defined as >20% of neighborhood households with income below federal poverty cutoff
Abbreviations: PR = prevalence ratios, CI = confidence interval

Health Disparities

The association of medical mistrust, clinical trial knowledge, and perceived clinical trial risk with willingness to participate in health research among historically marginalized individuals living in New York City Isabel Curro* Isabel Curro Laura C Wyatt Yousra Yusuf Victoria Foster Sonia Sifuentes Perla Chebli Julie A Kranick Simona C Kwon Chau Trinh-Shevrin Madison N LeCroy

Background: Medical mistrust, clinical trial knowledge, and clinical trial risk impact research participation yet are rarely studied among racial and ethnic groups.

Methods: Data were from a cross-sectional community needs assessment (n=1812). Multinomial logistic regression models examined associations of medical mistrust, clinical trial knowledge, and clinical trial risk with willingness to participate in health research (Yes [ref], No, Unsure) among Chinese, Korean, South Asian, Haitian, Hispanic, and Southwest Asian and North African (SWANA) NYC residents. One model was run for each group. Further disaggregated findings for Hispanic subgroups will be presented.

Results: Overall, 46.1% of participants reported willingness to take part in health research, ranging from 35.8% (Chinese participants) to 58.7% (South Asian participants). More medical mistrust was associated with less willingness to participate for Chinese (OR: 1.06, 95%CI: 1.00, 1.12) and Hispanic (OR: 1.08, 95%CI: 1.01, 1.14) participants; more willingness for Haitian participants (OR: 0.87, 95%CI: 0.81, 0.94); more uncertainty on willingness for Korean (OR: 1.13, 95%CI: 1.05, 1.22), South Asian (OR: 1.07 95%CI: 1.01, 1.12), and Hispanic (OR: 1.10, 95%CI: 1.05, 1.16) participants; and less uncertainty for Haitian (OR: 0.91, 95%CI: 0.84, 0.99) and SWANA (OR: 0.91, 95%CI:0.86, 0.97) participants. Clinical trial knowledge is linked to more participation willingness for Haitian participants (OR: 2.77, 95%CI: 1.15, 6.65); less willingness for Chinese participants (OR: 0.55, 95%CI: 0.34, 0.88); and more uncertainty on willingness for South Asian (OR: 2.09, 95%CI: 1.07, 4.07), Hispanic (OR: 1.81, 95%CI: 1.05, 3.11), and SWANA (OR: 2.71, 95%CI: 1.21, 6.03) participants.

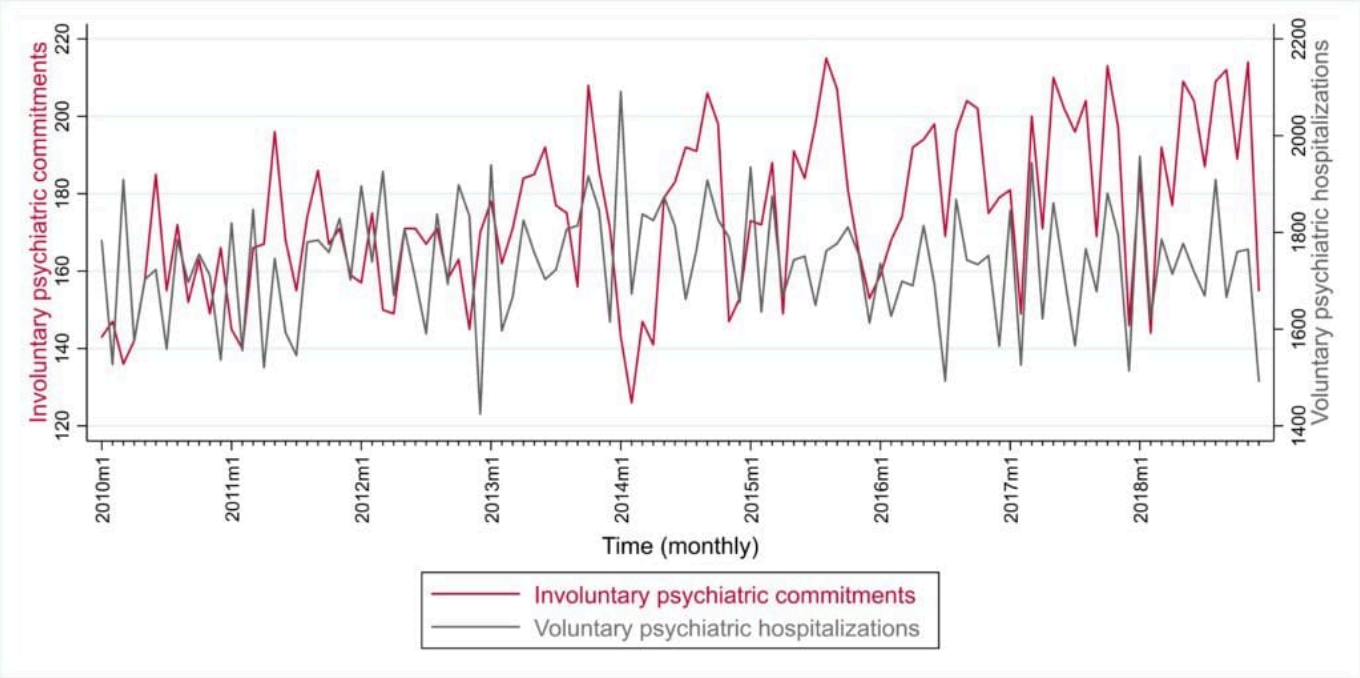
Conclusion: Willingness to participate in research and associations with mistrust, knowledge, and risk varied by group. Studying diverse groups can advance tailored engagement and equitable representation of underserved populations in research.

Health Disparities

Involuntary psychiatric commitments following the Krudttønden attacks in Denmark

Parvati Singh* Parvati Singh Geoffrey Carney-Knisely Lars H. Andersen Tim A. Bruckner

Terrorist attacks may reduce social tolerance of disordered behavior that, in turn, may increase involuntary psychiatric commitments in a population. We examine whether the Krudttønden terrorist attacks that occurred in February 2015 in Denmark correspond with a proximate increase in involuntary psychiatric commitments in the Danish population. We retrieved monthly count of involuntary psychiatric commitments (outcome) and voluntary (i.e. non-coercive) psychiatric inpatient admissions for Denmark from the Danish Psychiatric Central Research Register, from January 2010 to December 2018. We defined our exposure as a binary indicator of February 2015 (month of the Krudttønden terrorist attacks). Results from time-series analysis indicate 27 additional involuntary psychiatric commitments in February 2015 ($p < 0.05$), controlling for autocorrelation and the concomitant series of voluntary psychiatric inpatient admissions. We do not observe statistically detectable relations between the exposure and voluntary psychiatric admissions. Our findings suggest reduced social tolerance immediately following terrorist attacks.



Health Disparities

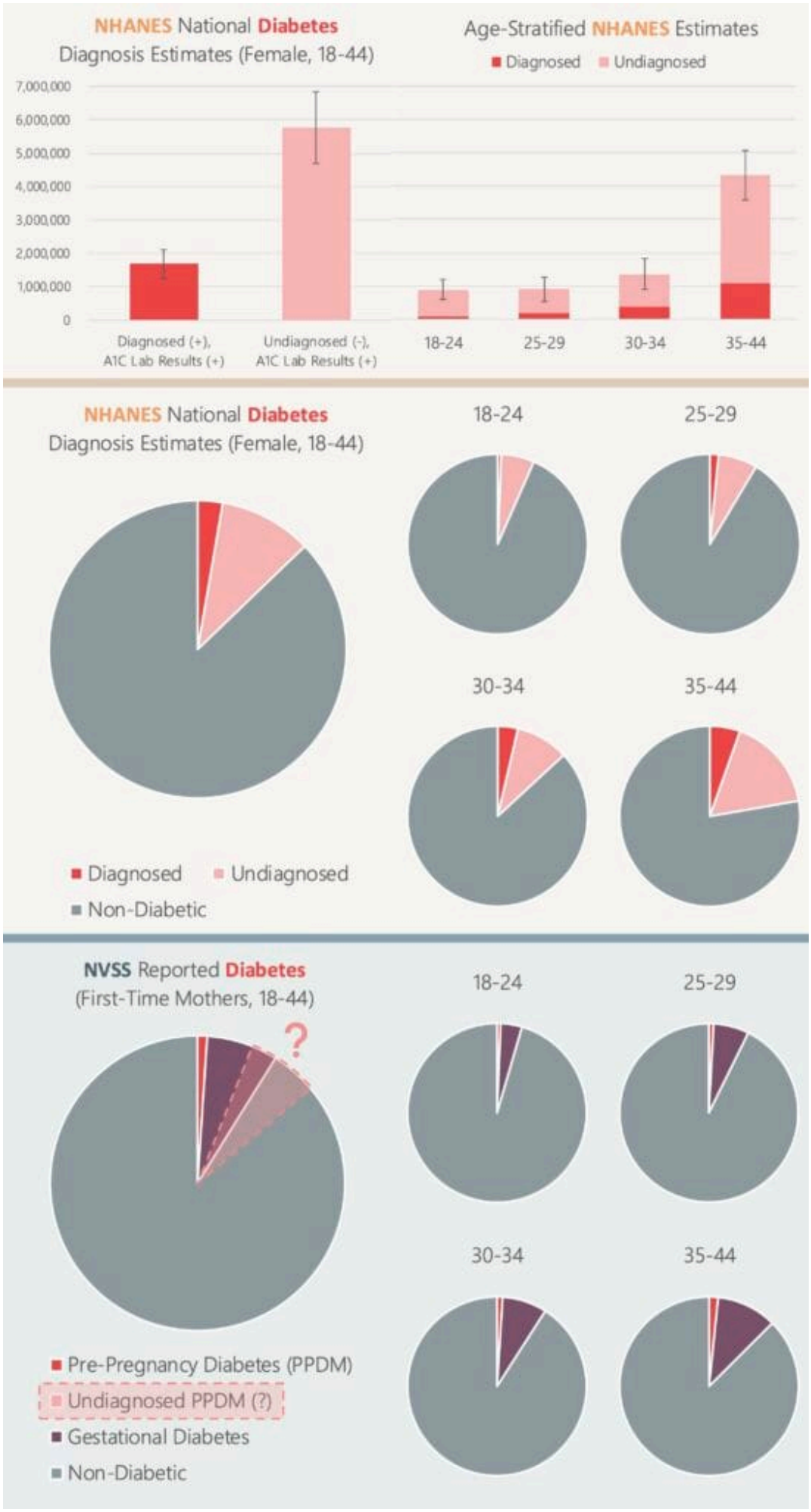
Leveraging Disease Misclassification to Estimate the Impact of Pre-Pregnancy Healthcare Access on Maternal Morbidity Ariana Mora* Ariana Mora Michael Kramer Joshua Wallach Mohammed K. Ali Timothy Lash

Background: Undiagnosed pre-pregnancy illness, which can be due to poor healthcare access, likely negatively impacts pregnancy outcomes since the disease is unknown and not medically managed. Increased healthcare utilization during pregnancy may lead to the diagnosis of these previously undiagnosed conditions, but it may also lead to disease misclassification. For example, pre-existing chronic diabetes (DMII) could be misclassified as gestational diabetes (GDM) if first evaluated in the setting of pregnancy. Thus, identifying DMII misclassified as GDM could serve as a proxy for inadequate pre-pregnancy healthcare, which is otherwise unmeasured.

Methods: We used the National Health and Nutrition Examination Survey (NHANES) to compare self-reported DMII diagnosis with clinically validated DMII status and identified individual health and socioeconomic factors predictive of DM misclassification. We then transported individual-level misclassification likelihoods to 2016-2023 natality data in the National Vital Statistics System (NVSS). Bias analysis will compare poor pregnancy outcome risks in reclassified DM births compared to the original NVSS DM classifications.

Results: Among NHANES reproductive age women (18-44), DMII diagnosis has sensitivity 0.24, specificity 0.99, PPV 0.75, and NPV 0.88. Reclassifying NVSS births to adjust for DMII underdiagnosis results in an additional 260,222 births with presumptive DMII (original: 100,713 DMII births). These are preliminary marginal estimates; modeled estimates will account for confounders affecting true underlying DMII and the diagnosis of DMII.

Summary: By leveraging externally informed bias adjustments of surveillance data, this research highlights potential changes to medical screening guidelines to reduce under/misdiagnosis of DM, improve biased estimates for poor pregnancy outcome risk factors, and support policies that increase pre-pregnancy healthcare access to reduce adverse pregnancy outcomes and disparities.


NHANES National Diabetes
Diagnosis Estimates (Female, 18-44)
Age-Stratified NHANES Estimates
Diagnosed
Undiagnosed
7,000,000
6,000,000
5,000,000
4,000,000
3,000,000
2,000,000
1,000,000
0
Diagnosed (+), A1C Lab Results (+)
Undiagnosed (-), A1C Lab Results (+)
18-24
25-29
30-34
35-44
NHANES National Diabetes
Diagnosis Estimates (Female, 18-44)
18-24
25-29
30-34
35-44
Diagnosed
Undiagnosed
Non-Diabetic
NVSS Reported Diabetes
(First-Time Mothers, 18-44)
?
18-24
25-29
30-34
35-44
Pre-Pregnancy Diabetes (PPDM)
Undiagnosed PPDM (?)
Gestational Diabetes
Non-Diabetic

Health Disparities

Residential Segregation, Housing, and Adverse Birth Outcomes Among Black Birthing People: The Case of South Carolina (1989-2020). Kristi Allgood* Kristi Allgood Annie Ro Yammei Xie Catherine VanderWoude Nancy Fleischer

Racialized legal residential segregation has been a barrier to homeownership for Black families in the US. This study aims to estimate an association between county-level Black:White (B:W) ratios in housing measures and adverse birth outcomes. Data on singleton, live births among Black birthing people between 1989 and 2020 in South Carolina (SC, n=527,577) were collected from birth certificates. County-level housing measures (B:W ratio of homeownership and home loan denials) were log transformed and standardized. Homeownership and area-level covariates (percent of residents below the poverty level and urban status) were obtained from the US Census Bureau while mortgage denials were from the Home Mortgage Disclosure Act. Unadjusted and adjusted mixed effects models with a random intercept were used to estimate the association between B:W disparities in housing measures and low birthweight (LBW) and preterm birth (PTB), separately. Among babies born to Black birthing people, about 12% were LBW and 12% were PTB. For the exposure measures, on average, Black people were 35% less likely to own a home and were about 2 times more likely to have a home loan denied than White people across SC counties. For every standard deviation increase in the proportion of White residents who owned a home relative to Black residents, the odds for LBW increased by 3% in the adjusted model (aOR: 1.03, CI: 1.1, 1.06). Similar results were observed for PTB (aOR: 1.05, CI: 1.03, 1.08). B:W disparities in home loan denial were not associated with LBW in any model and marginally associated with PTB (aOR was 1.01, CI: 1.00, 1.02). Identifying policy solutions to promote Black homeownership may protect against LBW.

Health Disparities

Lead exposure as a contributor to the Black-White racial disparity in blood pressure: evidence from NHANES 1988-1994 and 2017-2020 Mia Zhu* Mia Zhu Hannah Van Wyk Sung Kyun Park

Background: In the United States (US), racial disparities in blood pressure have persisted with Black people experiencing a greater risk of hypertension compared to White people. While disparities in lead exposure may explain some of this disparity, little is known about the mediating role of lead in racial disparities in blood pressure.

Methods: We used national-level, cross-sectional data of noninstitutionalized US adults aged ≥20 years from the National Health and Nutrition Examination Survey (NHANES), III (1988-1994) (n = 10,570) and 2017-2020 (n = 4,536). We examined the extent to which racial disparities in blood pressure were explained by disparities in blood lead in these two NHANES cycles using causal mediation analysis. We estimated natural direct and indirect effects and considered potential interaction between race and blood lead using 4-way decomposition.

Results: In NHANES-III, Black participants would have a 5.74 (95% CI: 4.94, 6.54) mmHg higher mean systolic blood pressure (SBP) compared to White participants if all adjusted covariates were held equal to that of the White population; 10% of this disparity was explained by differences in blood lead levels between Black and White participants. Similar trends were observed with hypertension. In NHANES 2017-2020, similar overall trends were observed. However, the proportion of racial disparities mediated by differences in blood lead between Black and White individuals reduced from 10% to 5%.

Conclusions: These findings suggest that racial differences in lead exposure may explain racial disparities in blood pressure, but the mediating role of blood lead has decreased since the 1980s.

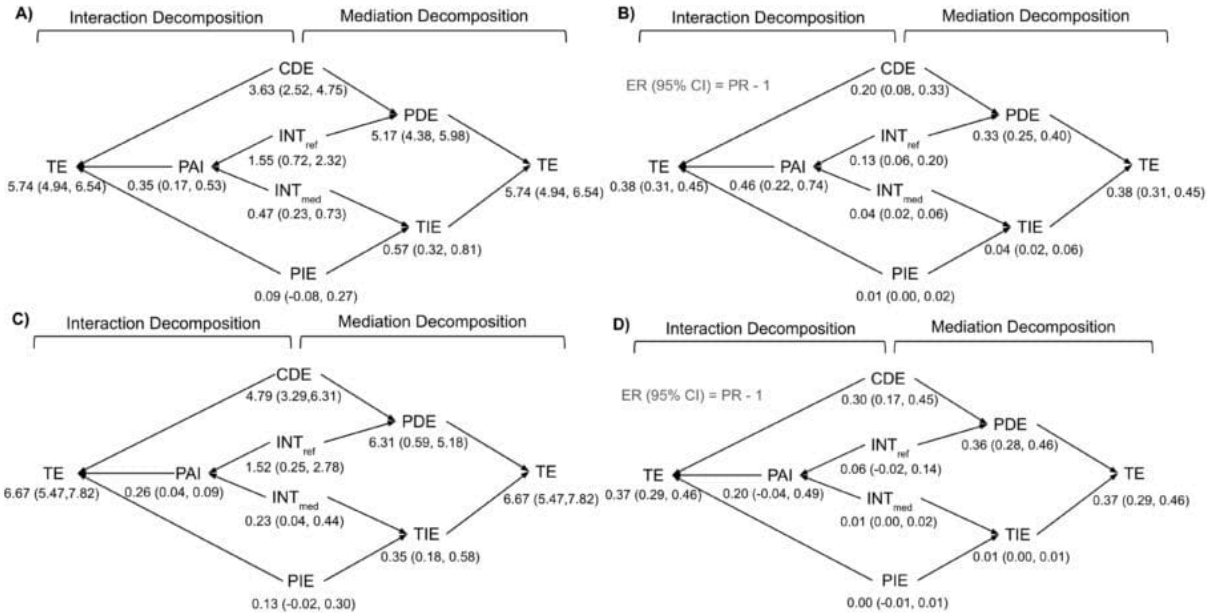


Figure 3: 4-way decomposition for NHANES-III 1988-1994 systolic blood pressure (A) and hypertension (B) and NHANES 2017-2020 systolic blood pressure (C) and hypertension (D). Abbreviations: TE: total effect, CDE: controlled direct effect, INT_{ref}: reference interaction, INT_{med}: mediated interaction, PIE: pure indirect effect, PDE: pure direct effect, TIE: total indirect effect, PAI: proportion attributable to interaction. Natural effects are randomized interventional analogues. Estimates for hypertension (B and D) were presented as excess relative risk (ER = PR - 1).

Health Services/Policy

Determinants of Homecare Use in Older Adults: a Systematic Review and Meta-analysis of Quantitative Studies Afshin Vafaei* Afshin Vafaei Marie Y. Savundranayagam Susan Phillips Maria C. Tavares Lauren Bal

Background: Homecare services are essential for supporting older adults to age in place, yet social disparities in their utilization reveal the need for a deeper understanding of the factors that drive homecare needs and use. The aim of this study is to identify health and social determinants of homecare use in older adults.

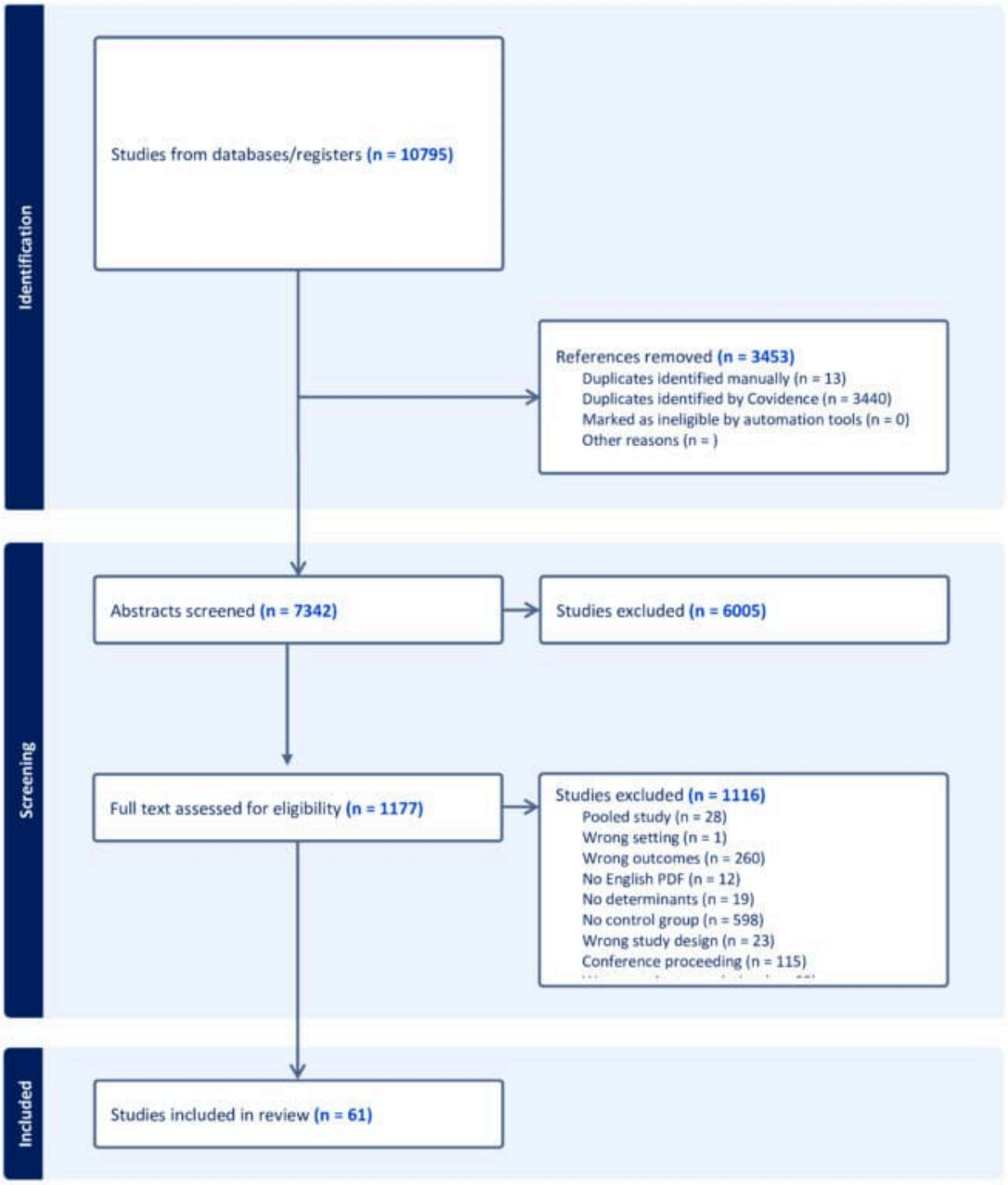
Methods: Following PRISMA, we conducted a systematic review (Jan 1, 2000 to April 10, 2024) of quantitative peer-reviewed epidemiologic studies among adults older than 65. The main inclusion criteria were incorporation of a form of homecare as an outcome and inclusion of at least one physical or social determinant. Studies focusing on individuals in long-term care or other institutional settings were excluded. Abstract and full-text screenings were performed in duplicate followed by extraction of data on homecare use and quantitative effect estimates of determinants.

Results: After abstract review of 7342 citations and 1177 full-text reviews, 61 articles met our inclusion criteria (figure 1). Physical ability, marital status, gender, and social isolation identified as the main determinants of homecare use. Ethnic minorities, despite greater needs often encountered obstacles in accessing homecare.

Next steps: Extracted quantitative data on effects estimates of determinants of homecare use (in form of RR or OR along with 95% CI) will be pooled by construction of DerSimonian-Laird random-effect models with inverse-variance weighting and heterogeneities between-studies will be quantified by I2 statistic.

Conclusions: Preliminary findings from the systematic review highlight significant social disparities in homecare access across various population groups. By addressing these gaps, this research will provide valuable insights for policymakers and healthcare providers to develop more equitable and effective homecare policies including facilitating aging in place.

Homecare in older adults



13th January 2025

covidence

Health Services/Policy

Exploring the Impact of Housing Type on Respiratory Health in New York City Adults: The Mediating Role of Indoor Environmental Quality Jin Choi* Jin Choi Byoungjun Kim

Respiratory diseases like asthma and chronic obstructive pulmonary disease (COPD) are major causes of morbidity in urban populations, especially among socioeconomically disadvantaged groups. Housing conditions, particularly in cities like New York, play a critical role in shaping respiratory health outcomes. This study examines the relationship between housing type and respiratory health, focusing on asthma and COPD among adults in New York City. It investigates various housing arrangements, including homeownership, public housing, rental assistance, and rent-controlled housing, and explores the mediating roles of indoor environmental factors, such as mold and cockroach infestations.

Results indicate that adults in public housing have significantly higher odds of asthma (OR = 2.15; 95% CI = 1.25, 2.84) and COPD (OR = 2.02; 95% CI = 1.74, 3.08) compared to homeowners. Similarly, individuals in rental assistance housing exhibit elevated risks for asthma (OR = 2.25; 95% CI = 1.17, 2.73) and COPD (OR = 1.95; 95% CI = 1.17, 2.79). Causal mediation analysis reveals that indoor environmental factors, such as mold and cockroaches, mediate these relationships. Specifically, mold mediates 52% of the asthma association (OR = 1.72) and 54% of the COPD association (OR = 1.61). Cockroach infestations mediate 54% of the asthma association (OR = 1.74) and 55% of the COPD association (OR = 1.51).

These findings underscore the importance of indoor environmental quality in shaping respiratory health, particularly among those in public and subsidized housing. The results highlight the urgent need for public health interventions to improve environmental conditions in these housing sectors. Prioritizing pest control, mold remediation, and building maintenance can reduce the burden of asthma and COPD, improving health outcomes for vulnerable populations.

Public health and housing policies addressing these environmental factors are essential for reducing respiratory health disparities. This research provides actionable insights for urban health policy, offering guidance for interventions in New York City and similar urban environments. By addressing these issues, we can work toward health equity and reduce the adverse effects of poor housing conditions.

Health Services/Policy

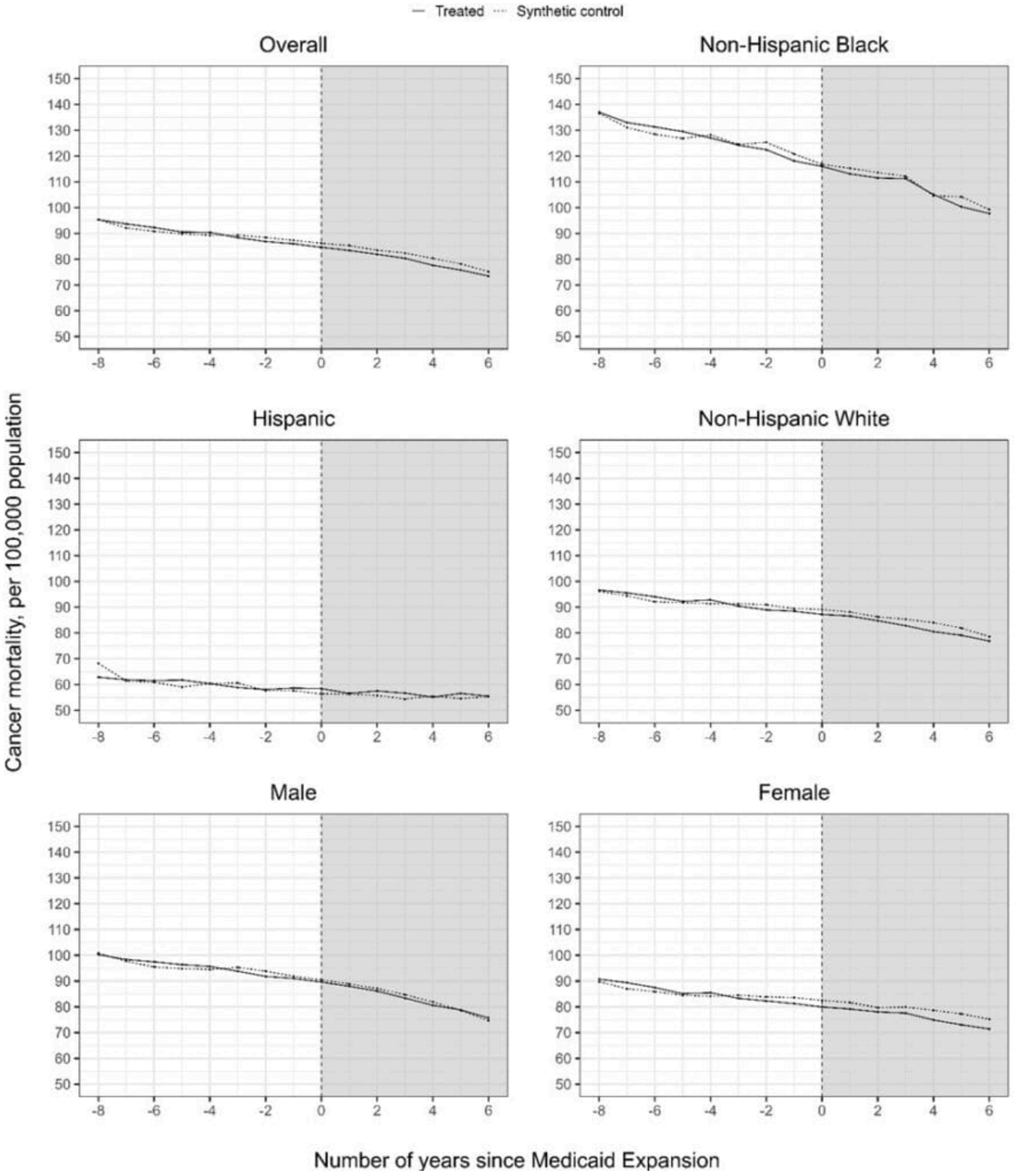
Policy Effect Heterogeneity of the Medicaid Expansion Program on Cancer Mortality Overall and by U.S. Region, Sex and Race/Ethnicity: A Generalized Synthetic Approach Mina Habib* Mina Habib Roch A. Nianogo

Background: Starting in 2014, the Patient Protection and Affordable Care Act aimed to expand Medicaid to cover individuals with incomes up to 138% of the federal poverty level. A Supreme Court ruling allowed states to opt out, creating a natural experiment to study Medicaid expansion's (ME) impact on cancer mortality. This study evaluated ME's effects on age-adjusted cancer mortality among individuals aged 25–64, overall and by U.S. region, gender, and race/ethnicity.

Methods: State-level data (2005–2019) from the U.S. Centers for Disease Control and Census Bureau were analyzed using a person-time weighted generalized synthetic control method. We adjusted for demographics, socioeconomic status, and primary care physician density to estimate mean differences (MD) per 100,000 persons per year. Thereafter, we assessed the presence of disparities across subgroups via a difference in Difference-in-Differences (DDD) model, using the group of most benefit as the reference.

Results: ME was associated with a modest overall reduction in cancer mortality (MD: -2.06; 95% CI: -4.24, 0.11). Subgroup analyses revealed significant reductions among women (MD: -3.02; 95% CI: -5.28, -0.77) versus men (MD: -0.59; 95% CI: -3.61, 2.42), with an imprecise DDD of -2.43 (95% CI: -6.19, 1.33). White Americans had the largest decrease (MD: -2.27; 95% CI: -4.15, -0.38) compared to Black (MD: -1.67; 95% CI: -6.19, 2.84) and Hispanic Americans (MD: 1.02; 95% CI: -9.54, 11.58), with imprecise DDDs. States in the Northeast had the largest decrease (MD: -4.46; 95% CI: -7.4, -0.89), followed by the South (MD: -2.59; 95% CI: -5, 0.57), West (MD: -1.03; 95% CI: -4.61, 3.29), and Midwest (MD: -0.71; 95% CI: -3.2, 2.47), all with imprecise DDDs.

Conclusion: ME appears to reduce cancer mortality; however, the impact on other subgroups, including racial minorities and males, remains unclear. Continued research is essential to understand and address these disparities.


Treated
Synthetic control
Overall
Non-Hispanic Black
Hispanic
Non-Hispanic White
Male
Female
Cancer mortality, per 100,000 population
Number of years since Medicaid Expansion

Health Services/Policy

What is the best measure to evaluate social prescribing programs in Australia? Rosanne Freak-Poli* Rosanne Freak-Poli Christina Aggar Yvonne Zurynski James R. Baker

Social issues underlie the majority of General Practitioners' (GPs) consultations, yet GPs lack the resources to offer holistic care. Social prescribing allows GPs to refer patients to link workers who co-design personalised plans for community-based, non-clinical supports that address non-medical needs. Despite growing global recognition, evaluation measures for social prescribing are inconsistent.

Aim

To identify critical outcome domains for evaluating the impact of social prescribing programs in Australia.

Methods

A three-phase Delphi study was conducted during the 2023 ASPIRE (Australian Social Prescribing Institute of Research and Education) conference. Pre-conference discussions among five academics identified potential outcome domains. At the conference, 85 service providers (58%), researchers (26%), policy professionals (19%), and commissioning specialists (15%), participated in the Delphi. Most were female (58%; 17% no gender disclosed), aged 35–54 years (57%), with over 10 years of professional experience (66%).

Results

Participants ranked emotional/mental health (mean 6.3±1.9SD), social wellbeing (6.0±1.2), and quality of life (QoL; 6.0±1.6) as the highest impact domains. When asked to identify the most important outcome, QoL was selected (Figure 1). Participants identified QoL as:

- A broad measure of holistic wellbeing
- Capable of calculating economic impacts
- Meaningful from the individual's perspective
- Inclusive of emotional, physical, and material wellbeing

The final Delphi survey focused on QoL items apt for evaluating the impact of social prescribing programs. The highest agreement was on health and physical wellbeing domains (94%), emotional wellbeing (93%), and material necessities such as financial, food, and housing security (92%).

Conclusion

QoL is the most valued outcome domain for evaluating social prescribing in Australia. Its ability to capture multidimensional wellbeing and economic impacts makes it a comprehensive and meaningful measure.

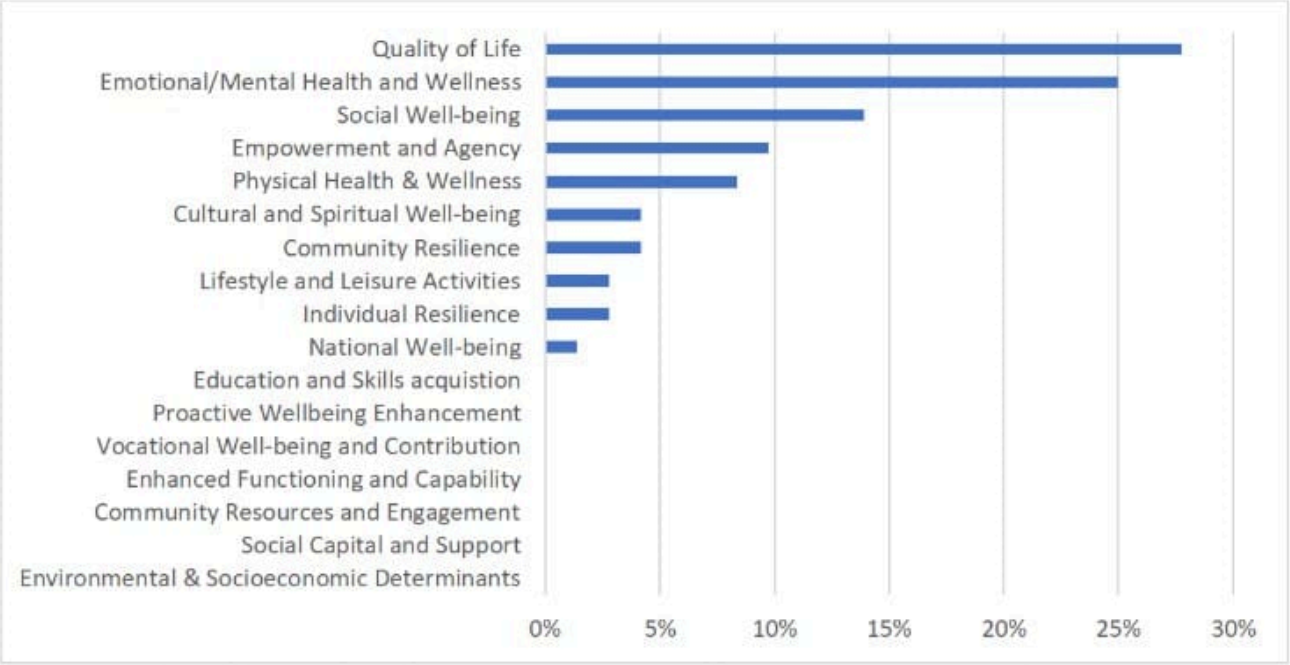


Figure: The 'most important' outcome for social prescribing in Australia as voted by 85 key stakeholders (service providers, researchers, policy professionals, and commissioning specialists)

Health Services/Policy

Relationship between surgical appropriateness, contextual factors, and pain trajectories following total knee replacement for knee osteoarthritis: A group-based trajectory modeling analysis Tristan Watson* Tristan Watson Arjumand Siddiqi Laura Rosella Peter Smith Gillian Hawker

Background: Total knee replacement (TKR) is a common intervention for individuals with knee osteoarthritis (OA) seeking pain relief and improved function. However, 20% of TKR recipients report minimal pain improvement, highlighting the need to identify the determinants of a good pain outcome following TKR. This study examines post-TKR pain trajectories and their preoperative determinants, including surgical appropriateness, surgical complication risk, and contextual factors.

Methods: We used data from the Best Evidence for Surgical Treatment study, a prospective longitudinal study of patients who underwent TKR in Alberta, Canada. Pain was assessed using the Western Ontario and McMaster Universities Arthritis Index. Surgical appropriateness was evaluated based on measures of TKR need (e.g., knee pain and disability), readiness/willingness, and patient expectations. Group-based trajectory modeling was used to examine pain trajectories over one year. Multinomial logistic regression explored the association between the baseline determinants and pain trajectory membership.

Results: Among 1374 TKR recipients, we identified three pain trajectories: “good outcome fast” [n = 158], “good outcome slow” [n = 1071], and “poor outcome” [n = 145]. Individuals in the poor outcome trajectory group had greater TKR need, but lower readiness/willingness for surgery and more unrealistic surgical expectations. Controlling for these factors, they were also more likely to have a postoperative complication, be male, have higher education, and have low back pain. The final model had moderate discrimination of the poor outcome but poor discrimination across all three pain trajectories.

Conclusions: We identified three distinct pain trajectories following TKR for knee OA. Surgical appropriateness and contextual factors were both associated with postoperative pain outcomes. Incorporating these factors may enhance patient outcomes and support TKR decision-making.

Health Services/Policy

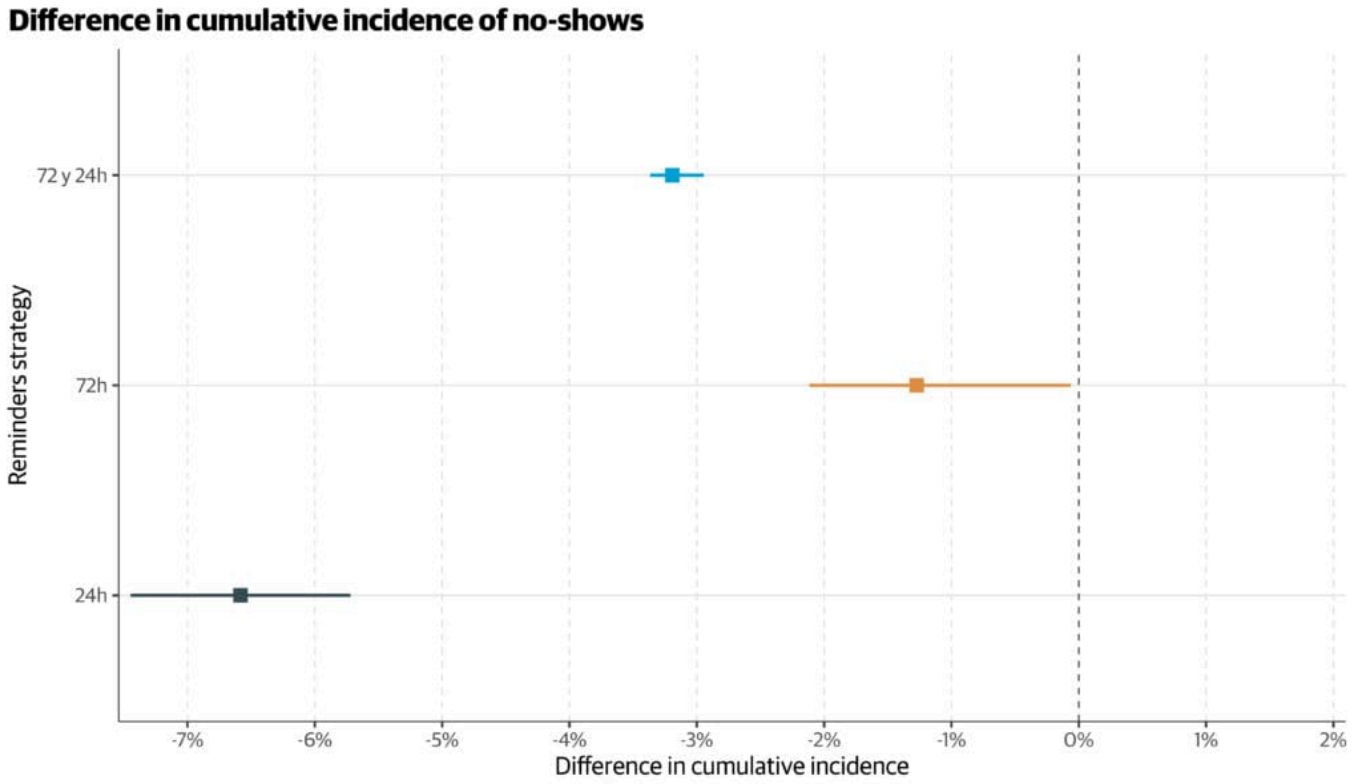
Reducing no-shows in public healthcare: Target trial emulation and cost-benefit analysis of WhatsApp reminder strategies to reduce appointment absenteeism Santiago Esteban*
Santiago Esteban Gastón Quintana Constanza Silvestrini Alejandro Szmulewicz

Missed medical appointments impact healthcare efficiency and increase operational costs. This study evaluated the comparative effectiveness and cost-benefit of different strategies that include WhatsApp reminders to reduce absenteeism in the Buenos Aires City public health system.

Methodology
A target trial was emulated using public health system data from May 2023 to May 2024. Inclusion criteria were: scheduled in-person medical appointments at least 72 hours in advance for prioritized specialties, and possession of a mobile phone. Four strategies were assessed: two WhatsApp reminders (72h and 24h prior), one reminder (72h), one reminder (24h), and no reminders. Reminders included options to cancel/reschedule. Time zero was set 72h before the appointment. Individuals were followed until appointment time or cancellation (patient or health system cancellation). The main outcome was the cumulative incidence (CI) of no-shows (missed or patient-canceled appointments). Secondary outcomes included cancellation and rebooking CI. The main causal estimand was the per-protocol effect. Effect estimation was done using the clone-censor-weight approach. Subgroup analyses considered age in years (0-12, 13-18, 19-40, 41-65, >65), timing of appointment booking (3-15, 16-30, 31-45, >45 days prior) and health facility type (primary care vs hospital).

Results
Data from 472,476 participants showed that a 24h reminder reduced no-show incidence by 6.58% (95% CI: -7.45% to -5.72%) compared to no reminders and had the highest cost-benefit ratio ($2.68 to $4.73 per Argentinian peso). The 72h reminder strategy yielded the best early cancellation and rebooking rates (1.59% increase, 12h prior). Subgroup analysis found greater effectiveness among adolescents and those booking appointments > 45 days in advance.

Conclusion
The 24-hour strategy was the most impactful and cost-effective. Future research should explore personalized messages and outreach for patients without compatible technology.


Difference in cumulative incidence of no-shows
72 y 24h
72h
24h
Reminders strategy
-7%
-6%
-5%
-4%
-3%
-2%
-1%
0%
1%
2%
Difference in cumulative incidence

Health Services/Policy

Telehealth, assets, and completion of mental health services after suicidal behavior: an analysis using electronic health records Catherine K. Ettman* Catherine Ettman Catherine K. Ettman Grace V. Ringlein Kyungeun Jeon Priya Dohlman Jason Straub Sazal Sthapit Peter P. Zandi Elizabeth A. Stuart

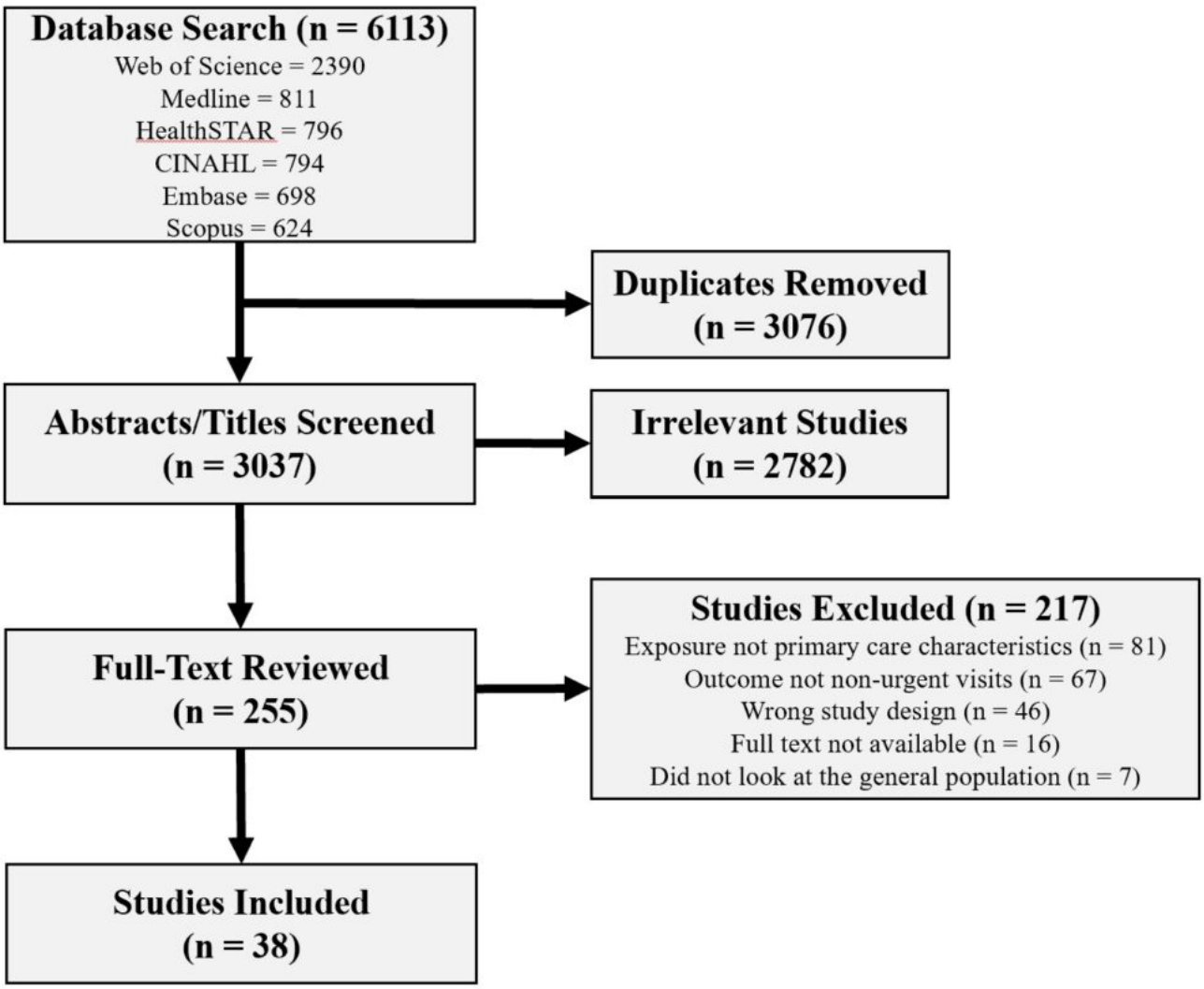
It is unknown how telehealth contributes to mental health services use following suicidal behavior and whether utilization differs across socioeconomic status. Using electronic health records from a cohort of patients with depression in a large urban health system, we assessed patterns in mental health services use after hospital-documented suicidal behavior defined by ICD-10 code for suicidal attempt, self-harm, or ideation (N=687 patients with 7,710 individual telehealth-eligible outpatient psychiatry appointments) from January 1, 2021 – June 30, 2024. First, we estimated whether telehealth was associated with appointment completion (versus no-show or same-day cancellation) in the 6 months following suicidal behavior using generalized estimating equation logistic regression, accounting for multiple appointments per patient, and adjusting for demographic characteristics and comorbidities. Then, we tested for heterogeneity by area financial assets (area deprivation) and social assets (marital status and employment) by adding interactions with telehealth to the models. We found that telehealth appointments had higher odds of completion than in-person appointments (aOR=1.52, 95%CI=1.28-1.80). While we found higher odds of completion of appointments of patients from low deprivation areas (high socioeconomic status) relative to high deprivation areas (aOR=1.62, 1.18-2.26) and married relative to unmarried patients (aOR=1.38, 1.03-1.86), with no significant differences by employment status, we did not find evidence of heterogeneity of the association between telehealth and appointment completion by area deprivation, employment status, or marital status. Telehealth appointments had higher completion than in-person appointments in the 6 months after suicidal behavior. The appointments of patients living in lower deprivation areas and who were married were also more likely to be completed.

LATEBREAKER

Health Services/Policy

Characteristics of Primary Care Associated with Non-Urgent Visits to the Emergency Department: A Systematic Review Antonio DiDomenico* Antonio DiDomenico Samantha Hajna Luke Turcotte Brent Faught

Having increased access to primary care services is associated with reduced emergency department (ED) visits, especially for non-urgent concerns. It is estimated that 10-40% of all ED visits worldwide are non-urgent. Seeking non-urgent care in the ED leads to poorer patient outcomes and greater costs to the healthcare system. While studies have been conducted on the predictors of non-urgent ED use, there is a need to synthesize existing evidence on the role of primary care on non-urgent ED use. We conducted a systematic review to identify primary care characteristics associated with non-urgent ED visits. We systematically searched for articles published since 2000 in Web of Science, Medline, HealthStar, CINAHL, Embase, and Scopus on the associations between outpatient primary care characteristics and non-urgent ED visits. A total of 3,037 studies were identified. After abstract screening, 38 studies underwent full review. Lack of after-hours care and office closure during regular business hours were the most cited characteristics associated with non-urgent visits. Other primary care characteristics associated with higher non-urgent ED use included low appointment availability, long wait-times, distant location, being difficult to reach by telephone, and limited services provision. Primary care characteristics associated with lower non-urgent ED use included using a patient enrolment model, team-based care, after-hours services, having a larger number of patients, use of an electronic health records system, and language concordance with patients. Targeting these factors in primary care settings may reduce non-urgent ED visits and thereby improve patient outcomes and reduce pressures on EDs.


Database Search (n = 6113)
Web of Science = 2390
Medline = 811
HealthSTAR = 796
CINAHL = 794
Embase = 698
Scopus = 624
Duplicates Removed (n = 3076)
Abstracts/Titles Screened (n = 3037)
Irrelevant Studies (n = 2782)
Full-Text Reviewed (n = 255)
Studies Excluded (n = 217)
Exposure not primary care characteristics (n = 81)
Outcome not non-urgent visits (n = 67)
Wrong study design (n = 46)
Full text not available (n = 16)
Did not look at the general population (n = 7)
Studies Included (n = 38)

LATEBREAKER

HIV / STI

Community-informed machine learning to identify factors associated with unmet social needs and adverse care outcomes among persons with HIV David B Hanna* David B Hanna Melissa Fazzari Earle C Chambers Dana Watnick Kathryn Anastos Mindy S Ginsberg Kevin P Fiori Uriel S Felsen

Introduction: Communities that would benefit most from epidemiologic research, especially historically marginalized communities like persons with HIV (PWH), are rarely engaged in model development. We worked with a group of stakeholders (community members, providers, social workers) to identify factors associated with having unmet health-related social needs among PWH and inform machine learning-based prediction models used to assess associations with adverse care outcomes.

Methods: In multiple stakeholder sessions, we reviewed known risk factors associated with social needs and elicited additional factors deemed relevant by stakeholders. Using EHR data from 2018-2023 from the ERC-CFAR Clinical Cohort of PWH in the Montefiore Health System (Bronx, NY), we used random forests to identify predictors of having social needs (among 65 variables), defined by AUC-based variable importance. We estimated propensity scores and used inverse probability weighting to assess the association of reporting social needs with time to virologic failure (>200 cp/mL) based on Cox regression, and with the 1-year rate of no-show visits based on negative binomial regression.

Results: Among 1,432 PWH (50% women, median age 55, 43% Black, 43% Hispanic), 34% reported at least 1 social need, most commonly housing issues (18%), food insecurity (15%) and transportation (12%). Domains identified by stakeholders included mental health, substance use, employment and religion. Random forests identified PHQ-2 (depression screening) score, number of past-year no-show visits and employment as having the highest importance. Using doubly-robust causal analysis, we estimated that if social needs were eliminated, virologic failure would be reduced by 43% (HR 0.57, 95% CI 0.40-0.80) and missed visits reduced by 60% (RR 0.40, 95% CI 0.29-0.55).

Discussion: Incorporating community perspectives into model building was feasible, identified key model features and led to more meaningful interpretation of findings.

HIV / STI

Educational Attainment and HIV Prevalence among Adolescent Girls and Young Women in Malawi: Estimating the Impact of Increased Secondary Education Completion using the Parametric G-formula Domonique Reed* Domonique Reed Katherine Keyes Jeanette Stingone Jessica Justman

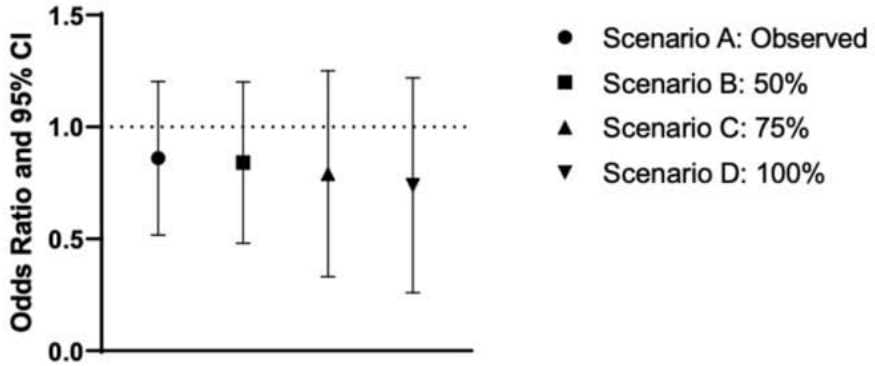
In Malawi, the completion of secondary education among adolescent girls and young women (AGYW) is low due to significant financial and gender inequality barriers. As Malawi reforms its education system to expand secondary education, understanding the impact of increasing educational attainment among AGYW on prevalent HIV is crucial. We modeled the impact of increasing the proportion of AGYW who completed secondary education on prevalent HIV.

We used data from sexually active AGYW enrolled in the Malawi Population-based HIV Impact Assessment (MPHIA; 2016), a nationally representative household survey. Our outcome of interest was HIV status, and our exposure was secondary education completion. Using a logistic regression-based parametric g-formula, we modeled scenarios where 31% (observed) of AGYW completed secondary education and hypothetical increases to 50%, 75%, and 100%.

Among 2,644 AGYW studied, 69% did not complete secondary education. Those without completion showed higher rates of HIV-positive partners (2% vs. 1%), sex work (7% vs. 4%), and age-disparate relationships (33% vs. 31%). Overall, HIV prevalence was 4%, with 5% among non-completers versus 3% among completers. For the observed scenario, there was a 14% (95% CI: 0.5-1.2) decreased odds of HIV among AGYW who completed secondary education (**Figure 1**). For 50%, 75%, and 100% scenarios, AGYW who completed secondary education had a 16% (95% CI: 0.5-1.2), 21% (95% CI: 0.3-1.3), and 26% (0.3-1.2) decreased odds of HIV compared to AGYW who did not complete secondary education, respectively; however, all estimates were not statistically significant.

Although all associations were not statistically significant, we observed a trend that increasing the proportion of AGYW who completed secondary education reduced the overall odds of prevalent HIV. As Malawi continues discussing educational reform, research supporting increases in secondary educational attainment is paramount.

Figure 1. Adjusted Odds Ratios and 95% Confidence Intervals for the Association between Prevalent HIV Status and Educational Attainment Proportion among Adolescent Girls and Young Women in Malawi. Models adjusted for community-level HIV prevalence, household transportation, partner's HIV status, age-disparate relationships, number of partners in the last 12 months, and condom use.



HIV / STI

Prevalence and correlates of obesity in HIV-positive and HIV-negative individuals in Puerto Rico: A clinic-based cross-sectional study Ana P. Ortiz* Ana Patricia Ortiz Jeslie M. Ramos-Cartagena Cristina Muñoz Cynthia M. Pérez Humberto M. Guiot Maribel Tirado

BACKGROUND: The prevalence of overweight and obesity among people living with HIV (PLWH) has increased since the introduction of antiretroviral therapy and due to the aging of this population. This trend contributes to an increased risk of metabolic disorders among PLWH. We aimed to compare body mass index (BMI) by HIV status in a clinic-based sample of adults in Puerto Rico (PR) and to identify factors associated with obesity in these groups. **METHODS:** This cross-sectional study used data from the baseline visit of the Anal Neoplasia Clinic at the University of PR Comprehensive Cancer Center (N=1,237). A physician-administered questionnaire collected sociodemographic, clinical, and lifestyle information, including anthropometric measurements. Pearson chi-square tests and multivariable logistic regression models were used to evaluate factors associated with obesity. **RESULTS:** Mean age of participants was 45±13.3 years. Most were men (67.5%) and PLWH (72.8%). Overall, 39.4% of participants were overweight (25≤BMI<30 kg/m2), 26.0% were obese (BMI≥30 kg/m2), 9.4% self-reported diabetes and 20.1% hypertension, with no significant differences by HIV status (p>0.05). Among PLWH, higher odds of obesity were seen among women compared to men (OR: 1.22, 95% CI: 1.14-1.31) and in individuals with hypertension compared to those without (OR: 1.26, 95% CI: 1.15-1.36). Among HIV-negative adults, higher odds of obesity were seen among women (OR: 1.19, 95% CI: 1.07-1.33), and those with hypertension (OR: 1.23, 95% CI: 1.08-1.40) and diabetes (OR: 1.24, 95% CI: 1.04-1.48) as compared to their counterparts. **CONCLUSIONS:** We observed a similarly high prevalence of obesity among PLWH and HIV-negative adults. Among PLWH, women and persons with hypertension had a greater burden of obesity. Findings underscore the need for targeted weight management interventions in this clinical setting to reduce the risk of cardiometabolic and obesity-related cancers in this high-risk population.

HIV / STI

Long-acting reversible contraceptives and the risk of sexually transmitted blood-borne infections among Canadians under 25 years of age Haylie Simmons* Haylie Simmons Nichole Austin Daniel Dutton Michelle Dimitris Sahar Saeed

Background

Sexually transmitted blood-borne infections (STBBIs) – specifically chlamydia and gonorrhea – are surging across Canada, especially among adolescent girls and young women. The use of long-acting reversible contraceptive (LARC) methods is also increasing among young women, but they do not offer any protection against STBBIs. It is therefore important to understand whether increased LARC access/uptake is associated with chlamydia/gonorrhea incidence rates among adolescent girls and young women under 25 years old.

Methods

We obtained data on monthly lab-confirmed chlamydia and gonorrhea cases among people under 25 from January 2016 to December 2021 from two provincial public health agencies. Since data on individual-level LARC use is not reliably captured in Canada, we used a policy that expanded LARC access at the population level in Ontario (known as OHIP+ in January 2018) as a proxy for LARC use. This created an opportunity to estimate the population-level impact of expanded LARC access on chlamydia/gonorrhea incidence using difference-in-differences. Ontario was selected as our treated group, and British Columbia (where no change in access occurred) as our comparator. Negative binomial models and marginal post-estimation were used to estimate the incidence rate ratio (IRR), and results will be stratified by sex.

Results

180,113 cases of chlamydia and 20,956 cases of gonorrhea were observed between January 2016 and December 2021 in Ontario and British Columbia. Preliminary results suggest the incidence rate ratio (IRR) for total gonorrhea cases for men and women under 25 was 1.24 (95% CI 1.07, 1.43), suggesting that expanded LARC access may be associated with increased gonorrhea rates at the population level (an absolute increase of 31 cases post-policy). The IRR for total chlamydia cases for people under 25 was 1.06 (0.92, 1.22), translating to an absolute increase of 67 cases attributable to expanded LARC access. Sex-stratified analyses are currently underway.

Conclusion

Given contemporaneous increases in LARC access/use and STBBI incidence among people under 25, it is essential to understand if the two are linked. We found that expanded LARC access may be associated with increases in gonorrhea incidence among people under 25.

HIV / STI

Assessing the link between long-acting contraception and risk of sexually transmitted blood-borne infections Haylie Simmons* Nichole Austin Farhan Khandahar

Background: Chlamydia and gonorrhea rates are surging across Canada, and people under 25 (particularly adolescent girls/ young women) are at increased risk. As disease incidence climbs, so does the promotion of long-acting reversible contraception (LARC) like intrauterine devices (IUDs). LARCs do not protect against sexually transmitted blood-borne infections (STBBIs), and LARC users are less likely to use secondary forms of contraception (e.g., barrier methods). This may put LARC users at increased risk of STBBIs.

Methods: We conducted a systematic review of evidence on LARC use and incident STBBIs (as defined by the Public Health Agency of Canada). Search engines included Medline, Embase, and CINAHL. We produced a narrative synthesis and a random effects meta-analysis (in progress) to summarize our findings; publication bias and study heterogeneity were assessed using funnel plots and I2 values. We adhered to PRISMA 2020 reporting guidelines. This review was preregistered in Prospero.

Results: Our initial search yielded 898 studies, 45 of which met our inclusion criteria. Approximately 44% focused primarily on chlamydia and/or gonorrhea; the remaining 56% assessed incident HIV (26%), HPV (18%), and other /aggregated STBBIs (12%). Sub-Saharan Africa was the most common location (~38%); there were no Canadian studies. Designs were mainly observational with very few (n=2) examining LARC/STBBI associations specifically among adolescents/young adults. Evidence on the association between LARC use and STBBI risk was strikingly contradictory, with roughly half reporting increased STBBI risk among LARC users and half pointing toward a null or protective association.

Conclusions: Our findings underscore the need for additional high-quality research on LARC use and STBBI risk given contemporary trends in contraception, particularly among younger people. Differences in study design and analysis likely obscure the true relationship between LARCs and STBBI risk.

HIV / STI

An enhanced PrEP/STI implementation strategy improves HIV oral pre-exposure prophylaxis persistence at an STI clinic in urban Malawi Grace E. Mulholland* Grace Mulholland Mitch Matoga Jane S. Chen Esther Mathiya Griffin J. Bell Beatrice Ndalama Tapiwa Munthali Naomi Nyirenda Naomi Bonongwe Claire Pedersen Edward Jere Mina C. Hosseinipour Zakaliah Mphande Irving F. Hoffman Sarah E. Rutstein

HIV remains a serious global health threat. Efforts to reduce incidence include scale-up of pre-exposure prophylaxis (PrEP), but effectiveness of PrEP hinges on coverage during periods of HIV risk. Persistent PrEP use is critical for those at elevated risk of HIV, including people with sexually transmitted infections (STIs).

The enhanced PrEP STI study ("ePrEP") explored a strategy to improve PrEP use, recruiting clients seeking STI care at an STI clinic in Lilongwe, Malawi. ePrEP provided assisted partner notification services and etiologic STI testing to participants who newly initiated PrEP in March-December 2022 (n=173). Participants were compensated for periodic study visits, even if they discontinued PrEP. Other clients who sought STI care and initiated PrEP in the same period (n=300) received only Malawi's standard PrEP care. We examined the effect of ePrEP participation on PrEP persistence, defined as continued engagement in PrEP services without missing ≥7 doses. We used routine PrEP records data to code persistence using visit dates, pill counts, and client-reported missed doses. Because ePrEP recruitment was not random, we used inverse probability weights to balance baseline differences in age, sex, and PrEP indication between ePrEP participants and other clients.

37% of clients were female. At PrEP initiation, median age was 27 (IQR: 23, 33), 22% had a partner with an unsuppressed HIV viral load, and 47% had bought or sold sex. Among ePrEP participants, 40% named ≥1 partner for assisted notification, and STI incidence during follow-up was 61.3 per 100 person-years. We estimated that, had all clients participated in ePrEP, 32% (95% CI: 25%, 40%) would have persisted on PrEP at 6 months, compared to 3% (95% CI: 1%, 5%) had all clients received only standard PrEP care.

ePrEP participation was strongly associated with higher PrEP persistence. Our findings suggest that ePrEP may be a promising strategy to improve PrEP persistence among people seeking STI care.

HIV / STI

A case-control study of virologic failure among people living with HIV enrolled in a NYC-based Medicaid special needs plan Emma Kohrt* Emma Kohrt Brianne Olivieri-Mui Rob Cavanaugh Brandon Dionne

Background: Viral suppression is essential for optimizing the health of people living with HIV (PLWH) and preventing HIV transmission. Therefore, there is a critical need to identify barriers to suppression. This study examined factors associated with virologic failure among PLWH enrolled in a Medicaid Special Needs Plan (SNP).

Methods: This matched case-control study used 2016-2018 claims data from Amida Care, a managed care organization administering a Medicaid SNP in New York City. Cases had at least one occurrence of virologic failure, defined as two consecutive viral load tests >200 copies/ml in a 4-month period. Controls had no instances of virologic failure. Both groups were enrolled in Amida Care for at least one year prior to the index date, or the date of the second viral load test in the 4-month period. Matching was performed using a 31-day window from the index date, age, and race. Conditional logistic regression models analyzed associations between exposures, (Social Deprivation Index (SDI) scores, gender, advanced care coordination, HIV stage, length of enrollment, and polypharmacy use) and virologic failure.

Results: The matched study sample included 2556 PLWH enrolled in Amida Care, with 62% male (n=1600), a mean age of 42.94 years (SD = 10.04), and a mean SDI score of 92.26 (SD = 13.91). Virologic failure was significantly associated with HIV Stage III diagnosis compared to Stages I/II (OR = 2.09, 95% CI: 1.69-2.58) and advanced care coordination for <6 months compared to never enrolled or enrolled for 6+ months (OR = 2.21, 95% CI: 1.36-3.58). Polypharmacy was associated with reduced odds of virologic failure (OR = 0.71, 95% CI: 0.54-0.92). While also significant, greater social deprivation (higher SDI scores) had little effect (OR = 1.01, 95% CI: 1.00-1.02).

Conclusion: By 6 months, advanced care coordination is no longer associated with virologic failure reflecting effective targeted efforts to increase engagement of high-risk PLWH in health care.

Infectious Disease

Environmental Lead Exposure and Clinical Infectious Respiratory Disease in an Underrepresented, Urban Sample of Children Eva Odiko* Eva Odiko Jing Nie Heather Lehman Marina Oktapodas Feiler

Objective: To examine the association between childhood blood lead concentrations and diagnosis of streptococcal pharyngitis or croup in an underrepresented, low-income sample of children residing in Philadelphia, PA.

Methods: This retrospective cohort study included medical record data on 14,148 children ≤14 years as part of the Temple University Hospital System from 2010-2020. Lead exposure was measured via blood lead concentration (BLC) in µg/dL as reported in the medical records. Infectious upper respiratory outcomes were measured from ICD codes and included streptococcal pharyngitis (strep) or croup. Covariates included age at blood lead collection, sex, race, ethnicity, social deprivation index, and insurance type. Logistic regression and Poisson models were fit to estimate odds ratios and 95% confidence intervals for the association between BLC and strep or croup, and the frequency of strep or croup occurrence respectively. Sex-stratified models examined potential effect modification by sex on the association between BLC and our outcomes.

Results: Among participants, 28% had BLCs above the current action level of 3.5 µg/dL set by the Centers for Disease Control and Prevention (CDC). Most children with either diagnosis had a BLC between 1 – 3.4 µg/dL. Observed findings reported 174% greater odds of BLC ≥3.5 µg/dL (1.93, 3.89) and 25% greater odds of BLC between 1 – 3.4 µg/dL (0.84, 1.86) among those with strep and croup, respectively, compared to children with no diagnoses. Stratified models showed stronger associations among males for both outcomes. Higher risk of frequent strep diagnosis was also observed for those with BLC ≥3.5 µg/dL, 2.45 (1.84, 3.26).

Conclusions: Observed findings suggest evidence of an association between BLC and strep or croup and even levels below the current set action level for blood lead. This supports evidence that no level of lead exposure is safe, and CDC set lead action levels are inadequate as health indicators.

Infectious Disease

Assessing correlates of protection against norovirus infection and disease Savannah M. Hammerton* Savannah Hammerton W. Zane Billings Ye Shen Amy K. Winter Andreas Handel

Norovirus is a major cause of acute gastroenteritis cases worldwide and in the United States. Despite this, correlates of protection against norovirus infection and disease outcomes are poorly understood, and no vaccines are available. We evaluated the relationships between pre-challenge GI.1 and GII.4 norovirus antibodies and clinical outcomes in two vaccine studies with post-vaccination challenge components. The first study assessed a monovalent GI.1 vaccine, and the second assessed a GI.1 and GII.4 bivalent vaccine. We analyzed histo-blood group antigen (HBGA) blocking titers, serum IgA and IgG, and total antibody ELISA (Pan-Ig). All antibody titers were genotype-specific. The outcomes were protection against PCR-confirmed infection, protection against vomiting or diarrhea any day post-challenge (VorD), protection against protocol-defined illness (PDI), and a modified Vesikari Scoring Scale for disease severity. We used Bayesian logistic regression models to assess antibody relationships with infection, VorD, and PDI, and gamma-poisson models to assess antibody relationships with Vesikari scores. We found differences in relationships between vaccine and placebo groups and inconsistent associations between antibodies and clinical outcomes. Our findings indicate that, currently, humoral CoPs may not reliably indicate protection against norovirus clinical outcomes.

Infectious Disease

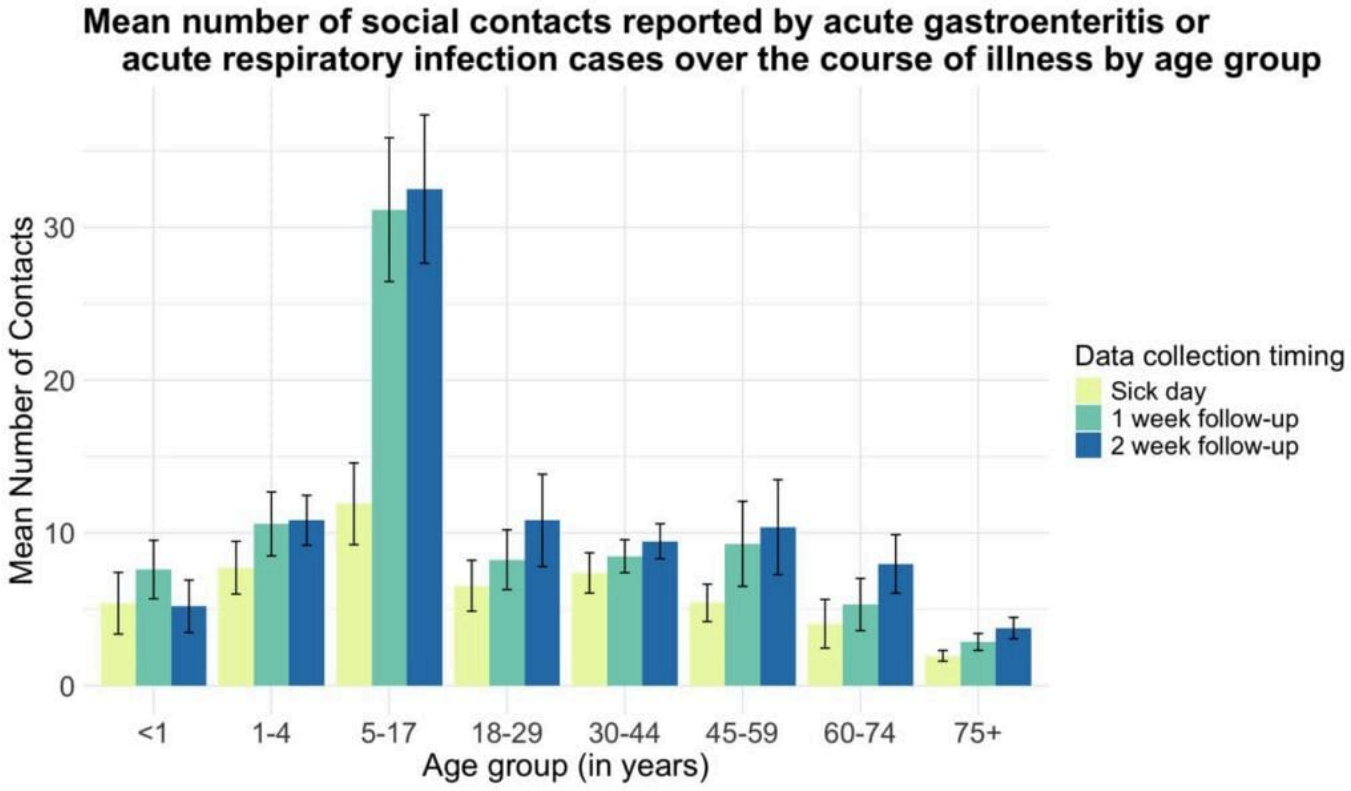
SickMix: How Do People Change Social Contact Patterns When They Are Sick? Grissel Lopes* Grissel Lopes Aarushi Tuli Judy Donald Mark Schmidt Samuel Jenness Benjamin Lopman Kayoko Shioda

Background: Sick individuals are the major drivers of infectious disease transmission, but there is limited empirical data on how they interact with others while infectious. We aimed to understand how acute gastroenteritis (AGE) or acute respiratory infection (ARI) cases and their household members (close contacts) modify their social behaviors over the course of illness.

Methods: We recruited cases of all ages who sought any type of healthcare service (e.g., telehealth, outpatient/inpatient care) at Kaiser Permanente Northwest clinics for AGE or ARI in 2024. Cases were asked to complete three longitudinal online social contact diaries: the first regarding their social contacts and behaviors on the day they felt most ill, and follow-up surveys at 1 and 2 weeks. Their household members were also invited to participate in the surveys.

Results: A total of 526 AGE/ARI cases completed all three surveys. Additionally, 834 household members of these cases consented to participate. The mean number of social contacts among AGE/ARI cases on the sick day was 6.4 (95% confidence interval [CI]: 5.2-7.7), which increased to 10.4 (8.5-12.3) at the 1-week follow-up and 11.9 (9.8-13.9) at the 2-week follow-up. On average, contacts at the 2-week follow-up were 1.84 times (95% CI: 1.79–1.88) higher than on the sick day, with the largest difference observed among those aged 5–17 years, who had a ratio of 2.73 (95% CI: 2.50–2.98). Stratifying by setting, contacts with household members remained stable over time, whereas contacts with non-household members increased as cases recovered.

Discussions: Our data collection is ongoing and is expected to conclude in May 2025. This study found that AGE/ARI cases reduced social contacts during the acute phase of illness and gradually increased interactions, especially with non-household members, as they recover. These data can help generate reliable estimates of transmission parameters and evaluate the impact of interventions.


Mean number of social contacts reported by acute gastroenteritis or acute respiratory infection cases over the course of illness by age group
Mean Number of Contacts
0
10
20
30
<1
1-4
5-17
18-29
30-44
45-59
60-74
75+
Age group (in years)
Data collection timing
Sick day
1 week follow-up
2 week follow-up

LATEBREAKER

Injuries/Violence

Evaluating the Effectiveness of a Hospital-Based Violence Intervention Program in Reducing Depression and PTSD Symptoms Among Gunshot Injury Survivors in Arkansas

Mofan Gu* Mofan Gu Nakita Lovelady James Selig Austin Porter Nick Zaller

BACKGROUND: Firearm violence resulted in 40,886 deaths and 31,652 injuries in the US in 2024. These injuries disproportionately impact young African American men in the US, often leading to untreated depression and PTSD. Hospital-based Violence Intervention Programs (HVIPs) provide trauma-informed care and social support to mitigate these effects. **METHODS**: Project HEAL Little Rock, Arkansas' first HVIP, was implemented at the University of Arkansas for Medical Sciences (UAMS) to address the mental health needs of gunshot wound survivors. Project HEAL staff identified enrolled African American male patients with gunshot wounds from UAMS emergency department. The patients were followed for 1 year post initial injury, and provided with a wide range of supports in healthcare, mental health, housing, employment, education, financial education, legal assistance, and many others, via one-on-one peer specialist check-ins and group sessions. Participants were asked to complete a set of survey questions including demographics, depression symptoms (PHQ-9), PTSD symptoms (PCL-5) at baseline, 3, 6, 9, and 12 months. We used mean scores and repeated measures ANOVA to examine symptom changes over time. **RESULTS**: As of March 2025, Project HEAL enrolled 55 African American male patients with gunshot wounds living in Little Rock, among which 15 completed all five assessments (the rest still ongoing). Mean PHQ-9 and PCL-5 scores declined over time (Figure 1), suggesting a potential dose response between HVIP and depression/PTSD symptom improvement. However, statistical significance was not reached ($p = 0.55$ and 0.56 respectively), likely due to small sample size. **DISCUSSION**: Project HEAL potentially contribute to improved mental health outcomes among survivors of firearm injury. This study serves as a pilot study for our upcoming randomized controlled trial (RCT). Findings highlight the potential of HVIPs to improve mental health in high-risk populations in rural America.

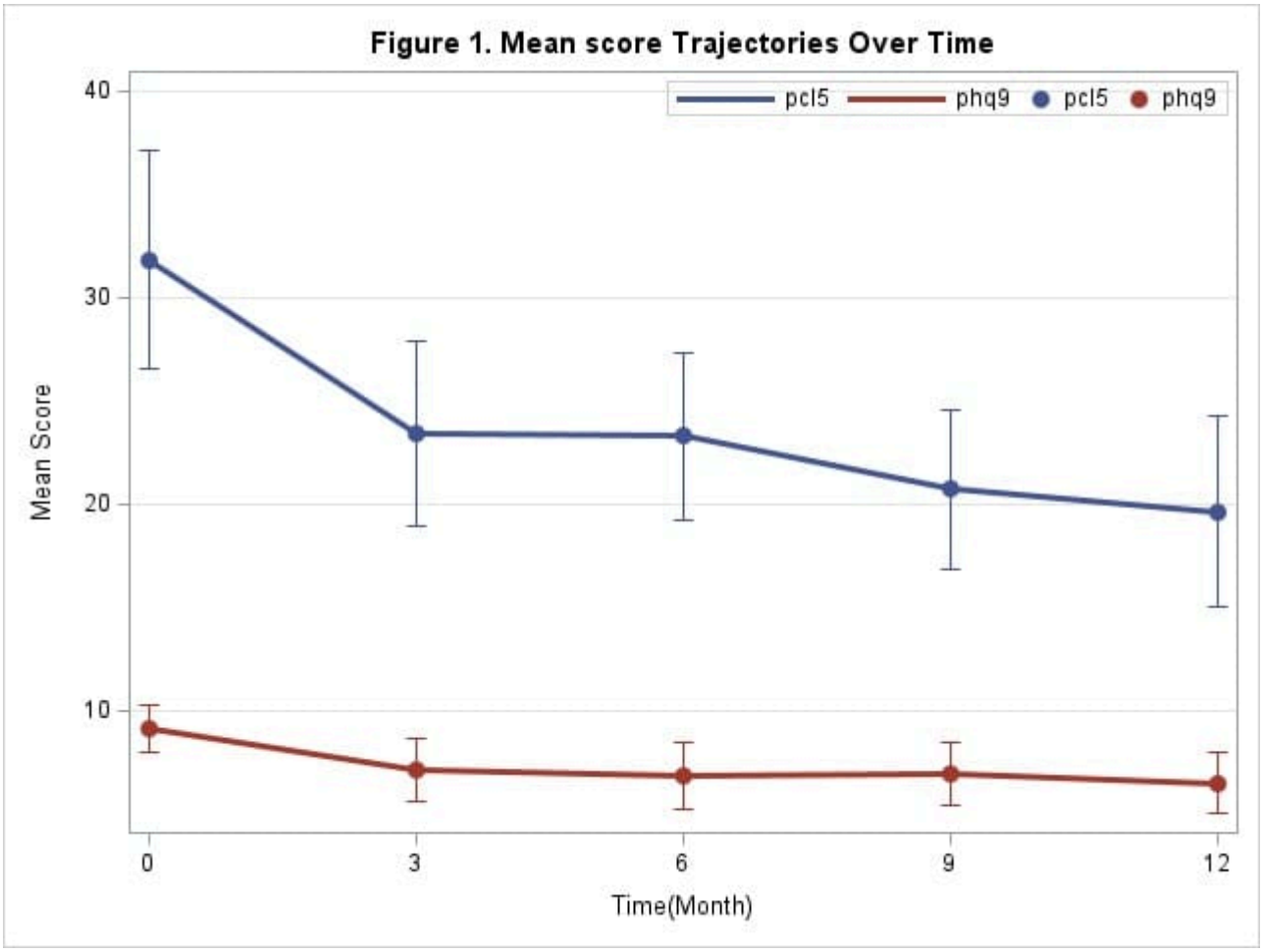


Figure 1. Mean score Trajectories Over Time
pcl5
phq9
pcl5
phq9
40
30
20
10
Mean Score
0
3
6
9
12
Time(Month)

Injuries/Violence

Timing of First Sexual Violence Victimization in Young Adults: Variations by Sexual and Gender Characteristics Xiyuan Hu* Xiyuan Hu Mary Ryan Baumann Mariétou Ouayogodé

Introduction

Sexual violence inflicts profound and enduring negative impacts on victim's health and quality of life. Research has documented that sexual violence significantly increases the risk of serious mental health conditions, substance use, lower education attainment, and reduced employment opportunities. The risk of experiencing sexual violence varies across sexual and gender characteristics (SGC), with females and non-heterosexual individuals facing disproportionately higher rates of victimization.

In this research, we examined the relationship between SGC and the timing of first exposure to sexual violence among young adults in the United States (US), distinguishing between physical and non-physical forms. Physical sexual violence encompasses any unwanted sexual activity involving physical contact, whereas non-physical sexual violence includes unwanted sexual acts that occur without direct physical contact. To our best knowledge, it is the first study to assess the relationship between SGC and the timing of sexual violence victimization for such a large cohort.

Method

Data Sources

The dataset comes from Add Health, The National Longitudinal Study of Adolescent to Adult Health, which was initiated in 1994. Add Health is a nationally representative school-based panel study of adolescents from grade 7 through 12 in the US. The cohort was tracked throughout young adulthood by four in-home interviews.

Add Health is the largest and most extensive longitudinal survey of adolescents. It collects longitudinal data about respondents' demographic, social, economic, psychological, and physical well-being along with contextual information on people and their communities. The data is divided into five waves, with Wave I occurring in September 1994-December 1995, Wave II in April-August 1996, Wave III in August 2001-April 2002, Wave IV in 2008-2009, and Wave V in 2016-2018.

In Wave IV, participants reported the dates and circumstances of significant life events during young adulthood, including experiences of both physical and non-physical sexual violence. In the present analysis, we used Wave IV data to examine the relationship between SGC and experiences of sexual violence, encompassing both physical (N = 4,816, events = 417) and non-physical (N = 4,811, events = 609) victimization.

Variables

The dependent variables were the timings of first victimization for both physical and non-physical sexual violence. Physical sexual violence was assessed through two questions: "Have you ever been physically forced to have any type of sexual activity against your will? Do not include any experiences with a parent or adult caregiver" and "How old were you the first or only time this happened?" Non-physical sexual violence was similarly measured using two questions: "Have you ever been forced, in a non-physical way, to have any type of sexual activity against your will? For

example, through verbal pressure, threats of harm, or by being given alcohol or drugs? Do not include any experiences with a parent or adult caregiver" and "How old were you the first or only time this happened?"

Sexual orientation was determined through self-identification. Participants who identified as "100% heterosexual (straight)" or "Mostly heterosexual, but somewhat attracted to same sex" were classified as heterosexual. Those who identified as "Bisexual, that is, attracted to men and women equally", "Mostly homosexual, but somewhat attracted to opposite sex", "100% homosexual (gay)" or "Not sexually attracted to either males or females" were classified as non-heterosexual. By combining sexual orientation with biological sex, participants were categorized into four SGC groups: heterosexual males, heterosexual females, non-heterosexual males, and non-heterosexual females.

Statistical Analysis

Given our focus on examining both the occurrence and timing of initial sexual violence victimization across different SGCs, survival analysis was determined to be the optimal analytical approach. Specifically, Cox proportional hazards regression was employed to estimate the hazard ratio of sexual violence victimization among different SGC groups.

The analysis controlled for several potential confounding variables: race (White (the reference), Black or African America, American Indian or Alaska Native, or Asian or Pacific Islander), education (less than high school (thw reference), high school, some college, college, more than college), and personal annual income.

We first presented descriptive statistics of the study population. Then, we examined the timing of first victimization for both physical and non-physical sexual violence using Kaplan–Meier survival estimates and multivariate Cox proportional hazards models. The risk period for sexual violence victimization was considered to begin at birth. For respondents who reported having experienced sexual violence, the age at first victimization was recorded as the event time. Respondemts who reported no sexual violence experiences were right-censored at their age during the Wave IV interview.

Results

Descriptive statistics

The mean age of participants was 29 years old. The sample was predominantly white (72%) and heterosexual (95%), with most participants having completed some college education (76%). Income levels varied by group, with heterosexual males reporting the highest income, followed by non-heterosexual males and heterosexual females, while non-heterosexual females reported the lowest income.

Among participants who experienced sexual violence, the mean age at first physical and non-physical sexual violence victimization was 16 years. Physical sexual violence was reported by 9% of the total sample, with disproportionately higher rates among non-heterosexual and heterosexual females. Among those who experienced physical sexual violence, heterosexual males reported the earliest mean age of victimization at 11 years. Non-physical sexual violence was reported by 13% of the sample, again with higher rates among non-heterosexual and heterosexual females. However, among those experiencing non-physical sexual violence, non-heterosexual females reported the earliest mean age of victimization at 13 years.

Timing of first physical sexual violence victimization

Kaplan-Meier survival estimates indicated higher hazards of physical sexual violence among non-heterosexual and heterosexual females compared to heterosexual males. Non-heterosexual males showed slightly elevated risk compared to heterosexual males. The log-rank test revealed significant differences between at least one of the four groups ($\chi^2 = 251$, $p < 0.001$).

The Cox proportional hazards regression models examined the association between SGC and time to first physical sexual violence victimization, adjusting for confounding factors (Figure 1). Compared to heterosexual males, non-heterosexual females exhibited the highest relative risk, with a hazard ratio of 12.33 (95% CI: 7.51, 20.23). Heterosexual females showed a hazard ratio of 7.97 (95% CI: 5.70, 11.13) relative to heterosexual males, controlling for race, education, and income. Non-heterosexual males revealed a marginally elevated hazard ratio of 2.29 (95% CI: 0.71, 7.41) compared to heterosexual males, all else held constant, though this was not statistically significant.

However, the Schoenfeld residual test indicated a violation of the proportional hazards assumption for both the SGC variable ($\chi^2 = 35$, $p < 0.001$) and the overall model ($\chi^2 = 46$, $p < 0.00$

Timing of first non-physical sexual violence victimization

Kaplan-Meier survival estimates revealed elevated risks of non-physical sexual violence among all groups compared to heterosexual males, including non-heterosexual females, heterosexual females, and non-heterosexual males. The log-rank test showed significant differences between at least one of the four groups ($\chi^2 = 324$, $p < 0.001$).

Cox proportional hazards regression models examining the association between SGC and time to first non-physical sexual violence victimization, with adjustment for confounding factors (Figure 1), revealed substantial group differences. Non-heterosexual females were found to have the highest relative risk, with a hazard ratio of 10.15 (95% CI: 6.70, 15.93) compared to heterosexual males. Heterosexual females showed a hazard ratio of 6.84 (95% CI: 5.29, 8.85) relative to heterosexual males, controlling for race, education, and income. Non-heterosexual males exhibited a hazard ratio of 3.25 (95% CI: 1.49, 7.09) compared to heterosexual males, all else held constant.

However, the Schoenfeld residual test indicated a violation of the proportional hazards assumption for both the SGC variable ($\chi^2 = 10$, $p = 0.021$) and the overall model ($\chi^2 = 30$, $p = 0.002$).

Discussion

We found that non-heterosexual females had the highest risk of experiencing both physical and non-physical sexual violence victimization compared to heterosexual males. Heterosexual females also faced significantly higher risk of experiencing both forms of sexual violence victimization compared to heterosexual males. Additionally, non-heterosexual males were at significantly higher risk of experiencing non-physical sexual violence victimization compared to other sexual and gender groups. While non-heterosexual males also showed an elevated risk for physical sexual violence victimization, the result were not statistically significant. Consistent with the prior research, these findings highlight the disproportionately high burden of sexual violence among certain sexual minorities and gender subgroups.

The findings have important implications. Childhood and adolescent sexual violence has long-lasting and detrimental influences on an individual's well-being. Females and non-heterosexual individuals, already facing systemic disadvantages, may be particularly vulnerable to negative consequences of such violence. Therefore, prevention and protection programs targeting children and adolescents should prioritize addressing the specific need of females and non-heterosexual individuals.

Limitations

The findings in this study should be interpreted with caution considering several limitations. First, participants may have been clustered at the school and state levels, but the study did not account for this potential clustering factor. Second, the impact of SGC on the timing of sexual violence victimization may vary over time; incorporating time-varying coefficients may better capture the potential dynamic effects. Third, the study's SGC classification was simplified due to limited access to gender identity data, preventing analysis of non-binary and other gender identities. Fourth, the study may be subject to residual bias from uncontrolled confounding factors like family socioeconomic status and community environments. Fifth, conclusions are based on data from young adults aged 25 to 34 in 2007-2009 and may not be generalizable to other age groups or more recent cohorts. Lastly, the findings may be affected by measurement bias, as individuals—particularly male participants—may underreport experiences of sexual violence due to social stigma and gender-based expectations around victimization.

Conclusion

Both non-heterosexual and heterosexual females were at a higher risk of experiencing physical and non-physical sexual violence victimization compared to heterosexual males. Non-heterosexual males also faced a heighted risk of experiencing non-physical sexual violence victimization. To mitigate the enduring consequences of sexual violence, prevention and protection services should prioritize interventions for females and non-heterosexual individuals during childhood and adolescence.

Panel A: time to first physical sexual violence victimization

Variable		N	Hazard ratio	p
Sexual and gender characteristics	Heterosexual males	2141	Reference	
	Heterosexual females	2482	7.97 (5.70, 11.13)	<0.001
	Non-heterosexual males	74	2.29 (0.71, 7.41)	0.17
	Non-heterosexual females	119	12.33 (7.51, 20.23)	<0.001
Race	White	3523	Reference	
	Black or African America	1116	0.89 (0.71, 1.12)	0.31
	American Indian or Alaska Native	34	0.86 (0.27, 2.68)	0.79
	Asian or Pacific Islander	143	0.67 (0.31, 1.41)	0.29
Education	Less than high school	345	Reference	
	High school	749	0.87 (0.58, 1.32)	0.51
	Some college	2104	0.90 (0.62, 1.29)	0.55
	College	982	0.47 (0.30, 0.73)	<0.001
	More than college	636	0.57 (0.36, 0.90)	0.02
Income		4816	1.00 (1.00, 1.00)	0.04

Panel B: time to first non-physical sexual violence victimization

Variable		N	Hazard ratio	p
Sexual and gender characteristics	Heterosexual males	2138	Reference	
	Heterosexual females	2480	6.84 (5.29, 8.85)	<0.001
	Non-heterosexual males	74	3.25 (1.49, 7.09)	0.003
	Non-heterosexual females	119	10.15 (6.70, 15.39)	<0.001
Race	White	3518	Reference	
	Black or African America	1116	0.72 (0.59, 0.88)	0.001
	American Indian or Alaska Native	34	0.76 (0.28, 2.05)	0.589
	Asian or Pacific Islander	143	0.65 (0.36, 1.18)	0.156
Education	Less than high school	345	Reference	
	High school	749	1.25 (0.85, 1.84)	0.251
	Some college	2099	1.29 (0.91, 1.83)	0.153
	College	982	0.78 (0.53, 1.16)	0.217
	More than college	636	0.88 (0.58, 1.32)	0.527
Income		4811	1.00 (1.00, 1.00)	0.050

Figure 1. Forest plot of hazard ratios for time to first physical and non-physical sexual violence victimization

Injuries/Violence

Location-specific musculoskeletal injury risk following mild traumatic brain injury among United States service members Alexander Ivan B. Posis* Alexander Ivan B. Posis Amy Silder James M. Zouris Daniel J. Crouch Pinata H. Sessoms Andrew J. MacGregor

Background: Mild traumatic brain injury (mTBI) is associated with greater risk of musculoskeletal injury (MSKI). However, it is unclear if the association of mTBI with risk of subsequent MSKI among a large cohort of United States (US) service members (SMs) with extended follow-up differs by specific MSKI location.

Methods: This retrospective cohort study included 777,811 SMs (mean ± SD age = 20.5 ± 3.4 years; 18.9% female; 53.7% White; mTBI = 2.6%) who joined between 2016-2020 and had medical record data until 2023. mTBIs and incident MSKI events were identified using International Classification of Diseases, 10th Revision, codes. We fit accelerated failure time models with a gamma distribution to estimate time ratios (TRs) and 95% CIs for the association of mTBI with subsequent overall MSKI and location-specific MSKI outcomes. All models were adjusted for demographic and military-relevant characteristics.

Results: During 1,589,903 person-years of follow-up, there were 543,463 MSKI events (342 MSKIs per 1,000 person-years). mTBI was associated with a 52% (TR = 0.48, 95% CI 0.46-0.51) reduction in time to overall MSKI relative to no mTBI. The most common MSKI locations were ankle/foot (22.9%), knee (16.3%), and lumbopelvic-hip (14.1%). mTBI was associated with reduced time to MSKI in all location-specific MSKI models. For example, mTBI was associated with reduced time to MSKI related to lower (TRankle/foot = 0.77, 95% CI 0.70-0.84; TRknee = 0.62, 95% CI 0.56-0.69; TRlumbopelvic-hip = 0.95, 95% CI 0.90-1.00) and upper (TRcervicothoracic = 0.19, 95% CI 0.16-0.21) body regions.

Conclusions: Among US SMs, mTBI was associated with faster time to subsequent MSKI. These associations differed by MSKI location. Findings highlight the importance of focusing on injury locations, such as lower body regions, which may be more prone to MSKI following an mTBI. This information can inform patient counseling on injury risk following mTBI.

Injuries/Violence

Polysubstance Use and Involvement of Fatal Motor Carrier Crashes Stanford Chihuri*
Stanford Chihuri

Motor carrier drivers play a crucial role in commerce and daily supply chain logistics, often facing high-risk conditions such as long hours, fatigue, and, in some cases, substance use as a coping mechanism. Despite stringent regulations, including mandated lower alcohol impairment thresholds and random drug testing, substance use may still contribute to motor carrier involvement in fatal crashes. However, the role of polysubstance use in these crashes remains underexplored. Using data from the Fatality Analysis Reporting System during 2007–2022, we assessed the association between polysubstance use (Blood Alcohol Concentration ≥0.01 g/dL and positive for any nonalcohol drug) and the risk of fatal crash involvement in motor carrier drivers. The study included 6,675 motor carrier drivers and 7,113 non–motor-carrier drivers involved in 6,393 fatal multivehicle crashes, with available toxicological testing data. Using McNemar's test to assess drivers involved in the same crashes, non-motor carrier drivers were significantly more likely than motor carrier drivers to test positive for any nonalcohol drug (29.0% vs. 6.4%, χ^2=920.94, P<0.0001), alcohol (15.8% vs. 1.0%, χ^2=832.69, P<0.0001), and a combination of both (6.8% vs. 0.3%, χ^2=381.87, P<0.0001). Conditional logistic regression revealed that motor carrier drivers had 53% lower odds of testing positive for any nonalcohol drug (odds ratio (OR) = 0.47, 95% confidence interval (CI) = [0.33, 0.68]), 83% lower odds for alcohol (OR = 0.17, 95% CI = [0.09, 0.33]), and 98% lower odds for polysubstance use (OR = 0.03, 95% CI = [0.003, 0.23]), after adjusting for age, sex, history of driving while intoxicated, previous accidents, speeding, and survival status. These findings highlight that, despite increasing drug use among the general driver population, motor carrier drivers have a significantly lower risk for drug-related fatal crashes, likely due to effective mandatory and random testing programs.

Injuries/Violence

Prevalence and Risk for Sexual and Dating Violence among LGBTQ+ Youth in California

Sabrina C. Boyce* Sabrina C. Boyce Emma Jackson Riley Saham Ricardo Vera Monroy Jay G. Silverman

LGBTQ+ youth experience disproportionately high risk for sexual violence (SV) and dating violence (DV), with more severe outcomes than heterosexual, cisgender youth. Yet, there are major gaps in measurement of sexual orientation and gender identity (SOGI) in nationally representative samples that limit understanding of the diversity of LGBTQ+ youth's experiences of violence and therefore, tailored prevention. This analysis addresses this gap by providing one of the first population-based estimates of how SV/DV risk varies within subgroups of LGBTQ+ youth. Cross-sectional data were collected from a census sample of 9,731 9th and 11th grade high school students from five school districts in Central and Southern California that voluntarily participated in the California Healthy Kids Survey (CHKS) and an additional SV/DV module during 2021-2022. Descriptive analyses were carried out to estimate the prevalence of each form of SV/DV for each LGBTQ+ subgroup. Bivariate and multivariate analyses provided estimates for the relative risk of violence across 18 LGBTQ+ subgroups based on intersections of SOGI. In this sample, 23.8% and 15.3% of LGBTQ+ youth report SV and DV, respectively, in the past 12 months. For SV, nonbinary youth, transgender boys, transgender girls, and cisgender girls who identify as pansexual and bisexual experience significantly higher risk relative to heterosexual cisgender girls, a group know to experience higher risk for SV/DV relative to heterosexual cisgender boys. For DV, bisexual and pansexual cisgender girls and nonbinary youth, and transgender boys experience significantly higher risk, relative to heterosexual cisgender girls. For both SV and DV, cisgender heterosexual boys experience significantly lower risk. Results from this study suggest that nonbinary and transgender youth, and cisgender girls who identify as pansexual and bisexual have the highest need for SV/DV prevention and support among LGBTQ+ youth.

Injuries/Violence

Application of IPV instrument in accurately identifying and abusive and unsafe relationships Alison Walsh* Alison Walsh Erin Kahle

Current survey instruments may underestimate intimate partner violence (IPV) prevalence in GBMSM (gay, bisexual, and other men who have sex with men) relationships, possibly due to incomplete capture of the full range of relationship abuse. This study evaluated the IPV-GBMSM scale's effectiveness in identifying self-reported abusive and unsafe relationships in 399 partnered GBMSM living with HIV (US, 2022-2024). The scale covers 18 emotional, physical/sexual, and controlling IPV behaviors over the 3 months prior to survey. Participants reporting the experience of any listed behavior were categorized as IPV victims. They also indicated if they felt safe in their relationship or considered their relationship abusive. IPV prevalence according to the IPV-GBMSM scale was calculated overall and by domain. The sensitivity, specificity, and positive/negative predictive values (PPV/NPV) of the scale for identifying unsafe and abusive relationships were analyzed. Overall IPV prevalence was 43.9%, with emotional, physical/sexual, and controlling IPV at 26.1%, 18.6%, and 24.9%, respectively. Of participants, 6.8% and 6.5% deemed their relationships unsafe or abusive. Sensitivity for identifying unsafety ranged from 0.6 (physical/sexual) to 0.8 (any IPV); specificity ranged from 0.6 (any IPV) to 0.9 (physical/sexual). Sensitivity and specificity for abusive relationships ranged from 0.7 (controlling) to 0.9 (any IPV) and 0.6 (any IPV) to 0.9 (physical/sexual). PPVs for safety and abuse were similar, at 0.2 (any IPV) to 0.3 (physical/sexual). All NPVs were near 1.0. Low PPVs suggest a disconnect between individual experiences of relationship abusive and threats to physical or mental health and the IPV-GBMSM instrument's assessment. Critical evaluations and the development of new tools to more accurately measure real-world IPV experiences and perceptions are essential.

Mental Health

The Effects of Problematic Smartphone Use on Adolescent Sleep and Mental Health: An Evaluation of Structural Associations Sheng-Hung Chu* Sheng-Hung Chu Yu-Ting Chin Pei-Wen Wu Pei-Tung Lin Jyun-Hao Guan Chien-Hung Lee

Background: Problematic smartphone use (PSU), which disrupts sleep patterns and reduces face-to-face social interactions, may significantly impact sleep problems and mental health. This study aimed to investigate the effects of PSU on sleep quality and depression in adolescents, as well as to explore their potential structural associations using structural equation modeling.

Methods: We examined 2,138 adolescents aged 14–19 years, randomly selected from 17 senior high schools in three areas with varying socioeconomic statuses in Taiwan. A questionnaire, consisting of 11 symptoms developed from the DSM-5 criteria for substance use disorder, was used to measure PSU. Participants with 0-1, 2-3, 4-5 and ≥6 DSM-5 symptoms were defined as no, mild, moderate, and severe PSU, respectively. The Pittsburgh Sleep Quality Index (PSQI) was used to assess sleep quality and disturbances, and the Center for Epidemiologic Studies Depression Scale (CES-D) was utilized to evaluate depressive symptoms. Generalized structural equation modeling was employed to analyze the relationships among PSU, sleep quality, and depression.

Results: The prevalence of DSM-5–defined mild, moderate, and severe PSU in adolescents was 12.9%, 17.6%, and 49.2%, respectively. Adolescents with mild, moderate, and severe PSU reported poorer sleep quality, with PSQI scores increased by 0.83, 1.05, and 2.09, respectively (all $P<0.05$). Adolescents with severe PSU had 3.1 higher CES-D scores for depressive symptoms. After adjusting for covariates, increased PSQI scores were significantly associated with higher CES-D scores ($\beta=1.78$, 95% CI: 1.64-1.92). Furthermore, sleep quality, latency, duration, disturbance, and daytime dysfunction mediated the relationship between smartphone usage time and depression scores.

Conclusion: Our findings indicate that PSU is linked to poorer sleep quality and depressive symptoms in adolescents, underscoring the need for targeted interventions to address PSU and improve mental health.

Mental Health

Investigating predictive value and effect estimates between two commonly used depression scales in via secondary data from HPTN 068, a conditional cash transfer trial of adolescent girls and young women in South Africa Valerie Lucas* Valerie Lucas Joanna Asia Maselko Molly Rosenberg Marie Stoner M Luz Reyes McNaughton Kathleen Kahn Audrey Pettifor

Intro

The Child Depression Index (CDI) and Center for Epidemiologic Studies Depression scale (CESD) are scales to measure and screen for depression. CDI is a version of the Beck Depression Inventory simplified for minors, and CESD is generally used for adults. Secondary data from HPTN 068 provided a unique opportunity to assess scale concordance in an adolescent female sample, a time period when minors transition to young adulthood.

Methods

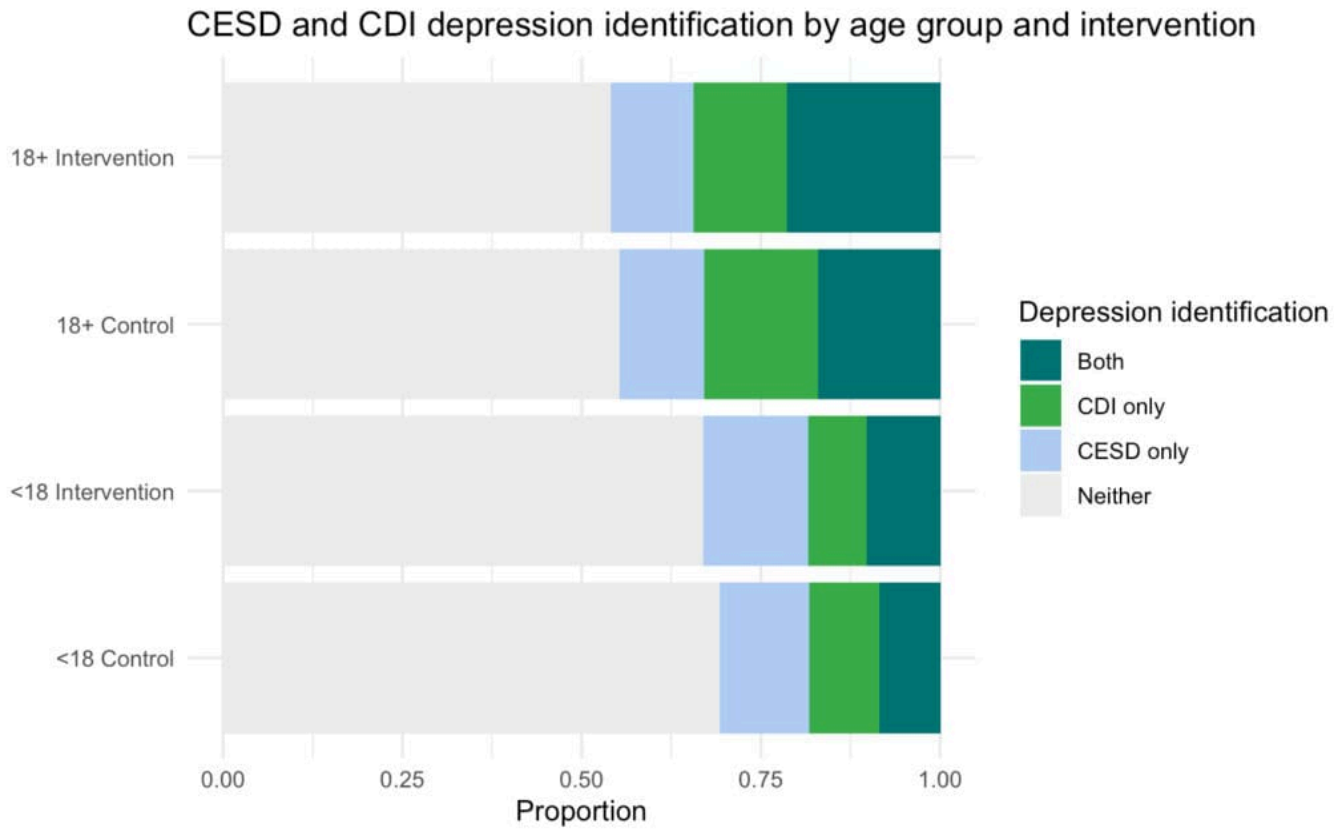
Young women (n = 2530) in rural South Africa were randomized 1:1 to a conditional cash transfer (CCT) or control. Participants were eligible to receive the CCT while they remained unmarried and maintained school attendance. Both the CDI and the CESD were administered at final study visit. Without a gold standard, we compared positive predictive values (PPV) of CDI and CESD for each other across age and intervention assignment and explored how choice of metric impacted CCT effect estimates.

Results

At study conclusion, participants had a median age of 18 (IQR: 17,18). The prevalence of depression was 26% via CDI and 27% via CESD. But PPV for CDI in detecting depression via CESD is only 53%, and the PPV of CESD for CDI is 57%. The PPV is lower for those <18 and higher for those 18+. For the <18 group, the PPV of CDI for CESD is 52%, and the PPV of CESD for CDI is 41%. For the 18+ group, the PPV of CDI for CESD is 57%, and the PPV of CESD for CDI is 62%. Comparing risk difference estimates, the CCT reduced depression by 0.7 percentage points (95% CI: -4.7, 3.4) via CDI and by 2.7 percentage points (95% CI: -0.9, 6.3) via CESD.

Conclusion

The PPV between CDI and CESD are surprisingly low, given the same stated construct and similar prevalence and effect estimates. The PPV of the CESD for CDI is greater than the PPV of CDI for CESD among 18+ participants, and vice versa for <18 participants. These differences suggest that CDI and CESD measure different underlying (sets of) constructs with age-based differences in depression symptoms.


CESD and CDI depression identification by age group and intervention
18+ Intervention
18+ Control
<18 Intervention
<18 Control
0.00
0.25
0.50
0.75
1.00
Proportion
Depression identification
Both
CDI only
CESD only
Neither

Mental Health

Population fraction of physician-diagnosed depression attributable to psychosocial stressors at work: Results of the PROspective Quebec Study on Work and Health Mathilde Lavigne-Robichaud* Mathilde Lavigne-Robichaud Ana Paula Bruno Pena Gralle Denis Talbot alain milot Gilbert-Ouimet, M. Brisson, C. Xavier Trudel

Background: Psychosocial stressors at work are risk factors for the incidence of depression. However, no previous prospective studies examined the fraction of diagnosed depression cases attributable to these work stressors.

Objective: To estimate the fraction of diagnosed depression events attributable to psychosocial stressors at work.

Method: This is a prospective study including 6,846 white-collar workers (1999-2001) free of depression in the year prior to baseline and followed up for 5 years. Psychosocial stressors at work were measured according to the job strain and effort-reward imbalance (ERI) models. Incident depression events were identified in medical databases with universal coverage. Attributable fractions (AFs) were estimated using the Kaplan-Meier method, with multiple imputation and inverse probability weighting applied to address selection and confounding biases.

Results: The estimated AF for job strain over 3 years was 16.8% (95% confidence interval [CI]: -5.2% to 38.9%). The AF for ERI over 3 years was 12.1% (95% CI: 1.5% to 22.8%). The AF for combined exposure to job strain and ERI was 42.0% (95% CI: 16.3% to 67.7%). Over a 5-year period, AFs for all exposures decreased but remained within the margin of the confidence intervals.

Conclusion: In the present study, psychosocial stressors at work were significant contributors to physician-diagnosed depression. Results suggest that a substantial proportion of incident depression cases—up to 42% in some exposure scenarios—could be prevented by reducing the prevalence of psychosocial stressors at work.

Mental Health

Racial and Rurality Disparities in Screening for Postpartum Depression in North Dakota (2017-2021) Andrew Williams* Andrew Williams Asma Ul Husna Juliana Antwi Kilyn Parisien Rylee Bergeron

Background: Postpartum Depression (PPD) is one of the most prevalent maternal health conditions affecting women after their childbirth, and a key contributor to maternal mortality. Undiagnosed PPD can lead to increased risk of substance use, suicidality, and poor maternal-infant bonding.. This study examined the intersection between race and rurality in regard to PPD screening in North Dakota (ND).

Methods: Data (weighted n=39,477) from the 2017-2021 ND Pregnancy Risk Assessment Monitoring System (PRAMS) were analyzed. Maternal race (White, American Indian, Other) and PPD screening were self-reported. County-level rurality was based on the 2013 National Center for Health Statistics Urban-Rural Classification Scheme for Counties. Logistic regression estimated odds ratios (OR) with 95% confidence intervals (CI) for the odds of PPD screening among AI and Other women, compared to White women. Models were fit overall and by rurality, adjusted for maternal sociodemographic and health factors.

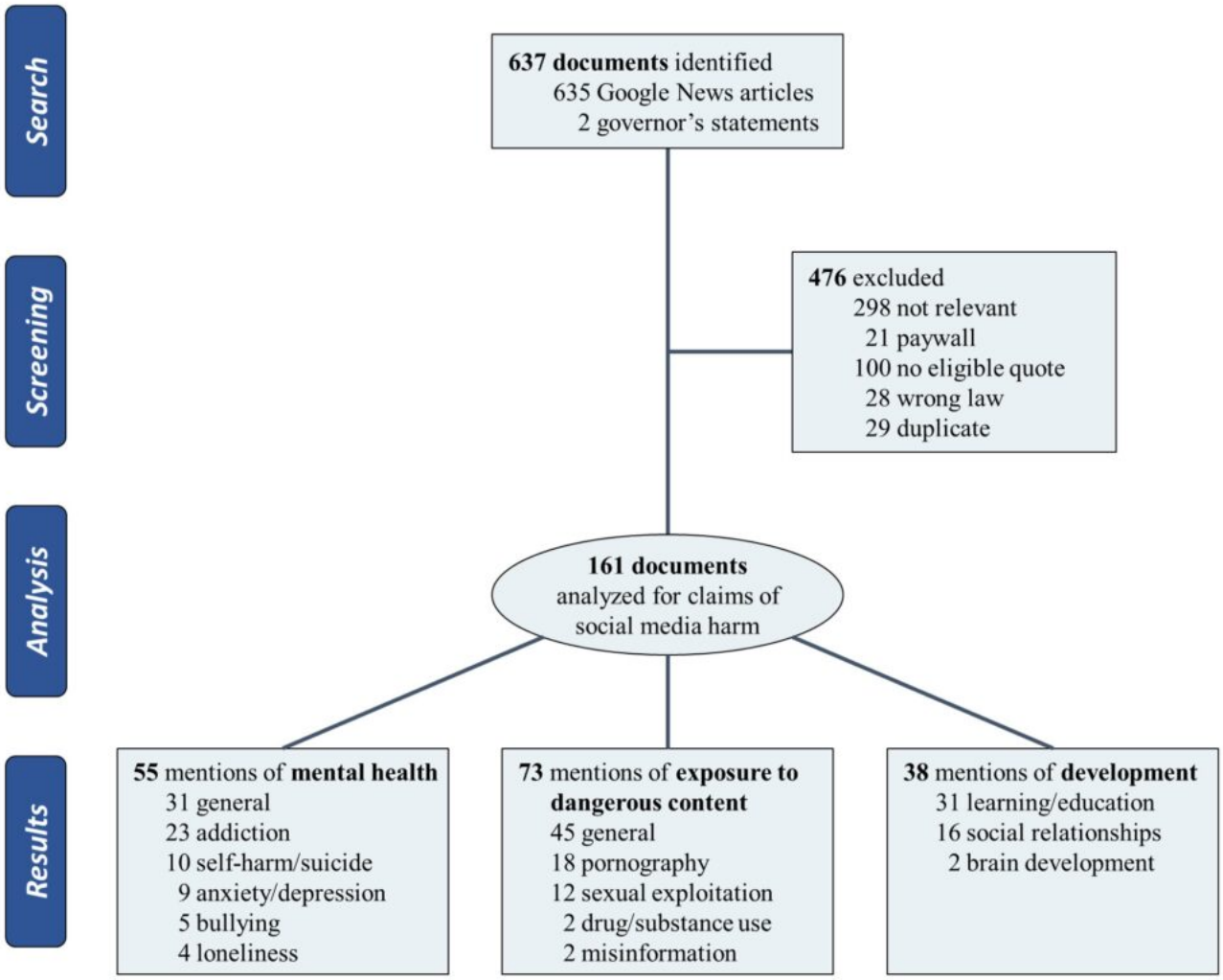
Results: Overall, 95% of women were screened for PPD, yet screening differed by race/ethnicity: 89% of AI women, 90% of Other race women, and 95% of White women ($p<.05$). In regression analyses, overall, AI women had 56% lower odds (OR:0.44, 95%CI0.27,0.71) of being screened for PPD compared to White women. We observed no differences for PPD screening among Other race women. The odds of PPD screening by race differed by rurality. Among rural women, AI women had 63% lower odds (OR:0.37, 95%CI:0.19,0.73) and Other race women had 67% lower odds (0.33, 95%CI:0.12,0.87) of PPD screening compared to White women. We observed no differences in PPD screening among urban women.

Discussion: This study shows significant disparity in postpartum depression screening in AI women and Other race women compared to White women. This disparity is more pronounced in rural settings of ND and may reflect the lack of access to postpartum healthcare in rural areas, and social stigma around mental health support.

Mental Health

US state regulation of adolescent social media use: Do policies match the evidence? Marco Thimm-Kaiser* Marco Thimm-Kaiser Katherine M. Keyes

The potential adverse effects of social media use on adolescent health and development have generated substantial scholarly and public attention. In response to the increasingly accepted thesis that social media use—at least if unregulated—is causing harm to adolescents, a growing number of state-level social media regulations are emerging in the U.S. These policy interventions are being designed in the context of mixed scientific evidence about the potential impacts of social media, forcing policy makers to weigh the need for proactive regulation to protect adolescents against the strength of the evidence that has accumulated to date. In this research, we explored the degree to which scientific evidence is used in arguments for state social media regulations. To this end, we conducted a media content analysis of elected government officials' statements about 69 state social media legislative initiatives that were adopted or enacted prior to September 2024, using Google News. We identified and screened 637 documents, of which 161 met inclusion criteria. We extracted three main themes connected to claims about social media-related adolescent harms: (1) harm to adolescents' mental health (mentioned in 55 articles), including six sub-themes (e.g., the dangers of social media or smartphone addiction, self-harm or suicide in connection to social media use, increases in adolescent anxiety and depression); (2) exposure to dangerous online content (73 mentions), including five sub-themes (e.g., access to pornography, risks of sexual exploitation), and (3) harm to adolescent development (38 mentions), including three-sub themes (obstacles to education and learning, negative impacts on adolescent social relationships, and adolescent brain development). Subsequently, we provide an overview of the strength of the evidence underlying common themes from the content analysis and recommendations for a research agenda designed to inform evidence-based policy.


Search
Screening
Analysis
Results
637 documents identified
635 Google News articles
2 governor's statements
476 excluded
298 not relevant
21 paywall
100 no eligible quote
28 wrong law
29 duplicate
161 documents
analyzed for claims of
social media harm
55 mentions of mental health
31 general
23 addiction
10 self-harm/suicide
9 anxiety/depression
5 bullying
4 loneliness
73 mentions of exposure to
dangerous content
45 general
18 pornography
12 sexual exploitation
2 drug/substance use
2 misinformation
38 mentions of development
31 learning/education
16 social relationships
2 brain development

Mental Health

Modifiable Lifestyle Factors for Perinatal Depression among Women with a History of Premenstrual Disorder: A Nationwide Register-Based Study in Sweden Jane Yan* Jane Yan Donghao Lu

Background: Perinatal depression (PND) is a major depression episode that occurs during pregnancy or postpartum. Recently, our work has identified that women with premenstrual disorder (PMD) are at high risk of PND, potentially due to the vulnerability to hormonal fluctuations. However, little is known about risk factors modifying the risk of PND in this high-risk group – women with PMD.

Aim: The study aims to estimate the risk of PND associated with modifiable lifestyle risk factors (smoking, snuff use, BMI) comparing women with and without PMD.

Methods: We conducted a prospective cohort study of all women who gave birth during 2003-2021 in Sweden. PMD diagnosed before pregnancy and PND (depression diagnosed during pregnancy or within one year postpartum) were identified from National Patient Register and regional primary care registers. Lifestyle risk factors in early pregnancy, including smoking, snuff use, and maternal BMI was obtained from the Medical Birth Register. Log-binomial regressions with robust estimator were used to calculate Risk Ratio (RR) of PND associated with individual lifestyle exposure, stratified on women with and without PMD, with adjustment for demographic and pregnancy characteristics and history of psychiatric disorders.

Results: In total, 1,236,980 women (2,195,838 pregnancies) were included in the study, with 22,914 (1.85%) diagnosed with PMDs before pregnancy. Compared to women without PMD, women with PMD were more likely to be born in Sweden, have a higher education attainment, and have a history of psychiatric. Among women without PMD, smoking or snuff use in early pregnancy was associated with 20-36% increased risk of PND when comparing to no use, while no pronounced association was found across BMI categories. Compared to women without PMD, women with PMD were at about two-fold risk of PND, independent of psychiatric history. Exposure to tobacco use moderately altered the association (e.g., RR changed from 2.06 (95%CI 2.01-2.12) (no smoking) to 1.75 (95%CI 1.40-2.17) (≥10 cig/day), whereas a 44% reduction of RR was observed from overweight/obesity (RR 2.17/2.18, 95% CI 2.08-2.27/2.05-2.31) to underweight (RR 1.74, 95% CI 1.42-2.13) in early pregnancy. Similar trends were noted regardless of psychiatric history, although among women without psychiatric history PMD was associated with about eight times higher risk of PND.

Conclusion: Women with PMD, particularly in absence of psychiatric history, were at high risk of PND. Such risk may be modified by body adiposity, but not by tobacco use, although future studies are warranted to confirm the causal relationship.

Mental Health

The association between antenatal depression with postpartum visit non-attendance: the mediating role of postpartum depressive symptoms Sabrina Karim* Sabrina Karim Hill L. Wolfe Lindsay S. Womack-Martenson Elizabeth Clark Angela Rohan

Introduction: Postpartum visits are important for timely interventions to prevent complications, yet 10-40% of U.S. women miss these visits. Identifying factors associated with non-attendance is important for improving visit rates. The role of mood disorders, particularly antenatal depression, is understudied. We examined the association between antenatal depression and postpartum visit non-attendance, and whether postpartum depressive symptoms (PDS) mediate the association.

Methods: This cross-sectional study used 2016–2022 Pregnancy Risk Assessment Monitoring System (PRAMS) data for women aged 18 or older with recent live birth (Unweighted n=210,854). Antenatal depression was identified based on report of experiencing depression during pregnancy. Outcome was self-reported postpartum visit non-attendance. PDS, the mediator variable, was determined by self-report of often/always feeling depressed, hopeless, and having diminished interest post-delivery. Descriptive and multivariable logistic regression analyses were conducted using sampling weights, with SAS PROC CAUSALMED assessing the mediation effect of PDS.

Results: One in ten women with a recent live birth reported not attending a visit at 4-6 weeks postpartum and 14% experienced antenatal depression. Non-attendees, compared to those who did attend, were more likely to be non-Hispanic Black (19% vs 13%) or Hispanic (25% vs 16%) women, enrolled in Medicaid during pregnancy (52% vs 32%), or had a history of intimate partner violence during pregnancy (4% vs 2%). Women who had antenatal depression had higher odds of postpartum visit non-attendance compared to those without antenatal depression (adjusted Odds Ratio 1.31, 95% CI 1.23-1.39). PDS mediated 13% of the association.

Conclusion: Our mediation results suggest that addressing PDS in women with antenatal depression may improve postpartum visit attendance.

Mental Health

Cognitive complaints predict persistent probable depression in U.S. military personnel

James K. Romine* Andrew MacGregor Amber Dougherty Diane Williams

Introduction: Depression is a significant health burden on the U.S. military and can lead to long-term quality of life issues and suicidal thoughts and behavior. While the military incorporates screening tools to identify depression, guidance on patient referral is lacking. As such, investigating additional criteria that could identify higher-risk individuals may help guide referral efforts.

Methods: 1,434 U.S. service members who responded to an initial health assessment upon return from deployment and screened positive for probable depression using the 2-item Patient Health Questionnaire (PHQ-2) were included. A subsequent health assessment was conducted 3-18 months later that also used the PHQ-2 and identified those with persistent probable depression. Fourteen health complaints were assessed in the initial assessment. A multivariable logistic regression model examined the predictive effect of these health complaints on persistent probable depression, after adjusting for demographic factors and time between assessments. ORs and 95% CIs were calculated.

Results: Overall, 26.9% of service members screened positive for persistent probable depression. In the multivariable regression, only two health complaints were statistically significant. Cognitive complaints, specifically “trouble concentrating on things” (OR 1.49, 95% CI 1.05-2.12) and “hard to make up your mind or make decisions” (OR 1.55, 95% CI 1.15-2.09), were associated with greater risk of persistent probable depression.

Conclusion: This study identified two cognitive complaints associated with persistent probable depression. These results may enhance military screening efforts. Service members who screen positive for probable depression with cognitive complaints may need referral for further care, a process that could be automated. Automated screening and referral efforts would allow more efficient provision of targeted medical care, which may help minimize the mental health burden in the U.S. military.

Mental Health

Posttraumatic stress disorder symptom remission and risk of incident type 2 diabetes

Kelsey Serier* Kelsey Serier Jeanine Nasser Karestan Koenen Jaimie Gradus

Posttraumatic stress disorder (PTSD) is a mental health condition with metabolic consequences. While individuals with PTSD are more likely to develop type 2 diabetes mellitus (T2DM), little is known about the impact of PTSD symptom remission on T2DM.

Using data from 41,106 women from the Nurses Health Study (NHS-II), we estimated the association between remitted and current PTSD symptoms and diagnosed incident T2DM between 2009 and 2019 using Cox proportional hazard regression. Lifetime trauma exposure and lifetime and past four-week PTSD symptoms were assessed in 2008. PTSD was defined as a score of 4 or higher on the Short Screening Scale for DSM-IV PTSD, with scores of 1-3 reflecting subthreshold PTSD. We defined remitted PTSD as endorsement of lifetime but not past month symptoms; current PTSD was defined as past month symptoms. Our comparison group for all analyses was women who experienced trauma but did not develop PTSD. We adjusted for confounders, including age, race, parental education, parental diabetes, somatotype at age 5, oral contraceptive use, and menopause status. We incorporated health behaviors (body mass index, diet, physical activity, alcohol use, and smoking) and antidepressant use as potential mediators.

Current PTSD had the strongest association with T2DM (HR = 1.56; 95% CI = 1.34, 1.82), followed by current subthreshold PTSD (HR = 1.15; 95% CI = 1.02, 1.28). The remitted PTSD groups had a comparable rate of T2DM to the trauma/no PTSD group (remitted subthreshold PTSD: HR = 1.01, 95% CI = 0.94, 1.19; remitted PTSD: HR = 1.03, 95% CI = 0.86 1.21). Associations for subthreshold (HR = 1.03; 95% CI = 0.92, 1.16) and current PTSD (HR = 1.18, 95% CI = 1.01, 1.39) were attenuated when considering mediators.

Overall, these findings suggest that while current PTSD symptoms may increase the rate of incident T2DM, remitted PTSD symptoms do not. PTSD symptom reduction may have important clinical implications for improving long-term metabolic health outcomes.

Mental Health

Recreational opportunities at Play Marin enhance health and well-being for adolescents in Marin City, CA Michaela F George* Michaela George Sabrina Angelonides Karina Leon Sizi Rios De Leon Reo Snyder Paul Austin

Background

Given the current mental health crisis among young adults, finding evidence-based interventions and community supported solutions is imperative. Using a mixed methods approach, we aimed to understand the impact of Play Marin (a community based organization focused on after school and sports programs) on overall health and well-being using data collected from current students, alumni, family members, and coaches through a holistic evaluation of the program.

Methods

In partnership with Play Marin, the research methodology consisted of quantitative and qualitative data collection through interviews and surveys. The interviews were conducted with current students and alumni of the Play Marin program, and parents and coaches also involved in the community. Quantitatively, we will compare survey data between current students and alumni of Play Marin and the national average using the YRBSS as a measurement tool.

Results

Preliminary results have revealed that recreational opportunities provided by Play Marin for adolescents and teenagers in Marin City, California resulted in an increase in mental and physical health, overall sense of belongingness within a community, and improved feelings of self-esteem and self-confidence. Current students and alumni were statistically significantly less likely to have poor mental health and higher physical activity than the national average according to the YRBSS.

Conclusions

Solutions to the mental health crisis may be ameliorated with increased recreational opportunities for adolescents and young adults through community engagement and positive interactions. Play Marin gives adolescents all the necessary tools and resources to have a healthier life and have lasting impacts in the future generation.

Mental Health

Area-level deprivation and suicide by restrictable methods: trends in Japan, 2000-2022

Yoshikazu Komura* Yoshikazu Komura Naoki Kondo Aoi Kataoka Keisuke Fukui Tomoki Nakaya Yuri Ito

Background

As method restriction is known to reduce suicide rates, identifying suicide methods commonly used in deprived areas is critical for developing suicide prevention strategies that minimize area-based disparity in suicide risk. We examined national trends in suicide rates by potentially restrictable methods, focusing on disparities by area-level deprivation levels.

Methods

This serial cross-sectional study used national vital statistics data of Japanese residents from 2000 to 2022. Area-level deprivation at municipality level was estimated based on the Japanese Areal Deprivation Index 2000. Suicide rates by potentially restrictable methods—pesticide poisoning, jumping from a high place, and intentional collision with moving objects—and their differences by area-level deprivation were estimated.

Results

From 2000 to 2022, 609,029 suicides were recorded (average suicide rate = 21.0 / 100,000 person-year), with 74,448 (12.2%) suicides by the three potentially restrictable methods. The disparity in suicide rate by pesticide poisoning decreased over time, while the disparity in rate by jumping persisted (rate difference [/100,000 person-years] in deprived vs. non-deprived areas: by pesticide poisoning in 2000, 0.20; in 2022, 0.02: by jumping in 2000, 0.17; in 2022, 0.36). In contrast, suicide rates by intentional collision were higher in non-deprived areas than deprived areas (rate difference [/100,000 person-years] in deprived vs. non-deprived areas: by intentional collision in 2000, −0.15; in 2022, −0.24).

Conclusion

We found that suicide rate disparity by pesticide poisoning decreased over time, while disparity by jumping persisted. These findings suggested that pesticide restrictions in Japan, implemented in 1999, have contributed to reducing suicide disparity associated with area-level deprivation, and installing barriers at high places boosts the current reduction of suicide disparity associated with area-level deprivation in Japan.

Mental Health

Neighborhood social capital and suicidality during the COVID-19 pandemic in the All of Us Research Program Azuna Sawada* Azuna Sawada Haku Chao Koichiro Shiba

Social capital—community traits such as networks, shared norms, and mutual trust—has been linked to lower suicide risk in neighborhoods. However, research using individual-level data is limited, particularly regarding how this association differs by types of social capital. Using publicly available census data, we assessed pre-pandemic levels of overall social capital and its specific types (bonding, bridging, and linking) at the 3-digit zipcode level in the US. We linked these data with individual-level responses from the All of Us Research Program (n=22,607), including participants who had complete data for all study variables and who completed the following surveys: the basic, lifestyle, and overall health surveys, as well as at least one wave of the COVID-19 Participant Experience Survey. We defined suicidality during the pandemic period as reported thoughts of suicide or self-harm in at least one survey wave between May 2020 and February 2021, using the 9th item of the Patient Health Questionnaire-9. We used generalized estimating equations to account for data clustering at the zipcode level. After adjusting for pre-pandemic characteristics (age, sex, race and ethnicity, educational attainment, employment status, homeownership, annual household income, health insurance, and neighborhood factors including poverty rate, unemployment rate, and income inequality), greater bonding social capital was associated with lower odds of suicidal ideation (OR for the highest social capital quintile compared to the lowest quintile = 0.81; 95% CI: 0.68 – 0.96), while there was no evidence of associations with suicidality for all other types of social capital. Bonding social capital—characterized by close ties between members of similar social groups—may be protective against suicidality during the time of crisis.

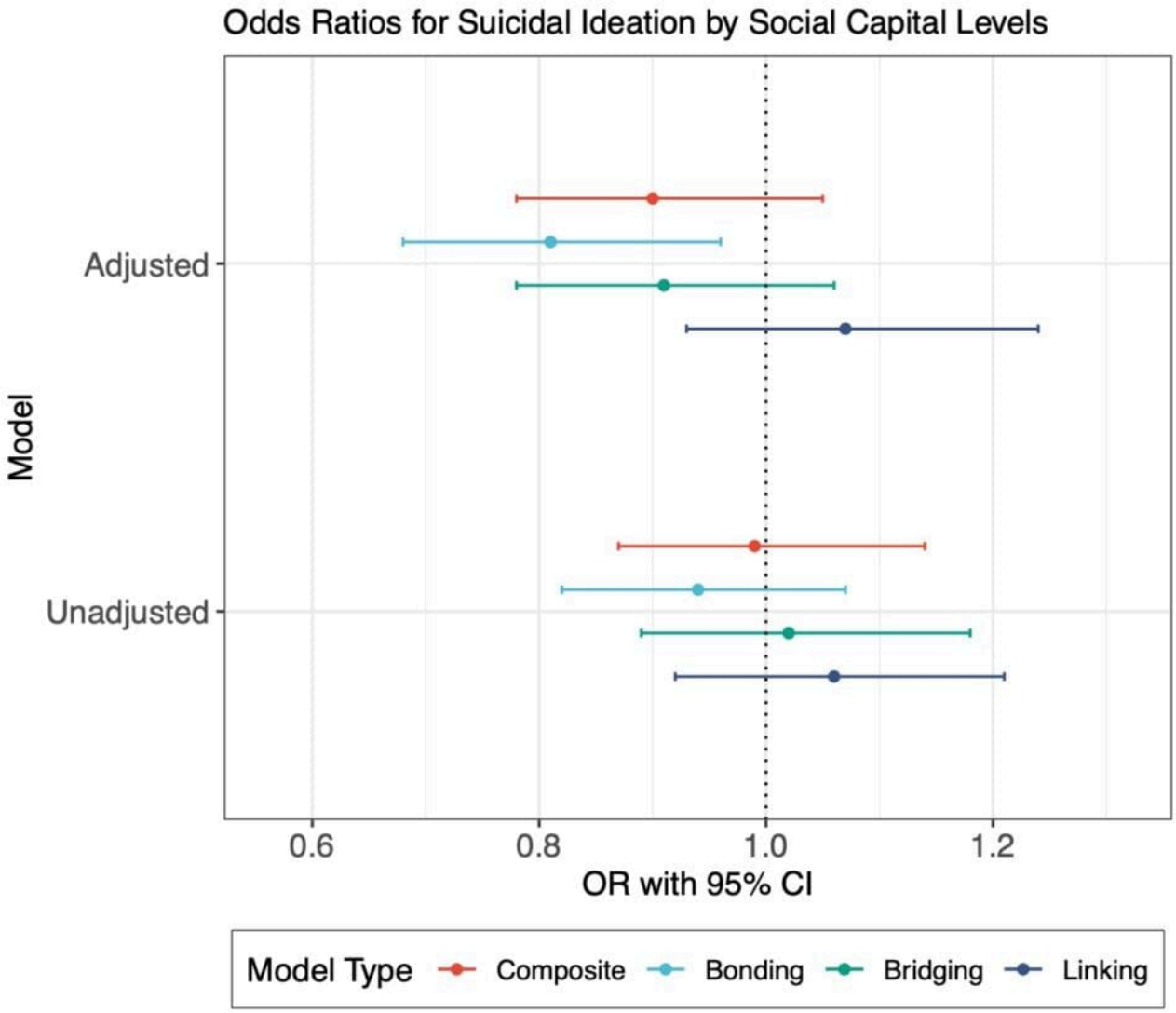


Figure. Odds ratios for the association suicidal ideation and social capital (highest vs the lowest quintiles) by type of social capital

LATEBREAKER

Mental Health

The Protective Power of Social Connectedness: Individual vs. Community Influences on Psychological Distress in Middle-Aged Black Adults Yu-Tien Hsu* Yu-Tien Hsu Katelyn Kostakis Shazel Muhammad Yusuf Ransome

Background: Social connectedness is a crucial determinant of mental health, yet its effects on Black adults remain understudied, particularly in distinguishing between individual and community-level influences. This study examined cross-sectional and longitudinal associations between social connectedness and psychological distress among Black adults at the individual- and neighborhood (census tract) levels.

Methods: Using data from the MIDUS (Midlife in the United States) study, we analyzed 897 Black adults aged 25-74 from an urban setting. Social connectedness was measured across six dimensions: neighborhood social cohesion, social integration, support from family and friends, contribution to the community, and spirituality. After extensive model diagnostics, we employed cluster-robust errors to account for clustering by census tracts. We constructed cross-sectional and longitudinal models using these cluster-robust errors with inverse probability weighting to address attrition, examining individual and census-level effects on psychological distress in immediate and long-term contexts.

Results: In longitudinal analyses, family support (b=-1.95, 95% CI=-3.01, -0.90) and friend support (b=-1.09, 95% CI=-1.66, -0.52) showed significant protective effects. Cross-sectional analyses confirmed these relationships, with family support (b=-1.83, 95% CI=-2.67, -1.00) and friend support (b=-0.95, 95% CI=-1.39, -0.50) remaining protective. Community contribution showed significant long-term but no immediate effects. Individual-level social connectedness played a more significant role than neighborhood-level factors.

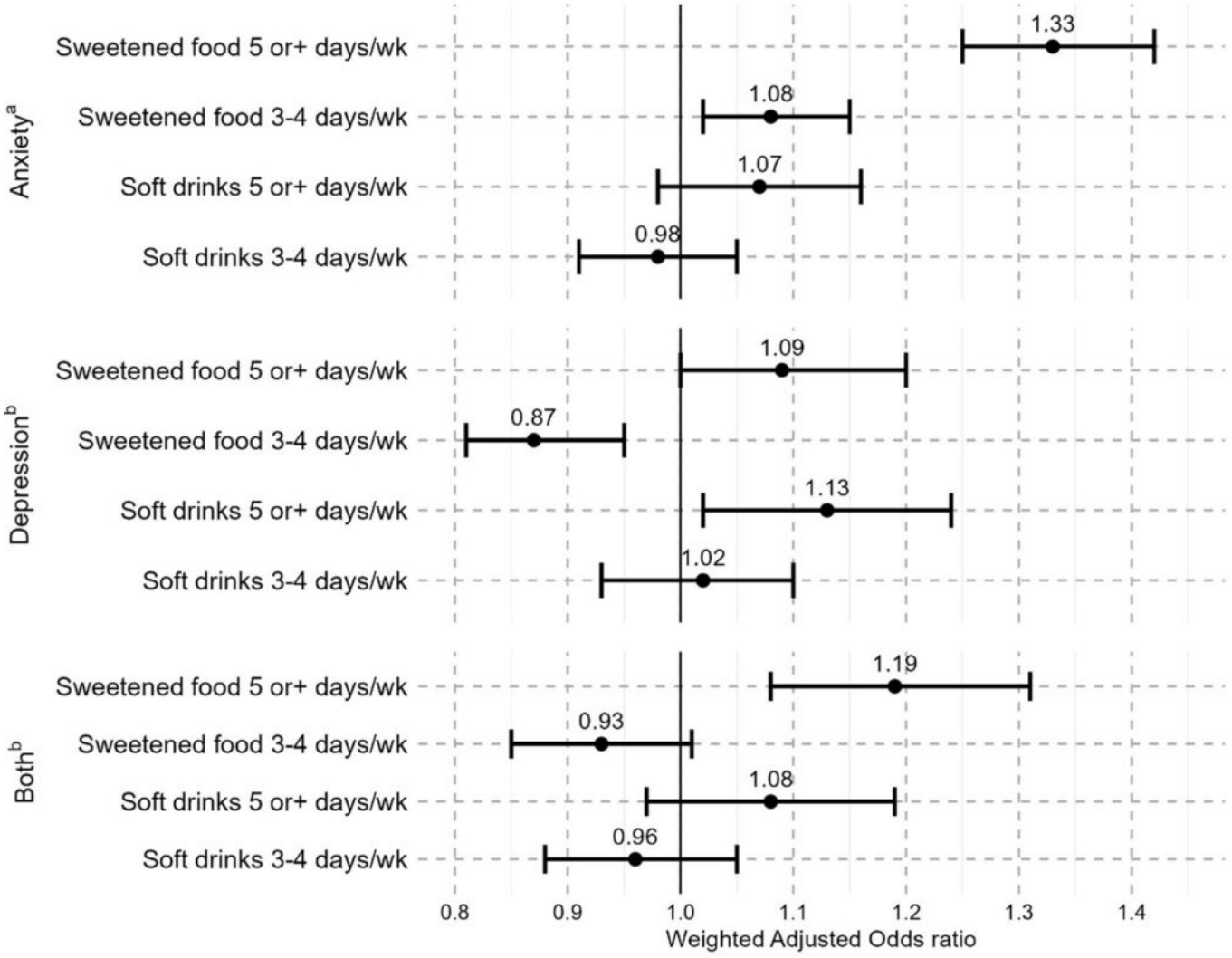
Conclusions: These findings underscore the primacy of individual-level social connections in protecting against psychological distress among Black adults. Mental health interventions should prioritize strengthening personal and family-centered social support networks while incorporating community engagement components for long-term benefits.

LATEBREAKER

Mental Health

Impact of soft drink and sweetened food consumption on mental health among Brazilian adolescents S. Cristina Oancea* S. Cristina Oancea Isabela Biagio Gisele Mara Silva Gonçalves Laura Soares da Silva André Luiz Monezi Andrade Luciana B. Nucci

Adolescence is a period that has a significant impact on development in adult life, as the various transformations during this stage can increase vulnerability to mental disorders such as anxiety and depression. Several factors influence mental health, among which inadequate nutrition stands out. This study investigates the association between the regular consumption of soft drinks and sweetened foods and symptoms of anxiety, depression, and both. The analysis included a representative sample of 117,495 Brazilian adolescents aged 13 to 17. Multivariable weighted and adjusted logistic regression models were used to investigate the association between the frequency of consumption of soft drinks and sweetened foods and mental health symptoms. Adjustment was made for sociodemographic variables, eating routine and dietary habits, physical activity practices, sedentary behaviors, cigarette use, episodes of binge drinking, and use of illicit drugs. Mental health symptoms were assessed using the Generalized Anxiety Disorder-2 (GAD-2) and Patient Health Questionnaire-2 (PHQ-2) scales. The results showed that consumption of sweetened foods 3-4 days and 5 or more days per week increased the risk of anxiety by 8% and 33%, respectively. Additionally, moderate consumption of sweetened foods (OR= 0.87) and soft drinks (OR= 1.13) was associated with symptoms of depression. Frequent sweetened food consumption was associated with both symptoms with a 19% higher risk (Figure 1). This association reinforces the relationship between high consumption of soft drinks and sweetened foods and mental health, highlighting the need for public policies and interventions that integrate nutritional and behavioral factors, aiming not only to improve adolescents' quality of life but also to ensure the maintenance of good habits for a healthier future.



[a]Adjustment was made for region of residence, sex, age, skin color/race, education level, type of school (public or private), habits of: having meals accompanied by an adult and using screens, and fast food,physical and sedentary activities,use of cigarettes, binge drinking, and use of illicit drugs.

[b]Adjustment was made for the same variables described above, except skin color/race.

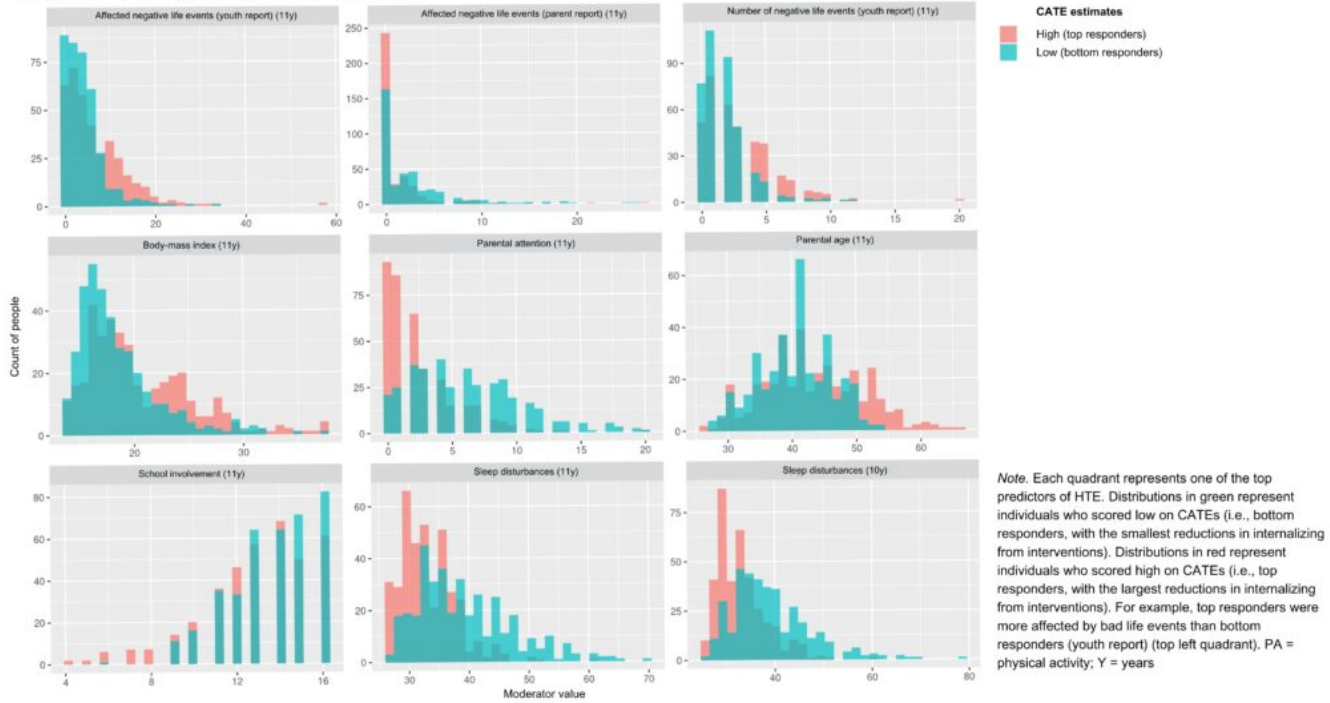
LATEBREAKER

Mental Health

Heterogeneity of treatment effects for hypothetical lifestyle interventions on depression risk in youth Lorenza Dall'Aglio* Lorenza Dall'Aglio Jordan W. Smoller Karmel W. Choi

Fifteen percent of youth experience depression. Primary preventive strategies (e.g., lifestyle interventions) are paramount. Yet, intervention data in youth are limited, and the heterogeneity of treatment effects (HTE) is understudied. We examined the profiles of youth with the greatest reductions in depression risk from lifestyle interventions, as emulated in a target trial. From the Adolescent Brain Cognitive Development Study, a cohort of US youth (NTraining=5,712, NTest=1,429), we used reports on recreational screen time (ST) and physical activity (PA) (12y), internalizing problems (Brief Problem Monitor, 13y), and its composites (anxiety, depression, somatic). Interventions were defined as meeting existing guidelines: 1) ST for max. 2h/day, 2) PA for min. 1h/day. Eighty demographic, socioeconomic, behavioral, and parental factors (10-11y) were leveraged as potential moderators of TEs. Causal Forest and the rank average treatment effect (RATE) estimated HTE. Variable importance analysis found key moderators which, in combination, most predicted higher conditional average treatment effects (CATEs) (i.e., greater treatment response). Intervening on ST or PA would decrease internalizing problems (CATEST=-0.35; SEST=0.05; p-valueST=3.71e-11; CATEPA=-0.16, SEPA=0.05, p-valuePA=0.002). HTE was found for PA (RATEPA=0.22, SEPA=0.06, p-valuePA=6.34e-05), not ST (RATEST=0.04, SEST=0.11, p-valueST=0.710). Results were driven by depression, not somatic or anxiety problems. Higher CATEs were observed for youth with greater adverse life events, body-mass index, parental age, and lower parental attention, school involvement, and sleep disturbances (Figure 1). To conclude, certain profiles of youth would most benefit from meeting recommended guidelines for PA (1h/day) to reduce their depression risk. While biases from observational studies must be considered, this work could inform the design of randomized controlled trials for targeted interventions in youth.

Figure 1. Distributions of factors determining heterogeneity in treatment effects for PA interventions on internalizing problems: Comparisons among top and bottom responders



Note. Each quadrant represents one of the top predictors of HTE. Distributions in green represent individuals who scored low on CATEs (i.e., bottom responders, with the smallest reductions in internalizing from interventions). Distributions in red represent individuals who scored high on CATEs (i.e., top responders, with the largest reductions in internalizing from interventions). For example, top responders were more affected by bad life events than bottom responders (youth report) (top left quadrant). PA = physical activity; Y = years

Mental Health

Causal relationship between schizophrenia and breast cancer: A two-sample Mendelian randomization study and polygenic risk score Ji Su* Ji Su Yang Nan Song Chul-Hyun Cho Chung Mo Nam Hyeon Chang Kim Sun Jae Jung

Introduction

Epidemiological observational research has identified a link between schizophrenia and breast cancer, but findings in Asian contexts show variations. The underlying cause of the higher breast cancer incidence among individuals with schizophrenia remains unclear.

Methods

A two-sample Mendelian randomization (MR) was performed to identify the causal association between schizophrenia and breast cancer. Genetic variants significantly associated with schizophrenia were obtained from the NHGRI-EBI GWAS Catalog. The study population included 2,165 breast cancer patients from the Seoul Breast Cancer Study (SeBCS) and 2,046 healthy controls from the Korea Genome Epidemiology Study (KoGES). A candidate gene association analysis was conducted for both breast cancer cases and controls, followed by MR using inverse variance weighting (IVW), weighted median, and MR-Egger approaches. Radial MR methods were applied to remove outliers and address pleiotropic bias. A polygenic risk score (PRS) was created with schizophrenia-associated SNPs and compared between the breast cancer and control groups.

Results

A causal association between schizophrenia and breast cancer was observed in the IVW method of MR analysis (OR=1.14; 95% CI, 1.01-1.28). The Radial MR analysis detected outliers, and consistent effect estimates were observed after removing these outliers (OR=1.14, 95% CI 1.01-1.28). A significant association was also found between schizophrenia PRS (per 1SD) and breast cancer risk (OR=1.18; 95% CI, 1.12-1.26).

Conclusion

The Mendelian randomization study corroborated findings suggesting a causal relationship between schizophrenia and breast cancer. These findings provide a basis for clinical guidelines addressing the high risk of breast cancer in patients with schizophrenia, including recommendations for breast cancer screening among women with schizophrenia.

Mental Health

The Effects of Daylight Saving Time Clock Changes on Mental and Physical Health Outcomes in Primary and Secondary Care in England Melanie A. de Lange* Melanie A. de Lange Kate Birnie Rebecca C. Richmond Chin Yang Shapland Sophie V. Eastwood Kate Tilling Neil M. Davies

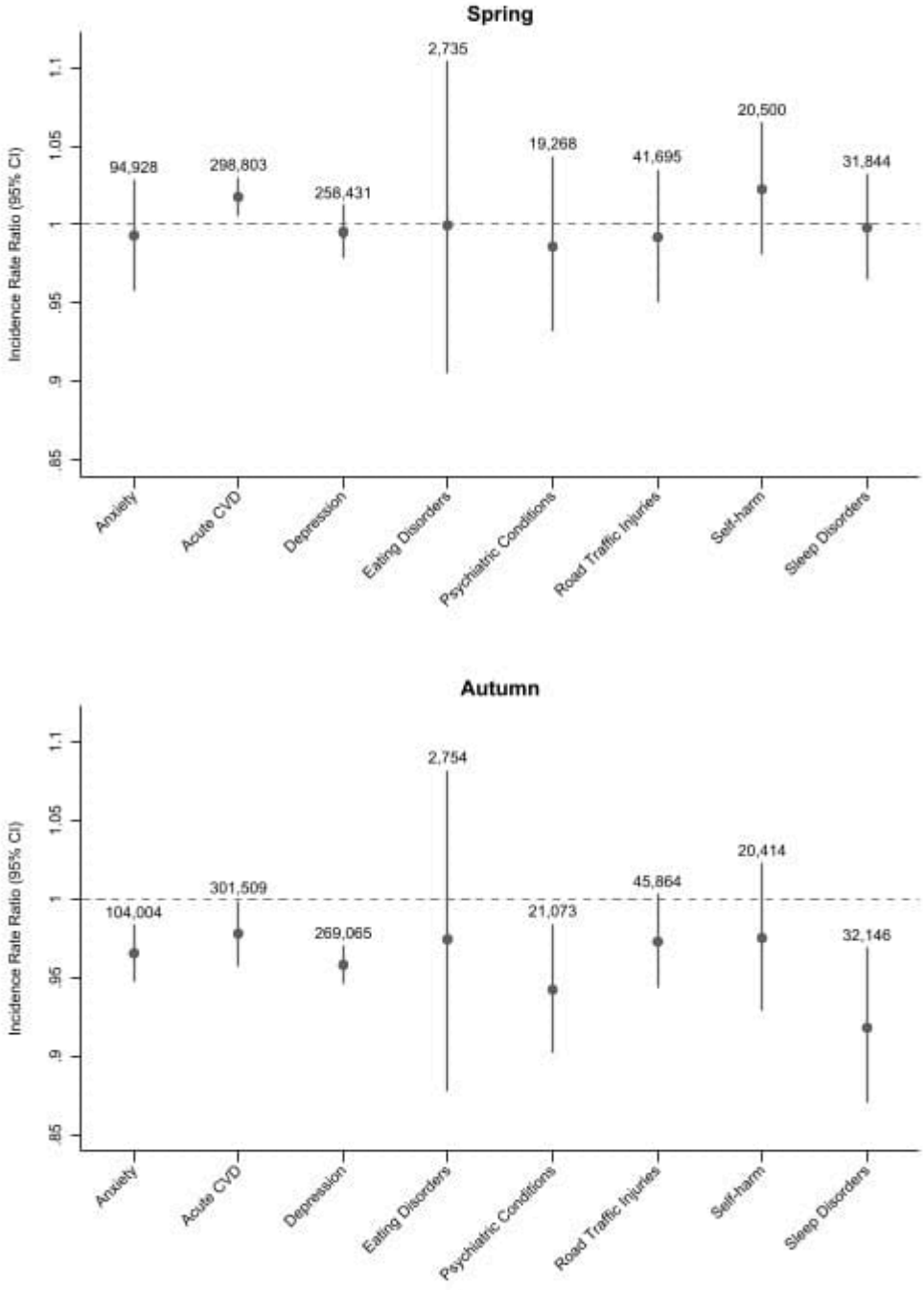
Introduction: The effects of daylight saving time (DST) transitions on health are the subject of intense debate, with the current literature fairly mixed. Few studies have looked at the effect on the health system as a whole and evidence from England is scarce. We aimed to explore the effects of the DST transitions on a range of health outcomes in a large dataset of linked English primary and secondary care records.

Methods: We used primary care records from the Clinical Practice Research Datalink (CPRD) Gold database linked to hospital admissions and emergency care visits. Patients were included if they had a code for acute cardiovascular disease (CVD), depression, road traffic injury, anxiety, self-harm, eating disorder or sleep disorder in their primary or secondary care record, or a code for a psychiatric condition in emergency care, in the 8-week period surrounding the Spring or Autumn clock changes between 2008 and 2019. Negative binomial regression models, adjusted for day of the week and region (and Easter weekend in Spring), compared event rates in the week after the clock changes to the control period (4 weeks before the transitions and weeks 2-4 after).

Results: In total 683,809 patients and 1,564,532 events were included in the study. In Spring we found an increase in acute CVD events in the week after the clock change (Incidence Rate Ratio: 1.02, 95%CI 1.01-1.03). In the week after the Autumn transition we found a decrease in acute CVD (IRR 0.98, 95%CI 0.96-0.999), depression (IRR 0.96, 95%CI 0.95-0.97), anxiety (IRR 0.97, 95%CI 0.95-0.98), psychiatric conditions (IRR: 0.94, 95%CI 0.90-0.98) and sleep disorders (IRR 0.92, 95%CI 0.87-0.97).

Conclusions: The Spring DST transition (when the clocks move forward an hour) was associated with an increase in acute CVD events. Meanwhile, the Autumn transition (when the clocks go back an hour) was associated with a reduction in acute CVD, sleep disorders and some mental health conditions.

Risk of mental and physical health outcome events in the week after the Spring and Autumn clock changes versus control period (England, 2008-2019)

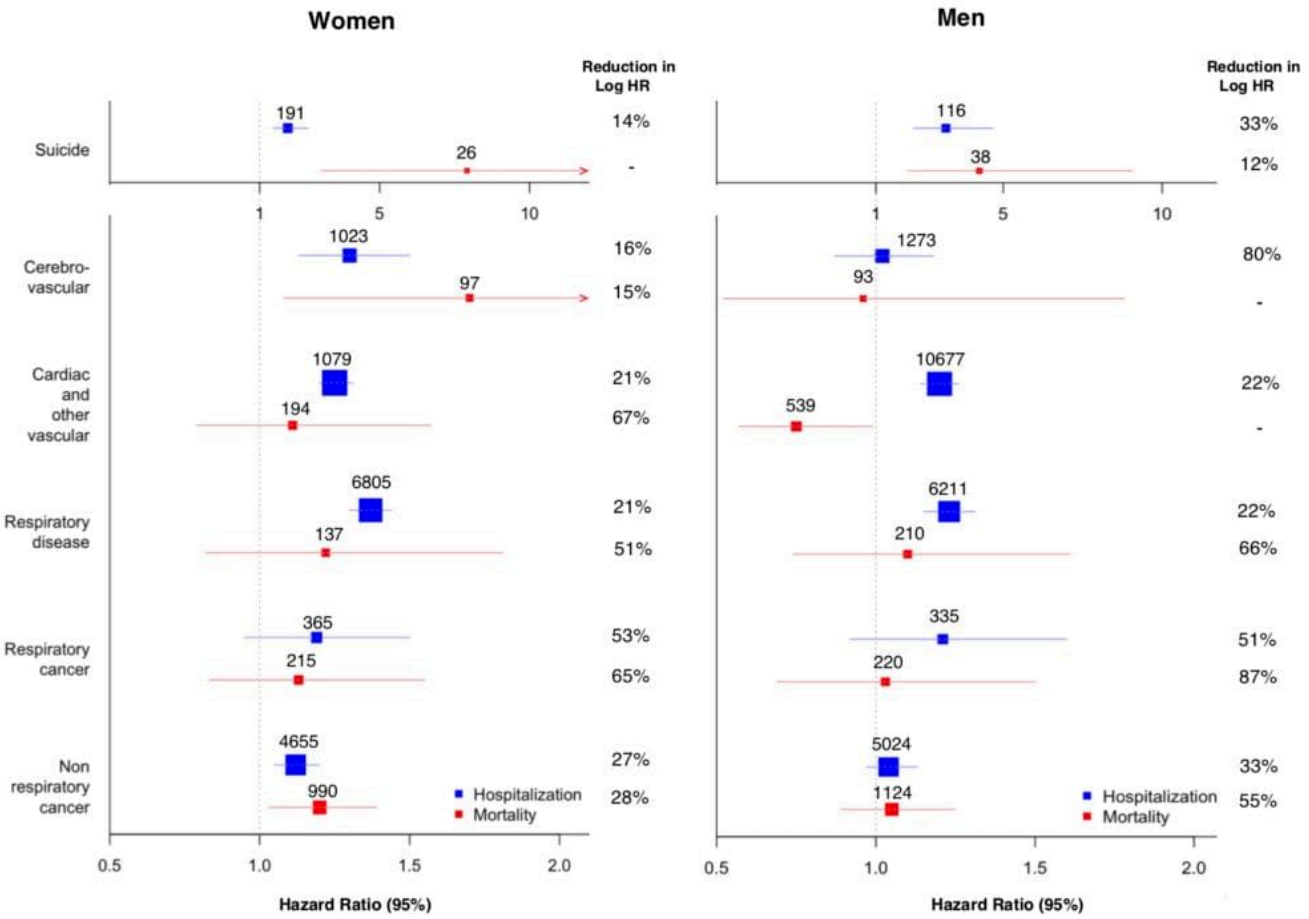


Numbers show total events per outcome in the week after DST transition and control weeks

Mental Health

The associations between major depressive disorder and the risks of mortality and hospitalization Sonali Amarasekera* Sonali Amarasekera Eo Rin Cho Susan Bondy Trevor Young Patrick Brown Prabhat Jha

Background: Major depressive disorder (MDD) may increase the risk of mortality and hospitalization from both suicide and chronic diseases. However, these associations must be interpreted cautiously due to potential confounding effects from demographic (age, sex), modifiable (smoking, alcohol, body mass index, physical activity) and social (socioeconomic status, marital status, family history of mental illness) factors. **Objective:** To estimate associations between lifetime MDD and cause-specific mortality and hospitalization by sex using UK Biobank data. **Design:** We conducted a retrospective cohort study of 113,196 participants (aged 40-69) assessed for lifetime MDD, with no medical or psychiatric comorbidities at baseline. **Methods:** Proportional hazards models assessed the effect of MDD on mortality and hospitalization rates due to suicide, vascular disease, respiratory disease, and cancer. We adjusted for age, modifiable and social factors. Residual confounding was evaluated by examining hazard ratios (HRs) and changes in the log-hazard after adjusting for confounders. **Results:** Lifetime MDD significantly increased the risk of suicide mortality in both sexes, with stronger associations observed in women (HR = 7.91; 95% CI = 3.05-20.54) than men (HR = 4.25; 2.00-9.06). Further, the log-hazard increased with confounder adjustment in women, and decreased in men (12%). MDD also significantly increased the risk of hospitalization from suicide attempts, but these associations were more sensitive to residual confounding as indicated by greater reductions in the log-hazard (14% in women, 33% in men). In both sexes, MDD was positively associated with hospitalization from cardiac and respiratory diseases. Associations with stroke were significant only in women. **Conclusion:** Lifetime MDD appears to increase risk of mortality and hospitalization due to suicide and certain chronic diseases. The strength of the associations and confounding effects vary by sex.



Estimates are adjusted for age, modifiable (smoking, alcohol use, body mass index, physical activity) and social (socioeconomic status, marital status, family history of mental illness) risk factors
Numbers above each square indicate number of events observed

Mental Health

Pubertal Timing and Depression: The Mediating Effects of Physical Activity and Body Dissatisfaction Dana Tarif* Dana Tarif Carol Joinson Abigail Fraser Jon Heron Ahmed Elhakeem

Background: Early pubertal timing has been found to be associated with adverse mental health outcomes, including depression. Although the majority of research has focused on girls, evidence suggests that early puberty is associated with depression in both sexes. However, the mechanisms underlying these associations remain unclear. Physical activity, a known protective factor against depression, has been found to be lower in early-maturing girls, while body dissatisfaction has been found to be higher in early-maturing girls and boys. This study aims to examine the potential mediating effects of physical activity and body dissatisfaction on the relationship between pubertal timing and depression in both sexes.

Methods: Data were analysed from 3806 (47% male) participants in a UK-based prospective cohort study, the Avon Longitudinal Study of Parents and Children (ALSPAC). Pubertal timing was assessed using age at peak height velocity (aPHV – males and females) and age at menarche (AAM), derived from repeated measurements collected from 7 to 17 years. Depression at 18 years was measured using the Clinical Interview Schedule-Revised (CIS-R). Mediators included accelerometer-measured physical activity (14 years), recorded as total counts per minute, and self-reported body dissatisfaction (14 years), measured using the Satisfaction and Dissatisfaction with Body Parts Scale. Confounders included socioeconomic status (SES), pre-pubertal BMI (9 years), adolescent BMI and depressive symptoms (13 years).

Analysis Plan: The analysis will include multivariable regression followed by counterfactual mediation analyses, using the parametric g-computation formula. We will evaluate the mediating effects of physical activity (model 1) and body dissatisfaction (model 2) on the association between pubertal timing and depression stratified by sex. Results will be adjusted for baseline and intermediate confounders. Findings from regression and mediation analyses will be presented.

Methods/Statistics

A novel estimand for quantifying vaccine efficacy against asymptomatic infections Elizabeth Rogawski McQuade* Elizabeth Rogawski McQuade Razieh Nabi David Benkeser

For preventive vaccines that do not confer sterilizing immunity, differences in vaccine efficacy by severity of disease are of interest. Such vaccines may prevent infections entirely in some individuals, but in others may only prevent clinical symptoms or lessen the severity of the clinical disease caused by infection. For these vaccines, it is common practice to report vaccine efficacy against both symptomatic disease and infection. Many studies additionally report a vaccine efficacy measure against asymptomatic infection, comparing the risk of asymptomatic infections in the vaccinated and placebo groups. Such estimates can be misleading because they mix the effects of vaccines preventing asymptomatic infections and of vaccines converting symptomatic to asymptomatic infections. When the latter effect is strong, vaccines can appear harmful with respect to asymptomatic infections (i.e., negative vaccine efficacy). In the context of the COVID-19 pandemic, these types of findings led to considerable confusion in the general population and may have led to increased vaccine hesitancy. In this work, we demonstrate how the typical formulation of vaccine efficacy against asymptomatic infections is not the most relevant estimand for quantifying the biological impact of vaccines on the infection process. Using a causal principal stratification framework, we suggest an alternative estimand for quantifying vaccine impact on asymptomatic infection that is a more natural analogue of the usual vaccine efficacy estimands against infection and symptomatic disease and which excludes vaccine effects that convert symptomatic cases to asymptomatic infections. We describe assumptions under which this estimand can be identified and estimated from randomized and observational studies, and we derive bounds for the estimand that do not require cross-world assumptions. We then apply these methods in the COVE study, a randomized trial of the Moderna COVID-19 (mRNA-1273) vaccine.

Methods/Statistics

Building an infrastructure to study longer-term, geospatial food access through residential history linkages Niyati Sudhalkar* Garth Rauscher Neng Wan

INTRODUCTION: Longer-term, cumulative geospatial access to food is an under-appreciated social determinant of health in cancer, given cancer's typically long latency period. We provide an overview of methods we use to construct longer-term food environments for epidemiologic cancer incidence and survival studies. METHODS: Identifiers are submitted to LexisNexis for linkage to their proprietary residential histories (RH) database. RH data are cleaned using SAS programs provided by NCI. We assign a primary address for each calendar year of RH (1990-2020). Food outlet data from the National Establishment Time Series (NETS) Database for the US Census combined statistical area (CSA) 176 (Chicago- Naperville, IL-IN-WI) were obtained for 1990-2020. Using Standard Industrial Classification (SIC) codes, type of food industry, trade name, and company name, food outlets are divided into healthy (supermarkets, grocery stores, etc.) and less healthy food sources (fast-food outlets, convenience, and gas stations, etc.). After building the appropriate, decade-specific street networks from TIGER/line shapefiles using ESRI's Network Analysis tool, we calculate driving (up to 5 miles) and walking (up to 1.5 miles) distances from each residence to each food outlet using the ESRI's Network Analysis Origin-Destination Cost Matrix (ODOM) solver. We define food access scores as inverse-distance weighted walking and driving distances to food outlets. Year-specific scores are summed to define the four final measures of 30-year cumulative, longer-term driving, and walking distance access to healthy and less healthy food sources. RESULTS AND DISCUSSION: Geospatial measures of longer-term (30-year) food access – when linked in epidemiologic studies to participants' residential histories – hold great promise for understanding how this crucial social determinant of health impacts cancer and other health conditions and for informing policy changes to make access to healthy food more equitable.

Methods/Statistics

Body Mass Index as a Negative Confounder? Evidence and solutions Zhu Liduzi Jiesisibieke* Zhu Liduzi Jiesisibieke Zhu Liduzi Jiesisibieke C Mary Schooling

Background: Adequate control for confounding is key to many observational study designs. Confounders are often identified based on subject matter knowledge from empirical investigations. Negative confounders, which typically generate type 2 error, i.e., false nulls, can be elusive. Such confounders can be identified comprehensively by using Mendelian randomization to search the wealth of publicly available data systematically. Here, to demonstrate the concept, we examined whether a common positive confounder, body mass index (BMI), was also a negative confounder of any common physiological attributes on health outcomes, overall and sex-specifically.

Methods: We used a Mendelian Randomization (MR) study to assess, overall and sex-specifically, whether BMI is a negative confounder potentially obscuring effects of potentially harmful physiological attributes. Inverse variance weighting was the main method. We assessed sex differences using a z-test.

Results: BMI was a potential negative confounder for Apolipoprotein B and total testosterone in men, and in both sexes for low-density lipoprotein-cholesterol, choline, phosphate, linoleic acid, polyunsaturated fatty acids and cholesterol.

Conclusions: Using BMI as an illustrative example, we demonstrate that negative confounding is an easily overlooked bias. Given negative confounding is not always obvious or known, using MR to identify potential negative confounders in observational studies may be helpful.

Methods/Statistics

Old tools to address persistent problems: assessing health disparities and differences with attributable fractions Alexander Keil* Alexander Keil Maria E Kamenetsky Maya Spaur Jessica M Madrigal Whitney R Robinson

Understanding disparities or differences in health across social and economic strata within populations is key to improving the overall health of populations. One focus of health disparities research in epidemiologic studies has been the differential impact of individual exposures among groups across which a health disparity exists. Current tools for assessing and understanding health disparities in epidemiologic data include evaluation of effect measure modification (EMM, does the impact of an additional unit of exposure vary across groups on some scale?) and decomposition analysis (to what extent is the disparity across groups mediated by the association between group membership and the exposure?). Despite common usage, these tools are limited. EMM evaluation fails to account for how the differential distribution of exposure across groups may impact disparities, while the decomposition analysis focuses directly on effects of group membership, which carries possibly untenable assumptions for making causal inferences and may not represent a modifiable factor.

Here, we make a modest proposal to adopt an existing, underutilized tool for assessing how exposures of interest impact health and health disparities: attributable fractions. Attributable fractions estimate the impact of eliminating exposure in a population, making them useful for studies of modifiable exposures that may or may not be equally distributed across population groups. Using synthetic examples, we demonstrate that attributable fractions can identify exposures that contribute to health disparities in settings in which there is no EMM. We demonstrate how attributable fractions can be extended, using tools like g-computation, to multiple exposures and settings where eliminating exposure is not feasible. This work demonstrates a set of tools for studying health disparities that focus on modifiable factors and thus better contribute to public health decision makers’ efforts to reduce health disparities.

Methods/Statistics

Understanding Depression as a Mediator Between HIV Stigma and Medication Adherence in Black Women with HIV Chandni Shahdev* Chandni Shahdev Serena Rajabiun Karyn Heavner Yan Wang Howard Cabral

Understanding Depression as a Mediator Between HIV Stigma and Medication Adherence in Black Women with HIV

Authors

Chandni Shahdev, MPH, BDS1, Serena Rajabiun, Ph.D., MA, MPH1, Karyn Heavner, Ph.D.1, Yan Wang, Ph.D., MA1, Howard Cabral, Ph.D.2

1Department of Public Health, Zuckerberg College of Health Sciences, University of Massachusetts Lowell

2Department of Biostatistics, Boston University School of Public Health

Abstract

Background: HIV stigma remains a critical barrier to medication adherence in Black Women Living with HIV (BWLWH), exacerbating mental health issues like depression. While previous studies have explored the separate effects of stigma and depression on medication adherence, little research has examined their combined impact, particularly how depression mediates the relationship between HIV stigma and adherence. Therefore, this study aims to explore depression as a mediator in the relationship between HIV stigma and medication adherence using the novel VanderWeele mediation analysis method.

The study will conduct secondary analysis of pre-post prospective nonrandomized convenience sample of 743 BWLWH with data collected from 2021-2023 as a part of Black Women First Initiative funded by the Health Resources and Service Administration (HRSA), HIV/AIDS Bureau (HAB), Ryan White HIV/AIDS program (RWHAP) Part F Special Project of National Significance (SPNS) and Minority HIV/AIDS Fund (MHAF) in response to National HIV/AIDS Strategy to address social health determinants of health for BWLWH in a culturally responsive manner. Twelve sites were funded to adapt interventions to improve HIV health outcomes.

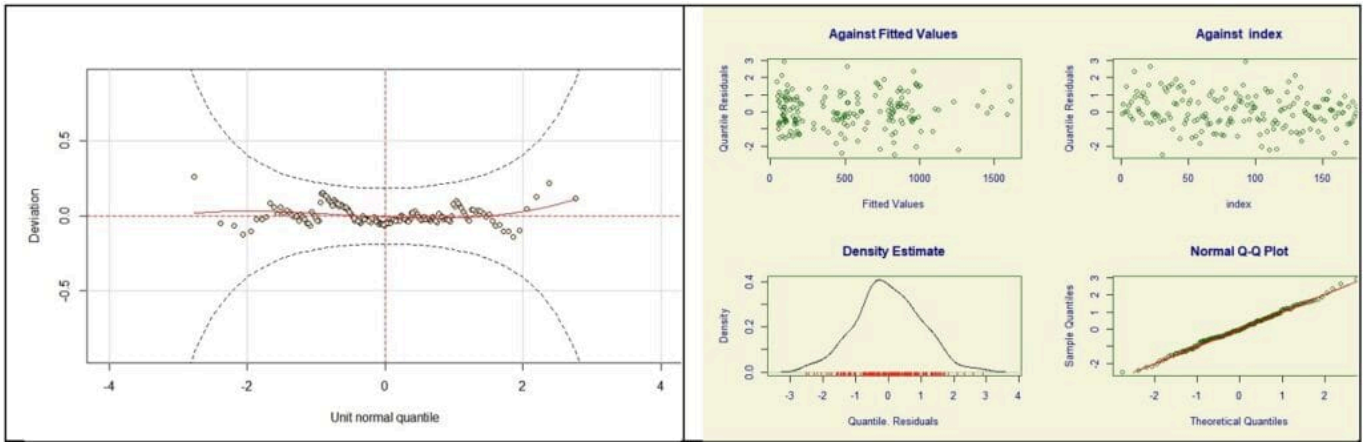
Method: We will test the hypothesis that depression mediates the relationship between HIV stigma and medication adherence. Causal mediation will be evaluated using bootstrapped samples (1,000 iterations) to calculate 95% confidence intervals. Covariates such as age, gender, and site-related variables will be included in the analysis. Statistical analysis will be performed using SAS 9.4, PROC CAUSALMED procedure.

Significance: The findings will inform the development of interventions that address both mental health and stigma, potentially improving HIV treatment outcomes for Black women.

Methods/Statistics

Analysis of Kidney Cancer Patients Using the SICHEL Regression Model within GAMLSS FrameworkAIM Tiago Almeida de Oliveira* Tiago Almeida de Oliveira Cleanderson Romualdo Fidelis Maria Carmen Escalante- Rojas Alessandro Gouveia Nunes Ana Patricia Bastos Peixoto

AIM: To evaluate kidney cancer progression using INCA clinical data and assess the SICHEL regression model's flexibility and robustness within the GAMLSS framework for handling asymmetric, heterogeneous, and overdispersed data. Kidney cancer is a significant public health concern due to its high mortality rates and the complex nature of its progression. Accurate modeling of clinical data is crucial for improving prognosis, guiding treatment decisions, and enhancing patient outcomes. This study introduces the SICHEL regression model, applied within the GAMLSS framework. By identifying key clinical factors that influence survival times, the study provides practical insights into disease progression, offering the potential to improve prognostic assessments and tailor treatments more effectively. The study focused on patients who experienced the event (death), and only positive times (in days) were considered. The number of days between diagnosis and death served as the dependent variable. Covariates included age, sex, diagnostic method, tumor extension, and morphology. To assess the model's performance, comparisons were made with Poisson and Negative Binomial models. These models were evaluated using the GAIC criterion to identify the best fit for the dataset. Results: For mean (μ) Parameter: Male sex ($p = 0.5185$) did not significantly affect time until death compared to females, while the "Malignant Neoplasia" morphology ($p < 0.001$) significantly reduced time until death compared to "Carcinoma." The "Investigation" diagnostic method ($p = 0.0756$) and "Metastasis" extension ($p = 0.0117$) significantly influenced time until death. Dispersion (σ) Parameter: Variations in data dispersion were observed, reflecting the impact of heterogeneity in the analysis. Shape (ν) Parameter: Male sex ($p = 0.0304$) was significantly associated with greater asymmetry in the time until death distribution, while "Malignant Neoplasia" ($p < 0.001$). The SICHEL model achieved the lowest GAIC value, indicating superior fit compared to Poisson and Negative Binomial models, due to its ability to accommodate data asymmetry, overdispersion, and variability. The SICHEL regression model, integrated with the GAMLSS framework, demonstrated flexibility and robustness in modeling times of kidney cancer patients.



Methods/Statistics

The dwindling yet lingering myths about use of p-values and confidence intervals in modern epidemiology Montana Kekaimalu Hunter* Montana Kekaimalu Hunter Anthony Russell Igor Burstyn George Maldonado

Background: Misinterpretation of statistical significance tests and confidence intervals has been a longstanding issue in epidemiology. Despite efforts by leading journals to discourage or ban such practices, the extent of misinterpretations in modern epidemiologic literature remains unclear.

Methods: We examined papers published in 2022 in three leading epidemiology journals (International Journal of Epidemiology, Epidemiology, and American Journal of Epidemiology) to assess the frequency and types of misinterpretations of p-values and confidence intervals. We randomly sampled 65 papers that assessed exposure-outcome relationships. Two authors independently reviewed the selected papers, cataloging misinterpretations according to guidelines published in 2016.

Results: Among the examined papers, 10 (almost one-seventh) contained misinterpretations of statistical significance. The most common error in seven papers was treating the p-value as a property of the phenomenon being studied rather than a characteristic of the test result. Three papers incorrectly interpreted 95% confidence intervals as having a 95% chance of containing the true effect size. Examples of misinterpretations included concluding no effect based on $p>0.05$, equating statistical significance with substantive importance, and using confidence intervals to judge “significance.” We also highlight some commendable uses of p-values.

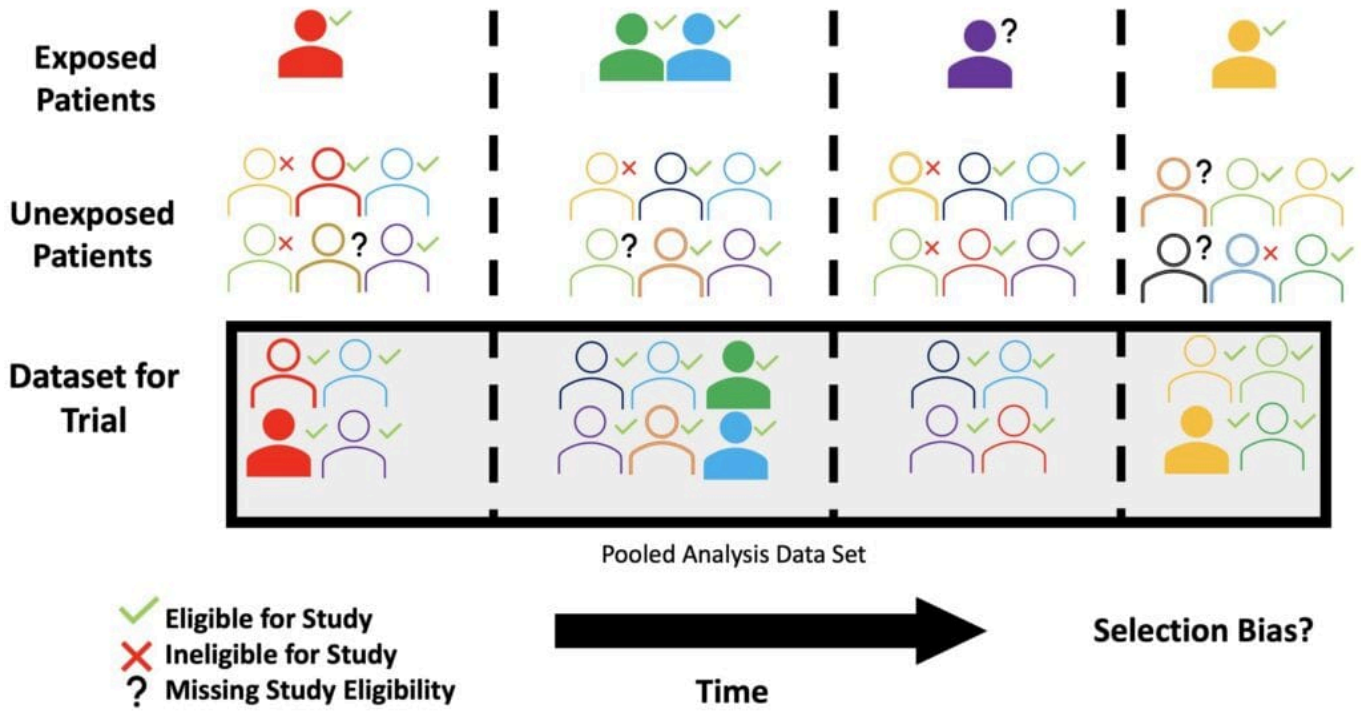
Conclusions: While misinterpretations of statistical tests were not widespread in top epidemiology journals, nearly one-seventh of the papers reviewed contained such errors. These findings highlight the need for continued efforts to improve the understanding and reporting of statistics in epidemiology.

Methods/Statistics

Adjusting for Selection Bias Due to Missing Eligibility Criteria in Emulated Target Trials

Luke Benz* Luke Benz

Target trial emulation (TTE) is a popular framework for observational studies based on electronic health records (EHR). A key component of this framework is determining the patient population eligible for inclusion in both a target trial of interest and its observational emulation. Missingness in variables that define eligibility criteria, however, presents a major challenge towards determining the eligible population when emulating a target trial with an observational study. In practice, patients with incomplete data are almost always excluded from analysis despite the possibility of selection bias, which can arise when subjects with observed eligibility data are fundamentally different than excluded subjects. Despite this, to the best of our knowledge, very little work has been done to mitigate this concern. In this work, we propose a novel conceptual framework to address selection bias in TTE studies, tailored towards time-to-event endpoints, and describe estimation and inferential procedures via inverse probability weighting (IPW). Under an EHR-based simulation infrastructure, developed to reflect the complexity of EHR data, we characterize common settings under which missing eligibility data poses the threat of selection bias and investigate the ability of the proposed methods to address it. Finally, using EHR databases from Kaiser Permanente, we demonstrate the use of our method to evaluate the effect of bariatric surgery on microvascular outcomes among a cohort of severely obese patients with Type II diabetes mellitus (T2DM).



Methods/Statistics

Enabling the Analysis of Patient-Level Data Across Jurisdictional Boundaries for Research Use: An Exploration of the Utility of the Likelihood Function Megan Harmon* Megan Harmon Na Li Tolulope Sajobi Jessalyn Holodinsky Tyler Williamson

Background: The secure and ethical handling of personal health information is a growing global concern, especially when sharing patient-level data across jurisdictions for research use. This study evaluates a novel methodology using the likelihood function to enable health data analysis without direct data sharing. The likelihood function carries all the information about the data for a specific model. By likelihood theory, log-likelihood functions from separate models can be combined to create an overall log-likelihood function, identical to that from a fully aggregated dataset.

Methods: We conducted a simulation study to evaluate the likelihood method for inter-jurisdictional health data analysis. A dataset of 200 observations was generated with a binary outcome (prevalence: 51%) and binary exposure (49% exposed), stratified across two jurisdictions. In Jurisdiction 1 (n=100), the outcome prevalence was 54% with 49% exposed; in Jurisdiction 2 (n=100), the outcome prevalence was 47% with 49% exposed. Logistic regression models were fit separately for each jurisdiction and for the combined dataset. Log-likelihoods from the jurisdictional models were aggregated to estimate regression coefficients for the overall population, which were compared to those from the fully pooled model.

Results: High heterogeneity was observed between jurisdictions (Q=50.10; I2=98%). Jurisdiction 1 showed a regression coefficient of 2.02 (SE: 0.46; log-likelihood: -57.82), and Jurisdiction 2 showed -2.81 (SE: 0.51; log-likelihood: -49.63). Aggregating log-likelihood functions yielded a regression coefficient of -0.28 (log-likelihood: -138.13), identically matching the fully pooled model.

Conclusion: Our findings demonstrate the potential of the likelihood-based method as a reliable and effective framework for cross-jurisdictional effect size estimation without sharing data. We offer a scalable solution for advancing health research globally while safeguarding patient privacy.

Methods/Statistics

Differences in Response Patterns by Socio-Demographic Characteristics in a Large Longitudinal Cohort Emanuela Mesesan* Emanuela Mesesan Daniela Dudas Mariah Landry Alpa V. Patel

Department of Population Science, American Cancer Society, Atlanta, GA

Background: Longitudinal prospective cohort studies are essential to understanding disease risk over time. Participant attrition may vary by factors such as age, race/ethnicity, or sex and could impact internal study validity. We examined response patterns over time in a large U.S. prospective cohort by demographic factors.

Methods: From 2006-2013, ~250,000 adults were enrolled in the American Cancer Society's Cancer Prevention Study-3 (CPS-3) and completed a baseline survey. In 2015 and every three years thereafter, participants received follow-up surveys to update exposure and health information. We examined response patterns by race (white, Black, Hispanic, Asian, other), baseline age (<35, 35-44, 45-54, 55-64, and 65+ years), sex (male, female), and education (

Results: Overall response decreased over time from 74% in 2015 to 66% in 2018 to 62% in 2021. Women consistently had higher response than men, an average 68% vs 63% respectively. Response rates among participants with higher educational attainment were more than 20% higher than participants with the lowest educational attainment. Response rates were steadily higher among older participants; participants aged 55 and older had more than 10% higher response rates than participants under age 45 at all-time points. White participants were more likely to respond over time, followed by Asian participants; and Black participants were less likely to respond.

Conclusion: In CPS-3, overall response to follow-up surveys declined over time. Response rates were highest among participants who were female, white, more educated, and over 55 years. Strategies to increase sustained engagement, particularly in men, non-white, less educated, and younger individuals, should be explored to minimize attrition over time.

Methods/Statistics

Statistical inference and effect measures in abstracts of major HIV and AIDS journals, 1987-2022: A systematic review Andreas Stang* Andreas Stang Henning Schäfer Ahmad Idrissi-Yaghir Christoph M. Friedrich Matthew P. Fox

Introduction: With the emergence of HIV/AIDS journals, the development of the reporting of statistical inference and effect measures in published abstracts can be examined from the beginning in a new field. The aim of this study was to describe time trends of statistical inference and effect measure reporting in major HIV/AIDS journals.

Methods: We included 10 major HIV/AIDS journals as ranked by the journal citation report in 2022 and analyzed all available PubMed entries for the period 1987 through 2022. We applied rule-based text mining and machine learning methodology to detect the presence of confidence intervals, numerical p-values or comparisons of p-values with thresholds, language describing statistical significance, and effect measures for dichotomous outcomes.

Results: Among 41,730 PubMed entries from the major HIV/AIDS journals (AIDS, AIDS Behav, AIDS Patient Care STDS, AIDS Res Ther, Curr HIV/AIDS Rep, Current Opin HIV AIDS, HIV Med, J Acquir Immune Deifc Syndr, J Int AIDS Soc, Lancet HIV), 31,665 contained an abstract. In the early years, most abstracts reporting statistical inference contained only significance terminology without confidence intervals and p-values. From 1988 to 2005, each year 30% of all abstracts contained p-values without confidence intervals. Thereafter, this reporting style continued to decline. The reporting of confidence intervals increased steadily from 1988 (11%) to 2022 (56%). Of the 17% of abstracts in 2017-2022 that included any effect measure, half reported odds ratios (51%), followed by hazard ratios (28%) and risk ratios (16%). Difference measures and number needed to treat or harm were very uncommon.

Discussion: Within the HIV/AIDS literature, there has been widespread use of confidence intervals. Most of the journals that we reviewed had a decrease in reporting only statistical significance without confidence intervals over time. The distribution of p-values shows little indication of p-hacking and this distribution looks very similar to the p-value distribution in the entire PubMed database. The HIV literature appears to more rely on confidence intervals than the previously reviewed literature.

LATEBREAKER

Methods/Statistics

Causal mediation analysis with a time-to-event mediator and outcome in the presence of competing risks: application to the Multi-Ethnic Study of Atherosclerosis (MESA) Ziqing Wang* Ziqing Wang Arce Domingo-Relloso Linda Valeri

Exposure to environmental metals has been linked to an increased risk of dementia, yet the underlying mechanisms remain unclear. Using data from the Multi-Ethnic Study of Atherosclerosis (MESA), we aim to quantify the potential mediating role of cardiovascular disease (CVD) incidence in the metal exposure-dementia relationship. Existing causal mediation methods for a time-to-event mediator and outcome are scarce. Also, they do not address informative dropout due to mortality, which is a competing risk for both CVD and dementia events. This may lead to biased or even reversed effect estimations, such as a misleading beneficial effect of metal exposure on dementia onset. Therefore, we propose a novel causal mediation framework based on multi-state survival models, where we define path-specific causal estimands that decompose the total effect into a direct effect, an indirect effect through the CVD event, and an indirect effect through the deterministic relationship between mortality and both the CVD and dementia events. This method will provide novel insights into the pathways linking metal exposure to dementia, and has the potential to be applied in aging studies in general.

Molecular

A state of the field: molecular epidemiology and bioethics Sarah Bassiouni* Sarah Bassiouni Jada Wiggleton-Little Emily Martin

Background: Molecular epidemiology is a subfield of epidemiology that has seen an explosion of work since its inception in the 1980s and the advent of novel molecular biological techniques that allowed us to answer questions we could not before. As molecular epidemiologists, we typically receive a great deal of training in the methods of epidemiology and molecular biology, but often a more limited training within the bioethics of using these techniques and framing our research questions. Given how scientific technologies continue to advance, it is imperative that molecular epidemiologists receive robust training in how to ground their research within a bioethical framework that balances the needs of population health with individual autonomy. Here, we discuss the current state of the research.

Methods: PubMed was searched for “bioethic*” or “bioethics” in conjunction with “molecular epidemiology” and “molecular epidemiolog*”.

Results: This resulted in 37 papers with some combination of these specific terms. The overwhelming majority of results were primary research papers studying infectious disease epidemiology or genetic epidemiology that mentioned bioethic* or bioethics in their background or discussion. Two papers discussed ethical challenges in HIV research and proposed recommendations for researchers in this topic. Another paper was an ethical reflection regarding the use of molecular typing techniques during outbreaks. Two papers discussed ethics within the subfield of genetic epidemiology.

Discussion: The paucity of peer-reviewed literature at the intersection of molecular epidemiology and bioethics represents a key opportunity that we as a sub-field have to strengthen our academic training pathways and available resources. This can further bolster the quality of the research we conduct, as well as improve the translation of our findings into public health policy.

Mortality

Mortality of World Trade Center (WTC) Responders by WTC Health Program Enrollment

Mst Afroza Parvin* Mst Afroza Parvin Rebecca D. Kehm James E. Cone Mark R. Farfel Rachel Zeig-Owens Baozhen Qiao David G. Goldfarb Moshe Z. Shapiro Tabassum Insaf Andrew C. Todd Charles B. Hall Paolo Boffetta Jiehui Li

Enrollment in the WTC Health Program (WTCHP) has been associated with lower all-cause and cause-specific (cancer and smoking related) mortality risk among WTC responders involved in rescue and recovery efforts in response to the 9/11 terrorist attacks. This study investigates whether differences in comorbidities account for the survival advantage associated with WTCHP enrollment. We followed 9,467 WTC responders in WTCHP and 18,963 not in WTCHP from enrollment to 2020. We ascertained deaths through linkage to NDI. We estimated adjusted HR (AHR) with 95% CI using Cox models and Fine and Gray's proportional sub-distribution hazards models respectively to determine the association of WTCHP enrollment with all-cause and cause-specific mortality. In calculating AHR, we initially adjusted for age, sex, race/ethnicity, and smoking status, and subsequently adjusted for various types of self-reported physical and mental health comorbidities using inverse probability weighting to balance the groups on comorbidities. We identified 1,658 deaths during follow-up period. Prior to adjusting for comorbidities, WTC responders in WTCHP had significantly lower risks of all-cause (AHR=0.72; 95% CI=0.65-0.81), cancer-specific (0.76; 0.63-0.93), heart disease-specific (0.74; 0.58-0.93), and smoking-related (0.71; 0.60-0.84) mortality compared to those not in WTCHP. However, after applying the weights of comorbidities, lower risks for all-cause (0.84; 0.76-0.94) and smoking-related (0.83; 0.71-0.97) mortality remained significant, but heart disease- (0.92; 0.73-1.14) and cancer-specific (0.84; 0.69-1.01) mortality risks became non-significant. When limiting to those with cancer, cancer-mortality (0.77; 0.60-0.99) was significantly associated with WTCHP enrollment. This study confirms that WTCHP enrollment is associated with reduced all-cause, cancer- and smoking-related mortality. Differences in comorbidities may explain some, but not all, of this survival benefit.

Neurology

Association of obesity with dementia over 24 years of weight history in the Framingham Heart Study Phillip Hwang* Phillip Hwang Rafeya Raquib Hanfei Xu Rhoda Au M. Maria Glymour Andrew Stokes

Background: Many studies of the association between obesity and dementia rely on weight status at a single point in time, making it difficult to adequately address bias associated with reverse causality. The objective of this analysis was to examine the association between maximum body mass index (BMI) and all-cause dementia without the consequences of reverse causality.

Methods: Longitudinal cohort study from the Framingham Heart Study. The follow-up period started from baseline Exam 13 (1972-1976) for the Original cohort and from baseline Exam 5 (1991-1995) for the Offspring cohort, and ended December 31, 2021. Maximum BMI (kilograms/meters2) over 24 years of objectively measured weight history before the beginning of follow-up for dementia. All-cause dementia was based on expert consensus using standard diagnostic criteria. Cox models were used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for the association between maximum BMI and dementia, with individuals in the normal BMI range (BMI 18.5-24) as the reference group, and adjusting for baseline age, sex, cohort, smoking, alcohol intake, education, and duration between exam of reaching maximum BMI and baseline exam.

Results: Among 6067 participants (mean [SD] age at baseline=62.4 [8.8] years; 55.5% female), 1303 (21.5%) developed dementia during the follow-up. A monotonic association was observed between maximum BMI and dementia, with obese II (BMI 35-39) significantly associated with increased risk of dementia (HR=1.35; 95% CI=1.07-1.71). A significant association was not observed for the overweight (BMI 25-29; HR=1.05; 95% CI=0.91-1.21) or obese I (BMI 30-34; HR=1.16; 95% CI=0.98-1.37) categories.

Conclusions: A monotonic association was found between maximum BMI over 24 years of weight history and subsequent all-cause dementia. Maximum BMI in the normal weight range was associated with the lowest risk of dementia in the sample, highlighting the importance of obesity prevention.

Neurology

The associations between personal air pollution exposures and cognitive function for post-thrombectomy patients. Yisi Liu* Yisi Liu Elise Dahlke Jacqueline Frank Jordan Harp Justin Fraser Keith Pennypacker

Stroke is the leading cause of long-term disability and the fifth cause of death in USA. Emergent large vessel occlusion (ELVO), as one of the most severe types of stroke (account for around 340,000 patients in USA each year) are responsible for higher dependence or death than other types of ischemic stroke. Thrombectomy, a standard procedure for some stroke patients, significantly lowers the risk of disability. However, patients still suffer from cognitive effect from the brain injury and the recovery vary widely between patients. This study aims to expand understandings on the impact of PM2.5 on cognitive recovery for post thrombectomy stroke patients.

This is a panel study nested in a prospective cohort at Kentucky that collect numerous neurocognitive test data and blood samples from 3-month to 2-year post thrombectomy. We employed the one-week personal air monitoring and the one-month at-home indoor air monitoring among stroke patients between three to six months post thrombectomy. We also collected information on cognitive function and nearly 200 different plasma proteins for each study participants at three months and six months post-thrombectomy, respectively.

We will present the spatial and temporal distribution of personal and indoor particulate matter (PM) exposures among stroke patients in Kentucky. Importantly, we will show the impact of PM exposures on cognitive function changes between 3-month and 6-month post thrombectomy based on mixed-effect linear regression models. Additionally, we will discuss associations between PM exposure and protein response post thrombectomy.

The study site (Kentucky) is located in the US Stroke Belt with some of the most medically underserved rural counties in the nation. Results from this study advance our understanding of the role of PM exposures on brain health in the stroke population and will inform potential new interventions to ameliorate the adverse effects of air pollution.

Neurology

The association between the DASH diet and resilience to neurodegeneration in memory, language, and executive function domains: Framingham Heart Study Tianyu Liu* Tianyu Liu Phillip H Hwang

Background

Emerging evidence suggests that the Dietary Approaches to Stop Hypertension (DASH) may improve brain health and reduce cognitive decline. However, more research is needed to understand its effects on neurodegeneration across different cognitive domains and age groups.

Methods

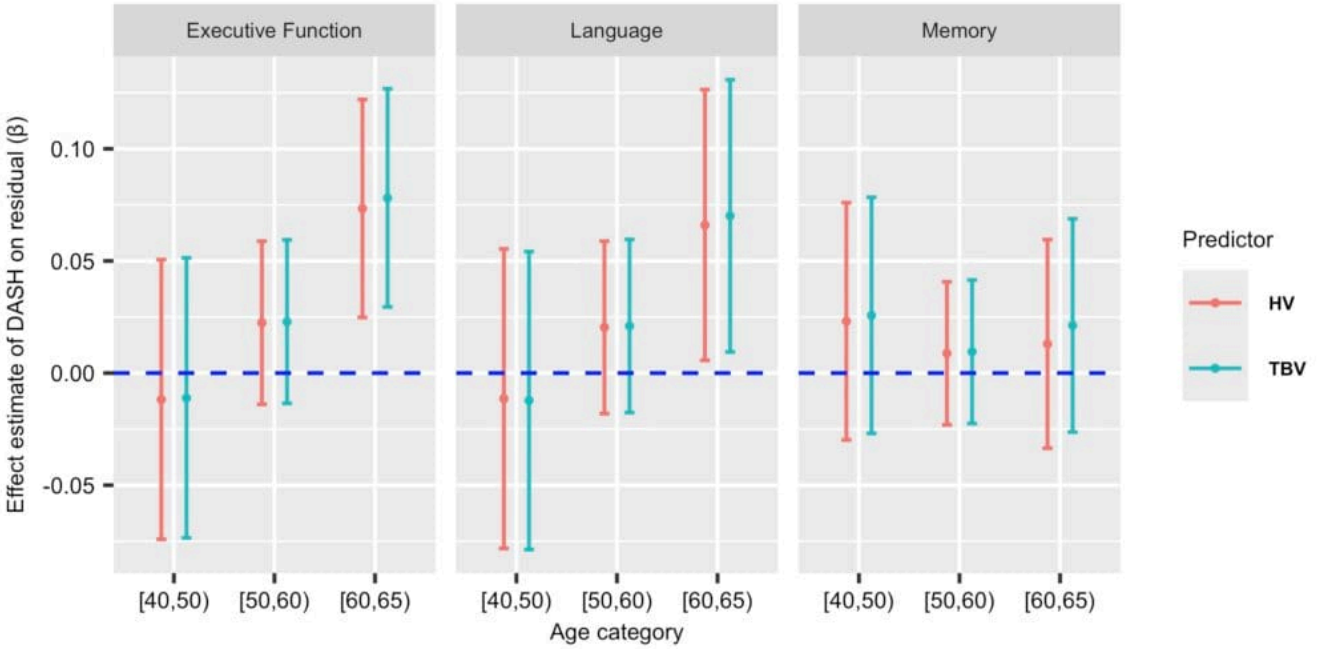
In total, 1163 subjects aged 40 to 65 who attended Exam 5 between 1991 and 1995 were selected from the Offspring cohort of the Framingham Heart Study and were followed until they underwent their first neuropsychological (NP) test at age 60 or older. DASH was calculated as both continuous and categorical (e.g., quartiles) variables based on food frequency questionnaires at baseline. The outcomes were six residuals for memory, language, and executive function scores from the NP exam, predicted by total brain volume and hippocampal volume based on structural brain magnetic resonance imaging. We used linear regression adjusting for age, sex, education, BMI, physical activity, smoking, alcohol, hypertension, and diabetes, and performed the subgroup analysis by three age categories with the cutoffs of 50 and 60.

Results

DASH score was positively associated with resilience to neurodegeneration in executive function predicted by both total brain volume (β = 0.03, 95% CI: 0.004-0.056) and hippocampal volume (β = 0.028, 95% CI: 0.003-0.148). The impact of DASH in the 60+ age group on resilience to neurodegeneration was stronger in language and executive function, with the estimates of the fourth DASH quartile as 0.216 (95% CI: 0.051-0.382) and 0.213 (95% CI: 0.081, 0.345) compared to the first quartile. In the age 50-60 group, people in the 2nd DASH quartile had a 0.096-unit (95% CI: 0.004-0.187) higher resilience to neurodegeneration in memory compared to the 1st quartile.

Conclusion

A high DASH score was associated with improved resilience to neurodegeneration in memory, language, and executive function domains, with stronger associations observed at higher DASH scores and among older adults.


Executive Function
Language
Memory
Effect estimate of DASH on residual (β)
0.10
0.05
0.00
-0.05
[40,50)
[50,60)
[60,65)
Age category
Predictor
HV
TBV

Neurology

The impact of physical activity on cognitive resilience in memory, language, and executive function: Evidence from Framingham Heart Study. Tianyu Liu* Tianyu Liu Phillip H Hwang

Background

Physical activity has been recognized as a key lifestyle factor that potentially mitigates the effects of neurodegeneration and preserves cognitive function. However, the relationship between physical activity and cognitive resilience in specific domains remains underexplored, especially regarding the moderating effect of age.

Methods

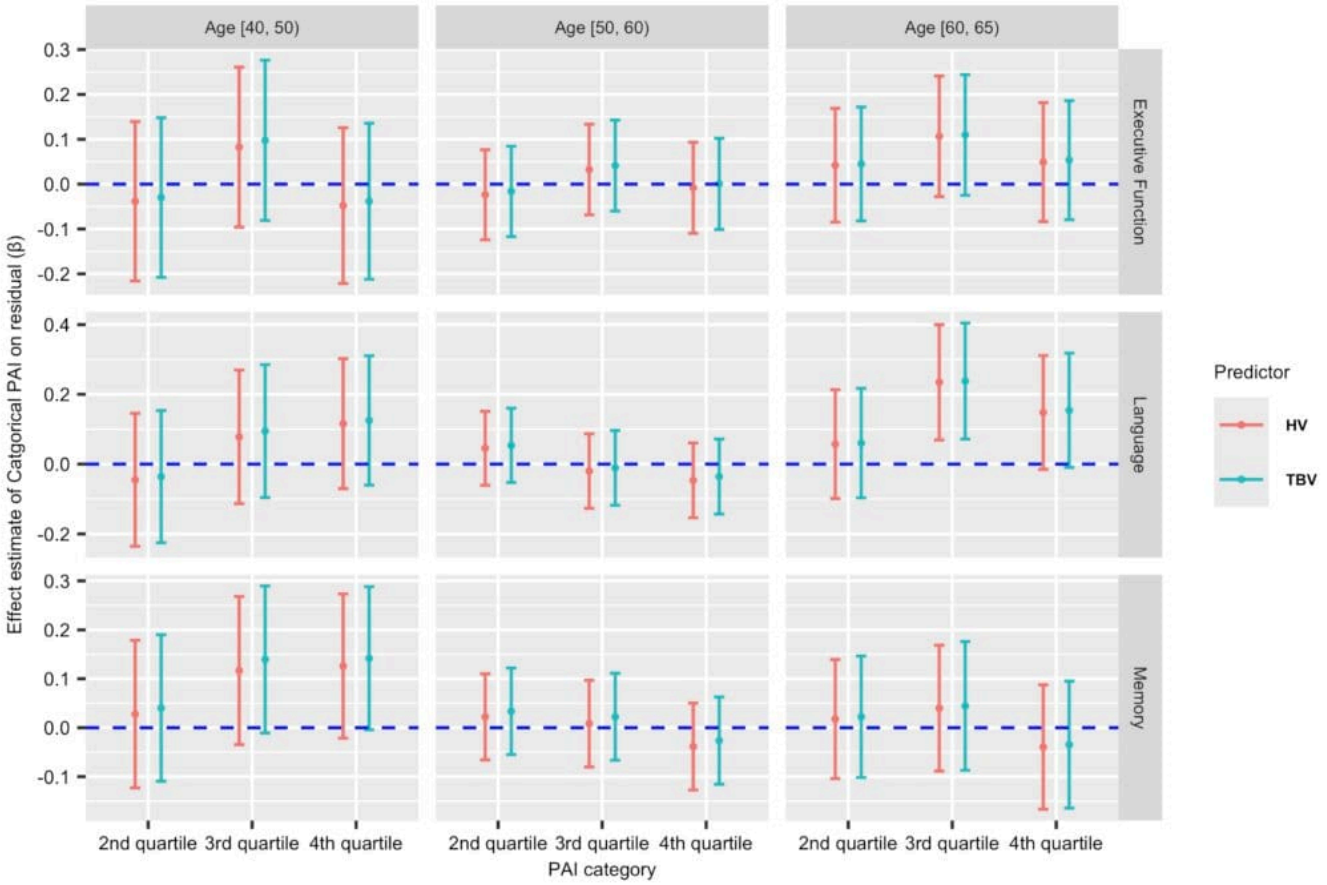
A total of 1,163 individuals aged 40 to 65 who attended Exam 5 between 1991 and 1995 were selected from the Offspring cohort of the Framingham Heart Study. They were followed until they concluded their first neuropsychological (NP) test over age 60. Physical activity was based on the physical activity index (PAI), which is a derived measure of total activity level based on a physical activity questionnaire. We used the residuals of memory, language, and executive function factor scores to assess the resilience outcome. These scores were predicted by total brain volume and hippocampal volume from structural brain magnetic resonance imaging. Linear regression was applied adjusting for age, sex, education, BMI, physical activity, smoking, alcohol, hypertension, and diabetes, and we performed a subgroup analysis by age categories with the cutoffs of 50 and 60.

Results

We found positive but insignificant associations between PAI and resilience to neurodegeneration across the entire population in memory, language, and executive function. For individuals aged over 60, the third PAI quantile was positively associated with the resilience in the language domain predicted by both total brain volume (β = 0.238, 95% CI: 0.072, 0.404) and hippocampal volume (β = 0.235, 0.069, 0.4) compared to the first PAI quantile. No significant relationships of PAI were observed in the other age groups analyzed in the subgroup assessment.

Conclusion

This long-term community-based cohort study suggests that higher physical activity levels play an important role in resilience to neurodegeneration, especially in the language domain among older adults.


Age [40, 50)
Age [50, 60)
Age [60, 65)
Executive Function
Language
Memory
Effect estimate of Catgorical PAI on residual (β)
0.3
0.2
0.1
0.0
-0.1
-0.2
0.4
2nd quartile
3rd quartile
4th quartile
PAI category
Predictor
HV
TBV

Neurology

Gene-Environment Interactions between Cumulative Lead Exposures and Genetic Risk Factors for Iron Burden on Parkinson's Disease Kanghong Shao* Kanghong Shao Cynthia Kusters Jeff Bronstein Adrienne Keener Danielle Thordarson Kimberly C Paul Beate Ritz

Background

Parkinson's disease (PD) has been linked to cumulative lead exposure. While the role of iron in PD remains unclear, considering iron accumulates in the substantia nigra and may contribute to PD etiology via oxidative stress, it has been suggested to interact with lead metabolism in PD development. However, few epidemiologic studies have investigated this interaction.

Methods

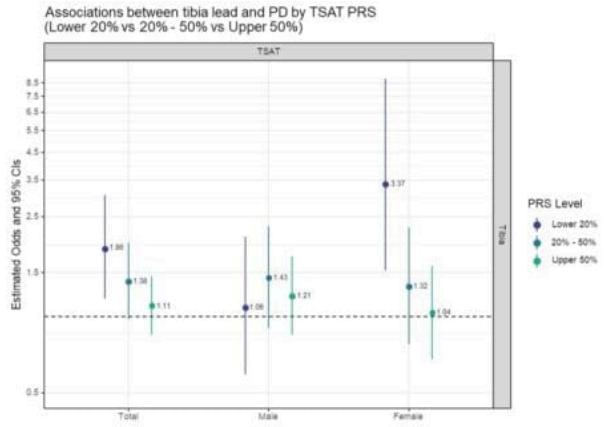
Tibia, patella, and blood lead levels were estimated using blood DNA methylation biomarkers among 523 PD patients and 236 population controls in the Parkinson's Environment and Gene (PEG) study, while polygenic risk scores (PRSs) for iron handling including total iron binding capacity [TIBC] and transferrin saturation [TSAT] were calculated based on single-nucleotide polymorphisms (SNPs) linked to iron metabolism and accumulation. We selected 11 SNPs associated with iron homeostasis. Logistic regressions were conducted to estimate effect sizes between lead biomarkers and PD stratified by each PRS's percentiles and each SNP's genotypes. The analyses were further stratified by gender.

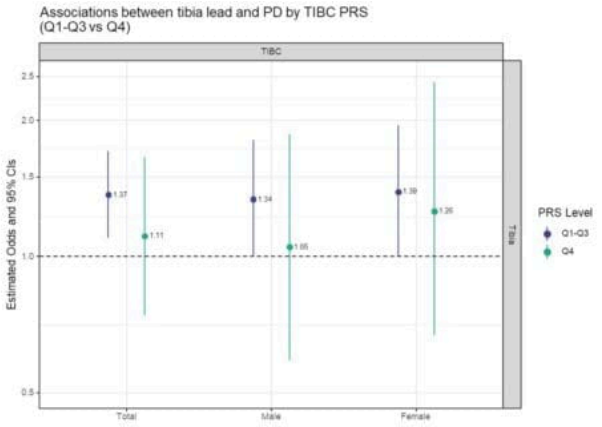
Results

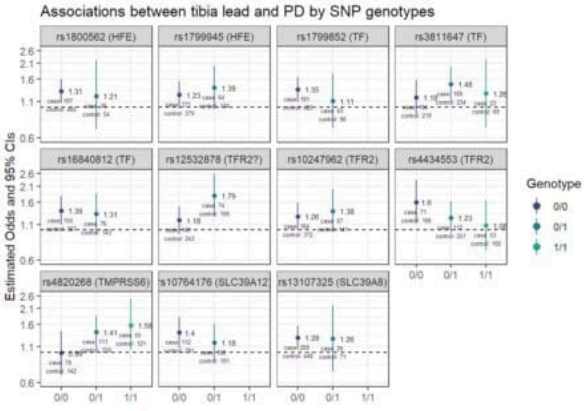
A low TSAT PRS (50th percentile) (OR = 1.11; 95% CI: 0.85, 1.45). A genetic profile of larger iron binding capacity also attenuates the effect size of cumulative lead exposure on PD (TIBC PRS Q4 vs Q1-Q3: OR = 1.11; 95% CI: 0.74, 1,66). The modifying effect of the TSAT but not the TIBC PRS was most pronounced and restricted to women (OR = 3.37; 95%CI: 1.53, 8.84).

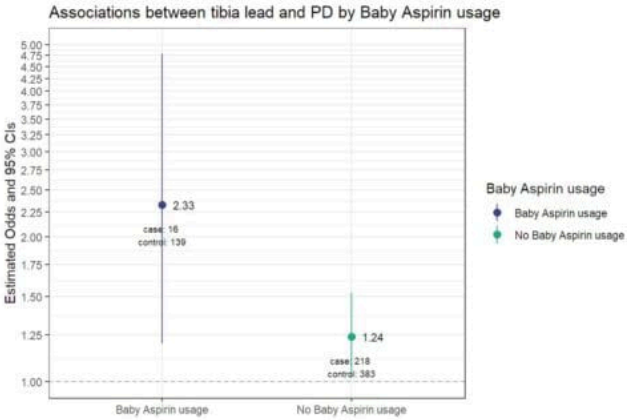
Conclusion

Genetic susceptibility to iron deficiency may exacerbate the effect of cumulative lead exposure on PD development, while genetic predilection to high iron load and total iron binding capacity reduces the harmful effect of lead. We saw evidence for larger modifying effects from a genetic predisposition to iron deficiency among women and none for men. Our findings suggested a protective role of iron against neurotoxicity of lead in PD.


Associations between tibia lead and PD by TSAT PRS
(Lower 20% vs 20% - 50% vs Upper 50%)
TSAT
Estimated Odds and 95% CIs
Total
Male
Female
PRS Level
Lower 20%
20% - 50%
Upper 50%


Associations between tibia lead and PD by TIBC PRS
(Q1-Q3 vs Q4)
TIBC
Estimated Odds and 95% CIs
Total
Male
Female
PRS Level
Q1-Q3
Q4


Associations between tibia lead and PD by SNP genotypes
rs1800562 (HFE)
rs1799945 (HFE)
rs1799852 (TF)
rs3811647 (TF)
rs16840812 (TF)
rs12532878 (TFR27)
rs10247962 (TFR2)
rs4434553 (TFR2)
rs4820268 (TMPRSS6)
rs10764176 (SLC39A12)
rs13107325 (SLC39A8)
Estimated Odds and 95% CIs
Genotype
0/0
0/1
1/1


Associations between tibia lead and PD by Baby Aspirin usage
Estimated Odds and 95% CIs
2.33
case: 16
control: 139
1.24
case: 218
control: 383
Baby Aspirin usage
No Baby Aspirin usage

LATEBREAKER

Neurology

Finding Prodromal Parkinson's Disease with the Movement Disorder Society's Prodromal Calculator and Electronic Health Records John Grady Heller* John Heller Kathryn Fitzgerlad

Background: Neurodegenerative processes leading to Parkinson's Disease (PD) may begin decades prior to diagnosis, and may become extensive before PD manifests. Early identification of prodromal individuals who may benefit most from earlier disease modification remains a critical need, and future disease modification clinical trials will likely need to utilize multiple key factors to recruit people with prodromal PD at the highest possible accuracy.

Methods: We adapted the Movement Disorders Society (MDS) Prodromal PD calculator to electronic health record (EHR) data to estimate the probability of prodromal PD among participants with REM sleep behavior disorder (RBD; i.e., a group with high expected rates of conversion to PD that is not diagnostically specific to PD) from the All of Us cohort. We identified persons with RBD using validated algorithms and calculated the rate of conversion from prodromal to diagnosed PD or 'phenoconversion' associated with a range of Prodromal PD probabilities using Cox proportional hazards models. We also derived the optimal cut-point for prodromal probability in this population for rates of conversion using 10-fold cross-validation (i.e., optimizing C-statistic and Youden's index).

Results: Of the 544 individuals with RBD (average age: 51.6±17.1 years; 55% male), 83 converted to diagnosed PD over an average follow-up of 3.7 (SD:1.9) years. Relative to individuals in this cohort with estimated prodromal PD probability less than 20%, those with probabilities exceeding 80% had an over 23-fold increase in rates of phenoconversion (23.79; 95% CI: 18.45, 39.69). We found a cut-point of 70% probability of prodromal PD as the optimal threshold most discriminatory for phenoconversion.

Conclusion: These results demonstrate that the MDS prodromal calculator applied to readily available EHR data can provide important discriminatory information in people with RBD. This may have implications for refining the identification of high-risk individuals.

Nutrition/Obesity

Depressive symptoms and obesity risk in Korean adolescents: A longitudinal analysis Dabin Jeong* Dabin Jeong Hannah Oh

Background: Studies suggest that there is a bidirectional association between obesity and depression. However, few studies investigated whether depression influences the risk of adolescent obesity using a longitudinal study design.

Objective: This study investigated the association between depressive symptoms and obesity risk among Korean adolescents using longitudinal data.

Methods: We conducted a longitudinal analysis using prospective cohort data from the Korean Child and Youth Panel Study (KCYPS; n=2,590 7th grade students) 2018-2022 (5-y follow-up). Depressive symptoms (score range 10-40) were assessed using the Korean version of the Symptom Checklist-90-Revised (SCL-90-R) and categorized into quartiles. Obesity was defined as BMI-for-age and -sex ≥ 95th percentile based on the 2017 Korean National Growth Charts. We performed generalized estimating equation models to account for correlation between responses within the subjects. We estimated odds ratio (OR) and 95% confidence intervals (CIs) for the associations between depressive symptom score and obesity risk, adjusting for potential confounders.

Results: Higher depressive symptom score was associated with higher obesity risk (highest vs. lowest quartiles: OR [95% CI]: 1.83[1.21-2.77]; p-trend=0.013) after adjusting for sociodemographic characteristics and parental obesity. The positive association persisted after additional adjustment for lifestyle factors (sleep duration, physical activity) and subjective health (OR [95% CI]: 2.00[1.29-3.09]; p-trend=0.005). When stratified by sex, similar positive associations were observed in both boys (OR [95% CI]: 1.60[0.94-2.75]) and girls (3.24(1.33-7.90); p-interaction=0.22).

Conclusions: Poor mental health may be one of the important predictors of adolescent obesity in Korea.

Nutrition/Obesity

Measuring sarcopenic obesity in older adults: development of age and sex-specific fat mass to fat-free mass ratio (FM/FFM) percentile curves using data from the Canadian Longitudinal Study on Aging Chris Kim* Chris Kim Claire Cook Hailey Banack

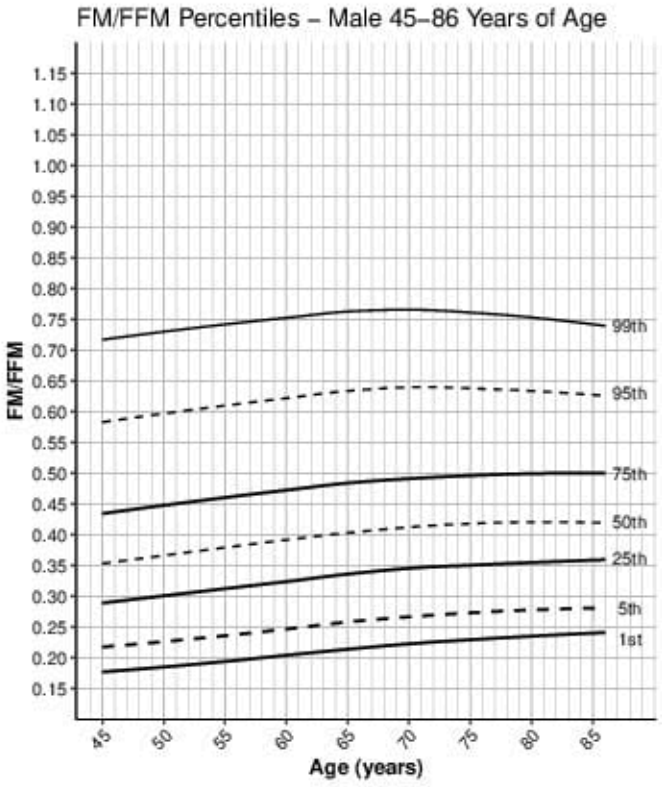
Chris Kim, MPH, Claire Cook, MPH, Hailey Banack, PhD

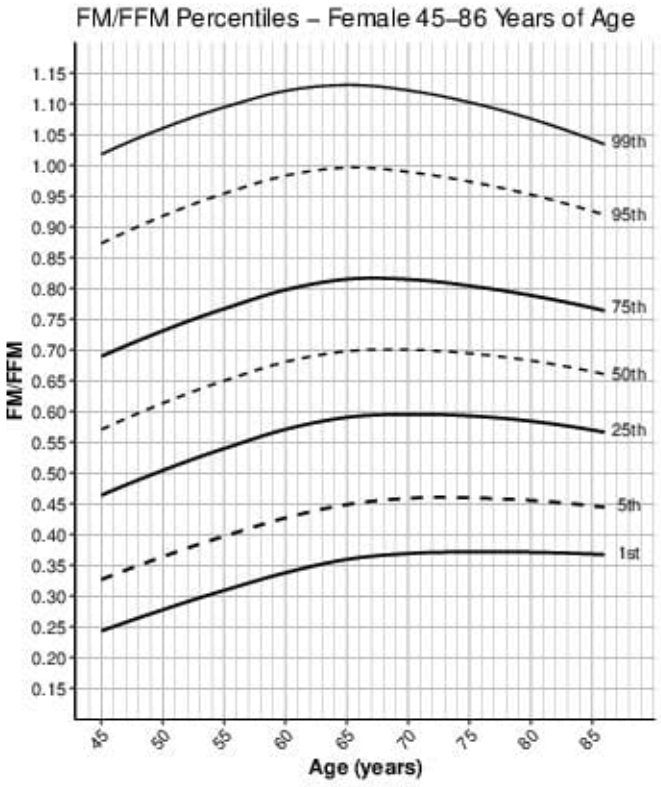
Background: Fat mass to fat-free mass ratio (FM/FFM) measures the relative contribution of fat mass (kg) and fat-free mass (kg) within an individual; a higher FM/FFM indicates a greater proportion of fat mass relative to lean body mass. The objective of this work is to develop age- and sex-specific FM/FFM percentile curves for older adults as a measure of sarcopenic obesity.

Methods Baseline data from the Canadian Longitudinal Study on Aging (CLSA) Comprehensive cohort were used (n=28,791). FM/FFM was calculated as the ratio of total body fat mass (kg) to total body lean mass (kg) from Dual-Energy X-ray Absorptiometry (DXA) scan. Age and sex-specific FM/FFM weighted percentile curves for the 1st, 5th, 25th, 50th, 75th, 95th, and 99th percentiles were calculated using the LMS method. LMS provides a summary of the changing distribution of the measurement of interest by the three curves, lambda for the skewness (L), mu for the median (M), and sigma for the coefficient of variation (S). The weighted percentile curves were then plotted with age on the x-axis and FM/FFM on the y-axis for males and females, respectively.

Results: The maximum FM/FFM was approximately 0.77 at age 70 for males and approximately 1.14 at age 66 for females (Figure 1). The median FM/FFM values in the same age ranges were approximately 0.41 and 0.70 for males and females, respectively. For both males and females, FM/FFM tended to increase until 65-70 years of age and decreased thereafter. Females experience increases in FM/FFM at earlier ages and decline at faster rates than males.

Conclusions: On average, males tended to have lower FM/FFM and had generally slower decline in FM/FFM than females. These patterns are similar to previous findings among older adults from US and China. Further research on sex differences in sarcopenic obesity among older adults is warranted.


FM/FFM Percentiles – Male 45–86 Years of Age
FM/FFM
Age (years)
99th
95th
75th
50th
25th
5th
1st


FM/FFM Percentiles – Female 45–86 Years of Age
FM/FFM
Age (years)
99th
95th
75th
50th
25th
5th
1st

Nutrition/Obesity

Association between parental body dissatisfaction and child feeding practices in a 2019-2020 statewide sample of Texas parents of second-grade students Kaitlin Brand* Kaitlin Brand Deanna Hoelscher Adriana Perez Raja Malkani

Introduction: Few studies have examined the relation between parent body size attitudes and child feeding practices in parents of elementary school children. The purpose of this study is to explore the association between parental body dissatisfaction and parent-reported child feeding practices in a diverse statewide population.

Methods: Validated self-reported survey data were collected from the parents of second-grade children (n = 1,083) participating in the 2019-2020 Texas School Physical Activity and Nutrition (Texas SPAN) study. Parental body dissatisfaction was dichotomized as desire to lose weight versus other. Child feeding practices included encouraging children to eat in the absence of hunger, offering sweets as a reward, and limiting snacks. Pearson Chi-square tests of independence were conducted, and three weighted logistic regression models were fit, adjusting for parent/child gender, family food insecurity, child race/ethnicity, parent age, and parent education level.

Results: Parents with body dissatisfaction were less likely to offer sweets as a reward (17% vs 26%, p = 0.009), but there were no differences in encouraging eating when not hungry or limiting snacks. Parents with body dissatisfaction had lower odds of encouraging eating when not hungry (AOR 0.68; 95% CI 0.42, 1.11), offering sweets as a reward (AOR 0.63; 95% CI 0.38, 1.01), and limiting snacks (AOR 0.58; 95% CI 0.29, 1.20) compared to parents without body dissatisfaction, after adjusting for covariates.

Discussion: Findings suggest that, among a racially/ethnically diverse population, parental body dissatisfaction may influence some feeding practices more than others. Further research to understand factors underlying these practices may be warranted.

Nutrition/Obesity

Trends in solid fat and oil consumption and their association with metabolic syndrome among U.S. adults: A trend analysis of NHANES 2007–2018 Miyuki Shimizu* Miyuki Shimizu Deirdre Tobias Sarinnapha Vasunilashorn

This study examines temporal trends in dietary fat consumption and its association with metabolic syndrome (MetS) prevalence among U.S. adults. We hypothesize that higher solid fat intake increases MetS prevalence, while higher oil intake decreases it. We conducted a repeated cross-sectional analysis using 2007–2018 U.S. National Health and Nutrition Examination Survey (NHANES) and Food Patterns Equivalents Database (FPED). The sample included 11,720 non-pregnant adults aged ≥20 years, excluding those with implausible energy intakes or missing data. Intake of solid fats and oils was assessed via 24-hour recalls. MetS was defined as having ≥3 of the following: elevated waist circumference, triglycerides, blood pressure, fasting glucose, or low high-density lipoprotein (HDL) cholesterol. We conducted multivariable regression models to estimate odds ratios (ORs) and 95% confidence intervals (CIs) for the association between fat intakes and MetS prevalence, adjusting for demographic, lifestyle, and dietary factors. From 2007 to 2018, MetS prevalence increased from 24% to 28%. During this period, mean solid fat intake decreased from 40 to 37 g/day, while oil intake increased from 22 to 31 g/day, reflecting a shift toward healthier oils in alignment with dietary guidelines. Higher solid fat intake was associated with increased odds of MetS (OR=1.20, CI:1.00–1.43), elevated waist circumference (OR=1.35, CI:1.11–1.64), and fasting glucose (OR=1.30, CI:1.06–1.59). In contrast, higher oil intake was not significantly associated with MetS (OR=0.87, CI:0.75–1.02), but was inversely associated with elevated triglycerides (OR=0.72, CI:0.61–0.84) and low HDL cholesterol (OR=0.86, CI:0.74–1.00). This study highlights a shift in the U.S. diet from solid fats to oils, in line with dietary guidelines. However, individuals who continue to consume higher amounts of solid fats are more likely to have MetS, suggesting that further public health efforts are necessary.

Oils intake	Low (Reference)	Medium (OR, 95%CI)	High (OR, 95%CI)	p-value**
Unadjusted model	1.0	0.97(0.84-1.12)	0.85(0.75-0.97)	0.02
Adjusted model*	1.0	0.98(0.84-1.15)	0.87(0.75-1.02)	0.02
Solid fats intake				
Unadjusted model	1.0	1.09(0.96-1.25)	1.20(1.04-1.38)	0.04
Adjusted model*	1.0	1.10(0.95-1.27)	1.20(1.00-1.43)	0.30

Table 3: Associations Between Dietary Fat Intake and Metabolic Syndrome in U.S. Adults (Unadjusted and Multivariable-Adjusted Odds Ratio)

*Adjusted for age, sex, race, education, exercise, smoking status, alcohol intake, total energy intake, fiber intake, and added sugar intake. ** p-values were calculated using dietary fat intake as a continuous variable to assess linearity.

Oils intake	Low (Reference)	Medium (OR, 95%CI)	High (OR, 95%CI)	p-value**
Elevated waist circumference	1.0	1.01(0.88-1.15)	1.13(0.98-1.30)	0.22
Elevated triglycerides	1.0	0.90(0.79-1.02)	0.72(0.61-0.84)	<0.001
Low HDL	1.0	0.93(0.82-1.06)	0.86(0.74-1.00)	0.05
Elevated blood pressure	1.0	1.09(0.91-1.29)	0.99(0.84-1.18)	0.47
Elevated fasting glucose	1.0	0.97(0.83-1.14)	0.95(0.80-1.12)	0.93
Solid fats intake				
Elevated waist circumference	1.0	1.16(0.98-1.37)	1.35(1.11-1.64)	0.002
Elevated triglycerides	1.0	0.96(0.82-1.12)	1.04(0.87-1.25)	0.50
Low HDL	1.0	0.95(0.82-1.09)	1.00(0.85-1.19)	0.71
Elevated blood pressure	1.0	0.97(0.86-1.10)	0.92(0.75-1.13)	0.23
Elevated fasting glucose	1.0	1.17(1.00-1.38)	1.30(1.06-1.59)	0.15

Table 4: Multivariable Adjusted Odds Ratio for Dietary Fat Intake and Metabolic Syndrome Components in U.S. Adults*

*Adjusted for age, sex, race, education, exercise, smoking status, alcohol intake, total energy intake, fiber intake, and added sugar intake. The results represent variables from a single model. ** p-values were calculated using dietary fat intake as a continuous variable to assess linearity.

LATEBREAKER

Nutrition/Obesity

Preconception diet and pregnancy outcomes: The PrePARED Consortium Emily Harville* Emily Harville Lixuan Ji Yuanhan Yu Janaki Sunderesan Ke Pan James Shikany Daniela Sotres-Alvarez Gita Mishra Erica Gunderson Lauren Wise

Objective To assess whether preconception adherence to dietary recommendations is associated with healthy pregnancy.

Methods We harmonized data on 17714 participants from 5 cohorts in the Preconception Period Analysis of Risks and Exposures influencing health and Development (PrePARED) consortium according to the Fédération International de Gynécologie et d'Obstétrique (FIGO) nutrition checklist score. Linear risk models used the total diet quality score as a predictor of composite healthy pregnancy/infant outcomes (no gestational diabetes or hypertensive disorders [HDP], vaginal birth, full-term, appropriate weight for gestational age), adjusting for demographics, smoking, and energy intake. Results were combined using a mixed model with random effects for study and weighted by the inverse of the variance.

Results In the Australian Longitudinal Study of Women's Health, greater adherence to FIGO recommendations was associated with a higher likelihood of healthy infant outcome (β [risk difference]=0.008, SE 0.007, per recommendation met). In Coronary Artery Risk Development in Young Adults, contrary to hypothesis, higher FIGO scores were associated with a lower likelihood of good pregnancy/infant outcome (β=-0.022, SE 0.006). FIGO scores were not appreciably associated with composite outcomes in the California Teachers Study, Hispanic Community Health Study, or Pregnancy Study Online. Pooled results did not indicate an association between FIGO score and outcomes (composite healthy pregnancy/infant: β=-0.004, SE 0.011), with the exception of an inverse association with preterm birth (β=-0.061, SE 0.057). In individual cohorts, inverse associations were also observed for cesarean section and HDP.

Conclusion Overall results did not show strong associations between preconception adherence to FIGO recommendations and pregnancy/infant outcomes, although some associations varied by cohort.

Occupational

Time-Varying Participation Patterns in a Workplace Health Promotion Program and Metabolic Health Hanae Nagata* Hanae Nagata Koryu Sato Koichiro Shiba Sho Takeda Naoki Kondo

Background: Workplace health promotion programs are widely implemented, but their long-term effects remain unclear. This study estimated the effects of time-varying participation patterns over a 5-year period on metabolic outcomes.

Methods: The Hakuhodo DY Group, a Japanese advertising company, introduced a voluntary health promotion program called “Checkup Championship” (Kenshin-sen in Japanese) during annual health checkup periods for its employees in 2019, applying behavioral science principles to enhance engagement compared to traditional methods. We used data from the health checkups of 3,697 employees (2,818 men and 879 women; mean age: 40.7 years) from 2018 to 2023. Our outcomes of interest were weight, waist circumference, BMI, blood pressure, LDL cholesterol and HbA1c in 2023. To assess the associations with these outcomes, we compared the participation patterns as follows: (1) consistent participation in all 5 years versus non-participation, (2) number of continuous participation sessions, and (3) continuous versus intermittent participation, such as participating every other year. We used longitudinal targeted maximum likelihood estimation (TMLE) to control for time-dependent confounding including exercise habits and other factors.

Results: Employees with consistent participation over 5 years showed significantly lower weight (-1.37 kg, 95% CI: -1.92 to -0.82), waist circumference (-1.16 cm, -1.78 to -0.55), BMI (-0.48kg/m2, -0.67 to -0.28), and LDL cholesterol (-3.86 mg/dL, -7.61 to -1.46) compared to non-participants. Sustained participation was associated with the outcomes when it was at least 4 years for weight and BMI, and at least 3 years for waist circumference and LDL cholesterol. Intermittent participation showed similar associations as the ones for continuous participation, but the association diminished with intermittent participation beyond two years. No significant differences in blood pressure or HbA1c were observed across any participation patterns.

Conclusion: Behavioral science-based workplace health promotion programs may improve metabolic outcomes of employees, when the participation was sustained at least for 3 to 4 years. These findings highlight the need for strategies that promote long-term engagement to enhance program effectiveness.

Occupational

Examining the relationship between long working hours and cardiovascular health using Life's Essential 8 Metrics: National Health and Nutrition Examination Survey (NHANES) 2011-2018 Annaliese Pena* Jee Won Park James Wallace Annaliese Pena Fadzai Nicola Dube Kareem Khairy Jee Won Park

Long working hours (≥55 hours/week), a growing trend in the workforce, represent a modifiable occupational risk factor with significant implications for cardiovascular health (CVH), yet the link between extended working hours and CVH remains insufficiently characterized. This study examined how long working hours influence overall CVH, and how the relationship differed by sex and depression, thus offering insights into the workplace-related determinants of cardiovascular health outcomes.

We used the National Health and Nutrition Examination Survey (NHANES) data from 2011 to 2018 to analyze 6,641 participants (age≥18 years). CVH was assessed using the American Heart Association's Life's Essential 8, which evaluates biobehavioral factors (e.g., diet, blood sugar). Adjusted multinomial logistic regression analyses for CVH (high/moderate/low) were performed as a function of working hours (35-40/41-48/49-54/55+ hours per week). We assessed for effect measure modification (EMM) by sex and depression by including relevant product terms in the model.

The adjusted ORs (95% CIs) for high and moderate versus poor CVH among participants with long working hours (55+ hours) compared to standard working hours (35-40 hours) were 0.82 (0.57-1.18) and 0.86 (0.63-1.17), respectively. There was some evidence for EMM by sex and depression. Specifically, the adjusted ORs (95% CIs) for high versus poor CVH among male and female participants were 0.67 (0.40-1.12) and 1.35 (0.78-2.32), and among those with and without depression were 0.31 (0.06-1.59) and 0.84 (0.57-1.25).

Our findings indicated that long working hours were associated with poorer CVH, particularly among male workers and those with higher depressive symptoms. These results emphasize the need for targeted interventions to mitigate workplace-related risks to CVH. Additional prospective studies are needed to establish the temporality of these associations and to capture the long-term effects of long working hours on CVH.

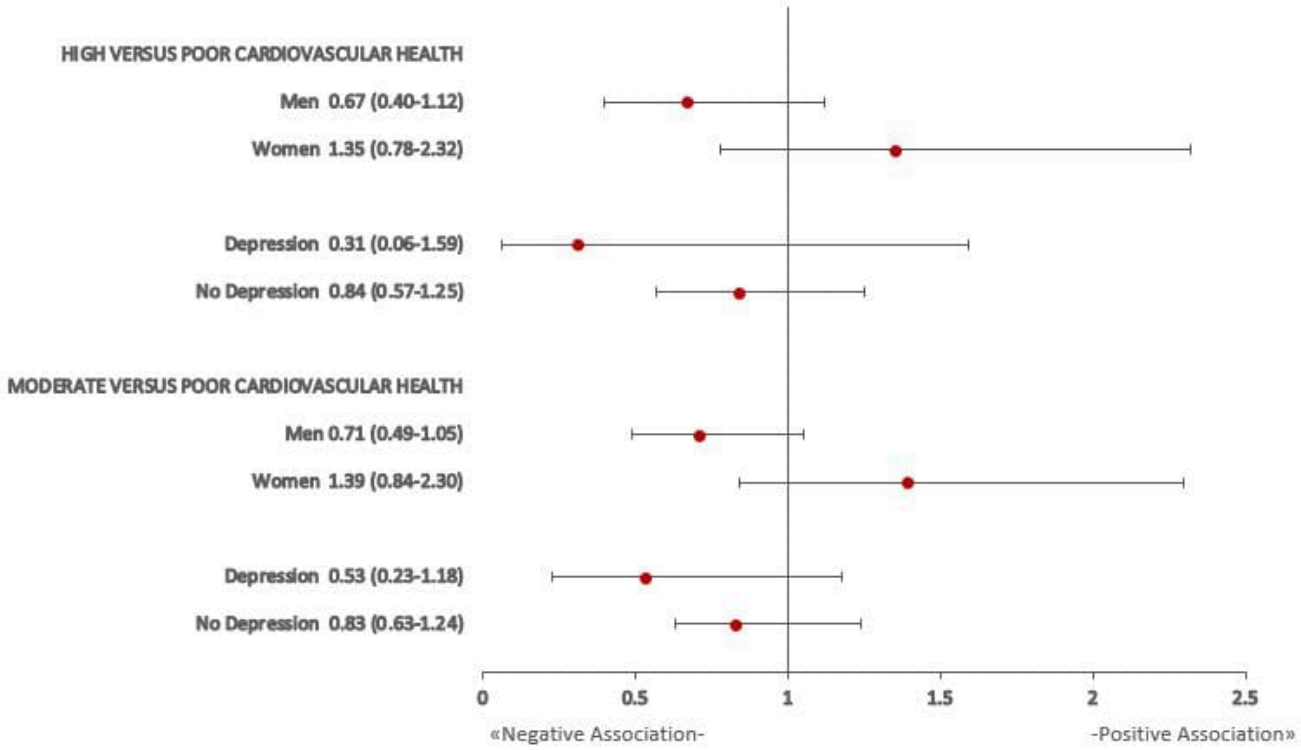


Figure. Adjusted odds ratios (95% CIs) for high and moderate cardiovascular health (versus poor) comparing those who worked long working hours (55+ hours/week) versus standard working hours (35–40 hours/week) by sex and depression status

Perinatal & Pediatric

Updated reference ranges for normal second trimester growth velocity Elizabeth Williams* Elizabeth Williams Maddy St. Ville Zhen Chen Jessica Gleason Dian He John Owen Roger Newman Edward Chien William Grobman Daniel Skupski Angela Ranzini Anthony Sciscione Jagteshwar Grewal Cuilin Zhang Fasil Tekola-Ayele Katherine Grantz

Monitoring fetal growth is essential, as deviations from normal growth are associated with adverse outcomes. However, clinical practice currently lacks a universally effective process for identifying pathologic fetal growth. Individualized growth assessment (IGA) has been proposed as an improvement, using second trimester (2T) ultrasound measurements to model individual third trimester (3T) growth potential. A criterion for using IGA is for a fetus to have a “normal” 2T growth trajectory, defined using reference ranges that were established in a small, racially homogeneous cohort (n=119, 88% White). However, these ranges have never been formally re-assessed.

To address this gap, we calculated updated 95% reference ranges for normal 2T growth velocity for head circumference (HC), abdominal circumference (AC), and femur length (FL) using the NICHD Fetal Growth Studies Standard Population (n=1,668). We compared the prior and updated ranges using t-tests and by comparing their 3T IGA classifications.

Compared to prior IGA reference ranges, we observed higher mean velocities and narrower ranges for all three parameters, with statistically significant differences for HC and FL. Applying the updated ranges to the full NICHD Fetal Growth Studies cohort (n= 2,447), 2-3% of fetuses previously identified as having normal 2T growth velocity were reclassified as abnormal. Among these 2-3%, fetuses with slower 2T growth were more likely to be flagged as overgrowing their 3T potential, and fetuses with faster 2T growth were more likely to be flagged as undergrowing their 3T potential using IGA (Table).

This apparent growth disparity between trimesters raises concerns about IGA methods pathologizing potentially healthy “catch-up” growth, calling into question the assumption that 2T growth velocity accurately predicts 3T growth potential. This finding underscores the need for a critical reappraisal of IGA to ensure its validity across diverse populations and growth patterns.

Table. Number of third trimester scans classified as below expected, expected, or above expected, by second trimester growth velocity classification

	Second-Trimester Growth Velocity Classification		
	Head Circumference		
Third Trimester Classification	**Below Normal** (N=28 fetuses; n=69 scans)	**Normal** (N=2,396 fetuses; n=6,253 scans)	**Above Normal** (N=8 fetuses; n=21 scans)
Below Expected	7 (10.1)[1]	299 (4.8)	0 (0)
Expected	62 (89.9)	5874 (93.9)	21 (100)
Above Expected	0 (0)	80 (1.3)	0 (0)
	Abdominal Circumference		
	Below Normal (N=37 fetuses; n=92 scans)	**Normal** (N=2,377 fetuses; n=6,225 scans)	**Above Normal** (N=33 fetuses; n=91 scans)
Below Expected	1 (1.1)	314 (5)	17 (18.7)
Expected	70 (76.1)	5520 (88.7)	68 (74.7)
Above Expected	21 (21)	391 (6.3)	6 (6.6)
	Femur Length		
	Below Normal (N=45 fetuses; n=104 scans)	**Normal** (N=2,327 fetuses; n=6,094 scans)	**Above Normal** (N=11 fetuses; n=34 scans)
Below Expected	1 (1)	135 (2.2)	6 (17.6)
Expected	93 (89.4)	5766 (94.6)	26 (76.5)
Above Expected	10 (9.6)	193 (3.2)	2 (5.9)

[1] n (column %)

Perinatal & Pediatric

Association of maternal body mass index with longitudinal fetal growth assessed by three-dimensional ultrasonography Kathryn A. Wagner* Kathryn Wagner Jessica L. Gleason Zhen Chen Wesley Lee William A. Grobman Roger Newman Cuilin Zhang Stefanie Hinkle Luis Goncalves Seth Sherman Daniel W. Skupski Robert Gore-Langton Angela C. Ranzini Edward Chien Ronald Wapner Sabrina Craigo Jagteshwar Grewal Katherine L. Grantz

There is a current obesity epidemic in the US; from 2016-2019, there was an 11% increase in women entering pregnancy with obesity. Maternal obesity is associated with fetal overgrowth, as assessed by two-dimensional (2D) ultrasonography. However, 3D ultrasonography can characterize fetal lean and fat tissue and organ volumes, which may provide additional insight into fetal metabolic programming. Therefore, we evaluated fetal 3D measures across pregnancy by maternal pre-pregnancy BMI.

In the NICHD Fetal 3D Study (2015-2019), fetal body composition and organ volumes were measured at up to five ultrasound scans from 15-40 weeks by certified sonographers. BMI (kg/m2) was categorized as normal (18-<25; n=1567), overweight (25-<30; n=767), or obese (≥30; n=468), based on self-reported pre-pregnancy weight and height. Trajectories of fetal 3D measures were modeled using linear mixed effect models. Overall and weekly mean differences in fetal growth were tested across BMI category, adjusted for covariates.

Fetuses of women with overweight or obesity had significantly larger fractional arm and thigh volumes, from 25-26 weeks through 40 weeks, and larger abdominal area and maximum abdominal subcutaneous tissue thickness (SCTT) between 29-40 weeks, compared to women with normal BMI. Proportional to fractional limb volume, fetuses of women with obesity had significantly smaller lean but larger fat limb volumes from 15-34 weeks. Fetuses of women with overweight BMI had significantly larger lung volume from 22-31 weeks, while fetuses of those with obesity had significantly smaller lung volume from 17-20 weeks, compared to normal BMI. No overall differences were observed among limb SCTT or other organ volumes.

Fetuses of women with obesity had larger abdominal and limb measures, characterized by greater fat but less lean tissue accumulation, compared to normal BMI. Higher fat to lean tissue ratio may have implications for risk of cardiometabolic dysfunction across the life course.

Perinatal & Pediatric

Effectiveness of Powdered Micronutrients in Complementary Feeding for Anemia Prevention in Primary Health Care: A Pragmatic Clinical Trial in an African Context Ana Raquel Ernesto Manuel Gotine* Ana Gotine Marly Augusto Cardoso

Introduction: Anemia continues to be a significant public health issue among children, particularly in vulnerable populations, requiring the evaluation of strategies for its prevention and control. **Aim**: To assess the effectiveness of micronutrient powders (MNP) for preventing anemia during the first year of life, distributed by health professionals at primary health care in Nampula, Mozambique. **Methods**: This pragmatic clinical trial was conducted across two health centers, involving 275 infants who were randomly assigned to either the intervention group (IG, n=135) or the control group (CG, n=135). The IG received 90 sachets of MNP to be consumed once daily for up to 180 days. Data were collected through a sociodemographic questionnaire, hemoglobin (Hb) measurements (HemoCue®), and rapid malaria tests (First Response® Malaria Antigen P. falciparum Card Test). Intention-to-treat statistical analyses were performed using Stata 18, with t-tests, Pearson's chi-square tests, and adjusted linear regression for Hb mean differences (before and after the intervention), with significance set at $p < 0.05$. **Results**: At baseline, infants aged 6 to 8 months had a mean Hb of 102.0 g/L (SD 11.0) in the IG and 104.0 g/L (SD 11.0) in the CG. Anemia rates (Hb <110 g/L) were 74% (95% CI 66–80) in the IG and 66% (95% CI 58–74) in the CG. After the intervention, at 12 to 14 months, the IG had a mean Hb of 106.2 g/L (SD 10.6) and an anemia prevalence of 56% (95% CI 48–66), while the CG had a mean Hb of 99.5 g/L (SD 11.7) and an anemia rate of 79% (95% CI 70–85). After adjusting for variables such as child's age, wealth index, maternal age and education, prenatal visits, and stunting at baseline, the IG showed an increase in the adjusted mean Hb difference of 0.28 g/L (95% CI 0.02–0.55), while the CG showed a decrease of -0.43 g/L (95% CI -0.72 to -0.15). **Conclusion**: The findings suggest that MNP supplementation, when distributed by health professionals, has a positive impact on hemoglobin levels, underscoring the importance of nutritional interventions in regions with high anemia prevalence during infancy.

Keywords: Anemia; iron deficiency, complementary feeding, micronutrients, home fortification.

Perinatal & Pediatric

Nationally-Representative Associations Between ASD Diagnosis and Irregular Sleep Patterns Chiashuan Chang* Chiashuan Chang Amanda E. Ng

Background: Irregular sleep patterns among children are a growing health concern, particularly among those diagnosed with autism spectrum disorder (ASD). While prior research has established that poor sleep is prevalent among children with ASD, limited studies have examined whether an ASD diagnosis itself predicts irregular sleep timing on a national scale. Furthermore, the role of sex differences in the ASD-sleep relationship remains unclear, with mixed findings reported. This study aimed to investigate (1) whether an ASD diagnosis is associated with irregular sleep timing among U.S. children aged 0–17, and (2) whether this association differs by sex. **Method:** This study analyzed parent-reported data on 11,611 children from the 2020 and 2022 National Health Interview Survey (NHIS) using complete case analysis (2.49% missing data). Descriptive analyses were conducted to summarize continuous and categorical variables. Bivariate analyses, including chi-square tests and Spearman's correlations, assessed associations between study variables. Multinomial logistic regression was employed to examine the relationship between ASD diagnosis and irregular sleep timing (bedtime and wake-up time), adjusting for demographic factors (e.g., sex, parental education) and psychological factors (e.g., anxiety, depression). An interaction term (sex × ASD diagnosis) was included to evaluate potential sex differences. **Results:** After adjusting for covariates, children with ASD, relative to those who did not have ASD, were less likely to having a regular bedtime on some days compared to having a regular bedtime every day. In contrast, children with ASD, relative to those who were not, are more likely to never have regular wake-up times compared to having consistent wake-up times every day (OR: 2.13). However, no significant moderating effect of sex was observed.

Perinatal & Pediatric

Lead Exposure During Key Neurodevelopmental Stages: A Target Trial Using Multimedia Biomarkers to Assess Children's Cognitive Function in Mexico City Victor Florez-Garcia*
Victor Florez-Garcia Alexander Keil Amy Kalkbrenner

Background: Lead exposure is particularly harmful to neurodevelopment when it occurs during pregnancy and early childhood. Quantifying the impact of exposure reduction can help policymakers establish evidence-based thresholds from a public health perspective. **Objective:** This study aimed to evaluate the causal effect of hypothetical interventions restricting the use of lead-glazed pottery in Mexico City during pregnancy and early childhood on children's cognitive performance. **Methods:** We used data from the Programming Research in Obesity, Growth, Environment, and Social Stressors (PROGRESS) longitudinal birth cohort in Mexico City. Lead exposure levels were assessed in blood, urine, and hair during both pre- and postnatal periods. Children's intellectual functioning was measured using the McCarthy Scales of Children's Abilities, focusing on verbal, perceptual, and quantitative domains, as well as the composite General Cognitive Index (GCI). Multimedia biomarker (MMB) indexes were developed using Weighted Quantile Sum Regression (WQS) and Principal Component Analysis (PCA). G-computation was applied to estimate adjusted observed and predicted effect sizes (β) along with 95% confidence intervals (95%CIs). **Results:** We observed an increase in the General Cognitive Index score, with a maximum gain of 0.60 points [95%CI: -0.25, 1.46]. The MMB-WQS method demonstrated a greater effect than MMB-PCA for perceptual and quantitative scales. The highest cognitive gains occurred with a 40% reduction in lead exposure, yielding improvements in perceptual [Δβ:0.77; 95%CI:0.24, 1.30] and quantitative abilities [Δβ:0.51; 95%CI: -0.05, 1.08]. **Conclusion:** Our findings suggest that reducing lead exposure during pregnancy and early childhood—particularly by limiting or banning lead-glazed pottery—could enhance children's cognitive development by 48 months of age in Mexico City.

Perinatal & Pediatric

Association between prenatal exposure to chemical and nonchemical stressors and adolescent well-being among extremely low gestational aged newborns (ELGANs) Jenna Frey* Jenna Frey Lauren Eaves T. Michael O'Shea Rebecca C. Fry

Humans are exposed to an array of stressors in their built and social environments throughout the life course. Exposure to chemical and nonchemical stressors—particularly during critical windows of susceptibility such as *in utero*—have been separately and jointly associated with adverse health outcomes. Aiming to identify associations between prenatal exposure and adolescent health, we hypothesize that higher levels of negative stressors will be associated with lower levels of well-being and increased internalizing/externalizing behaviors.

Participants in this analysis (N=219) were a part of the Extremely Low Gestational Age Newborn (ELGAN) cohort which is made up of individuals born before 28 weeks of completed gestation in three US regions. Chemical stressors (11 metals/metalloids measured in umbilical cord samples) and nonchemical stressors (SES composite variable including <12 years of educational attainment, Medicaid insurance use, "single" marital status, and food stamp use collected by a maternal interview at birth) were assessed. Three outcomes were measured at age 15. Overall wellbeing was measured through the PROMIS Global health self-report measure and internalizing and externalizing behaviors through the Child Behavior Checklist Youth Self-Report form. Metals were natural log-transformed for normality. Regression models were run for each of the 11 metals and the SES variable for each outcome.

In models adjusted for maternal age at birth and smoking status during pregnancy, the metals were positively associated with overall well-being: zinc (β=2.23, p=0.006), strontium (β=1.68, p=0.003), and barium (β=1.25, p=0.007). Adjusted models showed associations between the SES sum and internalizing behaviors (β=1.29, p=0.05) and the SES sum and externalizing behaviors (β=1.05, p=0.02). Next steps include testing for interaction between chemical and nonchemical stressors and evaluating mixtures effects of coexposure to multiple metals through quantile g-computation.

Perinatal & Pediatric

Fertility treatment and offspring neurocognitive functioning at 10 years Diane L. Putnick*
Diane Putnick Akhgar Ghassabian Thomas G. O'Connor Edwina H. Yeung

Some research suggests that children conceived with fertility treatment have increased risk of attention-deficit/hyperactivity disorder (ADHD) compared to those conceived without. However, subfertility rather than treatment may be the operative factor.

The Upstate KIDS longitudinal birth cohort of children conceived without and with fertility treatment was followed through 10 years (M=10.0; SD=.6). Children living within 2 hours of 4 clinic sites across New York state were invited for in-person assessments of neurocognitive functioning using the NIH Toolbox Cognition Battery (N=166). At those visits, 142 mothers and 144 children (87%; 99 singletons and 45 randomly-selected twins from the pair) completed the NIH Toolbox, validated tests measuring inhibitory control and attention, working memory, cognitive flexibility, processing speed, episodic memory, reading, and receptive vocabulary.

Analyses of variance and covariance estimated mean differences and 95% confidence intervals of cognitive scores among treatment (n=64) and no-treatment (n=80) groups. Groups were similar on child sex and age. Mothers in the treatment group were older, more likely to be college educated, and have private health insurance. There were no significant differences in child cognition for those conceived without and with fertility treatment (Table 1). Mothers who used fertility treatments scored lower on the flanker inhibitory control and attention and oral symbol digit test than nonusers after adjustment (Table 1), but similarly on other scales.

Findings suggest that children born following fertility treatment did not differ from those born without fertility treatment. However, mothers who used treatment scored lower on two tests measuring inhibitory control and attention and processing speed, which are core features of ADHD. If replicated, these findings suggest fertility treatment does not put children at risk for ADHD, but underlying subfertility may be associated with ADHD features.

Table 1
Unadjusted and adjusted comparisons of child and mother cognition measures by fertility treatment

NIH Toolbox Test	No treatment (n = 80) *M*(*SD*)	Treatment[1] (n = 64) *M*(*SD*)	Unadjusted B	Unadjusted 95%CI	Adjusted B	Adjusted 95%CI
Child						
Composite[a]	101.8(16.5)	105.3(16.0)	3.53	-2.00, 9.07	0.80	-5.21, 6.81
Fluid[a]	97.3(18.4)	98.2(14.4)	0.94	-4.73, 6.61	-0.11	-6.54, 6.32
Flanker inhibitory control and attention[b]	93.2(15.0)	91.5(12.2)	-1.69	-6.29, 2.91	-2.19	-7.41, 3.03
List sorting working memory[c]	103.2(14.1)	106.2(16.1)	2.93	-2.08, 7.94	1.53	-4.17, 7.23
Dimensional change card sort	97.5(15.4)	95.4(14.0)	-2.14	-7.05, 2.77	-2.90	-8.49, 2.68
Pattern comparison processing speed	94.6(22.4)	92.8(22.1)	-1.83	-9.21, 5.56	-1.39	-9.80, 7.01
Picture sequence memory[d]	102.6(14.9)	107.0(16.3)	4.40	-0.84, 9.64	3.74	-2.32, 9.81
Crystallized[e]	105.6(14.7)	109.4(17.3)	3.84	-1.45, 9.14	0.91	-4.95, 6.76
Oral reading recognition	103.8(15.4)	107.4(18.3)	3.69	-1.86, 9.24	1.57	-4.63, 7.77
Picture vocabulary	105.2(12.8)	108.4(16.0)	3.20	-1.55, 7.95	0.42	-4.90, 5.74
Mother (all Fluid)						
Flanker inhibitory control and attention[c]	92.4(14.9)	88.9(12.7)	-3.51	-8.18, 1.16	-5.58	-10.18, -0.97
List sorting working memory[c]	101.8(14.3)	106.5(13.9)	4.74	0.03, 9.44	3.25	-1.50, 7.99
Dimensional change card sort[c]	108.8(15.5)	106.4(16.5)	-2.33	-7.66, 3.00	-3.45	-8.98, 2.08
Oral symbol digit[c*]	93.6(13.5)	87.0(22.7)	-6.63	-12.71, -0.55	-7.60	-14.01, -1.18
Rey auditory verbal learning[c*]	28.4(5.1)	27.0(5.4)	-1.46	-3.21, 0.28	-1.51	-3.33, 0.32

Note. All scores were age-standardized except the mother's Oral symbol digit test and Rey auditory verbal learning test. Child models are adjusted for maternal age, race/ethnicity, education, pregnancy smoking and drinking, insurance status, gestational age at birth, plurality, and child sex. Mother models are adjusted for maternal race/ethnicity, education, pregnancy smoking and drinking, and insurance status.

[1] Treatment included in vitro fertilization, intracytoplasmic sperm injection, assisted hatching, frozen embryo transfer, gamete/zygote intrafallopian transfer, ovulation induction, and intrauterine insemination.

[a] ns for this analysis were 75 no treatment and 62 treatment.

[b] ns for this analysis were 80 no treatment and 63 treatment.

[c] ns for this analysis were 79 no treatment and 63 treatment.

[d] ns for this analysis were 76 no treatment and 63 treatment.

* Additionally adjusted for maternal age

Perinatal & Pediatric

Gestational weight gain and child growth and development in low and middle-income countries: an individual participant data meta-analysis Janaina Calu Costa* Janaina Calu Costa Nandita Perumal Uttara Partap Ilana Cliffer Dongqing Wang Enju Liu Molin Wang Wafaie W. Fawzi

Background: Gestational weight gain (GWG) influences maternal and child health with long-term impacts; however, evidence is mainly from high-income settings. We explored the association between GWG and long-term child growth and development in low- and middle-income countries (LMICs). **Methods:** Systematic literature searches (PubMed, Embase, Web of Science, and Cochrane) identified prospective cohorts and randomized trials from LMICs collecting pregnancy weight and child growth or neurodevelopment data. GWG adequacy was defined as the ratio of the observed over the recommended weight gain based on the Institute of Medicine guidelines. Child anthropometrics were summarized by age (15 days to 6 months, 6-12, 12-24, and 24-36 months). Neurodevelopment z-scores were derived from the 18-month assessment. Two-stage meta-analyses were used, with study-specific log-binomial or linear regression in the first stage and random-effects models for pooled estimates in the second. **Results:** Children born to women who had severely inadequate GWG, compared to those with adequate GWG, presented lower mean anthropometric z-scores at every age (27 studies, 86,540 mother-child pairs). Significant mean differences (MD) ranged from -0.14 to -0.30 standard deviations (SD) across different age groups for height-for-age, weight-for-age, and weight-for-height; and between -0.11 and -0.21SD for body mass index (BMI)-for-age. Children of women with severely inadequate GWG also showed lower neurodevelopment z-scores (7 studies): fine motor [MD = -0.08SD (95%CI -0.16, -0.01)], gross motor [-0.12SD (-0.19, -0.05)], receptive language [-0.10SD (-0.19, -0.01)], and socioemotional domains [-0.10SD (-0.20, -0.01)]. Pre-pregnancy BMI modified associations between GWG and child growth at up to 12 months. **Conclusion:** Suboptimal GWG was associated with short- and long-term child growth and development and support the need for interventions to improve women’s nutrition before and during pregnancy.

LATEBREAKER

Perinatal & Pediatric

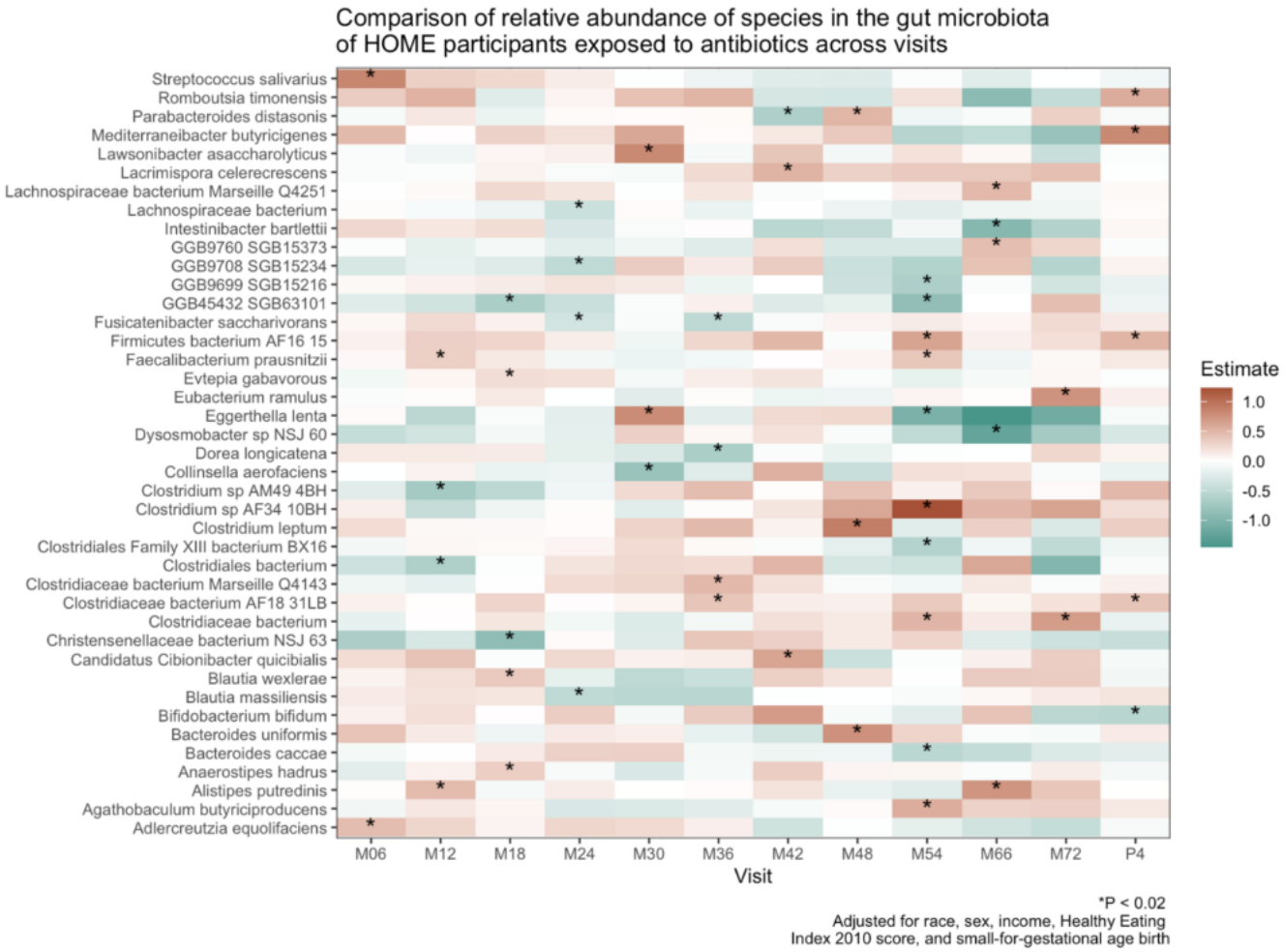
Antibiotic use in childhood and gut microbiome diversity in adolescents: The Health Outcomes and Measures of the Environment (HOME) Study Christian Daniele* Christian Daniele Melinda C. MacDougall Bruce P. Lanphear Jessie P. Buckley Aimin Chen Kim M. Cecil Kimberly Yolton Joseph M. Braun Hannah E. Laue

Background: Antibiotic use has been associated with reduced gut microbiome diversity, but it is unclear if antibiotic-induced dysbiosis at certain developmental windows has a long-term impact. This study examined the associations between antibiotic use during childhood with gut microbiome diversity in adolescents.

Methods: We collected antibiotic use with interviewer-administered questionnaires with primary caregivers up to 12 times between ages 6 months and 12 years. Additionally, children provided a fecal sample at age 12 years, followed by DNA extraction and metagenomic sequencing. Crude and adjusted linear regression models with generalized estimating equations (GEE) were used to determine associations of repeated measures of antibiotic use with Shannon diversity, inverse Simpson diversity, relative species abundances, and pathway relative abundances at age 12 years (adjusted for race, sex, income at follow-up, Healthy Eating Index 2010 score, and small for gestational age).

Results: The prevalence of antibiotic use ranged from 9.6% to 51.8% and was highest at age 12 months**.** Participants who reported antibiotic use at month 36 had lower Shannon diversity (adjβ: -0.12, 95% Confidence Interval (CI) = -0.24 – -0.01) and inverse Simpson diversity (adjβ: -4.82, 95% CI = -7.79 – -1.84) compared with those who did not. There were no significant associations in diversity indices found for other visits. Childhood antibiotic use was generally associated with reduced relative abundance of Eggerthella and Dysosomobacter sp. and increased relative abundance of Clostridium and Clostridiaceae spp. ($P < 0.02$), although estimates varied across exposure windows.

Discussion: Antibiotic use during childhood may lead to dysbiosis of gut microbiome composition and diversity. Further research is needed to determine whether this has broader health consequences.


Comparison of relative abundance of species in the gut microbiota of HOME participants exposed to antibiotics across visits
Streptococcus salivarius
Romboutsia timonensis
Parabacteroides distasonis
Mediterraneibacter butyricigenes
Lawsonibacter asaccharolyticus
Lacrimispora celerecrescens
Lachnospiraceae bacterium Marseille Q4251
Lachnospiraceae bacterium
Intestinibacter bartlettii
GGB9760 SGB15373
GGB9708 SGB15234
GGB9699 SGB15216
GGB45432 SGB63101
Fusicatenibacter saccharivorans
Firmicutes bacterium AF16 15
Faecalibacterium prausnitzii
Evtepia gabavorous
Eubacterium ramulus
Eggerthella lenta
Dysosmobacter sp NSJ 60
Dorea longicatena
Collinsella aerofaciens
Clostridium sp AM49 4BH
Clostridium sp AF34 10BH
Clostridium leptum
Clostridiales Family XIII bacterium BX16
Clostridiales bacterium
Clostridiaceae bacterium Marseille Q4143
Clostridiaceae bacterium AF18 31LB
Clostridiaceae bacterium
Christensenellaceae bacterium NSJ 63
Candidatus Cibionibacter quicibialis
Blautia wexlerae
Blautia massiliensis
Bifidobacterium bifidum
Bacteroides uniformis
Bacteroides caccae
Anaerostipes hadrus
Alistipes putredinis
Agathobaculum butyriciproducens
Adlercreutzia equolifaciens
M06
M12
M18
M24
M30
M36
M42
M48
M54
M66
M72
P4
Visit
Estimate
1.0
0.5
0.0
-0.5
-1.0
*P < 0.02
Adjusted for race, sex, income, Healthy Eating Index 2010 score, and small-for-gestational age birth

LATEBREAKER

Perinatal & Pediatric

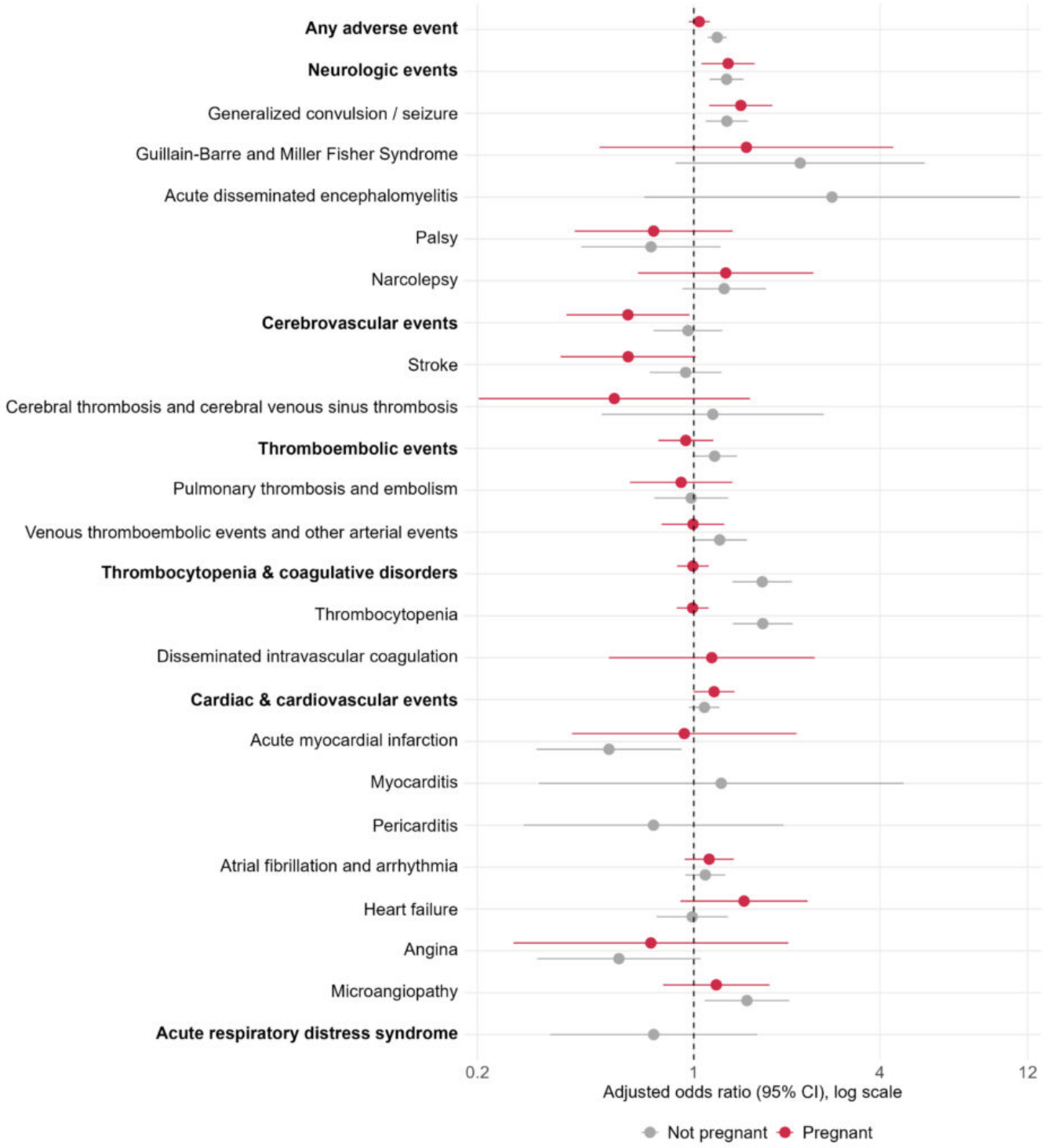
Should I wait? Methodological challenges in assessing vaccine safety in pregnancy and risk of adverse events following COVID-19 vaccination in women of reproductive capability, United States. Stacey Rowe* Stacey Rowe Sheena Sullivan Julia Koerber Flor Munoz Matthew Coates Onyebuchi Arah Annette Regan

Introduction: Pregnant people are commonly excluded from randomized controlled trials assessing vaccine safety and efficacy. Accordingly, vaccine safety in pregnancy is commonly assessed post-licensure using real world data. Previous studies have demonstrated the safety maternal vaccines, including COVID-19 vaccines. However, safety outcomes are rarely compared by pregnancy, and given pregnancy-induced immunologic changes, these outcomes may vary. We describe methodological challenges comparing outcomes by pregnancy; and quantify the incidence of adverse events given COVID-19 vaccination in women of reproductive capability, examining pregnancy as a potential risk modifier.

Methods: We conducted an exposure-matched cohort study capturing US women between 11 December 2020 and 30 September 2022. Public and private insurance claims for inpatient and outpatient medical encounters were used to identify pregnancy status, COVID-19 vaccination and medically-attended adverse events. Odds ratios for adverse events given COVID-19 vaccination were estimated using logistic regression models, with pregnancy as an effect modifier.

Results: Among 533,249 pregnant and 471,916 non-pregnant women, COVID-19 vaccine coverage was 15.2% and 57.4%, respectively. We identified 3,556 (120.6 per 10,000) adverse events among pregnant women, with no differences between those vaccinated and unvaccinated (aOR=1.04 [95%CI 0.96,1.13]). The crude incidence of adverse events was lower among non-pregnant women (n=3,581; 95.5 per 10,000); however, vaccination effects were stronger (aOR=1.19, 95%CI 1.11,1.28). The difference between pregnancy status was significant (p=0.011).

Conclusion: Adverse events following COVID-19 vaccination are rare among pregnant and non-pregnant women. Importantly, our study suggests that being pregnant does modify the effect of COVID-19 vaccines on the risk of adverse events, shifting estimates towards the null. The vaccine effects are stronger for non-pregnant women.


Any adverse event
Neurologic events
Generalized convulsion / seizure
Guillain-Barre and Miller Fisher Syndrome
Acute disseminated encephalomyelitis
Palsy
Narcolepsy
Cerebrovascular events
Stroke
Cerebral thrombosis and cerebral venous sinus thrombosis
Thromboembolic events
Pulmonary thrombosis and embolism
Venous thromboembolic events and other arterial events
Thrombocytopenia & coagulative disorders
Thrombocytopenia
Disseminated intravascular coagulation
Cardiac & cardiovascular events
Acute myocardial infarction
Myocarditis
Pericarditis
Atrial fibrillation and arrhythmia
Heart failure
Angina
Microangiopathy
Acute respiratory distress syndrome
0.2
1
4
12
Adjusted odds ratio (95% CI), log scale
Not pregnant
Pregnant

LATEBREAKER

Perinatal & Pediatric

Examining the effect of a continuous Medicaid enrollment policy on postpartum diabetes screening Teresa Janevic* Teresa Janevic Annabelle Ng Frances Howell Ashley Fox Ellerie Weber

Meeting clinical guidelines for patients with gestational diabetes, which recommend glucose screening within 6-12 weeks postpartum, has been challenging. Extending postpartum Medicaid coverage may increase screening. We leveraged the continuous enrollment provision of the Families First Coronavirus Act (FFCRA) to test if the incidence of postpartum diabetes screening increased during FFCRA. We used 2019-2021 claims data from the Transformed Medicaid Statistical Information System Analytic Files. We included n=352,218 Medicaid beneficiaries from 50 states and DC, who had a live or stillbirth from January 2019–June 2021 and a diagnosis of pre-existing or gestational diabetes. We defined three outcomes within 6 months postpartum: received OGTT screening, A1c screening, or either. Covariates included hypertension, maternal age, and severe maternal morbidity. We estimated interrupted time series models. We defined segments as before FFCRA (1/1/19-11/18/19), FFCRA with COVID-19 healthcare closures (11/19/19-6/30/20) and during FFCRA (7/1/20-6/30/21). We used a covariate-adjusted fixed effect linear regression model with state clustered standard errors. At baseline, 33.8% of patients received any screening within 6 months, 31.1% received an OGTT test and 14.0% received an A1c test. During the closure period, 4.7 per 100 fewer patients were screened postpartum (95%CI= -5.8, -3.5), with similar findings for both OGTT and A1c testing. Screening then rebounded with an increase of 0.5 per 100 additional patients screened per week (95%CI=-0.2, 1.3). After the closure period, testing was similar to the pre-FFCRA period (β=-0.8, 95%CI=-2.1, 0.5), suggesting continuous enrollment did not increase screening. Patterns for both OGTT and A1c testing were similar, as were adjusted coefficients. Findings suggest that interventions tailored to Medicaid enrollees eligible for postpartum extension policies are urgently needed to maximize the opportunity created to improve maternal health.

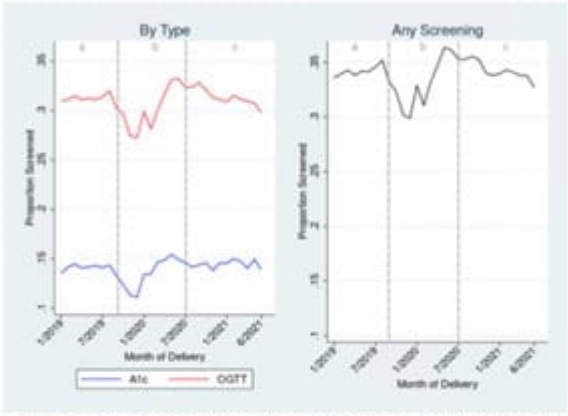


Figure 1. Unadjusted proportion of Medicaid beneficiaries with preexisting or gestational diabetes receiving diabetes screening within six months postpartum by month of delivery (a) before FFCRA, (b) FFCRA - COVID disruption, (c) FFCRA (N=352,218).

LATEBREAKER

Perinatal & Pediatric

Beyond survival: Investigating incident perinatal mental illness following severe maternal morbidity Maya Rajasingham* Maya Rajasingham Priya Premranjith Daniel Atkinson Rohan D'Souza Benicio N. Frey Sheryl Green Susan Jack Giulia M. Muraca

Introduction

Universal approaches to preventing mental health disorders in the perinatal period have not been successful; however, targeted interventions in high risk groups have shown promise. Individuals who experience severe maternal morbidity (SMM) may be one such group at uniquely high risk for perinatal mental illness, yet little is known about the mental wellbeing of individuals following SMM. Thus, we aimed to quantify the association between SMM and perinatal mental illness.

Methods

We conducted a population-based, propensity-score matched cohort study of nulliparous individuals who gave birth ≥20 weeks' gestation in Ontario, Canada (2012-2020) using linked administrative data obtained from ICES (formerly the Institute of Clinical Evaluative Sciences). Individuals with a history of mental illness were excluded. SMM and mental illness were identified using a validated algorithms of inpatient and outpatient diagnosis, intervention and billing codes. Individuals were followed until a mental illness diagnosis or the end of the follow up period (one year postpartum). Cox proportional hazard models were fit to evaluate the association between SMM and incident perinatal mental illness.

Results

The exposed, 5,517 individuals who experienced SMM between conception and six weeks postpartum, were propensity score-matched to 22,068 individuals who did not experience SMM on the same date. The incidence of perinatal mental illness was 13.0% in individuals with SMM and 9.3% among individuals without SMM. The risk of perinatal mental illness was 36% higher among individuals with versus without SMM (hazard ratio 1.36, 95% confidence interval 1.25-1.45). For both groups, mental illness was largely driven by mood and anxiety disorders.

Conclusions

SMM is associated with an increased risk of mental illness within one year postpartum. These findings underscore the importance of perinatal supports for individuals with SMM that address both their physical and mental health needs.

Perinatal & Pediatric

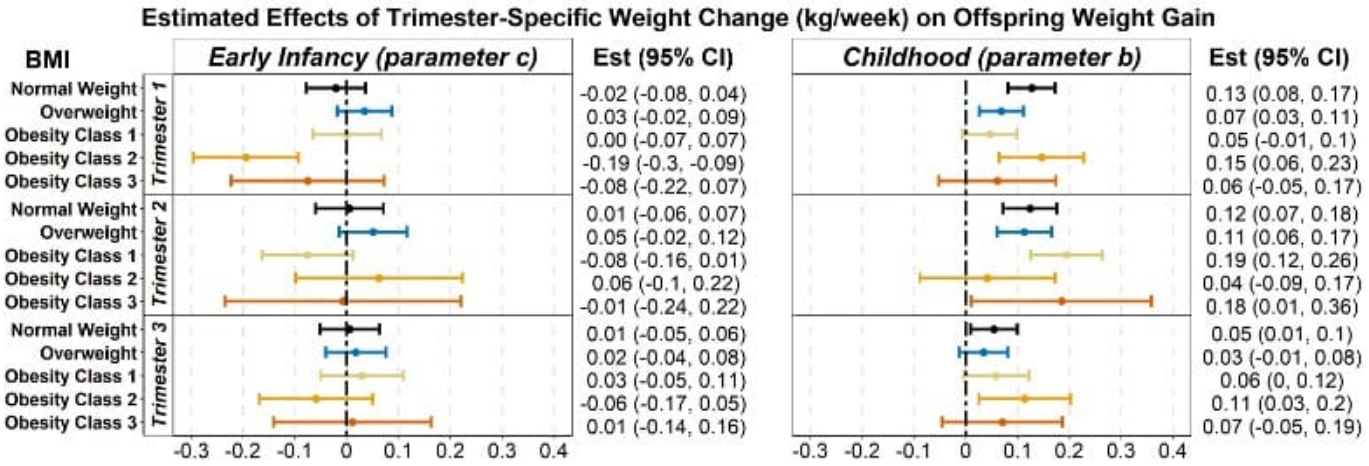
Gestational weight loss or gain and offspring growth in infancy and childhood: differences by trimester and pre-pregnancy BMI Anna Booman* Janne Boone-Heinonen Dang Dinh Anna Booman Byron A Foster Erin LeBlanc Natalie Rosenquist Rachel Springer Evelyn Sun Kimberly K Vesco

Background: Higher gestational weight gain (GWG) is well known to be associated with higher offspring body mass index (BMI), but less is known about associations with early childhood growth patterns that lead to high childhood BMI, especially in higher pre-pregnancy BMI groups.

Methods: We examined 18,228 children born to pregnant people receiving care from a national network of community health centers. We estimated nonlinear growth during infancy and linear growth in childhood using the Jenss model (birth to 5 years of age). In pre-pregnancy BMI-stratified analysis (normal weight, overweight, obesity class I, II, III), we calculated trimester-specific weight change using latent piecewise trajectory models, then modeled infancy (~0-12 months) or childhood (~12 to 60 months) weight gain parameters as a function of trimester 1, 2, or 3 GWG rate and maternal characteristics using linear regression.

Results: In general, higher trimester-specific GWG rates were not associated with early infancy weight gain, particularly in children of birthing parents with pre-pregnancy normal weight through obesity class I [range of estimates (95% CI): -0.08 (-0.22, 0.07) to 0.05 (-0.02, 0.12)]. In contrast, GWG was associated with faster childhood weight gain [range of estimates (95% CI): 0.03 (-0.01, 0.08) to 0.19 (0.12, 0.26)]. Notably, findings were mixed for pre-pregnancy obesity class II and III groups: for example, for obesity class II, trimester 1 GWG was associated with slower early infancy weight gain followed by faster childhood weight gain. In general, associations were stronger for trimester 1 and 2 than for trimester 3 GWG.

Discussion: Higher GWG in early pregnancy may lead to higher child BMI via faster growth in childhood, rather than in infancy. Given that rapid growth in infancy is more strongly linked to future risk of diabetes and other conditions, these findings suggest a need to understand the long-term impacts of GWG-induced childhood weight gain.



Perinatal & Pediatric

The Association of Maternal Intellectual and Developmental Disabilities with Adverse Birth and Infant Outcomes in California Catherine Psaras* Catherine Psaras Gretchen Bandoli Rita Ryu

Background. Intellectual and developmental disabilities (IDD) involve cognitive and adaptive deficits beginning before age 18–22. While fertility rates among individuals with IDD are rising alongside recognition of their reproductive rights, they still face significant social, healthcare, and health disparities during pregnancy. This study aimed to examine the relationship between IDD subtypes and adverse birth and infant outcomes. **Methods.** This population-based study analyzed linked data from California (2007–2021), including birth, infant death, discharge, emergency department, and ambulatory surgery center records. We compared singleton births to women with preexisting IDD (autism (ASD), cerebral palsy (CP), intellectual disability (ID), chromosomal abnormalities, and other IDD) to those without, using ICD codes to identify disabilities. The primary outcomes were NICU admission, small for gestational age (SGA), and very pre-term birth (PTB). Relative risks were adjusted for maternal age at birth. **Results.** The data included 6,430,534 singleton infants born from 2007–2021. 4,713 infants born among women with IDD (non-mutually exclusive subtypes: ASD: 458; CP: 1019; ID: 1817; chromosomal abnormalities: 1571; other IDD: 600). All five IDD subtypes were associated with increased risks for adverse infant outcomes. The strongest associations were observed in infants born to mothers with intellectual disabilities (RR [95% CI]: NICU: 3.12 [2.74, 3.56]; SGA: 1.86 [1.63, 2.13]; PTB: 2.87 [2.05, 4.01]) and chromosomal abnormalities (RR [95% CI]: NICU: 3.21 [2.87, 3.59]; SGA: 1.65 [1.47, 1.86]; PTB: 4.07 [3.07, 6.50]). **Discussion.** Women with IDD face significantly higher risks of adverse birth and infant outcomes. Given the increasing fertility rates in this population, further research is essential to develop strategies to prevent these outcomes and address associated disparities.

Perinatal & Pediatric

Combined effects of indoor environmental and outdoor PM2.5 influences on early asthma in the ECHO birth cohort consortium Akihiro Shiroshita* Akihiro Shiroshita Antonella Zanobetti Brent A. Coull Patrick H. Ryan Soma Datta Jeffrey Blossom Emily Oken James E. Gern Heike Luttmann-Gibson Eneida A. Mendonca Sima K. Ramratnam Sheryl L. Rifas-Shiman Joanne E Sordillo Veronica A. Wang Paloma I. Beamer Daniel J. Jackson Christine C. Johnson Gurjit K. Khurana Hershey Fernando D. Martinez Rachel L. Miller Katherine Rivera-Spoljaric Edward M. Zoratti Tina V. Hartert Diane R. Gold

Background: The individual effects of both indoor and outdoor environmental exposures remain unknown. This study aimed to evaluate the independent associations of water damage/home dampness, pets, dust mite allergen, and PM2.5 with childhood asthma development.

Methods: We included children from nine birth cohort sites from ECHO (Environmental Influences on Child Health Outcomes), including Project Viva and CREW (CAS, CCAAPS, CCCEH, COAST, EHAAS, IIS, URECA, and WHEALS). Exposures were (1) water damage/home dampness, dogs/cats at home, and dust mite allergen in the bed or bedroom during infancy/childhood, and (2) average ambient PM2.5 levels during the first three years of life. The self-reported history of water damage/home dampness and the presence of dogs and cats at home were collected by questionnaires. Dust mite allergen was measured by monoclonal antibody ELISA assays. We used previously validated predictive models to estimate the levels of PM2.5 at each participant's residential address. The outcome was time to asthma diagnosis from age 1 month to 5 years. We applied Cox proportional hazards models using both indoor environmental exposure and PM2.5 as exposures and adjusting for both individual-level and neighborhood-level confounders.

Results: We included 6,300 children with birth years between 1987 and 2016. We found a detrimental association of water damage/home dampness in infancy/childhood and a protective association of dogs in the home in infancy with risk of childhood asthma regardless of PM2.5 adjustment. The independent effect of having both water damage/home dampness and high PM2.5 relative to not having either was strongly associated with asthma development (hazard ratio: 1.97 [95% confidence interval: 1.19–3.26). There were no significant associations with cats in the home or dust mites.

Conclusion: Our study demonstrated that both outdoor air pollutants and indoor exposures should be considered together as risk factors for asthma.

Perinatal & Pediatric

Blood Lead Levels and Risk of Asthma amongst an Urban Clinical Cohort of Children Yijun Liu* Yijun Liu Jing Nie Heather K. Lehman Marina Oktapodas Feiler

Objective

To explore the association between peak blood lead levels (BLL) and subsequent asthma diagnosis in an urban clinical cohort of children who received health care through the Temple University Hospital System (TUHS) in Philadelphia, PA, between 2010 and 2020.

Study design

We conducted a retrospective cohort study using electronic health record (EHR) data from TUHS. Eligible participants included all children 10 years of age or younger with at least one laboratory measured BLL (N=14,217). Peak BLL (µg/dl) were extracted from laboratory test results in the EHR. Log-binomial regression models were fit to estimate the risk ratios (RR) and 95% confidence intervals (CI) between BLLs and asthma diagnosis (captured by ICD codes), adjusting for race, insurance, and age at blood sample collection. Secondary outcomes included asthma severity and exacerbations.

Results

A total of 3488 participants were diagnosed with asthma, the majority of whom were male (57.37%) and Black (59.78%). The mean age at blood sample collection for BLL measurements among those with asthma was 23.19 months (SD=16.02). Among all children, 27.24% had a peak BLL of ≥ 3.5 µg/dl. Compared to children with BLL <1µg/dl, adjusted RR of asthma diagnosis for those with a BLL of 1.0 – 3.4 µg/dl was 1.89 (95% CI 1.55–2.31), while risk for those with a BLL ≥ 3.5 µg/dl was 1.94 (95% CI: 1.56-2.40). Adjusted RR were slightly higher for males than females. No significant association was observed between elevated BLLs and asthma severity. However, higher BLLs were significantly associated with increased frequency of asthma events.

Conclusion

Children with higher BLLs had an increased risk of asthma diagnosis. Importantly, associations were observed for children with BLLs below the current CDC-set action level. These findings emphasize the importance of addressing environmental lead exposure to mitigate asthma risk in children, even among children with low-level exposure.

Perinatal & Pediatric

Racial and Ethnic Disparities in Mortality among Children with Congenital Heart Defects: A Scoping Review Jenil Patel* Jenil Patel Maria D. Politis Elijah H. Bolin Lydia Famuyide Wendy N. Nembhard

Background:
Congenital heart disease (CHDs) are the most common congenital anomalies, and mortality vary by race and ethnicity. This scoping review summarizes studies reporting CHD mortality by race and ethnicity, presenting an integrated summary of mortality metrics including rates, in-hospital mortality, and survival.

Methods:
We reviewed peer-reviewed studies from PubMed and Web of Science (1980–2019) reporting mortality among children under age 18 with CHDs by race and ethnicity. Outcome measures included hazard ratios (HRs), odds ratios (ORs), and Kaplan-Meier survival probabilities.

Results:
In total, 18 studies met inclusion criteria, spanning population-based analyses, post-surgical mortality, and survival probability estimates. Among population-based studies, mortality rates for non-Hispanic (NH) White children with CHDs ranged from 0.4 to 9.1 per 10,000 live births, and from 0.5 to 10.0 for NH Black children. Post-surgical mortality studies showed substantial variability, with rates for NH White children with CHDs from 0.2 to 57.0 per 1,000 and from 0.3 to 63.0 per 1,000 for NH Black children. Cox proportional hazard regression models reported HRs indicating higher mortality risks among NH Black and Hispanic children with CHDs compared to NH White children. In-hospital and survival rates in childhood were also disproportionately lower for NH Black and Hispanic children, as shown by ORs and Kaplan-Meier analyses from US states like Florida and Texas.

Conclusions:
Significant racial and ethnic disparities in mortality was consistently reported for children with CHDs, particularly in post-surgical and in-hospital settings. These findings underscore the need for targeted research to understand disparities and improve equitable healthcare access for CHD-affected populations.

Perinatal & Pediatric

Exploring Maternal Thyroid Hormones as Mediators in the Association Between Prenatal Exposure to Endocrine Disrupting Chemicals and Child Cognition in the SELMA study

Marlene Stratmann* Marlene Stratmann Chris Gennings Carl-Gustaf Bornehag

Background: Endocrine disrupting chemicals (EDCs) are associated with both thyroid hormones and neurodevelopment, yet, no previous studies have looked at the potential mediating effect of thyroid hormones on the association between EDC exposure and neurodevelopment.

Aims: To explore if the association between prenatal exposure to EDCs and child neurodevelopment is mediated by thyroid hormones, stratified by child sex and gestational age at the time of sample collection.

Methods: For 572 mother-child pairs from the Swedish Environmental Longitudinal, Mother and child, Asthma and allergy (SELMA) study, a mixture of 26 EDCs (phenols, phthalates,per- and polyfluoroalkyl substances and persistent chlorinated compounds) and thyroid hormones, as measured by a ratio between thyroxine (T4) and triiodothyronine (T3), were measured in maternal serum and urine. Neurodevelopment of the child was assessed with the Wechsler Intelligence Scale for Children. We used a weighted quantile sum regression index to divide the mixture into deciles and create one exposure variable. Linear regression analyses were adjusted for relevant confounders and stratified by sex, as well as early or late gestational age at time of sampling (<10 or ≥ 10 weeks gestation). Mediation was measured using the causal framework and the product method. Chemicals of concerns were identified in those that show a potential mediating effect by thyroid hormones.

Results: For boys (≥ 10 weeks gestation) the average causal mediation effect of the T4/T3 ratio was -0.32 (95% CI -0.82, 0.02), corresponding to a non-significant mediated proportion of 20%. For boys (<10 weeks gestation) and girls (<10 and ≥ 10 weeks of gestation), no mediation could be detected. Chemicals of concern for boys (≥ 10 weeks gestation) are PBA, BPF, TCP, MCiNP, MEP and MBzP.

Conclusion: These results point towards a potentially important mediating effect by TT4/TT3 ratio in the mother and a lower IQ in boys (≥ 10 weeks gestation).

Perinatal & Pediatric

Characterizing postnatal trajectories of breast bud diameter in male and female infants using latent class mixed models Paige E. Tomer* Paige Tomer Shanshan Zhao Natalie D. Shaw Virginia A. Stallings Andrea Kelly Walter J. Rogan David M. Umbach Mandy Goldberg

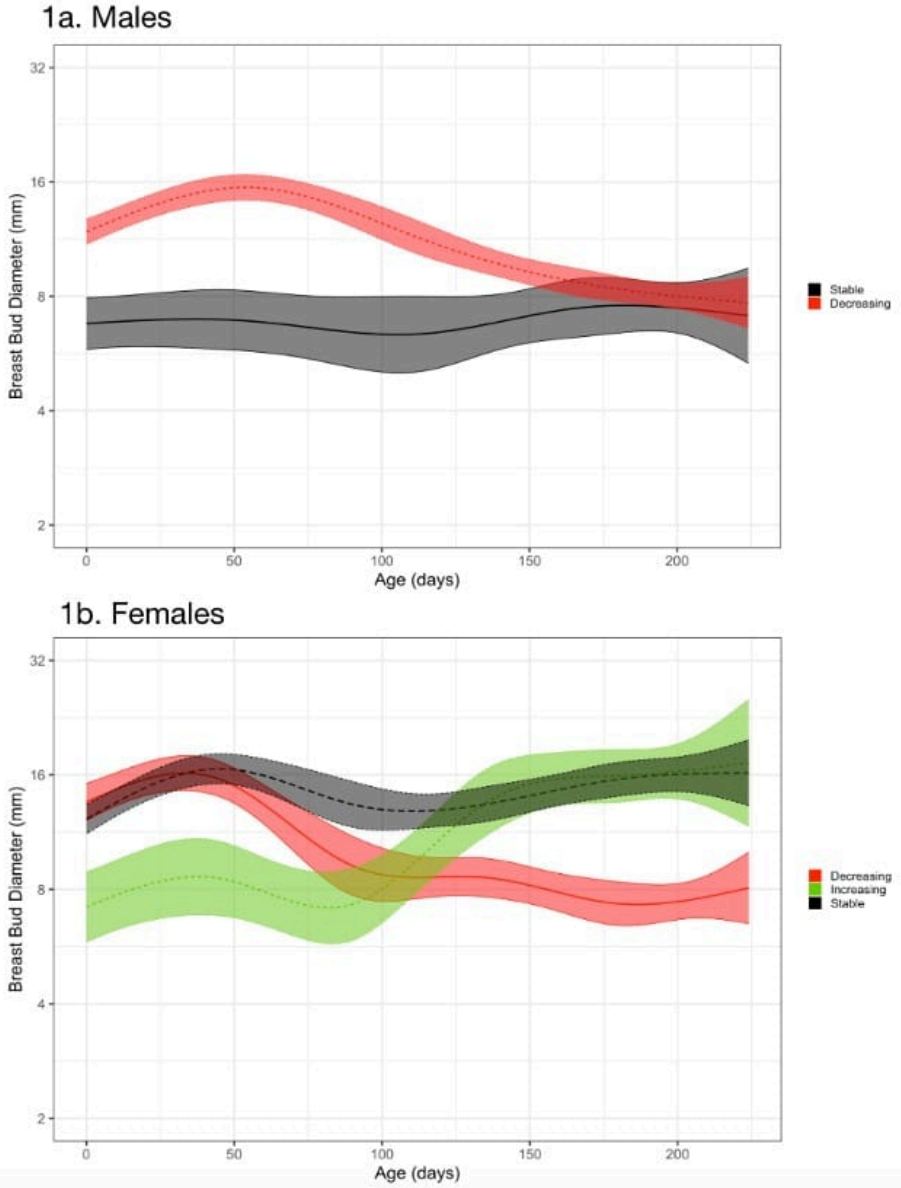
Background: Most infants are born with breast tissue that is expected to regress. The natural history of breast tissue across minipuberty, a period of sex-specific postnatal endocrine activity, has not been well-characterized. Our objective was to describe variation in sex-specific age trajectories of breast bud diameter across minipuberty.

Methods: We used data from 147 boys and 136 girls participating in the Infant Feeding and Early Development study, a longitudinal cohort of healthy, term infants enrolled during 2010-2013 from the Philadelphia area. Breast bud diameter was assessed via ultrasound within 72 hours of birth and every 4-8 weeks thereafter up to 24 weeks in boys and 32 weeks in girls. We log2-transformed the geometric mean of left and right breast bud diameters and applied latent class linear mixed models to cluster age trajectories of breast bud diameter in boys and girls separately. We selected the number of latent classes using several statistical metrics and visual inspection. We used the LCMM package in R 4.4.1 for model fitting.

Results: We identified two trajectory groups in boys: one with a larger diameter at birth that declined with age (n=115, 78%), the other with a smaller initial diameter that remained stable (n=32, 22%); the groups converged by age 24 weeks (Figure 1a). Three trajectory groups were identified in girls: stable (n=75, 55%), decreasing (n=42, 31%), and increasing (n=19, 14%) (Figure 1b). Compared to the stable group, the decreasing group had a similar diameter at birth that decreased with age, whereas the increasing group started with a smaller diameter and converged with the stable group by age 20 weeks.

Conclusions: We identified distinct patterns of breast bud diameter in male and female infants; patterns that may reflect differences in endocrine activity during minipuberty. Most infant girls maintained or experienced growth in breast bud tissue, while only a minority exhibited the expected regression by 32 weeks of age.

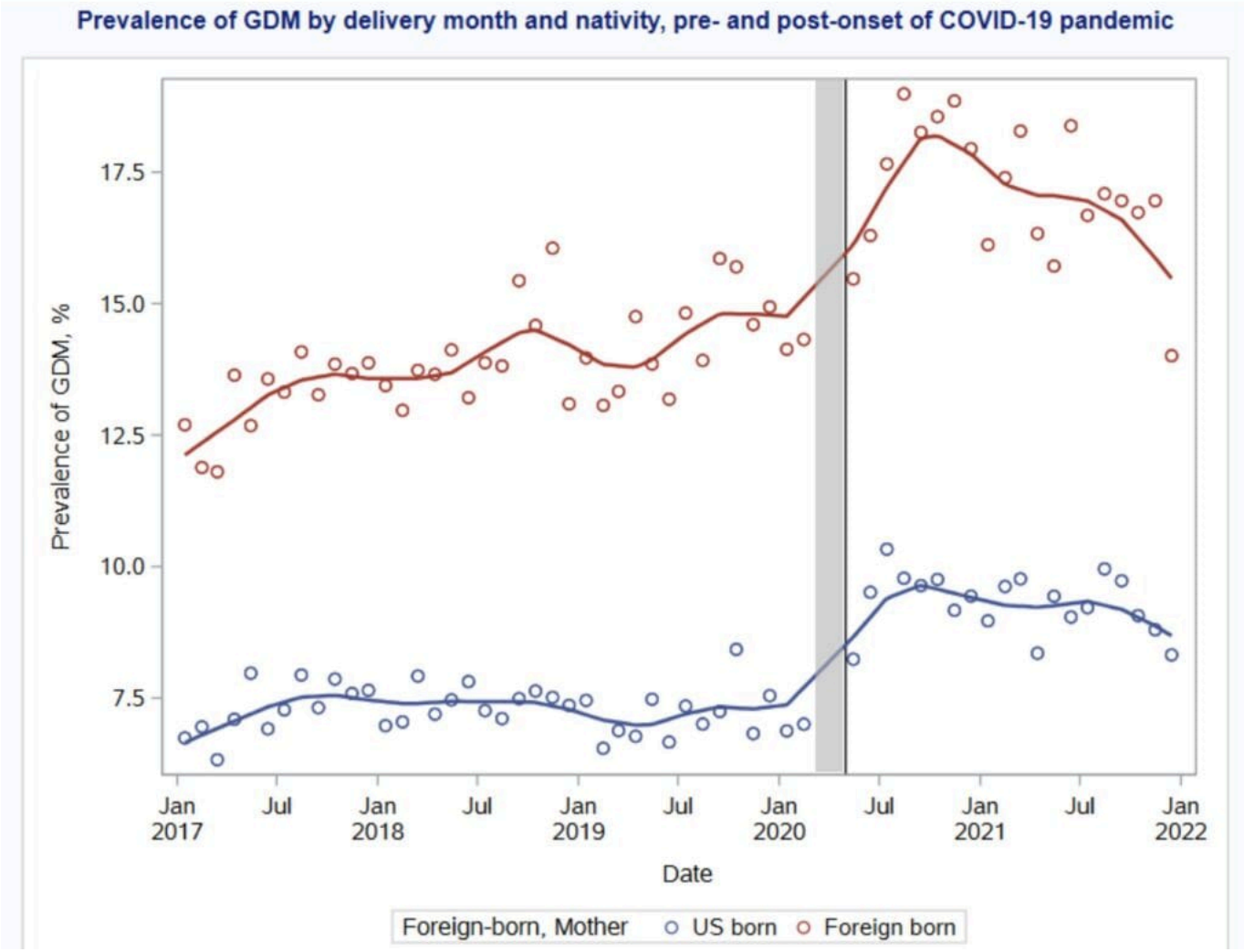
Figure 1: Predicted sex-specific age trajectories of breast bud diameter by latent class with 95% confidence intervals



Perinatal & Pediatric

The impact of the COVID-19 pandemic on gestational diabetes risk: Did immigrants fare worse? Natalie Boychuk* Natalie Boychuk Bohao Wu Katharine McCarthy Teresa Janevic

Gestational diabetes (GDM) is a common pregnancy complication with profound implications for future cardiometabolic risk. In New York City (NYC), immigrants are at higher risk of GDM, but the impact of the COVID-19 pandemic on GDM risk is unclear. We examined trends in GDM risk by month before and after onset of the COVID-19 pandemic and assessed if associations varied by nativity. We conducted an interrupted time series analysis of births to women without pre-pregnancy diabetes in NYC between January 2017-December 2021 using linked NYC birth record and hospital discharge data (n=402,025). We obtained maternal characteristics from the birth record. GDM was ascertained if indicated on either the birth or hospital record. Births were classified as pre-(January 2017-February 2020) or post-onset (May 2020-December 2021) of pandemic. We excluded births in March-April 2020. We constructed unadjusted and adjusted log binomial regression models and stratified by nativity. Half (50.7%) of women were foreign-born. GDM prevalence overall was 11.4%. After COVID onset, GDM risk increased by 5.3 per 100 deliveries (95% Confidence Interval [CI]: 3.7-7.0); this pattern persisted after adjusting for education, insurance, and parity (post vs. pre difference= 5.6, 95% CI: 4.0-7.2). Increases in GDM risk in the post-onset period were greater in foreign-born (post vs. pre= 8.3, 95% CI: 5.7-10.9) compared to US-born women (post vs. pre=3.4, 95% CI: 1.4-5.4). After the initial large increase, GDM risk decreased only slightly after the onset of COVID-19 by 0.08 percentage points per month (95% CI: -0.11, -0.04); this change was more pronounced in foreign-born (-0.14, 95% CI: -0.19, -0.09,) than US-born women (-0.03, 95% CI: -0.07, 0.01). GDM risk increased during the COVID-19 period, with marked disparities by nativity. While this trend appears to be receding, additional research is needed to understand the ongoing impact of COVID-19 on cardiometabolic health disparities in pregnancy.


Prevalence of GDM by delivery month and nativity, pre- and post-onset of COVID-19 pandemic
Prevalence of GDM, %
17.5
15.0
12.5
10.0
7.5
Jan 2017
Jul
Jan 2018
Jul
Jan 2019
Jul
Jan 2020
Jul
Jan 2021
Jul
Jan 2022
Date
Foreign-born, Mother
US born
Foreign born

Pharmacoepidemiology

Trends in Utilization of Chronic Asthma Medications among Publicly Insured Children in the US: 2003 – 2020 Celeste Ewig* Celeste Ewig Nicole Smolinski Almut Winterstein

Recent advances in our understanding of asthma treatments have led to additional considerations during clinical decision making. How these updates have affected utilization patterns of chronic asthma medications in pediatric patients with asthma remain uncharacterized. We aimed to describe the utilization of chronic asthma medications among publicly insured pediatric patients 2 to <18 years old with persistent asthma across relevant time periods of change.

We used Medicaid Analytic eXtract (MAX) and Transformed Medical Statistical Information System Analytic Files (TAF)national claims database. Individuals with persistent asthma defined as 1 hospital admission, or 3 outpatient visits with an asthma diagnosis identified from diagnosis codes, and a dispensing for a chronic asthma medication obtained from National Drug Codes, were identified within each calendar year The study period was divided into 3 periods: 2003 to 2008 (T1, FDA warnings for salmeterol in 2006 and montelukast in 2008), 2009 to 2014 (T2, post FDA warnings) and 2015 to 2020 (T3, post-approval of several biologic therapies). In each period, the proportion of pediatric patients with a dispensing of long-acting beta-agonists (LABA), montelukast, and asthma biologics was assessed using disproportionality analysis.

Our study included 1,953,516 pediatric patients (median age =6.7 years [IQR 4.3-10.2]). Males accounted for 59.9% of the population. The study population increased from 2003 to 2020 (T1=430,536, T2=591,941, and T3=820,179 individuals). Notable changes across time were observed in the proportion of the individuals using montelukast (T1=36.0% vs T3=33.1%, $p<0.001$), LABA (T1=2.5% vs T3 = 0.04%, $p<0.001$) and biologics (T1=0.1% vs T3=0.6%, $p<0.001$).

Although montelukast continues to be used by approximately a third of pediatric patients with persistent asthma, decline in utilization of LABA and increase in use of biologics appears to reflect advances in knowledge and uptake of newer therapies.

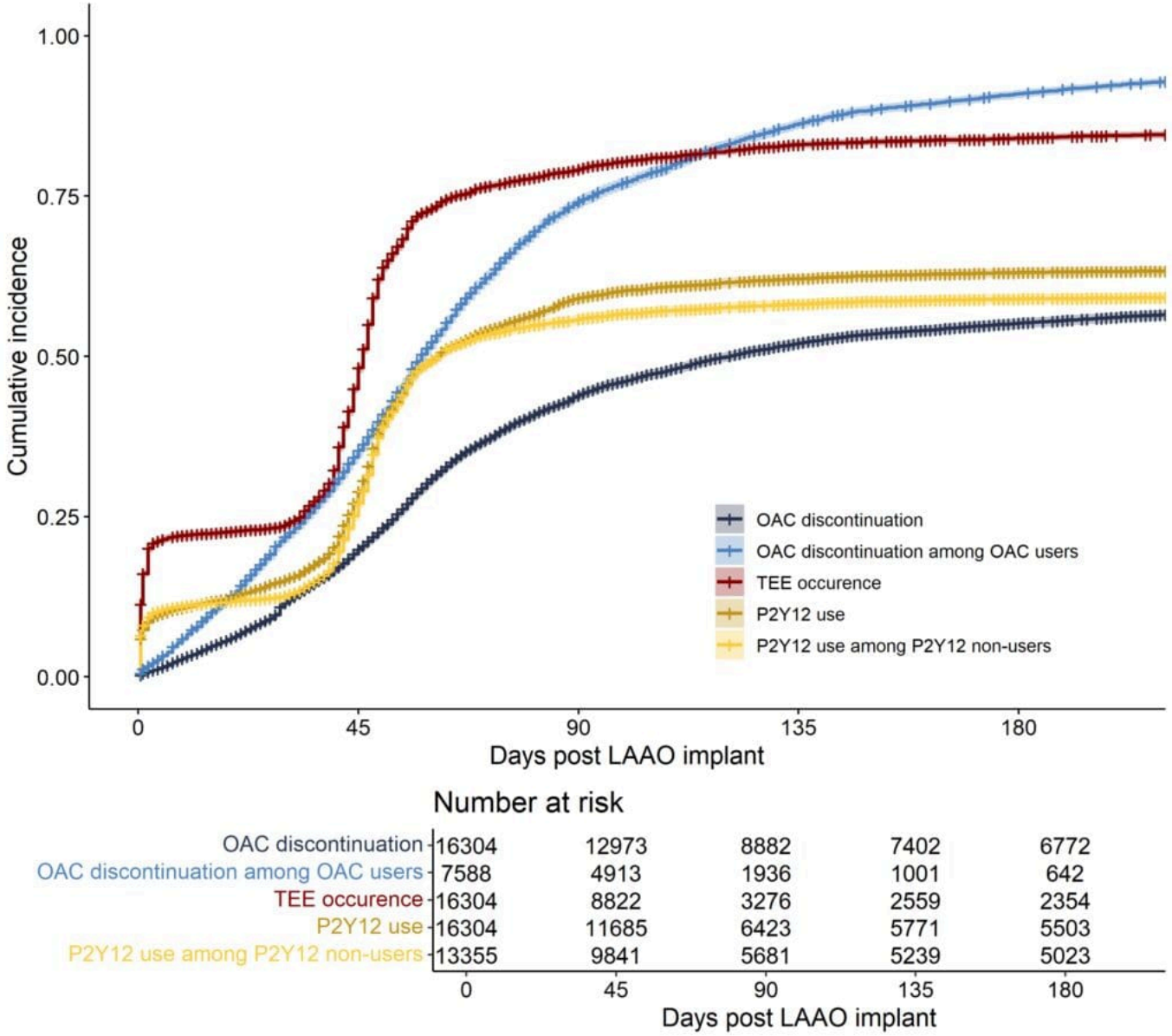
Pharmacoepidemiology

Anticoagulant Treatment after Left Atrial Appendage Occlusion in Older Atrial Fibrillation Patients Xiaojuan Liu* Xiaojuan Liu Sebastian Schneeweiss Daniel E. Singer Jerry Avorn Edwin K. Heist Joshua K. Lin

Introduction: Left atrial appendage occlusion (LAAO) offers an alternative to oral anticoagulants (OAC) for stroke prevention in atrial fibrillation (AF) patients. In March 2015, the LAAO device received approval alongside a specific postprocedural pharmacologic regimen including OAC therapy for 45 days followed by dual antiplatelet therapy for 6 months, yet real-world data on adherence to these protocols remains limited.

Methods: We established a cohort of 16304 AF patients who underwent first-time implantation of the LAAO device using Optum Clinformatics claims data 2015-2024. Patients aged <65 years or with a CHA2DS2-VASc score of <2 for males or <3 for females were excluded. We describe the rates of OAC discontinuation, defined as a ≥60-day gap in supply, transesophageal echocardiography (TEE) performed, and the use of P2Y12 inhibitors following implantation. Additionally, we examine the predictors of an unsuccessful occlusion and/or device-related thrombus, operationally defined as either: 1) continued OAC use following a TEE performed 30–90 days post-implant, or 2) continued OAC use beyond 90 days post-implant, regardless of whether TEE was performed.

Results and Conclusions: Among 16304 LAAO users, 3331 (20%) and 9532 (58%) discontinued OAC by 45 days and 6 months post-implant, respectively; these rates were 2675 (35%) and 6946 (92%) among 7588 patients who received OAC prior. Moreover, 10801 (66%) patients used P2Y12 inhibitors by 6 months post-implant; this rate was 8332 (62%) among 13355 prior P2Y12 non-users. TEE was performed in 7482 (46%) and 13950 (86%) patients by 45 days and 6 months post-implant, respectively (Figure). Factors associated with a higher likelihood of unsuccessful occlusion (or thrombus) included older age, Black race, and a longer duration of prior OAC use. These findings suggest moderate adherence to the LAAO postprocedural protocol. Further research is needed to assess the impact of these adherence patterns on clinical outcomes.



Number at risk

OAC discontinuation	16304	12973	8882	7402	6772
OAC discontinuation among OAC users	7588	4913	1936	1001	642
TEE occurence	16304	8822	3276	2559	2354
P2Y12 use	16304	11685	6423	5771	5503
P2Y12 use among P2Y12 non-users	13355	9841	5681	5239	5023
	0	45	90	135	180

Days post LAAO implant

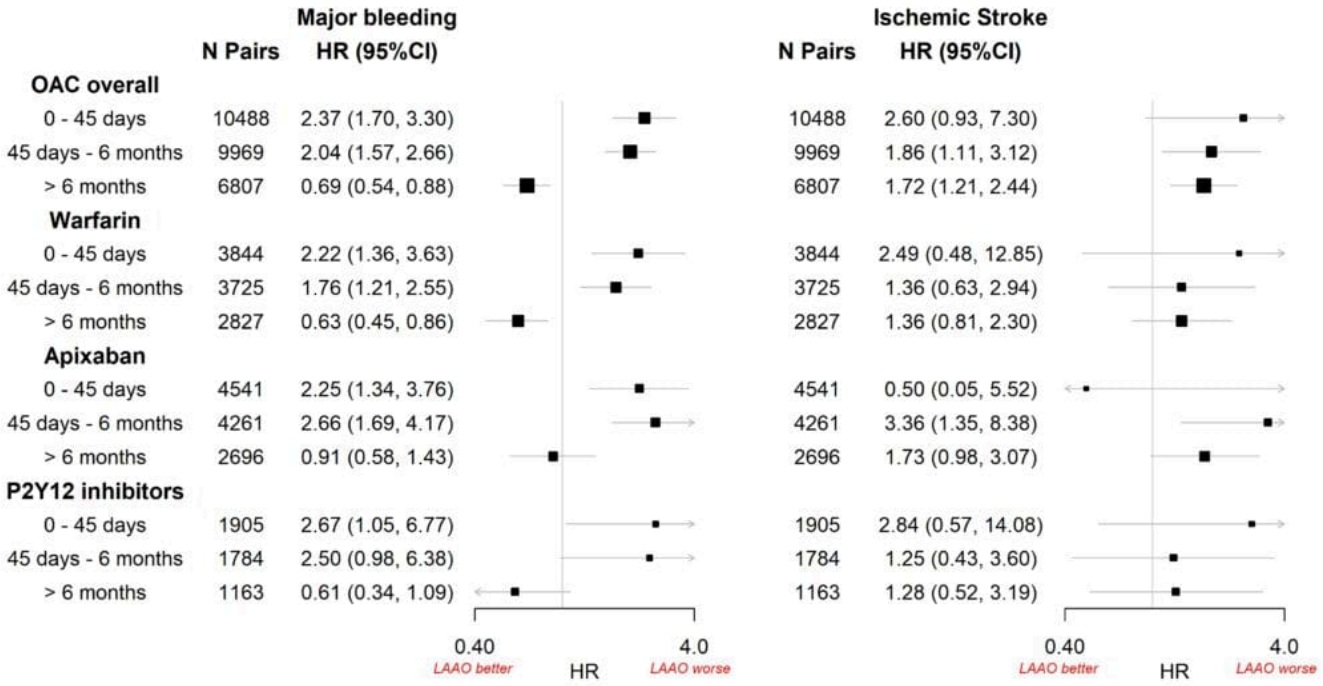
Pharmacoepidemiology

Comparative Effectiveness of Left Atrial Appendage Occlusion versus Oral Anticoagulants in Older Atrial Fibrillation Patients Xiaojuan Liu* Xiaojuan Liu Sebastian Schneeweiss Daniel E. Singer Jerry Avorn Edwin K. Heist Joshua K. Lin

Introduction: Real-world evidence evaluating left atrial appendage occlusion (LAAO) devices vs. oral anticoagulants (OAC) in patients with nonvalvular atrial fibrillation (AF) remain limited. We aimed to compare health outcomes between LAAO device users and OAC users.

Methods: A cohort study including 20992 AF patients aged ≥65 years with a CHA2DS2-VASc score of ≥2 (males) or ≥3 (females), using US Medicare claims data from 2016-2020. Patients who received LAAO in conjunction with OAC (warfarin, apixaban, rivaroxaban, or dabigatran) or with P2Y12 inhibitors on the index date were 1:1 matched to patients who received these medications alone via propensity score matching based on >80 pre-treatment covariates. Outcomes included hospitalization for major bleeding events, ischemic stroke, and all-cause death. Follow-up was censored at 2 years or upon treatment deviation (OAC discontinuation or LAAO implantation in OAC users, and OAC continuation beyond 90 days in LAAO users), and inverse probability of censoring weighting was applied to account for potential informative censoring.

Results and Conclusions: Patients' median age was 77; 46% were female. Compared to OAC-only users, LAAO users had a 2-fold risk of bleeding within the first 45 days (HR 2.37, 95% CI 1.70-3.30) and 45 days—6 months (HR 2.04; 1.57-2.66) post-implant, and a 31% reduced bleeding risk beyond 6 months (HR 0.69; 0.54-0.88). Additionally, LAAO users had a 70% higher risk of ischemic stroke beyond 6 months post-implant and before. This pattern was consistent across all individual OACs as well as P2Y12 inhibitors (Figure). No meaningful association between LAAO and mortality was observed over the 2-year follow-up. IPCW adjusted results remained unchanged. These findings highlight the heterogeneous effect of the LAAO device placement across outcomes and time periods following implantation, likely influenced by diverse antithrombotic regimens recommended at different stages post-LAAO.


Major bleeding
N Pairs
HR (95%CI)
OAC overall
0 - 45 days 10488 2.37 (1.70, 3.30)
45 days - 6 months 9969 2.04 (1.57, 2.66)
> 6 months 6807 0.69 (0.54, 0.88)
Warfarin
0 - 45 days 3844 2.22 (1.36, 3.63)
45 days - 6 months 3725 1.76 (1.21, 2.55)
> 6 months 2827 0.63 (0.45, 0.86)
Apixaban
0 - 45 days 4541 2.25 (1.34, 3.76)
45 days - 6 months 4261 2.66 (1.69, 4.17)
> 6 months 2696 0.91 (0.58, 1.43)
P2Y12 inhibitors
0 - 45 days 1905 2.67 (1.05, 6.77)
45 days - 6 months 1784 2.50 (0.98, 6.38)
> 6 months 1163 0.61 (0.34, 1.09)
0.40
LAAO better
HR
4.0
LAAO worse
Ischemic Stroke
N Pairs
HR (95%CI)
10488 2.60 (0.93, 7.30)
9969 1.86 (1.11, 3.12)
6807 1.72 (1.21, 2.44)
3844 2.49 (0.48, 12.85)
3725 1.36 (0.63, 2.94)
2827 1.36 (0.81, 2.30)
4541 0.50 (0.05, 5.52)
4261 3.36 (1.35, 8.38)
2696 1.73 (0.98, 3.07)
1905 2.84 (0.57, 14.08)
1784 1.25 (0.43, 3.60)
1163 1.28 (0.52, 3.19)
0.40
LAAO better
HR
4.0
LAAO worse

Pharmacoepidemiology

Disparities in Potentially Inappropriate Central Nervous System Medication Prescribing Among Sexual and Gender Minority Adults Chelsea Wong* Chelsea Wong Robert Cavanaugh Louisa H Smith Dae H Kim Carl G. Streed, Jr. Farzana Kapadia Brianne Olivieri-Mui

Central nervous system (CNS) medications: antidepressants, antipsychotics, hypnotic/sedatives, and anxiolytics; are used to treat mental health conditions but carry risks when used inappropriately. Sexual and gender minority (SGM) older adults face unique healthcare disparities, which may include differences in prescribing patterns and healthcare utilization. This study aimed to 1) assess the prevalence of inappropriate CNS medication prescriptions by SGM status and 2) evaluate whether SGM status moderates the association between prescribing and healthcare utilization.

Using All of Us electronic health record data, we included participants ≥50yo with no appropriate diagnosis for use of each of four CNS medication classes. A 1:5 SGM:non-SGM matched sample was created for each class to account for frailty, age, race & ethnicity, income, marital status, general mental health, and HIV status. Logistic regression assessed differences in inappropriate CNS prescriptions by SGM status, and negative binomial regression with offset evaluated whether SGM status moderated the association between CNS prescriptions and emergency department (ED) visits over 1 year.

The full sample included 6070 SGM and 118,498 non-SGM adults with matched samples ranging from 28,806-35,574 participants. SGM adults were more likely to have an inappropriate prescription for antidepressants (Odds Ratio [OR], 95% Confidence Interval: 1.15 [1.00,1.31]), antipsychotics (OR: 1.32 [1.10,1.59]), and hypnotic/sedatives (OR: 1.25 [1.09,1.43]). Inappropriate prescriptions across all four classes were associated with higher ED visits: antidepressants (Rate Ratio [RR]: 2.44 [1.84,3.25]), antipsychotics (RR: 3.33 [2.34,4.74]), hypnotic/sedatives (RR: 1.57 [1.18,2.10]), anxiolytics (RR: 2.22 [1.57,3.14]). SGM status was not modify these associations.

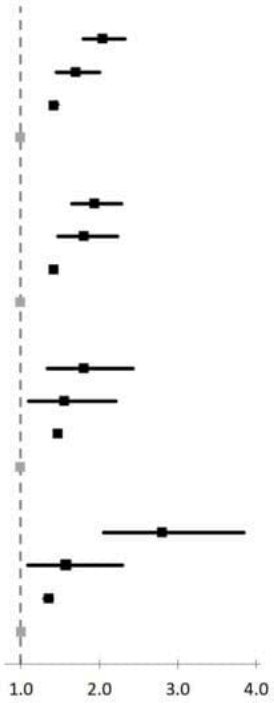
Our findings highlight disparities in prescribing patterns by SGM status among older adults and underscore the need for careful medication review among this population

Pharmacoepidemiology

Synergistic Risks: NSAIDs Use During Herpes Zoster Infection Doubles Stroke Risk – A Nationwide Case-Crossover Study Lin-Chieh Meng* Lin-Chieh Meng Hsi-Yu Lai Hui-Min Chuang Ho-Min Chen Liang-Kung Chen Fei-Yuan Hsiao

Background
Previous studies have suggested that herpes zoster (HZ) infection could trigger stroke, and the use of nonsteroidal anti-inflammatory drugs (NSAIDs), commonly prescribed for HZ pain management, has been associated with an increased risk of stroke. However, research evaluating whether NSAID use during HZ episodes may further elevate stroke risk remains limited.
Methods
Using a population-based claims database in Taiwan (2014-2020), we identified 336,075 patients with incident stroke. A case-crossover design compared exposure to HZ and NSAIDs between the focal period (1-30 days before stroke) and the referent period (366-395 days before stroke). Conditional logistic regression estimated adjusted odds ratios (aORs) for stroke risk associated with NSAIDs use during HZ episodes. Pre-planned subgroup analyses further examined such synergistic effects on stroke subtypes, across age groups (<50, 50-64, ≥65 years) and in patients with various comorbidities, including immunocompromised and autoimmune diseases, cardiometabolic risk factors, and renal and liver diseases.
Results
Combined HZ infection and NSAIDs use was associated with doubled stroke risk (aOR=2.05, 95% CI=1.80-2.33) compared to periods without either exposure. For specific stroke types, the adjusted ORs were 1.94 (95% CI=1.65-2.29) for ischemic stroke and 1.81 (95% CI=1.34-2.43) for hemorrhagic stroke. HZ episodes without NSAIDs (aOR=1.70, 95% CI=1.45-2.00) and NSAIDs use alone (aOR=1.42, 95% CI=1.40-1.44) showed lower but significant risk increment. In age-stratified analyses, individuals aged 65 years and older exhibited a significantly elevated stroke risk while concurrently utilizing NSAIDs during HZ episodes (aOR=2.24, 95% CI=1.92-2.62). Subgroup analyses demonstrated consistent elevated risks in patients with pre-existing comorbidities, particularly immunocompromised conditions and renal disease.
Discussion
Our findings demonstrate a significant synergistic effect between HZ infection and NSAIDs use on stroke risk, particularly among individuals aged 65 years and older or those with pre-existing cardiometabolic conditions. The optimization of pain management strategies during HZ episodes is paramount to mitigate the risk of stroke while ensuring effective management of HZ-associated pain.

Subgroup Exposure during period	Focal window n (%)	Referent window n (%)	Adjusted OR OR (95% CI)
Any stroke			
NSAIDs use during HZ episodes	771 (0.23)	387 (0.12)	2.05 (1.80- 2.33)
HZ episodes without NSAIDs use	443 (0.13)	273 (0.08)	1.70 (1.45- 2.00)
NSAIDs use only	77698 (23.12)	60401 (17.97)	1.42 (1.40- 1.44)
No exposure	257163 (76.52)	275014 (81.83)	ref
Ischemic Stroke			
NSAIDs use during HZ episodes	469 (0.24)	251 (0.13)	1.94 (1.65- 2.29)
HZ episodes without NSAIDs use	277 (0.14)	165 (0.08)	1.81 (1.47- 2.23)
NSAIDs use only	46066 (23.20)	35946 (18.11)	1.42 (1.40- 1.45)
No exposure	151713 (76.42)	162163 (81.68)	ref
Hemorrhagic Stroke			
NSAIDs use during HZ episodes	138 (0.15)	76 (0.09)	1.81 (1.34- 2.43)
HZ episodes without NSAIDs use	87 (0.10)	57 (0.06)	1.56 (1.10- 2.21)
NSAIDs use only	18824 (21.08)	14041 (15.72)	1.47 (1.43- 1.51)
No exposure	70248 (78.67)	75123 (84.13)	ref
TIA			
NSAIDs use during HZ episodes	164 (0.34)	60 (0.12)	2.81 (2.06- 3.85)
HZ episodes without NSAIDs use	79 (0.16)	51 (0.11)	1.58 (1.09- 2.30)
NSAIDs use only	12808 (26.54)	10414 (21.58)	1.35 (1.30- 1.40)
No exposure	35202 (72.95)	37728 (78.19)	ref



Pharmacoepidemiology

Disparities in Hospitalization Rates for Drug Overdose Among Pediatric Underrepresented Populations: An Epidemiological Analysis Aidin Gharavi* Aidin Gharavi Devon Lynn Ali Hamandi Ixchel Salazar Ryan Phan Leticia Rolon

Pediatric drug overdoses are a critical public health concern. Using the National Electronic Injury Surveillance System (NEISS) database, cases of children under 5 years old presenting to emergency departments and subsequently hospitalized during 2023 were extracted. Demographic information was compared to population estimates using Census.gov data, and Chi-square tests were utilized to determine significance, with p-values (P) <.05 being significant. The sample of 410 children under 5 years old represents an estimated 8,618 hospitalizations caused by drug poisoning to children under 5 years old in 2023 (95% CI: 4,715 – 12,521). Young children between 12 and 24 months old were the most likely group to present with drug poisoning, accounting for 37.6% of all overdoses, while children 4 years old were the least likely (8.5%). There was no significant difference in the hospitalization rates of males versus females (P: 0.49). Aspirin substitutes (n = 57) and Antihistamines (n=29) were the most common drugs mentioned, while aspirin accounted for 3.2% of hospitalizations. 44.0% of children were from an underrepresented group, defined as being either Hispanic and/or black. When comparing demographic information to 2023 population estimates by Census.gov, children from underrepresented groups were more likely to be hospitalized from drug poisoning (P: <0.001). Our findings indicate that pediatric drug overdoses disproportionately impact children from underrepresented groups. These incidents may arise from improper medication storage or inappropriate administration of medications. Targeted outreach and access to healthcare resources are necessary to reduce pediatric overdoses, especially in underrepresented populations. Public health campaigns should emphasize proper medication storage and dosing guidelines. Partnerships with community organizations and utilizing social media could help spread awareness and medication information.

Pharmacoepidemiology

Dynamic changes in first utilization of glucagon-like peptide-1 receptor agonists, sodium-glucose cotransporter-2 inhibitors, and metabolic/bariatric surgery; an analysis of OptumLabs data, 2010-2023 Paige Wartko* Paige Wartko Rui Zhang David Arterburn Eric Johnson Jennifer F. Bobb Chixiang Chen Lisa Ross Patrick J. O'Connor Rozalina G. McCoy

Background: Diabetes and obesity are leading contributors to morbidity and mortality. Treatment options have been changing, warranting assessment of recent patterns in utilization.

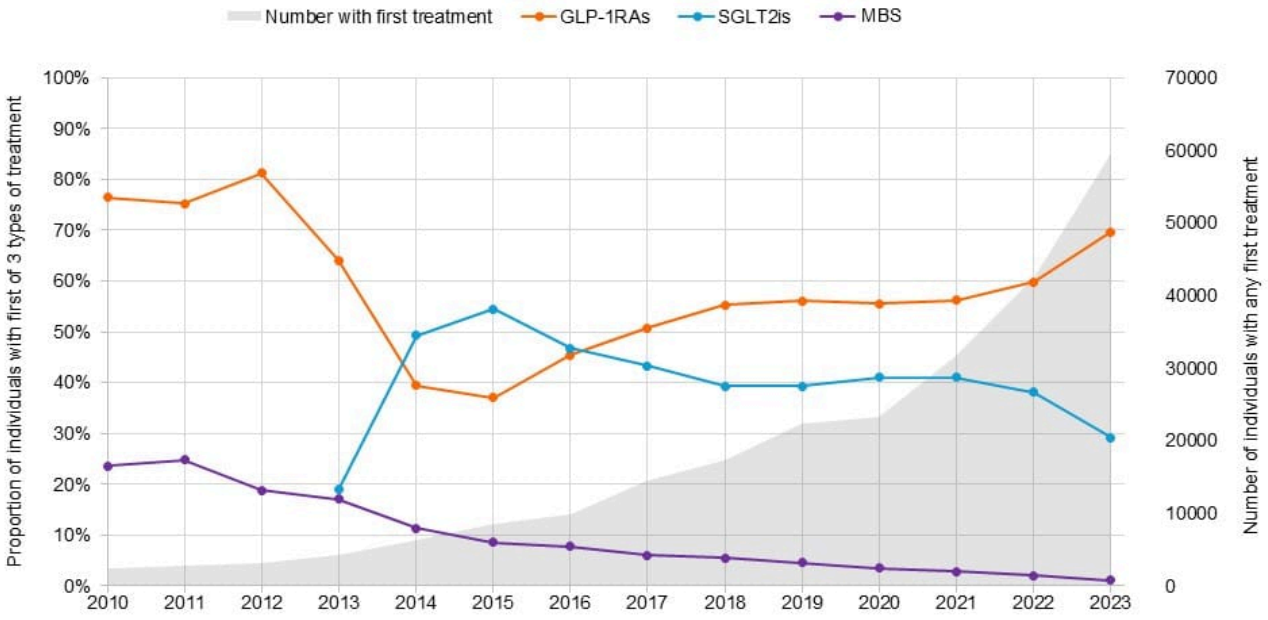
Objective: To assess frequency and recent temporal patterns in utilization of glucagon-like peptide-1 receptor agonists (GLP-1RAs), sodium-glucose cotransporter-2 inhibitors (SGLT2is), and metabolic/bariatric surgery (MBS).

Study design: We used claims from OptumLabs Data Warehouse (2010–2023) for enrollees in commercial and Medicare Advantage plans with diabetes and obesity to quantify the first utilization of GLP-1RAs, SGLT2is, and MBS overall and by year.

Results: We identified 248,069 individuals: 59% first used GLP-1RAs, 37% first used SGLT2is, and 4% first had MBS. Median age at first use of MBS, GLP-1RAs, and SGLT2is was 53, 60, and 63, respectively (all IQRs =17). The number of individuals using any treatment increased dramatically from 2010 to 2023 (Figure). The most common GLP-1RAs were semaglutide (41%), dulaglutide (24%), and liraglutide (16%). GLP-1RAs comprised 70% of studied treatments by 2023, with semaglutide accounting for 61% of GLP-1RA treatment. After approval in 2022, tirzepatide use increased precipitously, comprising 26% of GLP-1RA treatment by 2023. After SGLT2is' approval in 2013, they initially surpassed GLP-1RAs; after 2016, SGLT2is comprised a lower proportion of first treatment than GLP-1RAs. The most common SGLT2is were empagliflozin (63%), dapagliflozin (20%), and canagliflozin (18%). The proportion of MBS decreased over time, although the number of individuals getting MBS did not. Sleeve gastrectomy was more common than gastric bypass after 2012.

Conclusions: We observed rapid changes over time in utilization of different, potentially more effective, and/or less burdensome, treatments for individuals with diabetes and obesity. Further studies are needed to assess the impact of these shifting patterns on health outcomes.

First utilization of glucagon-like peptide-1 receptor agonists (GLP-1RAs), sodium-glucose cotransporter-2 inhibitors (SGLT2is), or metabolic/bariatric surgery (MBS), 2010-2023



Number with first of 3 types of treatment by year

GLP-1RAs	1879	2044	2486	2705	2488	3145	4468	7318	9540	12535	12877	17786	25339	41516
SGLT2is	0	0	0	797	3115	4624	4596	6247	6770	8792	9540	12986	16173	17431
MBS	582	674	575	720	716	729	762	873	947	1028	800	879	885	702
Total	2461	2718	3061	4222	6319	8498	9826	14438	17257	22355	23217	31651	42397	59649

Policing/Incarceration

Impact of jail-based methadone or buprenorphine treatment for opioid use disorder on Hepatitis C Virus outcomes immediately after release from New York City jails, 2011-2018

Sungwoo Lim* Sungwoo Lim Teena Cherian Sarah Braunstein Ellen Wiewel Zachary Rosner Monica Katyal Noa Krawczyk Maria Khan Sean Murphy Ali Jalali Philip Jeng Keith Goldfeld Ross MacDonald Joshua Lee

Hepatitis C virus (HCV) care services have been available in New York City (NYC) jails since the 2010s, with efforts to scale up screening and treatment. HCV treatment, while simplified over the last decade, takes weeks and can be complicated to coordinate for people transitioning from community to jail and, often, back in short time. In-jail methadone or buprenorphine treatment for opioid use disorder (MOUD) is associated with increased measures of stability following re-entry. This impact might translate into HCV outcomes in people with OUD but its evidence is limited. We tested whether in-jail MOUD is associated with first HCV ribonucleic acid (RNA) negative test result post-release at NYC healthcare facilities among individuals with OUD and HCV diagnoses prior to release. NYC jail-based patient electronic medical records were matched with NYC mortality and HCV registries. The cohort included 2817 adults who were incarcerated and released to the community in 2011-18. They experienced 4507 treatment (MOUD) and 2190 comparison (no MOUD) incarceration events. Outcome was time to the first test date post-release with undetectable RNA since the first HCV diagnosis. We conducted multivariable mixed-effect Cox regression analysis with demographic, health, and legal characteristics as potential confounders, and a frailty factor to address subsequent incarcerations by unique individual. The one-year post-release period was broken into the first month and remaining time to address the proportionality assumption violation. Treatment and comparison groups were similar except for percentages of males (79% vs. 90%), felony charge (27% vs. 59%), length of jail stay (median 20 days vs. 51 days), and injection drug use (75% vs. 70%). Adjusted HR for the outcome by in-jail MOUD was 4.96 (95% CI=1.74-14.12) within 28 days, and 1.14 (95% CI=0.81-1.59) for the remaining time. In-jail MOUD is associated with increased HCV clearance rates in the immediate post-release period.

Reproductive

Hair Relaxer Use and Anti-Mullerian Hormone Concentrations in a North American cohort

Lauren A. Wise* Lauren A. Wise Ruth J. Geller Dmitrii Krivorotko Geralyn Lambert-Messerlian Amelia K. Wesselink

Introduction: Hair relaxers (chemical straighteners) are used by millions of North Americans, particularly people of color. Relaxer use has been associated with an increased risk of hormone-dependent reproductive outcomes, including early puberty, subfertility, and uterine fibroids. The effect of hair relaxer use on concentrations of anti-mullerian hormone (AMH), a biomarker of ovarian reserve, has not been studied.

Methods: We analyzed baseline data from Pregnancy Study Online (PRESTO), a preconception cohort study of North American pregnancy planners (2015-2024). We restricted analyses to 838 females aged 21-44 years without a diagnosis of PCOS. Participants reported on lifetime hair relaxer use including age at first use, frequency and duration of use, and number of burns. We assayed AMH concentrations using picoAMH (Ansh labs). We used modified Poisson regression to estimate prevalence ratios (PR) and 95% CIs for associations between hair relaxer use and low AMH (<1.8 ng/ml to denote low AMH corresponding to <20% without evidence of polycystic ovarian morphology), adjusted for age, race, ethnicity, BMI, smoking, and history of subfertility.

Results: Overall, 2% of participants were current users and 10% were former users of hair relaxers; 15% of ever users began at ages <10 years. Median AMH was 5.5 ng/ml. Compared with never use of hair relaxers, PRs for current and former use were 2.01 (95% CI: 0.74-5.44) and 0.85 (95% CI: 0.54-1.34), respectively. Among ever users, prevalence of low AMH was highest for those with the greatest frequencies and durations of use (≥3 times/year vs. never use: PR=1.52, 95% CI: 0.65-3.56; ≥10 years vs. never use: PR=1.47, 95% CI: 0.46-4.67; frequency ≥3 times/year + duration ≥5 years vs. never use: PR=1.28, 95% CI: 0.51-3.18). No appreciable associations were seen with age at first use or number of burns.

Conclusion: Some measures of hair relaxer use were associated with a higher prevalence of low AMH, though precision was limited.

Reproductive

Prediction of endometrial tissue PFAS levels using serum biomarkers and demographic and reproductive factors: findings from the Investigating Mixtures of Pollutants and Endometriosis in Tissue (IMPLANT) Study Anna Z. Pollack* Maggie Fuzak Dr. Helen Chin Dr. Jenna R. Krall Vimalkumar Krishnamoorthi Kurunthachalam Kannan

Exposure to perfluoroalkyl substances (PFAS) is associated with adverse health outcomes. The IMPLANT Study measured PFAS in both serum and endometrium. Endometrium tissue is challenging to obtain and requires invasive surgical procedures. However, measurement of target tissue concentrations of PFAS is more relevant from toxicological point of view. This study aimed to develop prediction models to estimate PFAS concentrations in endometrial tissue based on serum concentrations, demographic characteristics, and reproductive factors

Using data from the operative cohort of the Endometriosis Natural History Diagnosis and Outcomes Study (N=433), which enrolled women undergoing laparoscopy or laparotomy for any indication who were not previously diagnosed with endometriosis, we developed multivariable linear regression and LASSO regression models. Predictor variables included serum PFAS concentrations (e.g., PFOS, PFOA, PFNA), age, BMI, parity, smoking, and menstrual status. The analysis focused on PFOS, PFHpA, PFOA, PFNA, PFDA, PFUnDA, and PFDoDA. Extreme outliers were removed based on the interquartile range (IQR) before analysis. Following these adjustments, the number of participants varied across models depending on the availability of complete data for each PFAS.

Serum PFAS concentrations were the strongest predictors of endometrial tissue levels, particularly for PFOS (R2=0.49; RMSE=3.02). Age and household income contributed to improved predictions for PFUnDA (R2=0.21;RMSE=0.09). However, moderate R-squared values across most PFAS (0.10-0.49) suggest that serum levels only partially predict eutopic tissue concentrations. This highlights that alternative approaches are necessary to better understand PFAS in eutopic tissue.

Reproductive

Comorbidities and complications: how the effect of cesarean delivery on postpartum rehospitalization varies by condition Ruby Barnard-Mayers* Ruby Barnard-Mayers Eugene Declercq Eleanor J. Murray Christina D. Yarrington Martha M. Werler

Introduction: Numerous studies have linked having a cesarean delivery to an increased risk of maternal morbidities. However, there is a lack of information on how different indications for cesarean deliveries modify these effects.

Objective: We aimed to understand how different indications of cesarean delivery act as potential effect modifiers for the effect of cesarean delivery on postpartum rehospitalization among nulliparous, term, singleton, vertex pregnancies in Massachusetts.

Methods: Data for this study come from the Pregnancy to Early Life Longitudinal data system, which uses birth certificate and hospital discharge records from all deliveries in Massachusetts from 2011 to 2018. Cesarean delivery, the exposure of interest, was based on both the birth certificate and discharge records. Postpartum rehospitalization included observational and emergency visits between 2 and 365 days after delivery. We examined EMM for five subgroups: chronic/acute disease, fetal conditions, uteroplacental abnormality, labor complications, and no documented indication. Within each of these groups we calculated adjusted RRs and RDs for the effect of cesarean delivery, compared to vaginal delivery, on rehospitalization adjusting for demographic and pregnancy characteristics.

Results: The risk of rehospitalization for vaginal deliveries was 20.5% for vaginal deliveries and ranged from 18% to 24% across the 5 indication groups for cesareans. The smallest effects were identified among birthing people with no indication (aRD: 0.05%) and with any chronic or infectious disease (aRD: 0.09%). The largest effect was among those with a uteroplacental abnormality (aRD: 2.91%; aRR: 1.22).

Discussion: We discovered modest evidence of EMM by indication for the effect of cesarean delivery on postpartum rehospitalization on both the relative and absolute scale. Our results suggest that birthing people with a uteroplacental or anatomic abnormality may benefit from a higher level of postpartum care.

Reproductive

Endometriosis diagnosis, severity, and location and serum anti-müllerian Hormone levels

Michelle Valenti* Michelle Valenti Karen V. Schliep Madeline Paulson Rachael B. Hemmert Matthew Peterson Melissa A. Furlong Zelieann Craig Anna Pollack Leslie V. Farland

Introduction: Endometriosis, a chronic, inflammatory condition, is often associated with pelvic pain and infertility. Anti-müllerian hormone (AMH), a marker of ovarian reserve, is associated with time to menopause and has been shown to be lower in those with endometriosis. The purpose of this study was to evaluate the association between incident endometriosis diagnosis, severity, and location with AMH levels measured prior to gynecologic surgery.

Methods: Data was acquired from the Endometriosis: Natural History, Diagnosis, and Outcomes Study, which recruited an operative cohort of women undergoing laparoscopy/laparotomy for any indication. Serum AMH levels (ng/mL) were log transformed and multivariable linear regression models were utilized adjusting for age (continuous and squared), body mass index (BMI), age at menarche, exogenous hormonal contraceptive use, and cigarette smoke exposure. Percent difference and 95% confidence intervals (CI) were calculated.

Results: In our sample (n=348), those with endometriosis (n=156) were slightly younger (32 years SD 6.8) than those without endometriosis (n=192) (33 years SD 7.3). Those with endometriosis had a lower BMI (26.7 kg/m2 SD 7.3 vs. 29.6 kg/m2 SD 9.0) and reported a higher proportion of infertility (41.0% vs. 18.8%) compared to those without endometriosis. Endometriosis diagnosis was associated with lower AMH levels (-20.6%, 95% CI -37.6, 1.0). Compared to those without endometriosis, stage I-II and stage II-IV endometriosis were associated with a 11.1% reduction (95% CI -62.25, -19.93) and 44.7% reduction (95% CI -62.3, -19.9), respectively. Ovarian endometriosis was associated with a 57.8% reduction (95% CI -71.9, -36.5) in AMH levels compared to those without endometriosis.

Conclusion: At surgical diagnosis, moderate to severe (Stage III-IV) and ovarian endometriosis were associated with lower AMH levels. This provides insight into the potential mechanism by which endometriosis may affect infertility.

Reproductive

Community Violence and Adverse Maternal and Infant Outcomes: Census Tract Homicides and Preterm Birth in California 2007-2018 John Halifax* John Halifax Caitlin Chan Shelley Jung Jennifer Ahern

The community environment has strong connections with adverse maternal and infant health outcomes in the United States. Community violence may be an important aspect of the environment, with potential to influence biological stress response mechanisms or maternal behavioral changes. Between community confounding leads us to examine within-community variation in violence in relation to birth outcomes. This work investigates the within community variation in homicides at the census tract level in three periods of gestation (preconception, trimester 1, and trimester 2) and preterm birth, with two post-birth exposure periods included as negative controls by temporality. Data are comprehensive for births in California in census tracts with at least one homicide from 2007-2018 (n=4.3 million observations among 6,714 census tracts).

Five average treatment effects contrasting exposure in each of the five periods vs entirely unexposed were estimated using data-adaptive longitudinal targeted maximum likelihood estimation (LTMLE). We aim to include census tract fixed effects to facilitate within-community comparisons, but large sample size has thus far produced analytic challenges. For computationally-feasible preliminary results, we used partition around medoids to cluster census tracts based on community-level covariates and an LTMLE estimator with fixed effects on these clusters for within-similar-community comparisons. Preliminary results on a data subset of 1,000 randomly selected census tracts find small associations that are not statistically significant, with exposure to community-level homicide showing some indication of an association with preterm birth during trimester 1. Future work will estimate these associations in the full dataset and use simulation studies to evaluate bias, variance, and computational feasibility of alternative LTMLEs that incorporate fixed effects or pool community-specific LTMLEs to be robust to between-community confounding.

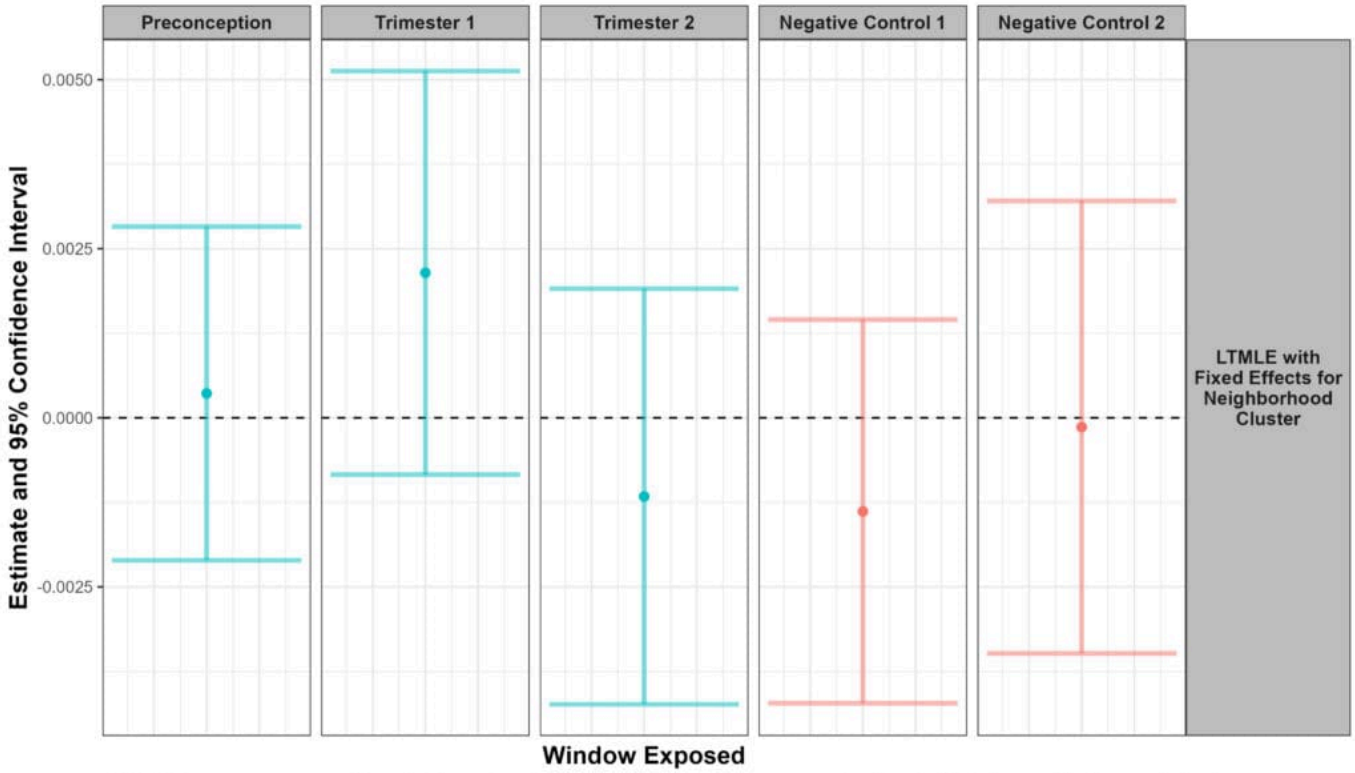


FIGURE. Average treatment effects for the contrast between exposure to a census-tract level homicide in the specified time period only and no exposure over the full course of pregnancy. Preliminary results are only for a subsample of 1,000 randomly sampled census tracts. Conception date is estimated as birth date minus gestational age at birth. Preconception period is defined as the 12-week period prior to conception date. Trimester 1 is defined as the 12-week period following conception date. Trimester 2 is defined as weeks 12-20 after conception date, truncated to ensure temporality of exposure before preterm birth. Negative Control windows 1 and 2 are defined as weeks 44-56 and 56-68 after conception date respectively, and both are after all births in the cohort. Neighborhood cluster membership is determined using the partition around medoids algorithm on baseline community-level covariates with the number of clusters k set to 0.10 the number of census tracts (in this case k=100).

Reproductive

Vitamin D, Free vitamin D, Iron, Ferritin, and Hemoglobin in Pregnancy: Findings from Kuwait Birth Cohort Study Abdullah Al-Taiar* Abdullah Al-Taiar Ali H. Ziyab Reem Al-Sabah Majeda S. Hammoud

Background: The association between vitamin D and iron, ferritin, or hemoglobin (Hb) levels remains controversial. This study aimed to estimate the prevalence of vitamin D deficiency and investigate its association with iron, ferritin, and Hb levels in pregnant women.

Methods: Pregnant women in their second or third trimester were recruited in the Kuwait birth cohort, a prospective study. 25-hydroxyvitamin D (25OHD) was assessed using electrochemiluminescence immunoassay, with deficiency defined as <50 nmol/L; while anemia was defined as having Hb <110 g/L. Free 25OHD was calculated from the concentrations of total 25OHD, vitamin D binding protein (VDBP) and albumin. Data on socio-economic status and lifestyle were collected using personal interviews. Simultaneous-quantile regression was used to examine the association between 25OHD levels and each iron, ferritin, and Hb levels while adjusting for potential confounders. Logistic regression was used to investigate the association between vitamin D deficiency and each iron, ferritin, and Hb levels while adjusting for potential confounders.

Results: Of all study participants, 55.93% (95%CI: 52.94-58.88%) had vitamin D deficiency, and 21.54% (95%CI: 19.21- 24.06%) had severe deficiency. Weak but significant correlations were found between 25OHD levels and iron (Spearman’s correlation coefficient (rs)=0.15; p<0.001), ferritin (rs=0.17; p<0.001), and Hb levels (r=0.14; p<0.001). There was also a strong association between vitamin D deficiency and anemia (p= 0.003). These associations remained evident after adjusting for confounding factors. Similar results were obtained when Free 25OHD was used instead of total 25OHD.

Conclusion: Vitamin D deficiency is common among pregnant women in Kuwait. There is a significant association between 25OHD and each iron, ferritin and Hb, which highlights the importance of routine screening for both anemia and vitamin D deficiency to guide appropriate prenatal supplementation.

Reproductive

Vicarious trauma: A pre-post analysis of exposure to a racially motivated mass shooting and adverse birth outcomes in South Carolina Abigail Kappelman* Abigail Kappelman Annie Ro Andrea Henderson Michael G. Smith Claire Margerison Nancy Fleischer

Introduction: We hypothesized that the mass shooting of Black churchgoers in Charleston, SC on June 17, 2015, constituted a racialized exogenous shock that would increase low birth weight (LBW, <2500g) and preterm birth (PTB, <37wks) in SC, with greater effect size for Black vs. White pregnant women and for women in Charleston County vs. the rest of SC.

Methods: We estimated the association between exposure to the event and adjusted odds of LBW and PTB using singleton birth certificates from SC from 2012-2016. Exposed infants were in utero on June 17, 2015 (estimated month of conception Sept 2014-June 2015); controls were in utero during the same periods the two years prior. Logistic regressions were adjusted for month and year of conception, trimester on event date, maternal race and age, and infant sex. Effect modifiers were maternal Black/White race and residence (Charleston Co./the rest of SC).

Results: We found no association between exposure and LBW (aOR 1.08 [95%CI 0.96-1.21]) or PTB (0.99 [0.89-1.11]) in the entire state (n=104471); associations did not differ by maternal race (both F test p>0.05). In Charleston Co. (n=9398), exposure was associated with higher odds of LBW (aOR 1.70 [95%CI 1.16-2.50]); this association did not differ by race (F test p>0.05). We did not find an association between exposure and PTB in Charleston Co. (aOR 1.29 [95%CI 0.90-1.86]) nor differences by race (F test p>0.05). In the rest of SC, though we found no overall association (LBW aOR 1.04 [95% 0.92-1.17]; PTB 0.97 [0.87-1.09]), we found a marginally harmful association for Black women only (LBW exposed x NHB aOR 1.12 [95%CI 1.01-1.24]; PTB exposed x NHB 1.12 [1.02-1.24]).

Conclusion: Though we found no overall association of exposure to the mass shooting on birth outcomes in SC, we found a significant association between the racialized “shock” and LBW for all pregnant women in Charleston Co., and between exposure and LBW and PTB for pregnant Black women only in the rest of SC.

LATEBREAKER

Reproductive

Maternal Pre-Pregnancy BMI and Miscarriage: a Burden of Proof Study Emily Desai* Emily Desai Ke Pan Mae Dirac Nicholas J. Kassebaum

Miscarriage, or spontaneous abortion, is a common cause of maternal morbidity. Maternal pre-pregnancy BMI has been shown to be associated with miscarriage, but studies vary in their risk estimates and the way in which they control for confounding. This study aims to evaluate the dose-response relationship between maternal BMI and risk of miscarriage, synthesizing all available data and quantitatively accounting for variations in study design and extent of control for confounding variables. We conducted a systematic review of the association between maternal BMI and miscarriage and included 24 studies. We developed a Directed Acyclic Graph to identify confounders and mediators and employed a Bayesian, regularized, trimmed meta-regression technique that accounts for heterogeneity among studies and accommodates non-linear dose-response relationships. No studies adjusted for the full set of identified potential confounders. Study population representativeness, exposure and outcome measurement, control of confounding, and selection bias were tested as bias covariates in our model. The lowest risk of miscarriage was at 19.41 kg/mˆ2 in our data. Before accounting for heterogeneity among studies, high and low BMI were significantly associated with higher risk of miscarriage, with an RR of 1.26 (95% CI:1.10-1.45) at BMI of 30 kg/mˆ2 and an RR of 1.13 (95% CI:1.05-1.22) at BMI of 15 kg/mˆ2, using conventional meta-regression bounds. After accounting for heterogeneity, the RRs were 1.26 (95% CI: 0.49-13.46) and 1.13 (95% CI: 0.69-1.92), respectively. These results suggest that available evidence is not able to distinguish whether the elevated risk of miscarriage among women with extreme BMIs is explained by confounding alone. Further research is needed to better understand this association. Longitudinal research studies controlling for age, socioeconomic status, smoking, diabetes, and other potential confounders are needed to inform public health planning and patient care.

LATEBREAKER

Reproductive

Pre-Pregnancy Cervical Procedures for Cervical Intraepithelial Neoplasia and Subsequent Risk for Delivering a Small-for-Gestational-Age Infant Cassandra N. Spracklen* Rachel Wacks Christian P. Daniele Laura Attanasio Elizabeth Bertone-Johnson Katherine W. Reeves

Background: In the United States, there are an estimated 11,500 incident cases and 4,000 deaths annually from cervical cancer. While the median age at diagnosis is 50 years of age, precancerous cellular changes, called cervical intraepithelial neoplasia (CIN), are mostly found during women's 20s and 30s. The association between pre-pregnancy cervical procedures for CIN and preterm birth (PTB) is well established. Several studies have suggested a link to low birth weight (LBW) using the same underlying biological mechanism as PTB, suggesting that structural changes from pre-pregnancy cervical procedures also leads to LBW. We believe this is artifact from collinearity between birth weight and gestational age. No studies, to date, have evaluated the potential relationship between cervical procedures and risk for small-for-gestational age (SGA) as a means to statistically disentangle LBW from PTB.

Methods: Within the Iowa Health in Pregnancy Study, a population-based case-control study of PTB and SGA infants, 2,709 women completed a computer-assisted telephone interview including a series of questions about their history of abnormal pap smear, colposcopy, and surgical procedures to remove cervical tissue for CIN (primary exposure). SGA outcomes were obtained from hospital delivery records. Multivariable logistic regression analyses were used to generate unadjusted and adjusted OR and 95% CI for the association between any pre-pregnancy cervical procedure and odds of delivering an SGA infant.

Results: In IHIPS, there were 793 (29%) SGA infants. Any pre-pregnancy cervical procedure for CIN was not associated with odds for SGA in unadjusted (OR: 1.07, 95% CI: 0.8, 1.43) or adjusted (aOR: 1.01, 95% CI: 0.59, 1.73) models.

Conclusions: Having a cervical procedure prior to pregnancy does not increase the odds of having an SGA infant, contradicting prior literature and suggesting that altering the cervical tissue can affect infant gestational age but not birthweight

Respiratory

Characteristics of Medically-Attended Respiratory Infections in High-Risk Adults Cameron Lee* Cameron Lee Maria

The clinical similarity of respiratory viruses and the lack of routine laboratory testing create knowledge gaps regarding their burden in adults. This study aimed to understand the symptoms and severe outcomes of medically-attended respiratory infections caused by non-influenza, non-RSV winter respiratory pathogens in adults with underlying high-risk conditions.

We conducted an observational study of medically-attended acute respiratory infections (MAARI) among high-risk adults. Data from re-tested respiratory specimens and electronic health records of participants in a test-negative influenza vaccine effectiveness (FluVE) study (2015-2020) were analyzed. Univariate analyses identified factors associated with respiratory pathogens and severe outcomes; multivariable logistic regression assessed the link between high-risk conditions and specific pathogens.

Among 3,575 participants with complete data, our sample population comprised of 65% female participants with 30% of the population aged 65 years and older. Primary analyses found no statistically significant associations between most sociodemographic characteristics and non-influenza, non-RSV respiratory pathogens. However, high-risk conditions were associated with certain pathogens: those infected with seasonal coronavirus were more likely to have chronic respiratory disease ($p < 0.01$) and those infected with adenovirus were more likely to have cardiovascular disease ($p < 0.01$) than other pathogens.

There were no significant relationships between sociodemographic characteristics or severe illness outcomes and infection with non-influenza, non-RSV respiratory pathogens. Future research should explore relationships between underlying disease and respiratory infection outcomes.

Respiratory

Free testosterone, estradiol, and asthma endotypes in Puerto Rican youth Yueh-Ying Han*
Yueh-Ying Han Franziska J. Rosser Glorisa Canino Juan C. Celedón

Background: Sex hormones may explain age- and sex-related differences in asthma. We examined whether free testosterone or estradiol level was associated with asthma endotypes in Puerto Rican youth, a group with high asthma burden.

Methods: We analyzed data from 320 Puerto Ricans aged 10-20 years with (cases) and without (controls) asthma in the Epigenetic Variation and Childhood Asthma in Puerto Ricans study (EVA-PR) and 334 Puerto Ricans aged 6-14 years in the Puerto Rican Genetics of Asthma and Lifestyle study (PR-GOAL). Using nasal epithelial transcriptomic profiles, EVA-PR participants with asthma were classified as having T2-high, T17-high, or T2-low/T17-low endotypes, and a machine learning approach based on blood eosinophils, total IgE, and atopy was used to predict T2-high asthma in PR-GOAL cases. Serum total testosterone, estradiol, sex hormone binding globulin (SHBG), and progesterone were measured, and free testosterone levels were calculated using testosterone and SHBG. Multinomial regression was used for the multivariable analysis of free testosterone, estradiol and asthma endotypes (with controls as the reference group), separately by sex.

Results: In the multivariable analysis in EVA-PR, 1-unit increment in free testosterone was associated with 1.08 times increased odds (95% confidence interval [CI]=1.03 to 1.15) of T17-high asthma in females. In males, 1-unit increment in estradiol was associated with 1.03 increased odds (95% CI=1.01 to 1.06) of T2-high asthma. Similarly, in PR-GOAL 1-unit increment in free testosterone was associated with 1.05 times increased odds of T2-low asthma in females. In males, 1-unit increment in estradiol was associated with 1.08 times increased odds of T2-high asthma.

Conclusions: In Puerto Rican youth, free testosterone was positively associated with T17-high asthma in females, and estradiol was positively associated with T2-high asthma in males. Sex hormones may influence asthma via T2 and non-T2 immune pathways.

Science Communication & Media

Leveraging semi-Bayesian data methods to communicate study results that inform policy

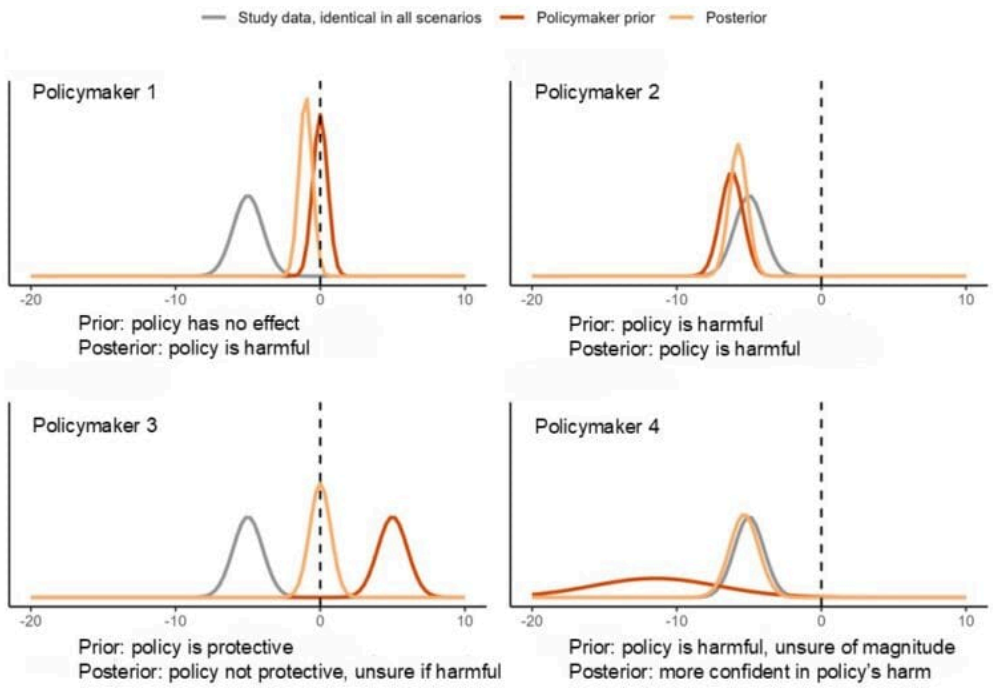
Simone Wien* Simone Wien Timothy L. Lash Melvin Livingston Whitney S. Rice Hannah L.F. Cooper Michael R. Kramer

Policymakers often informally incorporate their prior beliefs about a policy's effect when presented with new evidence from study data. This semi-formal Bayesian approach can conflict with the frequentist approach often used to guide inference. This discrepancy may make it difficult for epidemiologists to anticipate how policymakers will interpret study results. For example, a policy advocate may interpret protective results that are not statistically significant as confirmation that a policy improves health, while a policy skeptic may view those results as evidence that the policy is ineffective.

We adapt Greenland's semi-Bayesian data augmentation method to demonstrate how study results can be interpreted by different policymakers and to aid epidemiologists in developing arguments for varying prior beliefs. Using the effect of a policy on receipt of prenatal care as an example, we constructed priors reflecting different policymaker views and calculated their updated beliefs (posteriors) given hypothetical study data indicating a small but harmful policy effect (RD -5, 95% CL -7, -3 per 100 pregnancies). Per the method, priors and study data were operationalized as weighted estimates and pooled in lieu of a formal version of Bayes' theorem to calculate the posterior distribution.

This approach helps develop arguments tailored to a policymaker's posterior distribution (Figure 1). For instance, while Policymaker 3 may remain unconvinced that the policy is harmful given their prior belief in its protective effect, their posterior suggests that they may be more open to a discussion of how there is insufficient evidence that the policy is protective (RD 0, 95% CL -1.4, 1.4). Policymaker 1's posterior indicates that the data are sufficient to convince them that the policy is harmful; Policymaker 2 and 4's priors are reinforced given the data. We argue that this method helps epidemiologists frame results for policy audiences, including manuscript discussion sections.

Figure 1: Policymaker prior and posterior distribution for the effect of policy on any prenatal care, risk difference scale per 100 pregnancies



Science Communication & Media

Evaluating the Usability of a Health Technology Application to Combat Misinformation from the Community-Based Organization Perspective Amanda J Llaneza* Amanda Llaneza Muhammed Idris Ramadhan Malik Maya Korin Faven Araya Kristelle Pierre Rocio Baez Rodriguez Luz Claudio

Introduction: Health misinformation is a threat to public and environmental health. Health-related community-based organizations (CBOs) are trusted public health components of local communities. Health technology apps employed by CBOs have the potential to provide population-specific and culturally appropriate health information to combat misinformation. The objective of this study was to test the usability of a health technology application from the CBO perspective.

Methods: The Community Health Information Equity Forum (CHIEF), is an online platform developed to engage communities in dissemination of health messaging, built in collaboration for and with local communities in New York City. This study involved quantitative and qualitative methods to establish perceived usefulness, and perceived ease of use of the application from the perspective of members of CBOs. Participants completed a demographic survey, a series of tasks on the CHIEF app, commented on challenges and ease of use, and the Health Information Technology Usability Scale (Health-ITUES) post assessment survey. Frequencies and percent were used to describe the study sample, mean, and standard deviation were used to describe the overall Health-ITUES score, where a higher score (ranged from 1 to 5) indicated greater usability. A content analysis framework was utilized to systematically examine and interpret the qualitative data.

Results: Eight representatives from regional CBOs in New York City participated. All participants were female, 50% identified as Black/African American, 25% as Hispanic/Latino, and 25% as White. Most (75%) work in organizations that serve the borough of Brooklyn, 25% in the borough of Manhattan, and 67% were not currently satisfied with the current way their organization communicates with their constituents. The mean Health-ITUES score was 4.81 (SD: 0.17) for the CHIEF app. Patterns identified from the qualitative data were user experience design, functionality features, and outreach features.

Discussion: The CHIEF application demonstrated potential in serving as a trusted tool and means of interaction between community members and health-based CBOs.

Screening

Leveraging advocacy to shape public health data: The case of eating disorder surveillance among US youth Ariel Beccia* Ariel Beccia Sam Hahn Brittany Celebrano Allison Ivie S. Bryn Austin

Background: Eating disorders (EDs) are a growing public health threat for US youth, yet routine surveillance ceased when relevant items were removed from the CDC's Youth Risk Behavior Surveillance System (YRBS) in 2015. Here we report on a multi-sector campaign aimed at addressing this critical data gap. **Methods:** Our goal was to build support for the re-inclusion of items assessing EDs in the YRBS. Through strategic advocacy, communications, and community building, we targeted four key channels: Congress, community advocates, state YRBS coordinators, and media. **Results:** Our campaign generated significant momentum. Congressional engagement yielded two bipartisan letters to the CDC urging inclusion of ED items in the YRBS, along with provisions in federal budget bills. Community advocates organized a Capitol Hill advocacy day with direct engagement from Congressional members. Collaboration with state YRBS coordinators led to the formation of a formal working group, an online training program, and a proposal to the CDC calling for ED item inclusion. The campaign also garnered national media attention, further amplifying its message. These efforts culminated in a major victory: In July 2024, the CDC announced the addition of a binge eating item to the 2025 National YRBS – the first time in over a decade that representative data on EDs will be collected among US youth. Additionally, items assessing binge and restrictive eating were added to the recommended item pool for state-specific YRBS surveys. **Conclusions:** The CDC's decision to assess binge eating is a critical step toward strengthening ED surveillance in the US. Such data will make it possible to monitor trends in prevalence, identify spikes, and investigate inequities, ultimately informing more effective interventions. Our campaign also underscores the vital role that epidemiologists play in data advocacy efforts, highlighting how our expertise can shape public health priorities and drive meaningful change.

Screening

Liver Fibrosis Scores and Mortality in the Combined Cohort of World Trade Center Rescue/Recovery Workers Ankura Singh* Ankura Singh Rachel Zeig-Owens Nikolina Icitovic David G. Goldfarb Andrew C. Todd Christopher R. Dasaro Victoria Garrity David J. Prezant

Background

Higher liver fibrosis scores have been associated with elevated all-cause and liver disease-related mortality. We investigated whether liver fibrosis scores were associated with all-cause, liver disease-related and non-liver disease-related mortality as well as liver cancer incidence in workers who responded to the World Trade Center (WTC) on 9/11/01 (9/11).

Methods

The study included 43,870 WTC responders who were ≥18 on 9/11 and had blood drawn by 12/31/20 at a post-9/11 health exam. Aspartate aminotransferase-to-platelet ratio index (APRI), fibrosis-4 score (FIB-4), and nonalcoholic fatty liver disease fibrosis score (NFS) were calculated and categorized as low, intermediate or high fibrosis scores per established cutoffs. Deaths and liver cancer cases were identified via National Death Index records and state cancer registries, respectively. Cox proportional hazards regression models estimated HRs and 95% CIs for each outcome in those with intermediate and high vs low fibrosis scores, adjusting for sex, race, age, body mass index, smoking and alcohol use.

Results

There were 1,996 deaths, 81 liver disease-related deaths and 36 incident liver cancers in the cohort by 12/31/20. Participants with intermediate or high APRI (HR=1.73 CI=1.50-1.99 & HR=7.23 CI=5.63-9.29), FIB-4 (HR=1.18 CI=1.05-1.34 & HR=3.96 CI=3.22-4.85), or NFS (HR=1.61 CI=1.43-1.81 & HR=4.73 CI=3.78-5.93) had significantly greater risks of overall mortality vs those with low scores. Liver disease- and non-liver disease-related deaths were also elevated in those with intermediate or high scores. High APRI, FIB-4 and NFS and intermediate APRI and NFS were associated with liver cancer.

Conclusion

Intermediate and high liver fibrosis scores predicted all-cause, liver disease-related and non-liver disease-related mortality and high scores predicted liver cancer in WTC responders. Liver fibrosis scores may identify those at greater risk for mortality and liver cancer, even in a healthy worker cohort.

Screening

Carpal Tunnel Syndrome Severity Questionnaire: Diagnostic Accuracy Maik Zannakis* Maik Zannakis

Background America’s high incidence of carpal tunnel syndrome (CTS) is likely vastly underreported. Since CTS is a progressive disorder, early diagnosis is crucial for proper management. Symptoms questionnaires have been used for remote diagnoses, but heretofore have been fraught with inaccuracies. This study assesses the diagnostic accuracy of a new Carpal Tunnel Syndrome Severity Questionnaire (CTSSQ) when used as a tool to classify CTS severity.

Methods Screening data were collected via phone and email. The data were specific to CTS symptoms, results of EMG and NCV studies, and physician diagnostic impressions. Included patients demonstrated one of the three CTS severity levels (AAFP scale of Mild, Moderate, Severe). These patients then completed a CTSSQ online (N=68). Their prospective CTSSQ data were compared to pre-screen data. Diagnostic accuracy was evaluated for CTS severity level, comparing both sum- and algorithm-based scores.

Results For Mild CTS, the optimal cut-off score was 33 (sensitivity 88%, specificity 90%, AUC of 0.79). For Moderate CTS, the optimal cut-off score was 69 (sensitivity 91%, specificity 93%, AUC of 0.83). For Severe CTS, the optimal cut-off score was 91 (sensitivity 94%, specificity 96%, AUC of 0.85). The positive predictive value of the CTSSQ algorithm for diagnosing Mild, Moderate, and Severe levels of CTS was 89%, 91%, and 93%, respectively.

Conclusions The CTSSQ algorithm-based score performs well in identifying those patients with CTS as compared with similar measuring instruments. The more severe the CTS, the better the diagnostic validity of the tool for identifying the level of severity. Validating the diagnostic accuracy of the tool helps patients heretofore undiagnosed with CTS better comprehend their level of severity, with the intent of providing more impetus to seek immediate treatment.

Social

The socioecological framework for the field of epidemiology: aligning our work with justice and liberation Nadia Abuelezam* Nadia Abuelezam Jessie

Epidemiologists must look inward to work toward understanding how the field is shaped by recent sociopolitical events. Recent events, including the COVID-19 pandemic, Black Lives Matter, and the attacks on universities' equity, diversity, and inclusion work in the United States, are an opportunity to re-imagine how epidemiology can better serve more diverse populations in a domestic context. The history of epidemiology is firmly rooted in a positivist epistemological framework, meaning that our science has been controlled by the idea that reality is fully quantifiable; that numbers are objective; and, most problematically, that our biases and values do not shape our quantitative work. The positivist framework has limited our opportunities to extend our methodologies, prioritize community engagement, and focus on liberation as a goal of health equity work. We present a post-positivist view of the field through the construction of a socioecological framework for epidemiology (Figure 1). We consider the roles of epidemiologists as educators, public health practitioners, and members of the broader political communities in which they work. The framework names important action and reflection points from the individual- to the cultural-level of the socioecological framework. For example, at the institutional level, we suggest implementing and supplementing communications and advocacy training at every level of public health education through bolstering Council on Education for Public Health accreditation requirements. At the cultural level, we suggest exploring the value of Indigenous research models or standpoint theory, which is the idea that knowledge is fundamentally shaped by the social and political roles of the people who create it. By presenting this framework, we aim to instigate conversations on how the field of epidemiology can more closely align with justice oriented frameworks, viewpoints, and methodologies in order to serve more diverse populations.

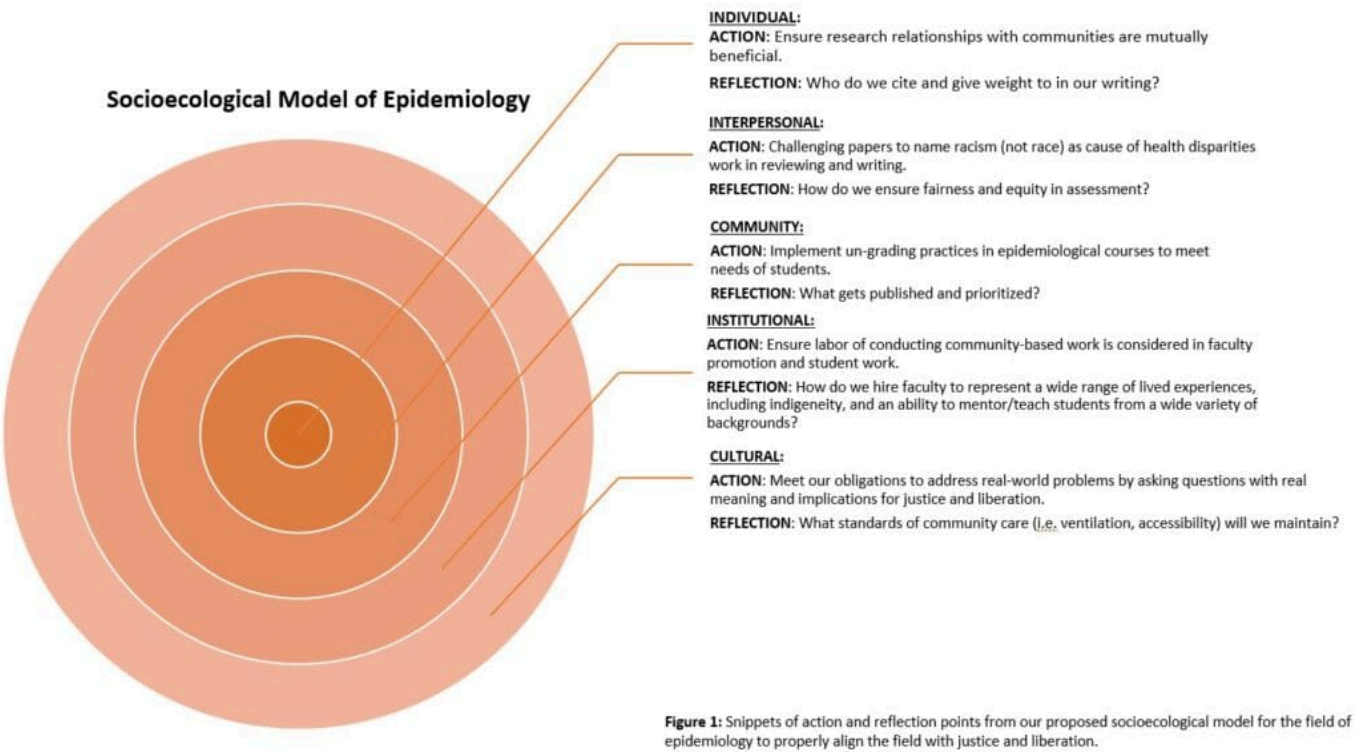


Figure 1: Snippets of action and reflection points from our proposed socioecological model for the field of epidemiology to properly align the field with justice and liberation.

Social

Solidarity-based epidemiology: re-distributing power inside and outside of the field Nadia Abuelezam* Nadia Abuelezam Jessie

We invite our colleagues in epidemiology to begin a conversation: what difference would it make if we took seriously the need to address differential power structures in epidemiology – both for epidemiologists ourselves and for those we serve? What is the nature of the solidarity required to transform the field? We present the tenets and framework for a “solidarity-based epidemiology” focused on delineating the professional obligations of epidemiologists (and epidemiology as a field). Drawing on Dr. Carol Gould’s sense of solidarity as the central tenet of any movement dedicated to addressing structural injustice, we imagine applying it to our own field to define solidarity-based epidemiology.

We believe solidarity involves changing underlying frameworks and methods related to how we ask questions, with the ultimate goal of re-distributing power to the most marginalized in order to advance their health. Epidemiologists have a role in this power redistribution through individual choice and cultural change within the field. For example, in thinking about how we might address the structural injustices experienced by disabled people, we suggest meeting disability advocates’ demands to ensure their ability to participate fully in all spaces (virtual and in person). To better serve our first-generation, lower income, or undocumented students, we suggest prioritizing funding schools with higher enrollments of these groups and providing unrestricted funds to ensure they can complete their education. Solidarity work requires intentional collaboration with previously ignored voices – a task difficult to accomplish without structural change in the discipline to allow for diverse methodological frameworks, study timelines, promotion timelines and research priorities to engage in this solidarity based work.

Through describing the tenets of solidarity-based epidemiology, we hope to inspire a conversation about cultural change in the discipline.

Social

Housing insecurity and adolescent mental health: A data-driven exploration of risk and resilience Sakurako Okuzono* Sakurako Okuzono Natalie Slopen

Background: Millions of U.S. households face difficulty paying rent and housing evictions, with families with children disproportionately affected by housing insecurity. Understanding heterogeneous responses to housing instability can lead to improved and tailored interventions. This study examined heterogeneity in the association between housing instability and subsequent mental health among U.S. adolescents to identify characteristics of at-risk and resilient subpopulations using a machine-learning approach.

Method: We used data from the Adolescent Brain Cognitive Development Study, a longitudinal cohort of 9-10-year-old U.S. adolescents. We included data from baseline to 3-year follow-up without missing exposure and outcome (n= 8,949). Using an ecological model, we selected 73 baseline variables as potential effect modifiers, reflecting a range of individual, family, neighborhood, and state-level characteristics. The exposure was housing instability one or two years after baseline. Mental health was assessed using the Child Behavioral Checklist at age 12. We estimated the average treatment effect via targeted maximum likelihood estimation and its heterogeneity (Conditional Average Treatment Effect: CATE) via the Generalized Random Forest algorithm (GRF), which allowed us to model complex multiple interactive effects. Last, we identified at-risk and resilient groups by taking the top and bottom deciles of the CATE estimate.

Results: 8 percent of participants experienced housing instability. Housing instability is associated with higher behavioral problems, and CATE obtained with GRF ranges from -0.5 to 1.1 (SD: 0.1). Comparing the at-risk and resilient groups, the at-risk group tended to belong to minoritized racial groups, have lower school involvement, and live in worse neighborhoods. We further identified that complex heterogeneity exists based on unique combinations of baseline characteristics.

Conclusion: By leveraging a data-driven approach, our study highlights the multifaceted nature of risk and resilience in response to housing insecurity and offers a framework for further research that can inform the development of targeted interventions.

Social

Financial assets and mental health after job loss Catherine Ettman* Catherine Ettman Grace V. Ringlein Rajesh Satpathy-Horton Elizabeth A. Stuart Sandro Galea

While there is strong evidence on the effects of job loss on mental health, there is less evidence about the role of wealth in protecting mental health following job loss. Using data from the CLIMB study, a longitudinal cohort of working-age U.S. adults (18-64 years) surveyed in Spring 2020, 2021, 2022, 2023, and 2024 (n=581), we assessed depressive symptoms following job loss and tested for effect heterogeneity by wealth. First, we estimated the effect of early pandemic job loss on depressive symptoms (PHQ-9 scores, 0-27) across 5 survey periods (2020-2024) using survey weighted, propensity score balanced generalized estimating equation (GEE) models. A doubly robust propensity score model was used to estimate the average treatment effect on the treated (ATET). Models included age, gender, race and ethnicity, housing status, savings, marital status, region, income, and previous depression diagnosis. Second, we estimated the effect of job loss on depressive symptoms stratified by savings groups, using GEE with survey and propensity score weights. The full model estimated an increase of 1.11 points (p=0.16) in depressive symptoms relative to no job loss on average across the 5 timepoints. Stratified models showed an increase of 0.92 points (p=0.17) for those with >$25,000 savings and a 1.11 point increase (p=0.30) for those with <$25,000 in savings. We found evidence of a small but non-significant effect of early pandemic job loss on depressive symptoms overall in U.S. adults from 2020-2024. While persons with lower savings had higher depressive symptoms, we did not find evidence of a significant difference in the effect of job loss on mental health across savings groups, potentially due to sample size.

Social

Following the power: social-class inequities in mortality from accidental poisonings, suicide, and chronic liver disease Jerzy Eisenberg-Guyot* Jerzy Eisenberg-Guyot Audrey Renson

Introduction: Hazardous working conditions fuel inequities in accidental-poisoning, suicide, and chronic-liver-disease mortality. Relational social-class theories suggest such hazards flow from power imbalances between workers, managers, and employers, social classes demarcated by power over property and labor. However, to our knowledge, no US studies using relational measures have analyzed social-class inequities in mortality from these causes. We addressed this gap.

Methods: We used the Mortality Disparities in American Communities dataset, which links the 2008 American Community Survey to the National Death Index through December 31, 2019. We classified respondents ages >18 as incorporated business owners (IBOs), unincorporated business owners (UBOs), managers, workers, or not in the labor force (NLFs) based on their employment, occupational, and business-ownership status. Then, using inverse-probability-weighted Aalen-Johansen survival curves, we estimated class inequities in mortality risks from the causes of interest, adjusted for age and gender. We also ran analyses subdividing workers by occupation and employment status, and by gender, race/ethnicity, and education.

Results: Our sample included 2,304,500 respondents and 132,000 deaths from all causes, 10,870 of which were from the focal causes. NLFs, UBOs, and workers had, respectively, 900 (95% CI: 800, 1000), 100 (95% CI: 0, 200), and 100 (95% CI: 0, 200) per 100,000 greater 12-year risks of mortality from the causes of interest than IBOs. Estimates remained largely unchanged after more thorough sociodemographic adjustment. Risks were especially elevated among unemployed, blue-collar, and service workers. Finally, inequities were similar within racialized groups, but were greater among men and the less-educated.

Discussion: We estimated class inequities in mortality from accidental poisonings, suicide, and chronic liver disease, aligning with theories linking the exploitation of labor to health inequities.

Social

Childhood adversity and vaginal microbiome diversity among pregnancy planners Andrea S. Kuriyama* Andrea S Kuriyama Julia C Bond Eliza Pentz Bernard L. Harlow Wendy Kuohung Doyle Ward Yael Nillni Renee Boynton-Jarrett Lauren A. Wise

Introduction: Childhood adversity (CA) can have long-term health effects, including impaired immune function and dysregulated cortisol levels, both hypothesized to cause dysbiosis of the vaginal microbiome.

Methods: We estimated the association between CA and the vaginal microbiome among 65 participants in Pregnancy Study Online, a preconception cohort study. At baseline, participants reported CA via the Adverse Childhood Experiences (ACE) scale and Brief Trauma Questionnaire (BTQ). Participants provided a vaginal swab sample within two weeks of enrollment that was analyzed with 16S rDNA sequencing. Higher microbiome diversity (associated with dysbiosis) was operationalized as 2 binary variables: 1) higher than the sample median of the Shannon Index (a metric for diversity of microbes in a single sample) and 2) ≥2 dominant operational taxonomical units (OTUs) – groups of related organisms comprising ≥10% of the microbiome. We calculated prevalence ratios (PRs) and 95% confidence intervals (95% CIs) using log-binomial regression, adjusting for race/ethnicity, parental education, and childhood .

Results: ACE scores 1-3 and ≥4 (vs. 0) were positively associated with Shannon Index >median (PR=1.10, 95% CI=0.55-2.19; PR=1.38, 95% CI=0.61-3.12, respectively) and ≥2 dominant OTUs (PR=1.15, 95% CI=0.58-2.29; PR=1.83, 95% CI=0.92-3.66, respectively). All ACE domains were positively associated with Shannon index >median and ≥2 dominant OTUs, except for household substance abuse and incarceration. Compared with participants who reported no abuse on the BTQ, those who reported sexual abuse only were more likely to have a Shannon Index > median. Across all BTQ categories, those reporting abuse were more likely to have ≥2 dominant OTUs than those reporting no abuse.

Conclusions: CA was associated with greater vaginal microbiome diversity, indicating that CA may have long-term effects on reproductive health.

Prevalence ratios for childhood adversity in relation to vaginal microbiome outcomes (n=65)

		Shannon Index > median			≥2 dominant Operational Taxonomic Units (OTUs)		
	Total N	N (%)	Crude PR (95% CI)	Adjusted PR (95% CI)*	N (%)	Crude PR (95% CI)	Adjusted PR (95% CI)*
Cumulative ACE Score							
0	14	5 (35.7)	1.00 (ref)	1.00 (ref)	6 (42.9)	1.00 (ref)	1.00 (ref)
1-3	37	17 (46.0)	1.29 (0.59,2.82)	1.10 (0.55,2.19)	19 (51.4)	1.20 (0.61, 2.37)	1.15 (0.58,2.29)
≥4	14	9 (64.3)	1.80 (0.81,4.02)	1.38 (0.61, 3.12)	11 (78.6)	1.83 (0.94,3.56)	1.83 (0.92,3.66)
ACE domains							
Household mental illness	32	18 (56.3)	1.58 (0.73,3.39)	1.17 (0.55,2.46)	18 (56.3)	1.31 (0.67,2.58)	1.18 (0.58,2.37)
Household substance abuse	18	10 (55.6)	1.56 (0.69,3.52)	1.00 (0.63,1.57)	12 (66.7)	1.56 (0.78,3.09)	1.48 (0.74,2.96)
Household incarceration	4	3 (75.0)	2.1 (0.85,5.18)	0.97 (0.43,2.23)	3 (75.0)	1.75 (0.76,4.01)	1.50 (0.37,6.07)
Parental separation/divorce	20	11 (55.0)	1.54 (0.69,3.45)	1.38 (0.47,4.10)	11 (55.0)	1.28 (0.62,2.64)	1.71 (0.67,4.39)
Domestic violence	11	7 (63.6)	1.78 (0.77,4.10)	1.37 (0.53,3.57)	8 *72.7)	1.70 (0.84,3.43)	1.38 (0.68,2.78)
Physical abuse	14	8 (57.1)	1.60 (0.69,3.69)	1.49 (0.52,4.22)	9 (64.3)	1.50 (0.73,3.08)	1.17 (0.79,1.73)
Emotional abuse	12	15 (55.6)	1.56 (0.71,3.39)	1.47 (0.59,3.62)	16 (59.3)	1.38 (0.70,2.73)	1.42 (0.71,2.82)
Sexual abuse	27	8 (66.7)	1.87 (0.83,4.19)	1.22 (0.70,2.13)	9 (75.0)	1.75 (0.88,3.48)	1.96 (0.57,6.70)
Brief Trauma Questionnaire							
No abuse	41	19 (46.3)	1.00 (ref)	1.00 (ref)	19 (46.3)	1.00 (ref)	1.00 (ref)
Physical abuse only	7	2 (28.6)	0.62 (0.18,2.08)	0.87 (0.44,1.69)	4 (57.1)	1.23 (0.60,2.54)	1.30 (0.68,2.49)
Sexual abuse only	12	8 (66.7)	1.44 (0.86,2.42)	1.20 (0.78,1.85)	10 (83.3)	1.80 (1.19,2.72)	1.88 (0.77,4.59)
Both physical and sexual abuse	5	2 (40.0)	0.86 (0.28,2.65)	1.01 (0.51,2.02)	3 (60.0)	1.29 (0.59,2.85)	1.32 (0.61,2.89)

Note: ACE=adverse childhood experiences; PR=prevalence ratio; CI=confidence interval;

*Adjusted for race/ethnicity, highest level of parental education, and economic resources as a child

Social

Human flourishing and sleep quality by age group among South Korean adults: A cross-sectional study Jaeyoung Ha* Jaeyoung Ha Sung-il Cho

Introduction: While sleep quality has been linked to psychological predictors, such as happiness and life purpose, its relationship with broader dimensions of subjective well-being (i.e. human flourishing) remains understudied.

Methods This study surveyed 1,217 South Korean adults aged 19–64 years through simple random sampling. Human flourishing was assessed using the Flourish Index (FI), which includes two items across five domains: happiness and life satisfaction, health, meaning and purpose, character and virtue, and close relationships. Total flourishing scores (0–100) were calculated by summing domain scores, with higher values indicating greater flourishing. Sleep quality was measured using the Pittsburgh Sleep Quality Index (PSQI; 0–21, higher scores indicating poorer sleep quality). Regression models were adjusted for sociodemographics and health behaviors, including gender, education, marital status, income, depression, anxiety, alcohol, and tobacco use.

Results Flourishing scores were significantly related to sleep quality across all age groups, even after adjusting for covariates The associated flourishing domains differed by age. For those aged 19-29, Happiness and Life satisfaction (beta (SE): -0.273 (0.090) p=0.002), and Close social relationships (beta (SE): -0.122 (0.054), p=0.025) were significant. Health was the significant factor for those aged 30-39 (beta (SE): -0.118 (0.061), p=0.05). aged 50-59 (beta (SE)=-0.136 (0.071), p=0.05), and aged 60-64 (beta (SE)=-0.266 (0.100), p=0.009).

Conclusion Sleep quality correlates with different aspects of flourishing across age groups. For individuals aged 30 and older, health was strongly linked to sleep quality, while happiness and relationships were more significant for those aged 19-20. Further research should examine the age-specific associations between sleep quality and human flourishing.

Figure 1. Flourishing scores by domain and age group in a sample of 1,217 Korean adults.

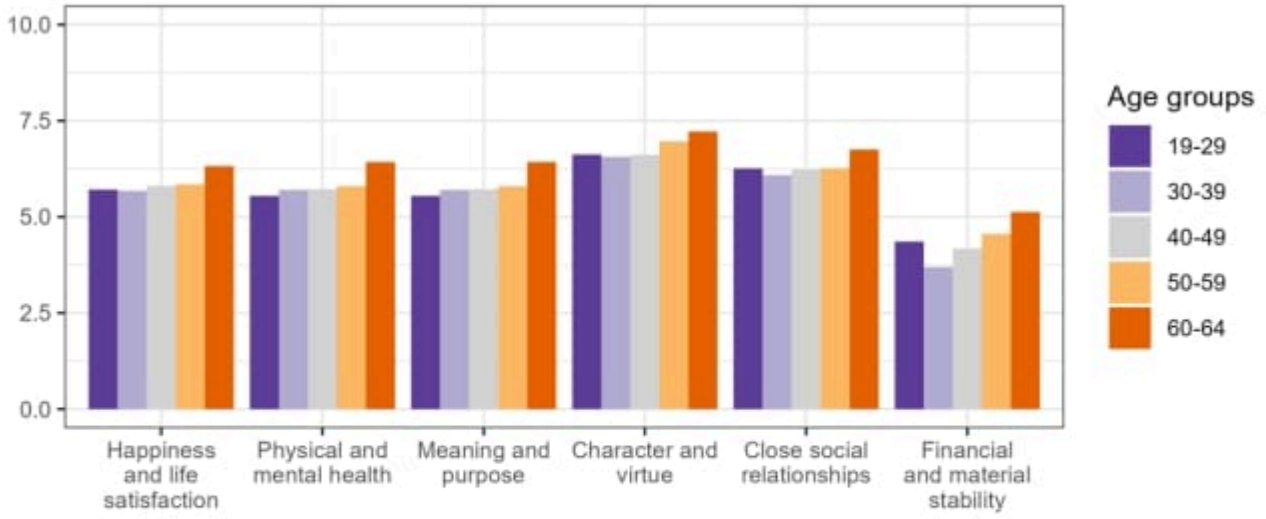
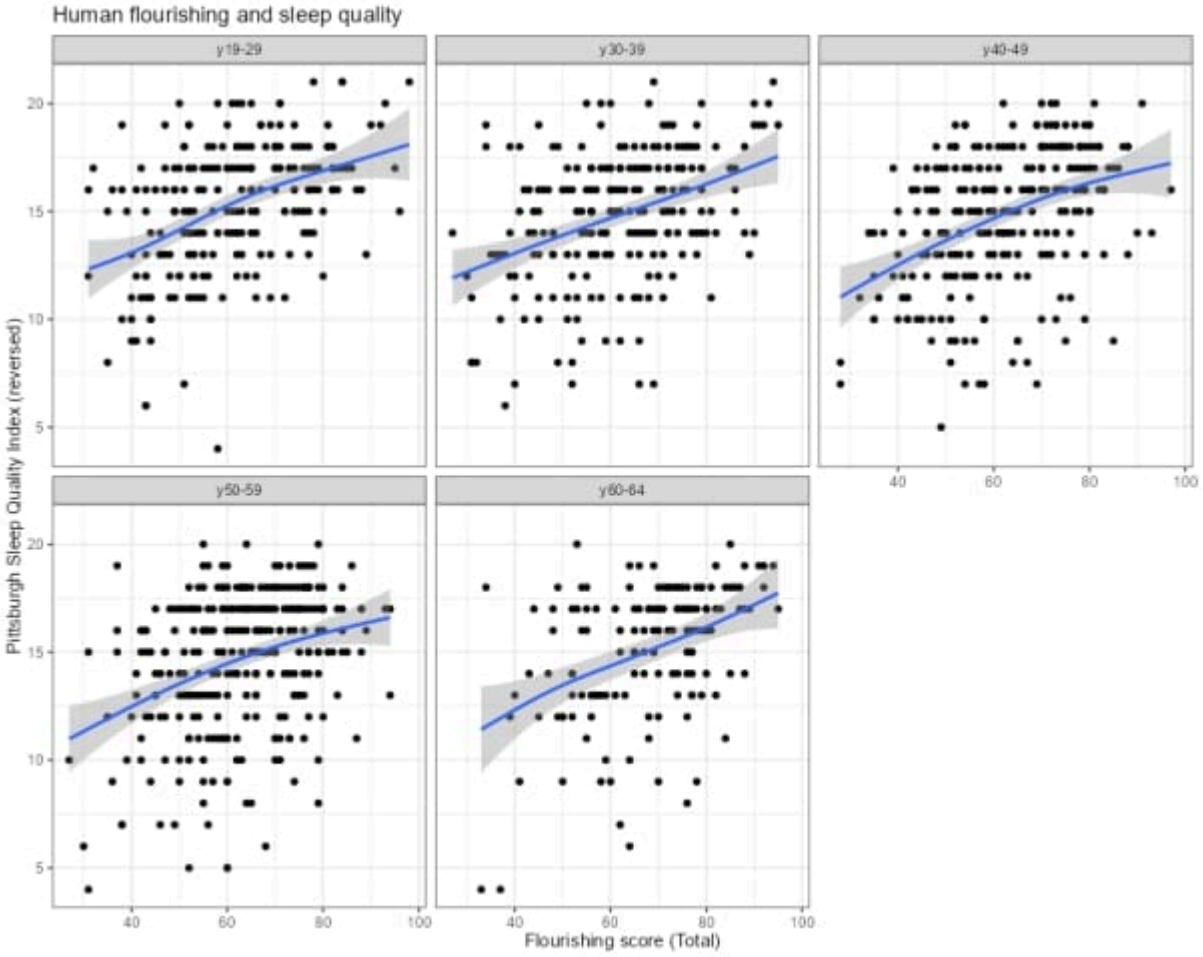


Figure 2. Correlations between human flourishing and sleep quality by age groups.



Social

Health status and voting participation among US citizens Jordan Baeker Bispo* Jordan Baeker Bispo Jingyi Tian Ahmedin Jemal Farhad Islami

Background: Increasing voter participation was recently added as a core objective of Healthy People 2030. In addition to structural barriers, poor health and chronic disease burden may hinder civic engagement, but few studies have examined this relationship at the national level. This study examines associations between health status and voting among US citizens, overall and by age, sex and race/ethnicity.

Methods: Data are from the 2023 National Health Interview Survey. The dependent variable was self-reported voting participation (yes/no) in the most recent local election. Health indicators included overall self-rated health (SRH), disability status (yes/no), and history (ever diagnosed: yes/no) of five common chronic diseases (heart disease, stroke, cancer, chronic obstructive pulmonary disease [COPD], and diabetes). Associations were modeled using survey-weighted logistic regression with adjustment for respondent sociodemographic characteristics.

Results: Data from more than 25,000 respondents were analyzed. Overall, the prevalence of voting was significantly lower for those with fair/poor versus excellent/very good SRH (adjusted prevalence ratio [aPR]=0.87, 95%CI=0.83-0.90), and for those with a disability (aPR=0.87, 95%CI=0.83-0.91) or history of stroke (aPR=0.89, 95%CI=0.83-0.95), heart disease (aPR=0.95, 95%CI=0.91-0.99) or COPD (aPR=0.91, 95%CI=0.86-0.97) than those without. Conversely, cancer history was associated with higher voting participation (aPR=1.06, 95%CI=1.03-1.11). In stratified analyses, associations were similar for males and females. Associations with SRH, COPD, diabetes and stroke were stronger among NH White respondents, and associations with cancer were stronger at younger ages.

Conclusions: Poor overall health and chronic disease history, with the exception of cancer, were linked to lower voting participation. Efforts are needed to expand voting accessibility among adults with health-related barriers to civic engagement.

Social

Who is lonelier: in-home or long-term residential care? Rosanne Freak-Poli* Rosanne Freak-Poli Barbara Barbosa Neves Chilot Agegnehu Pei-Chun Ko

Background

Surgeon General Murthy has declared that America has an “epidemic” of loneliness and has likened its public health risks to smoking. People in later life and people with ill health are particularly vulnerable to loneliness.

Aim

To compare loneliness, social isolation, and social support by living situation among Australia’s most health-vulnerable older adults.

Methods

495 Australians receiving the highest care tier under the government subsidy system were recruited. Surveys were conducted online and in-person between October 2023 and July 2024.

Results

Participants in long-term residential care (n=279) were older (mean±SD 85.81±7.83 vs. 82.34±7.28 years, $p<0.001$), more likely to be born in Australia (67% vs. 58%, $p=0.01$), speak English as their first language (90% vs. 80%, $p=0.03$), and report having never had a partner (19% vs. 6%, $p=0.001$) compared to those receiving in-home care (n=216). No significant differences were observed for gender, sexual orientation, Aboriginal or Torres Strait Islander status, or education level.

The prevalence rates are disheartening. Across multiple measurements, at least 30% are lonely, 40% have low social support, and around half are socially isolated (Figure). Long-term residential care participants tended to be less lonely and have more social support, but be more socially isolated than in-home care recipients (Figure).

Conclusion

This study represents the largest research sample of high-tier recipients. We found that individuals receiving in-home care experience more loneliness and lower social support, despite having lower social isolation compared to those in long-term residential care. Given the known benefits of social interaction for health and well-being, these findings have critical implications for policies that assist people to remain at home in later life. However, the disheartening prevalence rates highlight the need for strategies to enhance social connection among older adults in both settings

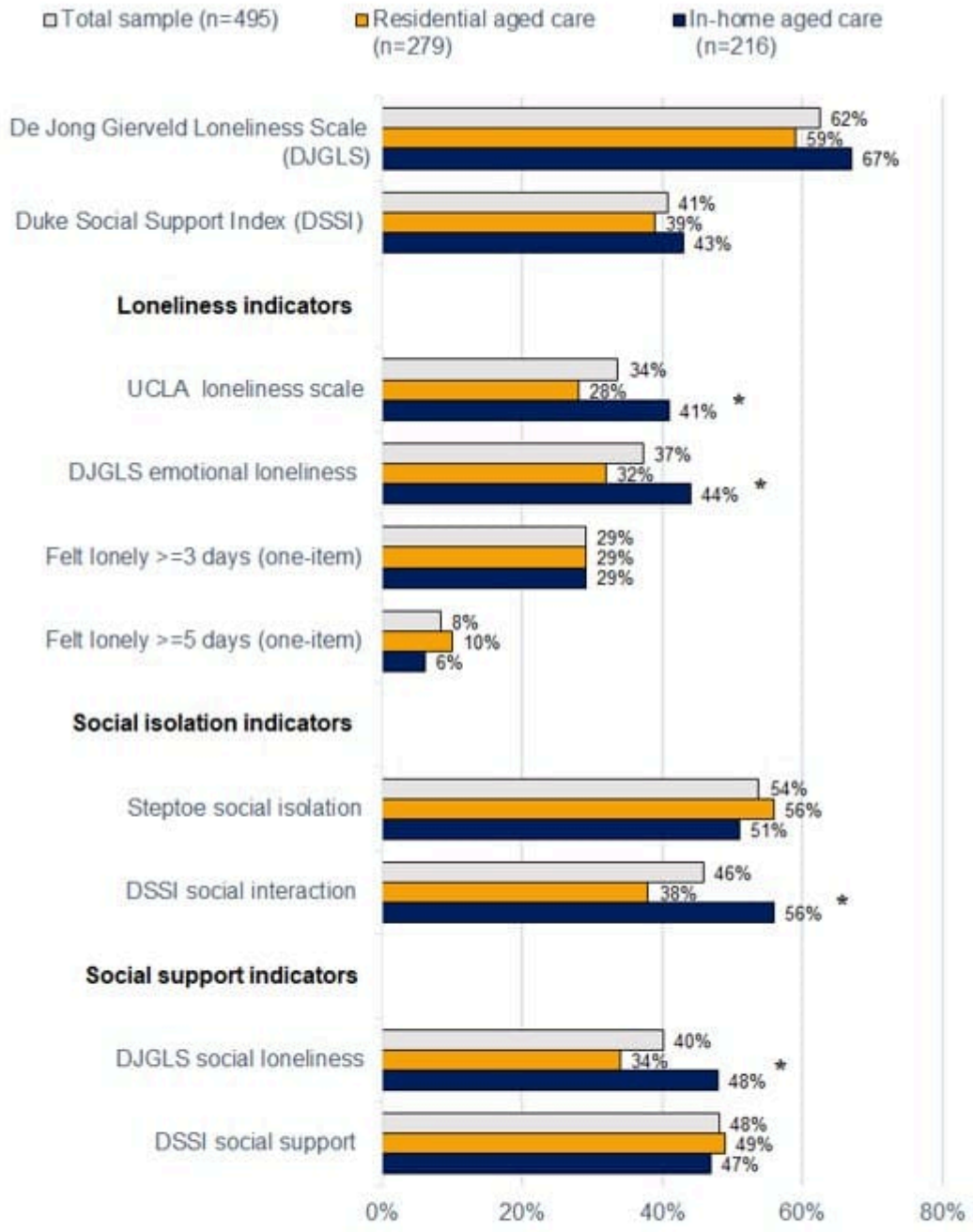


Figure: Comparisons of loneliness, social isolation and social support among Australians in long-term residential (n = 279) and in-home (n = 216)care

Higher values indicate the positive or negative outcome based on the measurement name. *p<0.05.

Social

Punitive school discipline is associated with lower odds of contraceptive use in adolescence and higher odds of sexual victimization in early adulthood Jillian Hebert* Jillian Hebert Catherine dP Duarte Kelsey Holt Anusha M Vable

Punitive school discipline practices, like suspension or expulsion, are common exposures in US schools with implications for disrupted positive peer and trusted adult relationships. While linked to increased risk for various adverse physical and mental health outcomes, no work has evaluated associations between punitive school discipline and adolescent contraceptive use or sexual victimization in early adulthood. We hypothesize that punitive school discipline increases vulnerability to sexual victimization and risk for engaging in unprotected sex. In National Longitudinal Study of Adolescent to Adult Health data, we used confounder adjusted logistic regressions to estimate associations between punitive school discipline (3-levels: no discipline, ever suspended, ever expelled; measured in grades 7-12) and (1) adolescent contraceptive use one year later (yes/no in last encounter; in past year) and (2) sexual victimization (yes/no without physical force; with physical force) measured 14 years later when students enter early adulthood (ages 24-32). 22% of participants experienced suspension and 4% experienced expulsion at baseline. While suspension was not associated with contraceptive use during the last sexual encounter or in the last year, compared to no punitive school discipline, suspension was associated with higher odds of experiencing sexual victimization in early adulthood (with physical force OR: 2.11, 95%CI: 1.61, 2.76; without physical force OR: 1.74, 95%CI: 1.36, 2.20). Compared to no punitive school discipline, expulsion was associated with lower odds of contraceptive use (in last encounter OR: 0.57, 95%CI: 0.36, 0.93; in past year OR: 0.62, 95%CI: 0.39, 0.98) and higher odds of experiencing sexual victimization without physical force (OR: 1.98, 95%CI: 1.14, 3.31). Results suggest exposure to punitive school discipline may shape sexual experiences in adolescence and early adulthood and may be an important modifiable risk factor for long-term sexual health.

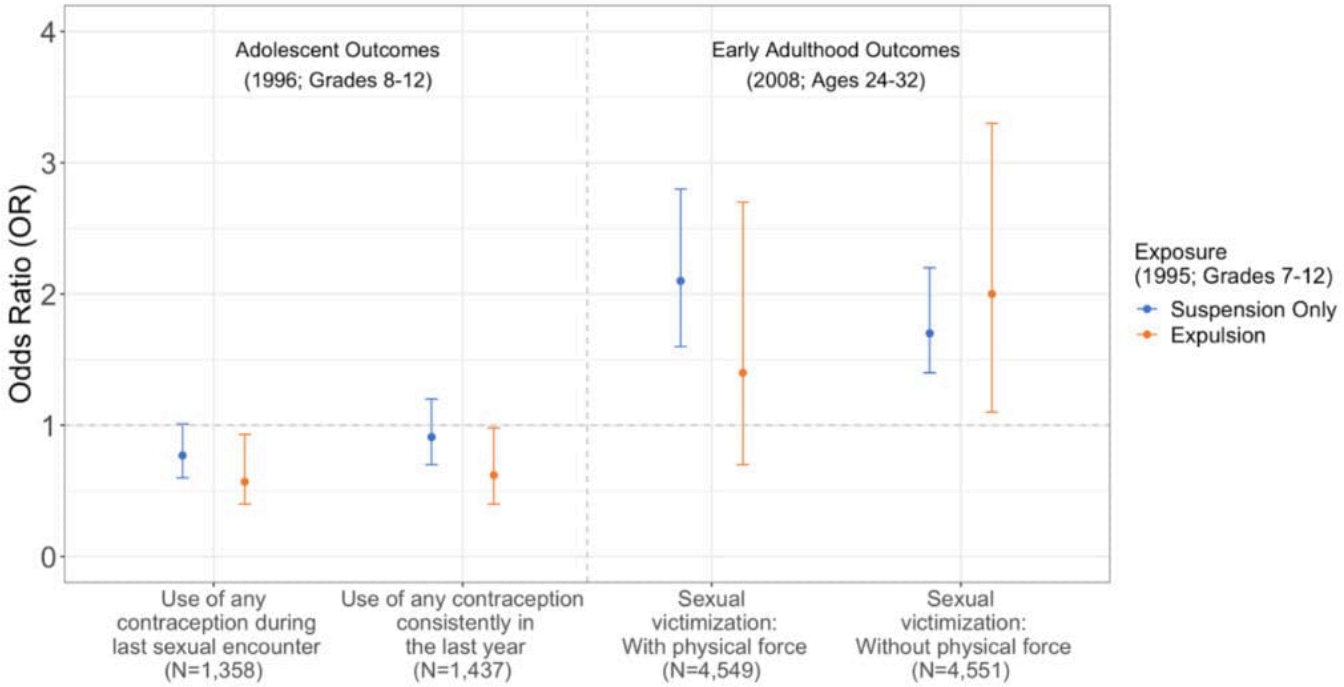


Figure 1. Associations between punitive school discipline and contraceptive use or sexual victimization

Structural

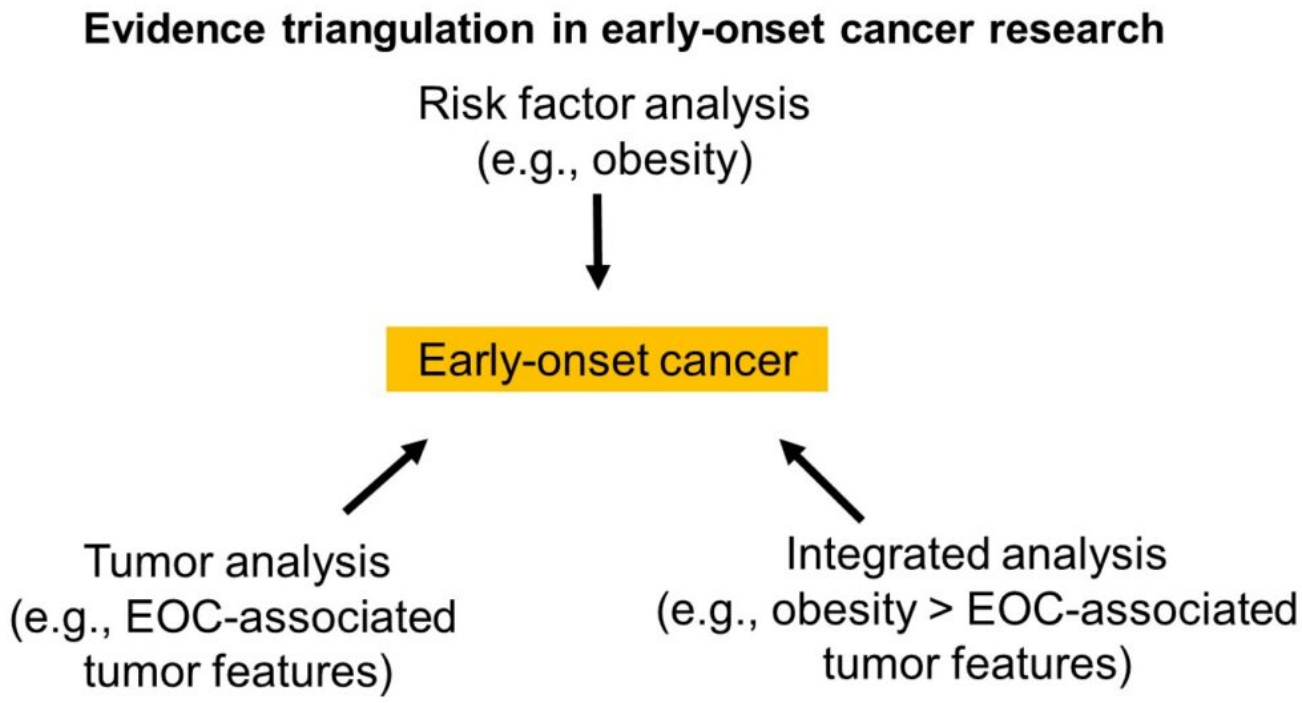
State-Level Weight Stigma: A novel measure using Project Implicit data and case-study application Alexis Miranda* Alexis Miranda Brittany Charlton Colleen Reynolds Bryn Austin Ariel Beccia

Objective: The importance of studying root causes of health inequities (e.g., structural racism) is established, yet few studies have explored the health effects of structural forms of weight stigma on health. Our objective was to develop a measure of weight stigma at the state level and perform an illustrative case study using preterm birth, an outcome known to be associated with other systems of oppression like racism. **Methods:** Using data from Project Implicit, a nonprofit that administers implicit association tests to help identify implicit bias, we compiled several individual-level indicators of weight stigma into a composite score and categorized states according to their level of weight stigma, based on quartiles of the state-level average. Case study data were drawn from the longitudinal Growing Up Today Study; participants were followed beginning in 1996 and a lifetime pregnancy history was assessed in 2019. We fit unadjusted logistic regression analyses with generalized estimating equations to account for clustering by multiple births to estimate associations between state-level weight stigma and preterm birth. **Results:** Individuals residing in states with the highest quartile of weight stigma score (Q4) had 1.49-times the odds of preterm birth compared to those living in the lowest quartile of weight stigma score (95% CI: 1.00, 2.22). The predicted probability of preterm birth in the lowest exposure quartile (Q1) is 0.070; 0.058 for those in Q2; 0.062 for those in Q3; 0.10 for those in Q4. **Conclusions:** Findings from this study suggest that weight stigma at the state level may be associated with preterm birth. We have demonstrated the effective use of this novel measure and the relative ease in which it can be applied to future studies of weight stigma and health. Future work should examine cumulative exposure to weight stigma over the life-course and consider additional methods to operationalize this exposure in conjunction with individual-level measures.

Study Design

Evidence triangulation in early-onset cancer research Tomotaka Ugai* Tomotaka Ugai Shuij Ogino Satoko Amanda Phipps Ulrike Peters

The incidence of early-onset cancer, commonly defined as cancers diagnosed in adults below 50 years old, has increased in many countries. Evidence suggests that early-onset cancer is different from later-onset cancer and that early-life and long-term exposure can influence early-onset cancer risk decades later. However, key challenges in causal analyses of these exposures exist. For example, studies of early-onset cancers may be susceptible to recall bias, shorter follow-up, small sample size of young participants and early-onset cases, and confounding. To address these challenges, we took the following approaches. As an example, we illustrated our approaches using our early-onset colorectal cancer (CRC) research utilizing the resources of the Nurses' Health Study (NHS), Health Professionals Follow-up Study, and Genetics and Epidemiology of Colorectal Cancer Consortium. First, we compared clinicopathological characteristics of early-onset cases with those of later-onset cases in a cross-sectional case-only analysis. We identified long interspersed nucleotide element-1 (LINE-1) DNA hypomethylation, immunosuppressed features, and pks+ Escherichia coli colibactin mutational signatures as early-onset CRC-associated features. Second, we conducted a pooled analysis of case-control studies to examine the association between long-term exposures and the risk of early-onset CRC, showing that obesity [OR, 1.3 (1.2-1.3)], alcohol [OR, 1.2, (1.0-1.6)], fast insulin [OR, 2.4, (1.3-4.2)], and type 2 diabetes [OR, 1.3 (1.0-1.7)] were associated with early-onset CRC risk. Third, we conducted an integrative analysis of long-term exposures and early-onset CRC-associated tumor features in a prospective cohort design. We have shown that long-term alcohol intake is associated with increased incidence of CRC with tumor LINE-1 hypomethylation [HR: 1.7 (1.0-2.7)] and that insulin-resistant promoting dietary scores are associated with increased incidence of CRC with pks+ Escherichia coli [HR: 4.1 (1.7-9.8)]. Ideally, we hope to validate these associations in early-onset CRC after we collect more tissue from early-onset CRC. These combined approaches will strengthen causal inferences by integrating results from different approaches, leading to evidence triangulation in early-onset cancer research.


Evidence triangulation in early-onset cancer research
Risk factor analysis
(e.g., obesity)
Early-onset cancer
Tumor analysis
(e.g., EOC-associated
tumor features)
Integrated analysis
(e.g., obesity > EOC-associated
tumor features)

Study Design

Development of a Community-Based Collaborative Study to Understand & Mitigate Manifestations of Structural Racism in Cancer Care Settings Emma Herbach* Emma Herbach Samantha McCoy Gabrielle Harris Isis Nelson Erin Kobetz Antonia Leavitt Brandon Mahal Amanda Rivera

Purpose: To describe the collaborative development of a community-based pilot study to document manifestations of structural racism throughout the cancer continuum and generate actionable patient-driven solutions.

Methods: Co-creation of this initiative began with a community cancer survivor sharing her story during a cancer center outreach event. A partnership flourished during informal interviews, which highlighted the hardships of her cancer journey due to failures in healthcare, and specifically cancer care, settings. Informed by her insights, we developed a protocol to systematically collect data about the cancer care experiences of marginalized survivors.

Results: The resulting pilot study aims to (1) characterize the cancer care journey of breast and gynecologic survivors from populations impacted by structural racism and (2) develop patient-driven recommendations to address multilevel manifestations of structural racism in cancer care settings. This transformative mixed methods study marries the need for in-depth patient narratives and robust quantitative measurements of quality of care with focus groups and surveys.

Two key perspectives from our community partner shaped the focus of and approach to this work: (1) the importance of being heard and (2) taking action to remediate past harms. Being heard and valued is critical to healing from the hardships of navigating cancer care. To ensure the expertise of survivors is incorporated into study procedures, we hired 4 community members as paid members of the research team. By elevating the patient voice to multidisciplinary healthcare stakeholders, their first-hand accounts will be heard by people in positions of power who may rarely hear the realities of navigating cancer as someone in a racialized body. Beyond just talking about hardship, doing something is equally important. Thus, the recommendations generated through this work come directly from survivors, who will collaboratively determine what resources are needed to ameliorate barriers to high-quality cancer care.

Conclusions: This collaborative research initiative to understand how structural racism manifests in cancer care settings is a critical step towards mitigating inequitable care and outcomes among cancer patients.

Development of a Community-Based Collaborative Study to Understand & Mitigate Manifestations of Structural Racism in Cancer Care Settings

E. Herbach[1], S. McCoy[2], G. Harris[3], I. Nelson[3], E. Kobetz[1], A. Leavitt[4], B. Mahal[1,5], A. Rivera[1,5]

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[2]Cancer Survivor
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FIERCE
Fighting Structural Inequality in Cancer Care

Background

- Structural inequalities drive disparities along the continuum of cancer care **(Figure 1)**
- Gaps in knowledge exist about how high-level mechanisms manifest in healthcare settings from the patients' perspective
- Direct survivor experiences are needed to fully understand barriers to care

Purpose

- To describe the collaborative development of a community-based pilot study to document manifestations of structural racism throughout the cancer continuum and generate actionable patient-driven solutions

Methods

- Interviews with community cancer survivor who experienced hardships throughout her cancer care due to failures in healthcare settings
- Drove development of a transformative mixed methods study to systematically investigate the cancer care experiences of marginalized survivors

Figure 1: Theoretical Framework.
Adapted from Alcaraz et al Ca Cancer J Clin 2020; 70:31-46

Community Partner Insights

Two key perspectives from our community partner shaped the focus of and approach to this work:

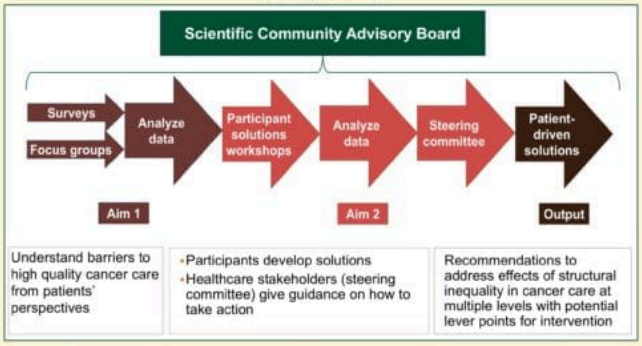
1. The importance of being heard
- Being heard and valued is critical to healing from the hardships of navigating cancer care

2. Taking action to remediate past harms
- Beyond just talking about hardship, *doing something* is equally important

Community-Informed Study Design

- Ensure the expertise of survivors is incorporated into study procedures
  - Scientific Community Advisory Board – 5 community members become paid members of the research team
- Elevate the patient voice to multidisciplinary healthcare stakeholders
  - Patients' first-hand accounts heard by people in positions of power who may rarely hear the realities of navigating cancer as someone in a racialized body

Figure 2: Study Design



The resulting pilot study aims to:

1. Characterize the cancer care journey of breast and gynecologic survivors from populations impacted by structural racism
2. Develop patient-driven recommendations to address multilevel manifestations of structural racism in cancer care settings

Conclusion

- A pilot study that marries the need for in-depth patient narratives and robust quantitative measurements of quality of care to generate patient-driven solutions that ameliorate barriers to high-quality cancer care

Eligibility Criteria

- Breast and gynecologic cancer survivors from South Florida
- Completed active treatment at least 6 months and less than 10 years ago
- Speak English, Spanish, or Haitian Creole
- Identify as Black/African American, Hispanic, Asian, Indigenous, or mixed race or ethnicity

Research reported in this poster was supported by The Office of the Executive Dean for Research at the University of Miami Miller School of Medicine, Dean's Diversity Council Research Action Team Pilot Award number UM DDC 2024-01.

S/P indicates work done while a student/postdoc

Substance Use

Investigating the association between the presence of chronic disease and alcohol consumption as mediated by perceived mental health and social support: A path analysis

Amy B. Crandall* Amy B. Crandall Jason Mulimba Were Roman Pabayo

Background: Having a chronic disease is a source of stress that may contribute to alcohol misuse. However, less is known about mechanisms that link chronic disease to alcohol misuse. This study aimed to determine whether perceived mental health and social support mediate the association between chronic disease presence and alcohol use.

Methods: Cross-sectional data was obtained from the 2019-2020 Canadian Community Health Survey. Individuals not using a proxy were included (n = 38,557). Chronic disease presence was defined as a binary measure based on self-reported diagnoses, perceived mental health was measured using a five-item Likert scale, and social support was measured using the five-item Social Provision Scale. Alcohol consumption was categorized as an ordinal variable (no use to daily use). Path modelling with weighted least squares estimation was used, and all coefficients were standardized with z-scores.

Results: A 1-SD increase in chronic disease presence was associated with a 0.068-SD decrease in alcohol consumption after adjusting for confounders (95% CI: -0.098, -0.039). A 1-SD increase in chronic disease presence was also associated with 0.177-SD lower perceived mental health (95% CI: -0.210, -0.144), while a 1-SD increase in perceived mental health was associated with a 0.277-SD increase in social support (95% CI: 0.259, 0.295). Indirectly, a 1-SD increase in chronic disease presence was associated with a 0.002-SD decrease in alcohol consumption via the mediated perceived mental health and social support pathway (95% CI: -0.003, -0.001).

Conclusion: Findings from this study indicate that chronic disease is associated with decreased alcohol consumption, with perceived mental health and social support mediating this relationship. It is proposed that campaigns focused on mental health and the risks of alcohol use for people with chronic diseases are essential for maintaining low alcohol consumption in this population.

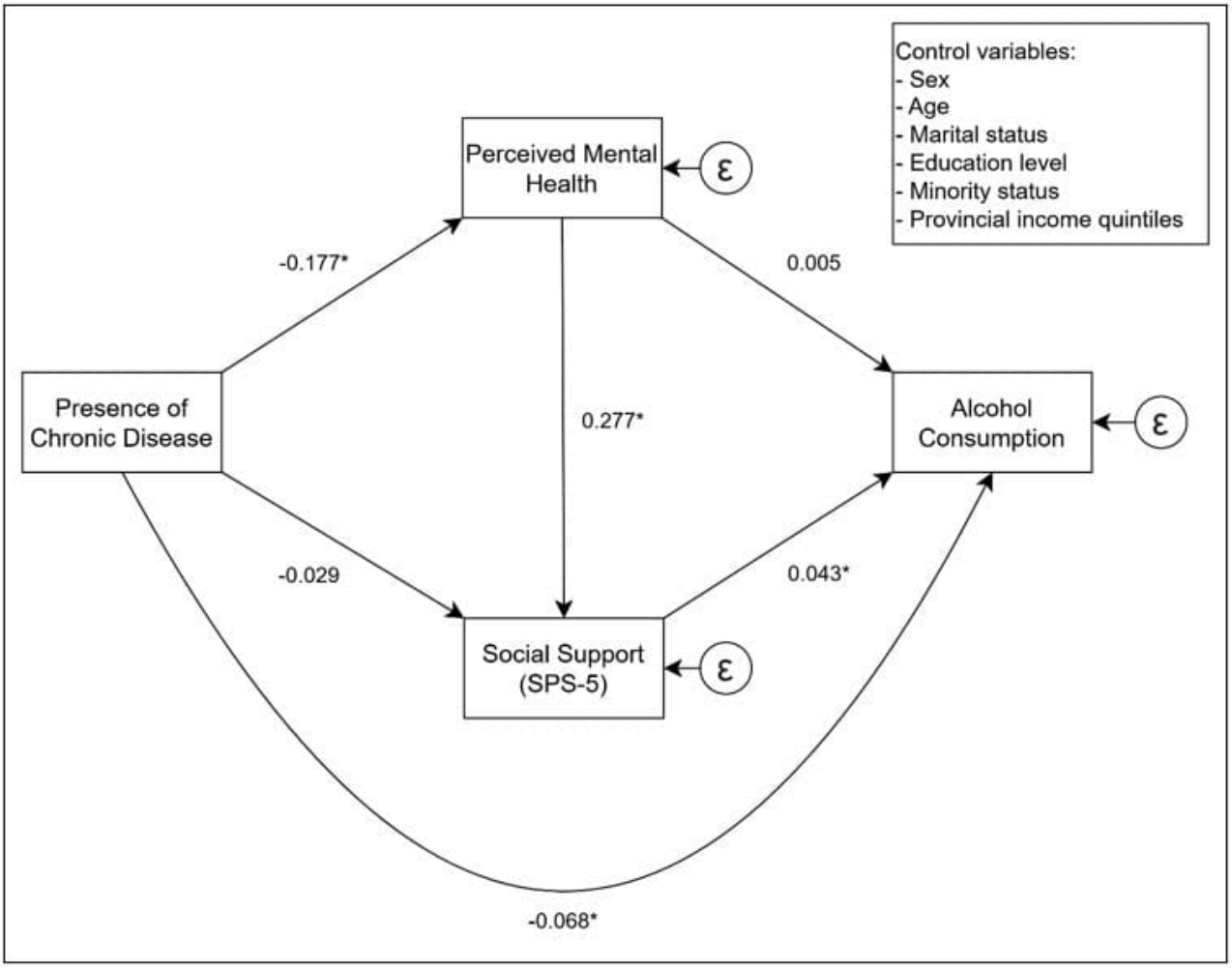


Figure 1. Path diagram and standardized coefficients of the resulting path analysis between the presence of chronic disease and alcohol consumption via perceived mental health and social support.

Note. * = p < .001

Substance Use

Alcohol tax policy, alcohol consumption, and depressive symptoms in the Health and Retirement Study Peter Toyokazu Buto* Peter Buto Minhyuk Choi Scott C. Zimmerman Justin S. White Laura Schmidt Stacy Sterling Shelli Vodovozov Yvette Cozier Suzanna M. Martinez Rhoda Au Felicia W. Chi M. Maria Glymour

Evidence suggests a bidirectional relationship between alcohol consumption and depressive symptoms, but the magnitude of effects can be challenging to estimate. We used an instrumental variable (IV) analysis to assess whether tax-induced alterations in alcohol consumption influenced depressive symptoms.

Our sample included those who joined the Health and Retirement Study (HRS) in 1998 or later, and followed them through 2018. We linked state-level alcohol tax rates from the Alcohol Policy Information System to HRS participants based on current state of residence in each year.

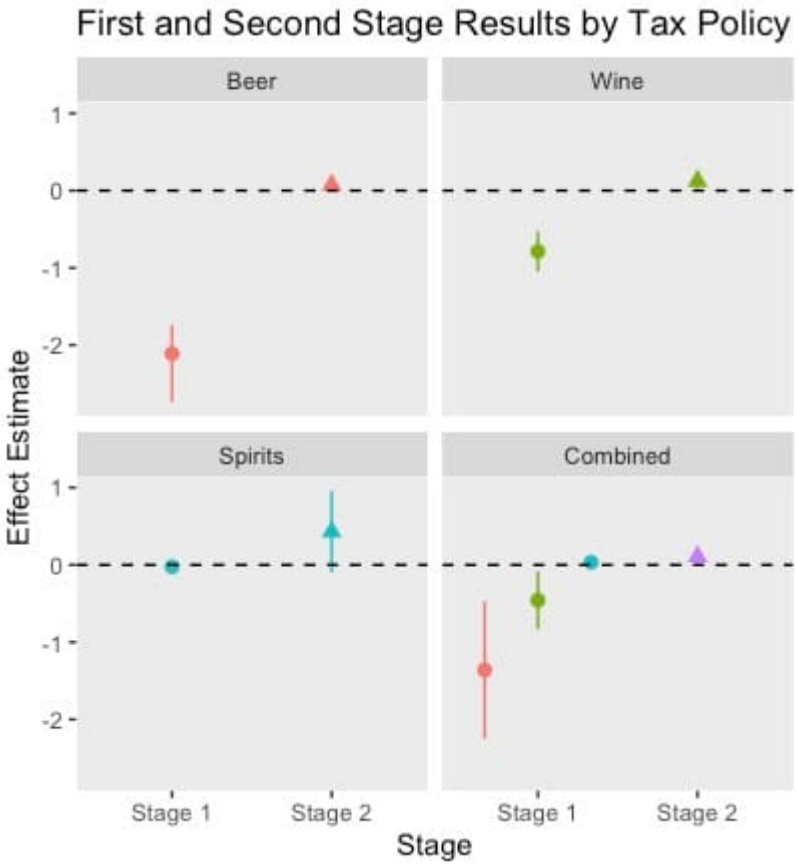
Alcohol consumption was measured as the average number of drinks per week in the last three months. Depressive symptoms were assessed using a modified version of the 8-item Centers for Epidemiologic Study-Depression (CES-D). Covariates included age, sex, race/ethnicity, education, and state of residence.

We examined the association of state-level taxes with alcohol consumption. Alcohol tax was modeled separately as the tax on beer, wine, or spirits per gallon and combined. We then conducted two-stage least squares IV for the effect of alcohol use on CES-D.

Our final analytic sample (n=20,774) had an average follow-up of nine years. The average taxes for beer, wine, and spirits over this period across all states were $0.34, $1.22, and $7.29 per gallon, respectively.

For every $1/gallon increase in beer tax, alcohol consumption on average decreased by -2.11 (-2.74, -1.74) drinks/week. Using the combined taxes as an instrument, the IV estimated effect of each additional drink per week was an increase of 0.11 (0.01, 0.20) points of CES-D score. Estimated effects when individually using beer, wine, or spirit taxes as an IV varied slightly but were statistically indistinguishable.

Alcohol taxes were associated with decreased alcohol consumption. These differences, which varied by the type of alcohol tax, were further associated with increased depressive symptoms.


First and Second Stage Results by Tax Policy
Beer
Wine
Spirits
Combined
Effect Estimate
1
0
-1
-2
Stage 1
Stage 2
Stage

Substance Use

Advanced Machine Learning for Substance Overdose-Related Mortality Prediction Sukanya Krishna* Sukanya Krishna Marie-Laure Charpignon Maimuna Majumder

In the US, the substance overdose epidemic claimed over 81,000 lives in 2023 alone. More accurate predictive models are needed to guide public health interventions. Traditional statistical methods like Seasonal Autoregressive Integrated Moving Average (SARIMA) have limitations in capturing nonlinear trends, long-term dependencies, and policy interventions. We investigate deep learning (DL) approaches—Long Short-Term Memory (LSTM) networks and Temporal Fusion Transformer (TFT) models—to improve overdose-related mortality predictions.

Using publicly available mortality data from CDC WONDER, this study trains and evaluates LSTM and TFT models against SARIMA, assessing accuracy via mean absolute percentage error (MAPE) and precision via prediction interval (PI) length. Preliminary results show that LSTM models (batch size 5, 9-month lookback, mean squared error loss) achieved comparable MAPE to SARIMA for training data (LSTM: 5.93%; SARIMA: 4.75%) and lower MAPE for validation (LSTM: 2.99%; SARIMA: 4.00%) and testing data (LSTM: 15.24%; SARIMA: 16.23%), suggesting predictive improvements (Figure 1). TFT models will further integrate socioeconomic and behavioral risk factors to enhance explanatory power and capture complex interactions between past trends and socio-behavioral responses. Future work will incorporate uncertainty estimation methods like conformal prediction and Monte Carlo dropout to improve reliability in overdose mortality estimates.

This research aims to demonstrate that DL models may outperform SARIMA in predicting substance overdose mortality and provide insights into future epidemic trends – overall, by substance, and by geography. Our findings have the potential to refine resource allocation and intervention strategies, contributing to a more data-driven response to the overdose crisis. This work represents a critical step toward leveraging machine learning to address complex public health challenges.

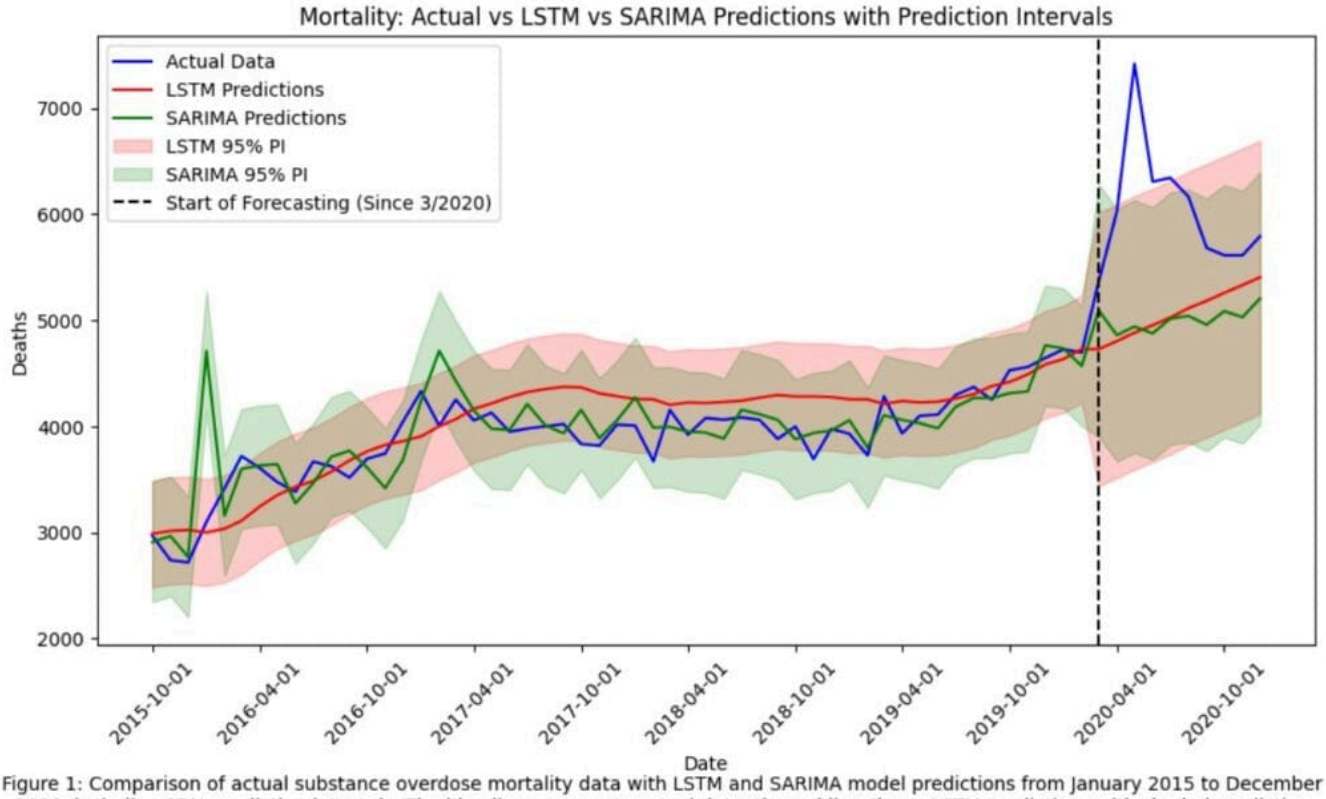


Figure 1: Comparison of actual substance overdose mortality data with LSTM and SARIMA model predictions from January 2015 to December 2020, including 95% prediction intervals. The blue line represents actual data, the red line shows LSTM predictions with shaded prediction intervals, and the green line shows SARIMA predictions with shaded prediction intervals. A vertical dashed line marks the start of forecasting in March 2020. The time period spanning January 2015 to December 2018 was used to train models, while the time period spanning January 2019 to February 2020 was used for validation. The pandemic period spanning March 2020 to December 2020 constitutes the testing dataset/period.

Substance Use

Parental incarceration and offspring cigarette, alcohol, and cannabis use: A systematic review Shadiya L. Moss* Shadiya Moss Emilie Bruzelius Katherine M. Keyes

Background: Exposure to parental incarceration is associated with poor mental and physical health among adolescents; however, the impact of parental incarceration on adolescent substance use is unclear. In this review, we systematically appraise the extant literature investigating the association between parental incarceration and substance use among offspring ≤18 years of age.

Methods: A structured search of PubMed, Embase, PsychInfo, National Criminal Justice Reference Service, and Web of Science databases was conducted using search terms related to the concepts of parental incarceration and adolescent alcohol, cannabis, and cigarette use in the United States from 1984 to January 2022. Studies were independently screened for inclusion and data extraction. The primary outcomes were adolescent cigarette, alcohol, and cannabis use. Data extraction also focused on the role of moderators and mediators when applicable.

Results: Data from 10 studies were included. Studies suggested that parental incarceration was associated with an increase in adolescent cigarette and cannabis use. Findings for adolescent alcohol use were less clear, with included studies reporting negative, null, and positive associations. Only three studies assessed effect modification, showing that the association between parental incarceration and adolescent alcohol and cannabis use may be moderated by gender, age, and race. No studies included mediation effects.

Conclusions: In conclusion, while there is an increased interest in the health and well-being of offspring exposed to parental incarceration, research on offspring substance use outcomes is still underdeveloped. Studies included in this review suggest that parental incarceration was associated with higher cigarette and cannabis use, but studies were inconclusive regarding adolescent alcohol use. This review provides an overview of gaps in the literature and a call for research to understand if there is an association between parental incarceration and adolescent alcohol use, and if there are causal relationships between parental incarceration and adolescent substance use outcomes more generally, including effect modification and mediation.

Substance Use

Change in maternal e-cigarette use during pregnancy and preterm birth Xiaozhong Wen*
Xiaozhong Wen Aye Moe Dhruvi Patel Gabrielle Hastings Kayla Elaine Manney

Objective: We aimed to examine the associations between changes in e-cigarette and cigarette use during pregnancy and the risk of preterm birth. Methods: We conducted a secondary data analysis within Phase 8 of the Pregnancy Risk Assessment Monitoring System (PRAMS, 2016-2021). Use of e-cigarettes and cigarettes before and during late pregnancy was self-reported. Gestational age was obtained from birth certificates, and preterm birth was defined as gestational age less than 37 weeks. Multivariable logistic regression models were used to estimate the OR and 95% CI for preterm birth associated with changes in e-cigarette and cigarette use during pregnancy, adjusting for socio-demographics, pregnancy-related characteristics, and other substance use. Results: Discontinuation was 78.9% among exclusive e-cigarette users, 53.8% among exclusive cigarette users, and 48.2% among dual users. The prevalence of preterm birth was 8.1% in the total sample and 7.7% among non-users of e-cigarettes/cigarettes. Among 30,809 pre-pregnancy exclusive cigarette users, quitters had a lower risk of preterm birth than continuous smokers (8.8% vs 12.0%; confounder-adjusted OR, 0.74 [95% CI, 0.66-0.82]). Among 4,090 pre-pregnancy exclusive e-cigarette users, quitters did not have a significantly different risk of preterm birth from continuous vapers (8.3% vs 11.0%; adjusted OR, 0.80 [0.55-1.15]). Among 6,428 pre-pregnancy dual users, compared to continuous dual users, those who continued smoking only (11.2% vs 9.9%; adjusted OR, 1.19 [0.86-1.65]) or continued vaping only (8.8% vs 9.9%; adjusted OR, 0.94 [0.61-1.46]) did not have a significantly different risk of preterm birth, but complete quitters had a lower risk of preterm birth (6.4% vs 9.9%; adjusted OR, 0.69 [0.51-0.92]). Conclusion: Discontinuation of e-cigarettes and/or cigarettes was common during pregnancy. It was associated with a substantial reduction in the risk of preterm birth among exclusive cigarette users and dual users.

Substance Use

Association Between Prescription Opioid Misuse and Polysubstance Use Among Adolescents in the U.S.: Exploring Associations with Engagement in Risky Health Behaviors Asef Raiyan Hoque* Asef Raiyan Hoque

Introduction:
Polysubstance use is the simultaneous use of multiple substances. The fourth wave of the opioid epidemic is emerging and will be driven by polysubstance use. There is growing public health concern about prescription opioid misuse and engaging in concurrent multiple substance use among high school students. Prescription opioid misuse is associated with higher engagement in risky health behaviors including driving, substance use, sexual, and suicide-related behaviors. The objective of this study was to first investigate the association between prescription opioid misuse and polysubstance use among adolescents. Additionally, the study explored the relationship between opioid misuse and adverse health behaviors among adolescents reporting polysubstance use.
Methods:
This study utilized the 2017-2021 Youth Risk Behavior Surveillance System nationally representative data of high school students. Pearson's chi-square tests compared the differences between the participants. A multivariate regression model was used to compare prescription opioid misuse and polysubstance use. Additionally, logistic regression analyzed the association between opioid misuse, polysubstance use, and engagement in selected risky health behaviors.
Results:
The findings showed a significant association between prescription misuse and polysubstance use. Moreover, opioid-misusing adolescents who engaged in polysubstance use showed mixed results for engaging in other risky health behaviors. Notably, adolescents who misused prescription opioids and engaged in polysubstance use had a significantly higher likelihood of reporting suicide-related behaviors, such as feelings of hopelessness.
Discussion:
As the fourth wave of the opioid epidemic emerges, the findings from this study highlight the intertwined nature of opioid misuse. Public health policy should address concurrent multiple substance use and educate on the associated behavioral risks to prevent adverse outcomes among adolescents.

LATEBREAKER

Substance Use

Effect of Menthol Flavor on E-Cigarette Users' Puffing Behavior & Toxicants Exposure: A Crossover Clinical Trial among US Young Adults Sreshtha Chowdhury* Sreshtha Chowdhury Tarana Ferdous Simanta Roy Wasim Maziak

Background: Electronic nicotine delivery systems (ENDS) have emerged as the most prevalent tobacco products among the youth in the United States, with flavors being one of the major drivers for use. Limiting flavors to menthol and tobacco for ENDS "pod-mods" was one of the first major actions taken by the FDA to reduce the spread of ENDS among young people. However, menthol flavor can present a potential risk given its popularity among young people in the US and its puffing and nicotine-enhancing properties when studied in cigarettes. This study examined the effect of menthol flavor on e-cigarette users' puffing behavior & toxicant exposure.

Methods: In this within-subject clinical cross-over study, 67 young current e-cigarette users completed two lab sessions and vaped up to 60 minutes ad libitum, preceded by 12-hour nicotine abstinence. Participants used the same e-cigarette device in two separate sessions, differing by flavor (menthol/tobacco) in random order. Next, the puffing topography parameters recorded during each vaping session were replicated using a digital playback smoking machine for each participant to measure the toxicant emissions (14 aldehydes) at an Aerosol Research Laboratory.

Results: The result shows the median topography parameters were significantly higher during the menthol-flavored ENDS sessions compared to the tobacco flavor, i.e., puffing time: 1.18 minutes, vs. 0.92 minutes, p= 0.0114; total inhaled volume: 1367.19 ml vs. 1223.06 ml, p=0.0199; total puffs: 30 vs. 28.5, p=0.0733. Additionally, higher median values were observed for 11 among 14 aldehydes for sessions with menthol condition compared to the sessions with tobacco condition (i.e., formaldehyde: 0.56 vs. 0.50 µg/session, p=0.6154; acetaldehyde: 9.31 vs. 8.15 µg/session, p=0.4769; crotonaldehyde: 0.39 vs. 0.32µg/session, p=0.0518).

Conclusion: Using a sensitive within-subject design, the results of this study suggest that menthol flavor enhances ENDS users' puffing behavior and toxicant exposure. It highlights that limiting menthol flavor could play an important role in reducing ENDS harm and addictiveness among young people.

LATEBREAKER

Substance Use

Pictorial health warning labels are effective in reducing subjective measures, behavioral responses and toxicant exposure: a crossover study Natasha Shaukat* Natasha Shaukat Simanta Roy Sreshtha Chowdhury Zoran Bursac Taghrid Asfar Wasim Maziak

Background
This study aims to assess the impact of six evidence-based WP-specific pictorial health warnings (HWs) placed on the WP device on puffing behavior, toxicant exposure, subjective smoking experiences, harm perception, motivation and intention to quit among young WP smokers in Florida.
Methods
In a crossover experiment, a total of 100 WP smokers completed two 45-minute ad-libitum WP smoking sessions (without HW vs. with HW on the device) after a 12-hour abstinence. Exhaled Carbon Monoxide (eCO) was measured before and after each session, while puff topography was recorded throughout the smoking session. Additionally, participants completed survey questionnaires before and after the WP smoking sessions assessing subjective smoking experiences. Based on the distribution, we used the student's t-test, Wilcoxon sign rank test, and Chi-square test to examine mean differences in puffing parameters, eCO, and subjective measures between smoking conditions (PHWL vs. no-PHWL) among study participants.
Results
The mean e-CO boost (34.16 vs. 26.58) ($p= 0.01$) was higher in the no-HW condition compared to the HW condition. Differences were also observed between the two conditions for puff topography. For example, median smoking time (46.4 min vs 45.3 min; $p<0.001$), median puffing time (4.35 min vs. 4.22 min; $p<0.001$), average puff duration (3.13 sec vs. 2.90 sec; $p=0.03$), and the total number of puffs (95.0 vs. 84.0; $p=0.04$) were lower in the HW compared to no-HW conditions. Subjective measures also demonstrated differences between the two conditions, including greater suppression of the urge to smoke (14.98 vs. 7.51; $p<0.001$), reduced puff liking (4.01 vs. 3.63; $p = 0.01$), and reduced puff satisfaction (4.11 vs. 3.65; $p = 0.01$) following exposure to HW compared to no-HW conditions. WP harm perception ($p=0.30$), motivation to quit ($p=0.06$), and intention to quite ($p=0.66$) were higher among participants after smoking the WP with HW compared with WP without HW.
Conclusion
Using an evidence-based approach, a large sample size for clinical studies, and an efficient and sensitive within-subject design, this study demonstrates that pictorial HWs on WP devices effectively reduce smoking behavior, toxicant exposure, and subjective experiences while increasing harm perception, intention, and motivation to quit WP smoking.

Substance Use

Randomized experiment for the effect of warm delivery of tobacco 21 toolkits to retailers in New Orleans James Buckley* James Buckley Daisy Dai

Background: Tobacco use is the leading cause of preventable death worldwide, causing more than 480,000 deaths each year in the United States. The federal Tobacco 21 (T21) law signed in December 2019 raised the minimum legal age of tobacco sales from 18 to 21 years nationwide. The "Tobacco Nation" region, a collection of 13 U.S. states in the South and Midwest, has higher adult and youth smoking prevalence and poorer health outcomes while also lacking effective tobacco control policies laws and tobacco prevention spending relative to the rest of the U.S.

Methods: 100 tobacco retail establishments in the New Orleans metropolitan area were identified and visited twice by covert buyers aged 18-20. The buyer attempted to purchase a tobacco product and recorded if the store pulled down the product and if ID was asked for. A T21 toolkit, composed of T21 materials from the FDA, was delivered to 50 stores in the sample. Following delivery, a second visit occurred where the same attempt to purchase was made by a covert buyer. McNemar's test was used to compare violation between rounds of inspections overall and by group.

Results: Overall, 37% of stores in the first wave were in violation of T21 laws. 45.83% of the stores in the toolkit group and 28.84% of the stores in the no-toolkit group were in violation of T21 laws during the first inspection. Overall, 24.24% of stores in the second wave were in violation. 21.27% of the stores in the toolkit group and 26.92% of the stores in the no-toolkit group were in violation. The decrease in violations was significant for the toolkit group(p=0.02) and not significant for the no-toolkit group(p=0.85).

Conclusions: The stores which received a T21 toolkit saw approximately a 44% decrease in T21 violations while stores which did not receive a toolkit saw negligible change. This study highlights the importance of retailer education in effectively enforcing youth tobacco use prevention laws.

Translational & Implementation Science

Barriers and facilitators of critical care nursing workflow using electronic health records

Alison Trinkoff* Alison Trinkoff Ayse P. Gurses Hyang Baek Janelle Faiman Daniel France T Ryan MIles Oluseyi Daodu Patience Osei Kelly Gleason Dawn Luzetsky Judy Ascenzi Stephanie Morgenstern Charlotte Seckman Shijun Zhu Shilo Anders

Background: Nurses spend the most time of any profession using the Electronic Health Record (EHR), mostly for clinical workflow and to document care provision. However, there has been minimal inquiry into the usability of EHR as designed for nursing care, and EHR demands among nurses are a growing concern. Using a Human Factors/Systems Engineering approach, we specifically targeted nurses' EHR use during critical clinical events and transitions, including admissions, discharges, and medication administration, while they were caring for extremely high acuity patients.

Methods: In this multi-centered, multi-method study, 40 critical care nurses were observed and interviewed using a qualitative approach combining semi-structured interviews and observations of nurses while using the EHR in their natural work environment. Interviews were recorded using Zoom/MS Teams with transcripts enabled. Data were coded using MaxQDA and checked for inter-rater reliability across study sites for consistency and accuracy. For this analysis, we focused on nurse-identified barriers or obstacles to care from the EHR system, along with EHR facilitators beneficial to their work.

Results: Major barriers of EHR use included time demands associated with locating up-to-date information and needing to prioritize patient-care activities over charting. Other barriers were associated with the inability to customize the EHR to specific critical care environments. Major EHR facilitators included EHR promotion of communication across teams and disciplines, especially during admissions, as this was viewed as a team activity, and assisting with organizational aspects of task load and communication across teams.

Conclusions: Input from nurses can identify EHR barriers requiring redesign and enhance features that promote optimal utility for clinical workflow, building on strengths of the EHR system. Human factors qualitative approaches yielded details that can be addressed through EHR modifications in implementation studies. Future research will relate EHR system features to missed nursing care and medication errors, quantitatively.

Women’s Health

Child bereavement and maternal incident hypertension in the Nurses’ Health Study II

Karolina Edlund* Karolina Edlund Alexandra Hillcoat Shaili Jha Jae Hee Kang Karestan Koenen Christy Denckla

Background: Cardiovascular disease remains the leading cause of morbidity and mortality among women, and prevention has focused on risk factors such as hypertension. While trauma is a known predictor of women’s cardiovascular health, the impacts of bereavement-related trauma are underexplored. As 12% of US adults experience child loss by age 50 and bereaved mothers bear greater risk of health sequelae than bereaved fathers, pathways linking child loss and hypertension among women warrant investigation.

Methods: Using data from 31,326 women in the Nurses’ Health Study II (Mage in 1989 = 34.53 years [SD = 4.65], 94% White) with a median follow-up of 11 years (IQR = 2), we ran Cox proportional hazards models to explore associations between history of child loss assessed in 2008 and self-reported clinician-diagnosed hypertension thereafter, adjusting for sociodemographic covariates. We excluded individuals if they reported hypertension or myocardial infarction/stroke, used antihypertensives, died, or were lost to follow-up prior to 2008. To explore effect measure modification by psychological sequalae, we fit models stratified by lifetime posttraumatic stress disorder (PTSD) and baseline clinically significant depressive symptoms.

Results: The prevalence of incident hypertension, lifetime PTSD, and clinically significant depressive symptoms was 18%, 10%, and 17%, respectively. Women with a history of child loss exhibited 1.09 (95% CI = 1.05, 1.13) times the adjusted hazard of incident hypertension compared to non-bereaved women. Estimates were elevated among women with a history of PTSD (HR = 1.16 [1.09, 1.22]) or clinically significant depressive symptoms (HR = 1.18 [1.09, 1.27]) relative to those without (HRno PTSD = 1.01 [0.95, 1.07]; HRno depression = 1.04 [1.00, 1.09]).

Conclusion: Women bereaved of a child are at moderately increased risk of incident hypertension. Further investigation is needed into the psychological sequelae of child loss as prevention targets.

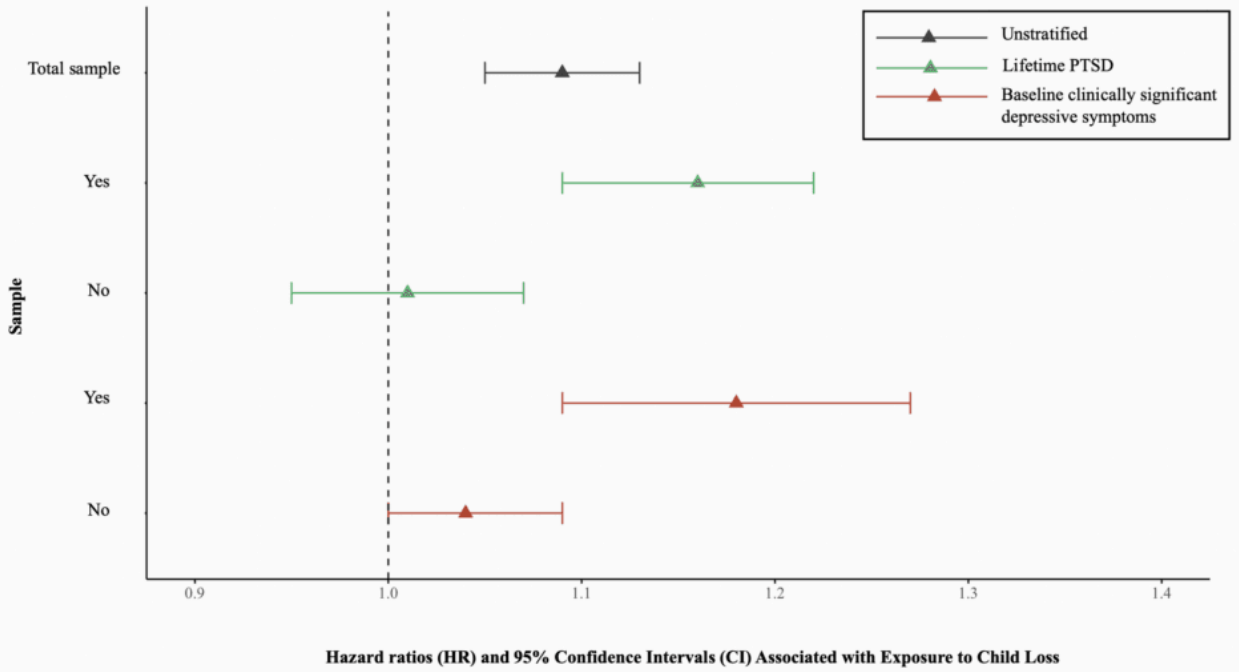


Figure 1. Hazard ratios (HR) and 95% confidence intervals (CI) for the association between history of child loss assessed in 2008 and self-reported clinician-diagnosed hypertension thereafter, stratified by effect modifiers of interest: lifetime PTSD and clinically significant depressive symptoms at baseline. All models adjusted for age in 1989, race, mother's education, father's education, family history of hypertension, alcohol intake between ages 15 and 17, BMI at age 18, smoking status at age 18, physical activity between ages 18 to 22, oral contraceptive use in 1989, and AHEI diet score in 1991.

Women’s Health

Recent and Chronic Exposure to Personal Care Products and Urinary Biomarker Concentrations of Non-persistent Endocrine Disrupting Chemicals in the Study of Environment, Lifestyle and Fibroids Angela L. Jeffers* Angela Jeffers Caroll A. Co Samantha Schildroth Lauren A. Wise Quaker E. Harmon Donna D. Baird Kyla W. Taylor

Background: Exposure to endocrine-disrupting chemicals (EDCs), such as parabens, phthalates, and phenols, through personal care products (PCPs) has been linked to adverse health effects. Using data from the Study of Environment, Lifestyle and Fibroids, we conducted an untargeted analysis to assess the association between urinary biomarkers of 31 EDCs and self-reported recent (24-hour) and chronic (12-month) PCP use.

Methods: EDC biomarker data were available for 434 individuals with a secondary follow-up visit from 2014-2016. We applied dimension reduction using variable clustering to 25 biomarkers with >70% of values above the limit of detection. Associations between levels of PCP use and individual EDC biomarkers were assessed using an unadjusted lognormal accelerated failure time (AFT) model with a significance threshold of $\alpha=.01$. Separate AFT models were fitted for each PCP-metabolite pair, with both chronic and recent PCP use treated as categorical variables.

Results: Clustering of 25 EDC biomarkers identified 9 distinct clusters. The parabens, monoethyl phthalate, and benzophenone-3 (BP3) cluster was associated with chronic sunscreen, face/body/hand/fade cream, foundation, and eye makeup use; triclosan to chronic face/hand cream use; and dibutyl and monobenzyl phthalates with chronic and recent douching. Di-isononyl phthalate metabolites were associated with chronic nail polish use, while alternative phthalates were associated with chronic foundation and shellac use. Recent makeup use was associated with higher BP3 and paraben levels. Recent condom use was associated with higher di-isobutyl phthalate metabolites.

Conclusions: Our findings suggest that EDC biomarkers cluster by parent compound and associations between EDC biomarkers and PCP use are influenced by factors such as product type and frequency of use. Habitual PCP use may be necessary for significant biomarker accumulation, emphasizing the importance of biomarker collection timing and frequency of use.

Women’s Health

A case-control study of environmental chemical exposure and adenomyosis risk Kristen Upson* Kristen Upson Mandy Hall Kwalton Holly R. Harris Sawsan As-Sanie Victoria L. Holt

Adenomyosis, marked by endometrial glands and stroma within the myometrium, can confer debilitating symptoms. As estrogen is central to disease pathogenesis, environmental chemicals that are endocrine disruptive may alter adenomyosis risk. We investigated this hypothesis among female enrollees ages 18-59 of an integrated healthcare system in Washington State. Cases had incident, pathology-confirmed adenomyosis diagnosed 2001-2006 (n=386). We employed two control groups: randomly selected age-matched enrollees with intact uteri (“population controls”, n=323) and hysterectomy controls (n=233). Data on occupational and non-occupational exposure to chemical groups were collected by in-person interview. We conducted logistic regression to estimate adjusted ORs and 95% CIs, comparing cases to population and hysterectomy controls. Our data suggested increased adenomyosis risk with ever exposure to epoxy resins (cases vs. population controls: OR 1.8, 95%CI: 0.9-3.6; hysterectomy controls: OR 1.4, 95%CI: 0.7-2.9) and heavy metals (population controls: OR 1.5, 95%CI: 0.8-2.7; hysterectomy controls: OR 2.0, 95%CI: 1.0-4.1). Our data also suggested twice the risk of adenomyosis with lead exposure (population controls: OR 2.2, 95%CI: 0.8-6.3; hysterectomy controls: OR 2.0, 95%CI: 0.6-6.1); lead exposure mostly occurred from non-occupational sources (paint, home renovation, soldering, and stain glass work). The association with mercury exposure was inconsistent (cases vs. population controls: OR 1.1, 95%CI: 0.5-2.3; hysterectomy controls: OR 1.7, 95%CI: 0.7- 4.5). No association was observed with solvent exposure; results were inconclusive for exposure to herbicides, insecticides, fungicides, and rodenticides given few exposed participants. Results from our case-control study suggest that exposure to epoxy resins and heavy metals, particularly lead, are associated with increased adenomyosis risk. Given the exploratory nature of our analysis, further research is warranted.

Women’s Health

Kidney Function and Biomarkers of Folate and Vitamin B12 Status in Women of Reproductive Age in Southern India Doreen Larvie* Doreen Larvie Heather M. Guetterman Erin G. Sley Beena Bose Christina B. Johnson Amy Fothergill Arick Wang Shameem Jabbar Mindy Zhang Christine M. Pfeiffer Yan Ping Qi Charles E. Rose Jennifer L. Williams Saurabh Mehta Rebecca Kuriyan Prakash B. Narasimhan Krista S. Crider Julia L. Finkelstein

Background: Red blood cell (RBC) and serum folate concentrations may be altered in individuals with impaired kidney function. However, there is limited population-level data among women of reproductive age (WRA), including in settings without exposure to folic acid fortification.

Methods: We examined the associations of estimated glomerular filtration rate (eGFR) with biomarkers of folate and vitamin B12 in WRA (n=966; 15-40 y; not pregnant/lactating) in a population-based biomarker survey in Southern India. RBC and serum folate, serum creatinine, total vitamin B12, holo-transcobalamin, methylmalonic acid (MMA), and homocysteine were evaluated in archived samples (2017-2019). Serum creatinine was used to calculate eGFR (a measure of kidney function), using the Chronic Kidney Disease Epidemiology Collaboration equation. eGFR stages (stage 1: ≥90, 2: 60-<90, 3: 30-<60, and 4: <30 mL/min/1.73 m2) and eGFR <90 mL/min/1.73 m2 [lower eGFR and higher stages (compared to higher eGFR values and lower stages) indicate impaired kidney function] were considered in analyses. ANOVA was used to compare continuous nutritional biomarkers by eGFR stage.

Results: A total of 96.3% of WRA were at eGFR stage 1 (n=930), 3.5% were at stage 2 (n=34), and <1% were at stage 3 (n=1) or stage 4 (n=1) (geometric mean: 118 [95% CI: 117-119 mL/min/1.73 m2]). In univariate analyses, WRA with eGFR <90 vs.≥90 mL/min/1.73 m2 had lower serum folate concentrations (12.3 [10.4-14.4] vs.16.6 [16.1-17.2] nmol/L, p=0.003). However, there were no differences for serum folate <7.0 nmol/L vs. ≥ 7.0 nmol/L, RBC folate concentrations, or biomarkers of vitamin B12 status [e.g., homocysteine, and MMA], comparing eGFR <90 vs. ≥90 mL/min/1.73 m2.

Conclusions: In this population, those with impaired kidney function had lower serum but comparable RBC folate concentrations. Further research on folate biomarkers and kidney function may enhance screening and biomarker assessment to improve women’s health.

Women’s Health

Patterns of telehealth use during pregnancy and postpartum among commercially-insured women with live births, 2019—2021 Adit Doza* Adit Doza Lijing Ouyang Donatus U. Ekwueme Romeo R. Galang Brenda Bauman Lisa Romero Wanda Barfield Shanna Cox

Background: The use of telehealth has undergone a significant transformation in the aftermath of the COVID-19 pandemic. This study is designed to assess the shifts in telehealth utilization among pregnant and postpartum women from 2019 to 2021. It also aims to assess differences in telehealth use between rural and urban areas and describe the most frequently utilized services.

Methods: We used the Merative MarketScan Commercial database for women aged 15-49 who had a live birth delivery between 2019 and 2021, with continuous insurance enrollment for 10 months pre-delivery and 12 months post-delivery. We described patient characteristics stratified by telehealth user (TU) vs non-telehealth user (NTU) for all cohorts based on year of delivery. The major diagnostic categories (MDCs) were used to assess service types of telehealth use.

Results: The total telehealth visits during pre-delivery and post-partum periods were 60,655 in 2019; 204,935 in 2020; and 276,425 in 2021. An increasing proportion of telehealth visits occurred in the pre-delivery period (2.8% in 2019, 24.2% in 2020, and 46.1% in 2021). Across all cohorts, a higher proportion of TUs had diabetes (9.9%-12.8% vs. 6.2%-7.3%), hypertension (6.0-6.6% vs 3.7%-4.4%), and depression (6.4%-7.6% vs. 1.3-2.3%) compared to NTUs. Lower proportion of TUs lived in rural areas compared to NTUs (6.6%-7.3% vs 11.2%-13.0%). The MDC for mental health services was present for greater than 50% of telehealth visits during postpartum for all cohorts.

Conclusion: Increased telehealth visits among pregnant and postpartum women may relate to more accessible care or increased mental health needs. Further research may determine if increased telehealth use improves maternal and birth outcomes.

Women’s Health

Impact of recreational cannabis legalization on prenatal cannabis use Summer Sherburne Hawkins* Summer Hawkins Rebekah Levine Coley Christopher F Baum

Cannabis use among pregnant women has increased more than 60% over the past decade during a time of increasing liberalization of cannabis policies. However, gaps remain in understanding the effects of legalization on prenatal cannabis use and whether they vary across groups.

Using 2016-2021 data on 94,347 women from 21 states and DC in the Pregnancy Risk Assessment Monitoring System, we conducted fixed effects probit regression models to examine the impact of recreational cannabis legalization on prenatal cannabis use controlling for demographics, other cannabis policies, year and state fixed effects. We included interactions to test for differential effects by demographic (age, education, race/ethnicity) and higher-risk (depressive symptoms, prenatal smoking) strata. We report average marginal effects.

Overall, 5.8% of women reported prenatal cannabis use. Nine states and DC legalized recreational cannabis by 2021. Recreational cannabis legalization increased prenatal cannabis use by 2.13 percentage points (0.021; 0.008, 0.034), with differential effects by race/ethnicity (p=0.02) and prenatal smoking (p=0.02). Recreational cannabis legalization increased use among white women by 2.57 percentage points (0.026; 0.012, 0.040), but not among other racial/ethnic groups. Legalization also increased use among women who smoked prenatally by 9.90 percentage points (0.099; 0.048, 0.150), but not non-smokers. There were trend interaction effects by education (p=0.07) and depressive symptoms (p=0.06), suggesting increased use post-legalization among women with less education and depressive symptoms. There was no evidence of age interactions.

Results indicate that recreational cannabis legalization had unintended consequences of increasing prenatal use, particularly among women who were white and from higher-risk groups. We will further test spillover effects of legalization on other substances to better understand the broader effects of cannabis policies on pregnant women.

Women’s Health

LA Cervix Care: Improving Cervical Cancer Prevention in Louisiana Rachel Thevenot* Rachel Thevenot Caleigh Foto Deborah G. Smith, PhD, MPH, BSN Donna Williams, MS, MPH, DrPH Jennifer E Cameron, PhD Bilikisu “Reni” Elewonibi, PhD, MPH Jerry Mclarty, PhD Michael E Hagensee, MD, PhD Jennifer DeLeon

Cervical cancer is largely preventable through HPV vaccination and early detection, yet it remains a public health challenge. This study aims to identify barriers preventing women from accessing cervical cancer preventive tools and design strategies to overcome them. We will screen 1,500 women from both urban and rural areas for high-risk HPV using self-administered swabs and surveys. A smaller group will join focus groups to help develop educational materials to reduce fear. Women with hrHPV detected will be referred to colposcopy as per standard care, and the rate of successful referrals will be measured. hrHPV-positive women will be screened for a potential marker of cancer development, hypermethylation, to explore the validity of this triage test. The study, launched in September 2024 at the Medicine Primary Care Clinic at UMC in New Orleans, has enrolled 32 women, with eight participants having hrHPV present. Participants expressed high satisfaction and acceptance of the self-administered vaginal swab, with most samples demonstrating high quality. Surveys have been collected, and hrHPV-positive women have been referred for gynecological follow-up. The Shreveport site began recruiting women from over 20 rural clinical sites using a Mobile Health Unit to improve access in rural communities, enrolling four women in December 2024. The baseline study will take 12-18 months. We will identify and address key barriers to follow-up gynecological care, including logistical issues (improving access and navigation), educational needs (developing culturally sensitive materials), and emotional support. The long-term goal is to develop a care delivery model that eliminates cervical cancer in Louisiana.

Women's Health

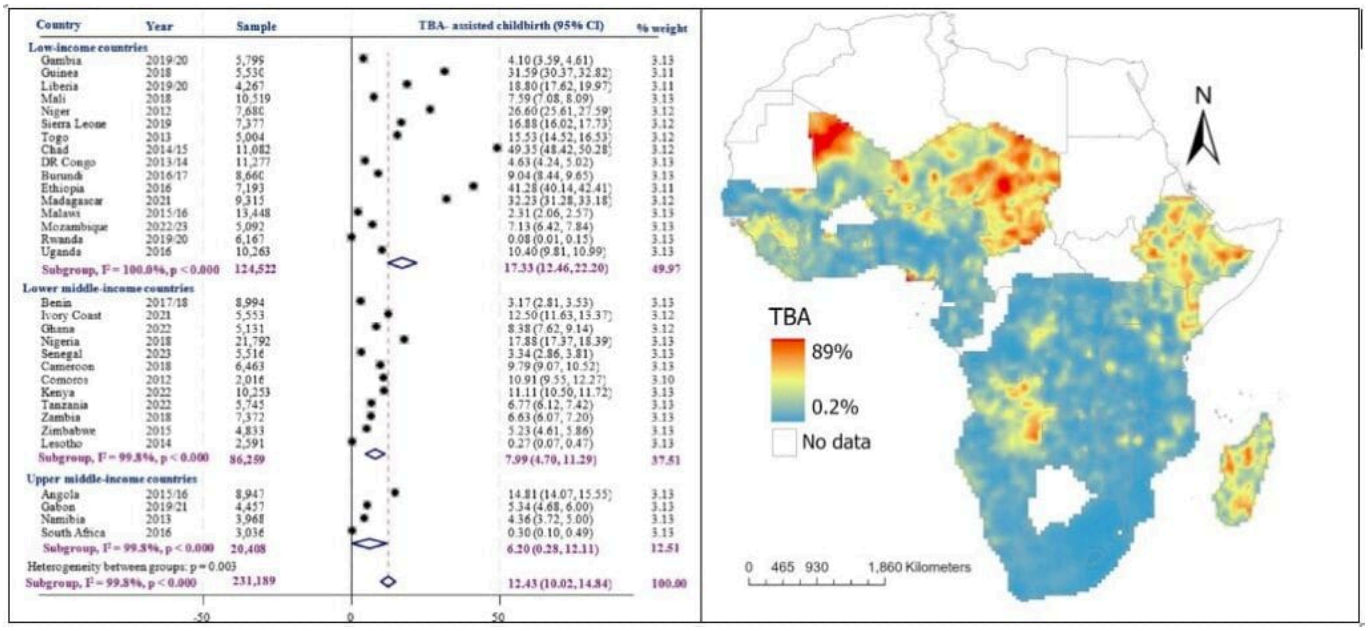
Mapping traditional birth attendance in sub-Saharan Africa between 2012 and 2023; analysis of data from demographic and health surveys. Daniel G. Belay* Daniel G. Belay Gizachew A. Tessema Jennifer Dunne Kefyalew Addis Alene Tefera Taddele Theodros Getachew Richard Norman

Background: Traditional birth attendance (TBA) remains common in Sub-Saharan Africa (SSA), impacting maternal and neonatal mortality rates. This study aimed at producing high-resolution geospatial estimates and identifying predictors of TBA-assisted childbirth in SSA.

Methods: We used the latest Demographic and Health Survey (DHS) data (2012-2023) from 32 SSA countries. Our sample included 231,189 reproductive-aged women who had given live birth to a child within the past five years. A multilevel binary logistic regression model was employed to identify the predictors of TBA-assisted childbirth, accounting for individual, household, and community-level factors. Geospatial analysis identified geographic hotspot areas where TBA is most prevalent.

Result: The proportion of TBA-assisted childbirth among reproductive-aged women in SSA was 12.43% (95% CI: 10.02%, 14.84%), ranging from 0.3% (South Africa) to 49.4 % (Chad). Hotspot clusters of TBA-assisted childbirth were found in Chad, Ethiopia, Madagascar, Guinea, and Niger. TBA-assisted childbirth was associated with women with community low women literacy (AOR=2.82; 95% CI; 2.57, 3.09), low household wealth status (AOR=1.42; 95% CI; 1.34, 1.49), and residing in rural areas (AOR=2.95; 95% CI; 2.68, 3.24) or had major problems with distance from the health facilities (AOR=1.22; 95% CI; 1.17, 1.26).

Conclusion: Significant geographic variation in TBA-assisted childbirth among women in SSA indicates the need for targeted health interventions to improve access to skill delivery services and empower women through financial and literacy initiatives.



LATEBREAKER

Women’s Health

Preconception care receipt and Pre-pregnancy hypertension among Black Women in the US: 2016-2021 Shanika Jerger Butts* Shanika Jerger Butts Michael E. Thompson Lorenzo N. Hopper Sharon Watson Stella Kim Janaka Bowman Lewis

Introduction

Preconception care is individualized health care designed to optimize health prior to pregnancy to reduce future pregnancy complications and adverse childbirth results by addressing health conditions and risk factors prior to conception. Promoting preconception care for preventing pregnancy-related illnesses and death is needed for all women, but especially among those who are at highest risk. This study evaluated the trends, patterns and provider interactions related to preconception care receipt among US Black women of reproductive age and how Black women with and without hypertension are receiving preconception care services.

Methods This study used data from Pregnancy Risk Assessment Monitoring System (PRAMS) from 2016-2021 with a sample of Black women, intending to become pregnant, across 44 states, District of Columbia, New York City and Puerto Rico (n= 16,071). Multivariate logistic regression models evaluated the association between pre-pregnancy hypertension and preconception care reception.

Results After adjustment, hypertensive Black women had significantly decreased odds of 21% (OR: 0.79, CI: 0.72-0.87) to have received a health care visit with a provider 12 months prior to pregnancy, compared to their counterparts who did not have hypertension prior to pregnancy. An inverse dose-response relation was found as Black women obtained more education and household income, a statistically significant odds of receiving preconception care services decreased.

Conclusion Further research is needed on the offer, reception, and results of health promotion and health education on preconception care services for Black women during childbearing years. However, these findings confirm that hypertensive Black women who intentionally began pregnancy had lower odds of having received preconception care services compared to Black women who did not begin pregnancy with hypertension. Given that women with chronic conditions would have more reasons to receive care prior to pregnancy, this finding was disconcerting.

LATEBREAKER

Aging

Reproductive history and brain imaging: The CARDIA study Emily Harville* Emily Harville Ilya Nasrallah Kristine Yaffe CE Lewis Erica Gunderson

Background: Almost two-thirds of people living with Alzheimer's are women. Reproductive history is associated with later-life cardiometabolic health, and, while cardiometabolic health is associated with dementia and Alzheimer's, the literature linking reproductive history and cognitive health is limited and inconclusive.

Methods: Data from 471 women (mean age=54.0, range 43-61) participating in the CARDIA Brain MRI study were used. MRIs measures of brain volume, white matter fractional anisotropy, and cerebral brain perfusion were generated. Reproductive history was self-reported. Gravidity, parity, and history of pregnancy complications (miscarriage, gestational diabetes, low birthweight, preterm birth) were examined as predictors of total brain volume and volume of regions of interest relative to memory or identified in previous studies, using linear models with control for age, total cranial volume, and gravidity (when relevant).

Results: Total volume and total white matter volume were highest in those who were gravidity/parity 1 or 3+. Ventricle volume was highest in nulligravida/nullipara. There were no associations between gravidity/parity and any other volume measure. History of preterm birth, low birthweight, miscarriage, or gestational diabetes were not associated with any of the volumetric measures. Higher gravidity and parity were generally associated with higher cerebral blood flow, and gravid women also seemed to have greater fractional anisotropy and lower trace in white matter. Other reproductive history measures were not associated with these outcomes.

Conclusions: Gravidity and parity were associated with some global brain measures at midlife, generally in the direction of better brain health in parous compared to nulliparous women. History of pregnancy complications were not associated with these outcomes, perhaps due to low power or to lack of a genuine association.

LATEBREAKER

Aging

Impact of Driving Mileage on Depression Prevalence Among Older Adults During the COVID-19 Pandemic: A Longitudinal Poisson Regression Analysis Anni Wang* Anni Wang
Guohua Li

Background: Previous studies indicate that depression status and use of antidepressant medication are associated with driving behavior and safety among older adults. It is unclear, however, whether changes in driving patterns are predictive of depression. Using longitudinal data for a sample of active older adult drivers, we examined the association between annual driving mileage and depression status during 2019 through 2022.

Methods: Data for this study came from the Longitudinal Research on Aging Drivers project, in which naturalistic driving data for 1,095 drivers aged 65-79 years at baseline were available. Poisson regression models were employed to analyze the association between driving mileage and depression status, adjusted for history of depression and demographic factors, since they effectively adjust for the varying time each participants was observed. Models were run separately for each year to assess trends over time and observe the influence of COVID-19, to compare pre-pandemic (2019) and pandemic periods (2020-2022).

Results: During the study period, the prevalence of depression increased from 6.21% in 2019 to 7.12% in 2022 while the average annual driving mileage decreased from 8740.11 miles in 2019 to 5920.32 miles in 2022. Poisson regression modeling revealed an inverse relationship between annual driving mileage and depression status. With adjustment for demographic factors and history of depression, the rate of depression decreased by 8.61% for every 1,000-mile increase in annual driving mileage (adjusted RR 0.91, 95% CI: 0.88, 0.95).

Conclusion: Our results indicate that the prevalence of depression among older adults increased during the COVID-19 pandemic and that reduction in driving mileage is associated with increased rates of depression in a dose-response fashion.

LATEBREAKER

Aging

Retirement from the Labor Force Among Unpaid Caregivers: A Matched Case-Control Study
Derek Manis* Derek Manis Wenshan Li Reiko Okamoto Stacey Fisher Colleen Webber Vanessa Taler Douglas Manuel Amy Hsu

Objective: To examine the caregiving factors, sociodemographic characteristics, and self-reported health of caregivers who retired from the labor force to provide full-time, unpaid care to their care recipient.

Design: Matched case-control study.

Setting and Participants: Caregiver respondents from the Canadian Longitudinal Study on Aging baseline (2011-2015), follow-up 1 (2015-2018), and follow-up 2 (2018-2021) cycles who indicated that they retired from the labor force to provide care (i.e., cases). These respondents were matched 1:1 without replacement to caregiver controls who did not retire to provide care on birth year (+/- 1 year), sex, and region of Canada.

Methods: Caregiving-related variables (e.g., type of care and intensity, care recipient's sex, relationship to the caregiver, co-residence status), sociodemographic variables (e.g., income, immigration, race, sexual orientation, marital status), and self-reported health were examined. Conditional logistic regression was used to model adjusted associations with being a caregiver who retired from the labor force to provide care.

Results: There were 336 caregivers who retired to provide care and who were matched to 336 caregivers who did not retire due to caregiving (mean age 70 years, 73% female; N = 672). Factors related to caregiving burden and type were strongly associated with retirement from the labor force to provide care full-time, whereas caregivers' self-reported physical and mental health and household income were not associated with the decision to retire.

Conclusions and Implications: Caregivers' decisions to retire from the labor force were mostly driven by their care recipients' care needs. These findings substantiate the imperative for comprehensive workplace policies that accommodate varied caregiving responsibilities and duties. Increasing access to affordable congregate care options may be another strategy that could reduce caregiver burden and retirement from the labor force to provide care.

LATEBREAKER

Aging

Biological Aging and Autoimmune Disease Incidence: A Large Prospective Cohort Study
Choa Yun* Choa Yun Minkyo

Background: While accelerated biological aging is linked with various age-related disorders, its role in autoimmune disease risk is unclear. This study investigates the association between biological aging and autoimmune disease risk in a large prospective cohort.

Methods: We analyzed 470,020 UK Biobank participants without 41 autoimmune diseases ascertained using ICD codes and self-reported diagnosis at baseline. Biological aging was estimated using 18 biomarkers via the Klemera-Doubal method (KDM), PhenoAge, and homeostatic dysregulation (HD). Hazard ratios (HR) and 95% confidence intervals (CI) were estimated using Cox proportional hazards models to assess the association between biological aging and autoimmune disease incidence, adjusting for age, sex and potential confounders. We also fitted a time-varying model by including an interaction term between biological and chronological age.

Results: During a median follow-up of 12.7 years, 38,169 participants (56% females) developed autoimmune diseases. A 1-SD increase in KDM (HR 1.18, 95% CI 1.16–1.19), PhenoAge (1.27, 1.25–1.28), and HD (1.18, 1.16–1.20) was significantly increased disease risk. In sex-stratified analyses, a 1-SD increase in KDM (HRmale 1.15, 95% CI 1.13-1.16 vs. HRfemale 1.26, 95% CI 1.24-1.29) and HD (1.21, 1.19-1.24 vs. 1.19, 1.17-1.22) were associated with higher risk of autoimmune diseases in females, while PhenoAge showed a higher risk in males (1.32, 1.30-1.34 vs. 1.24, 1.22-1.25). The HRs for all biological aging measures show a consistently elevated risk of autoimmune diseases, higher at younger ages and decreasing slightly with age, but remaining above 1 across all ages.

Conclusion: Accelerated biological aging was associated with an increased risk of developing autoimmune diseases, with variations noted across sex and slightly higher risk at younger ages. These findings suggest that biological aging may inform risk stratification and primary prevention efforts for autoimmune diseases.

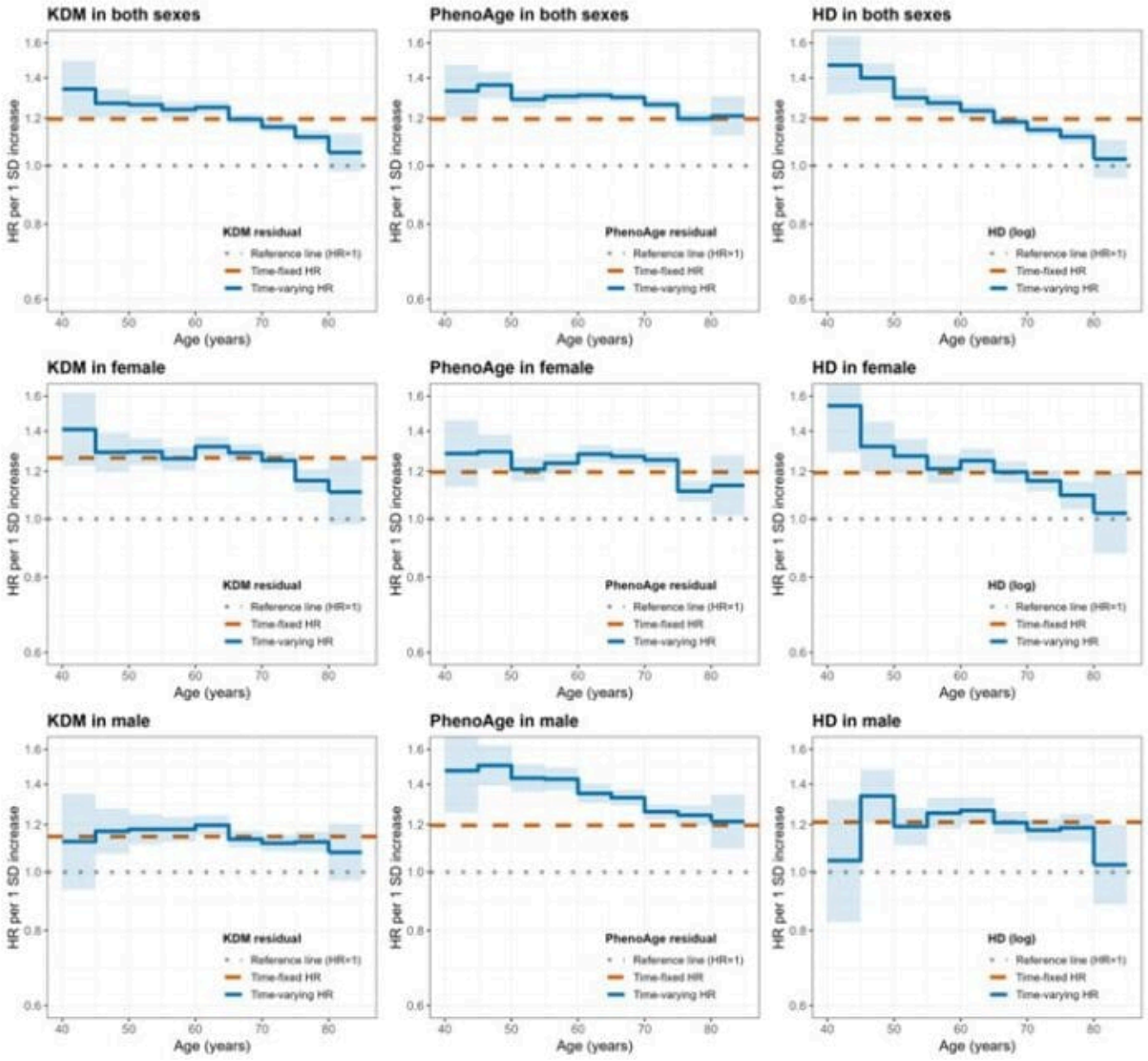


Figure 1. Time-varying hazard ratios for risk of autoimmune disease per 1 standard deviation increase in biological age measures by chronological age in UK Biobank

Time-varying hazard ratios were calculated by fitting a model that included interaction terms between each biological age measure (Klemera-Doubal method [KDM], PhenoAge, homeostatic dysregulation [HD]) and chronological age, segmented into 5-year intervals.

Aging

The effect of regular physician home visits on the prevention of hospitalization among older adults starting long-term care in Japan Yoko Hamasaki* Yoko Hamasaki Masao Iwagami Yuta Taniguchi Jun Komiyama Yuji Ito Taeko Watanabe Naoaki Kuroda Ai Suzuki Nanako Tamiya

Background: Demand for home healthcare is increasing as the population ages. The Japanese healthcare system can reimburse physician home visits.

Aim: We examined whether physician home visits could reduce the risk of hospitalization among older adults starting long-term care, overall and by subgroups, which we identified by a clustering analysis in our previous study.

Methods: This retrospective cohort study included community-dwelling adults aged ≥65 years who started long-term care in City A, Japan, between October 2014 and March 2019. We defined the exposure status of regular physician home visits within 3 months after the care-need certification and followed them from 3 months as a landmark analysis. We excluded participants who were hospitalized or died before the 3-month landmark time point. All-cause hospitalization was assessed using the cumulative incidence function and competing-risk Cox regression. The analysis was conducted for all the participants and also by subgroups of people with (i) mild physical, (ii) mild cognitive, (iii) moderate physical, (iv) moderate multicomponent, and (v) severe multicomponent subtypes, clustered using 74 items on physical and cognitive functions, behavioral problems, and medical procedures in the Japanese standardized survey for care-needs certification.

Results: Of 3,120 participants (median [IQR] age, 83 [77-87] years; female, 60.6%), 6.2% used physician home visits. Median follow-up was 402 (201–730) days, and 1,118 were hospitalized. Overall, physician home visits were associated with fewer hospitalizations (adjusted HR 0.71, 95% CI 0.54-0.93). By subgroup, we observed a lower risk of hospitalization (adjusted HR 0.18, 95% CI 0.07-0.47) only in the severe multicomponent subtype (Figure).

Conclusions: We found physician home visits were associated with a lower risk of hospitalization, driven by the result in the most severe subgroup. These findings inform individualized care decisions and personalized care strategies.

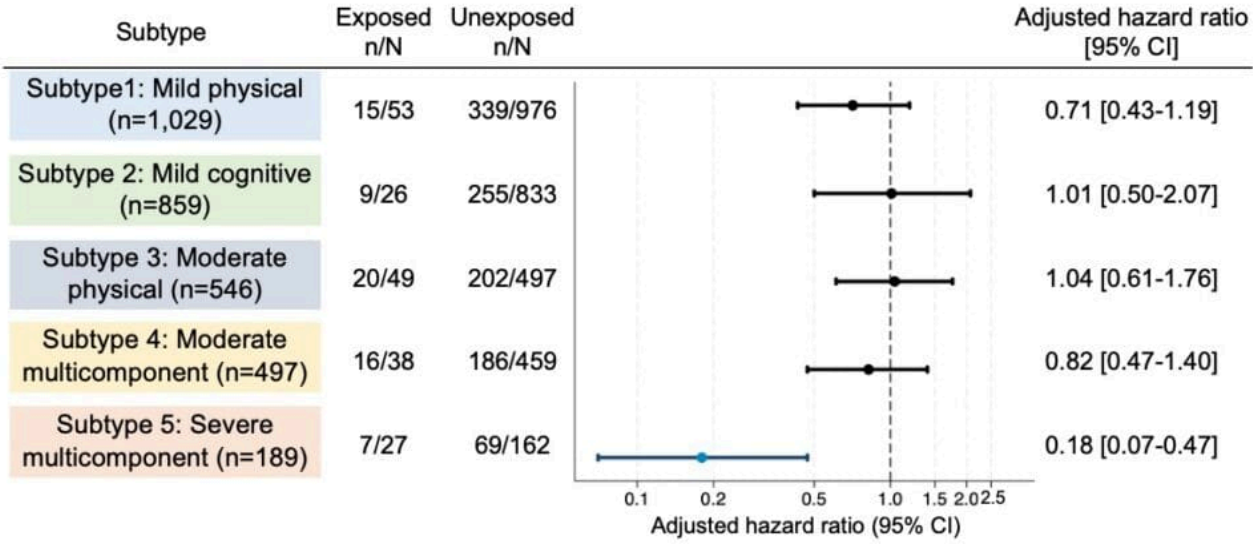


Figure. Association between physician home visits and hospitalization among subtypes of older adults requiring long-term care

All the regression models were adjusted for age, sex, care-need level, history of hospitalization, and use of home-visiting nurse services. n=No. of outcome, N=No. of participants.

Aging

Parental age at the birth of the last child and mid- to later-life memory decline in rural South Africa Meredith L. Phillips* Meredith Phillips Joshua W. Brown Jaroslaw Harezlak Christina Ludema Molly Rosenberg

Background: The prevalence and incidence of cognitive impairment and decline are growing, especially in low- and middle-income countries. Having children later in life has been associated with better health outcomes and may be associated with improved cognitive health. We aimed to estimate the association between age at the last birth and memory function and decline in older adults in Rural South Africa.

Methods: Using data from the "Health and Aging in Africa: A Longitudinal Study of an INDEPTH Community in South Africa" (HAALSI) cohort, we calculated participants' ages at the birth of their last child, restricting to parents who had not experienced child loss (n=1,961). Longitudinal episodic memory was assessed at three points from 2014/15-2021/22. We fit sex-stratified linear mixed-effects models to estimate the association between age at last birth on memory function and decline, adjusting for age, education, literacy, childhood health, country of birth, father's occupation, and household assets.

Results: Of the 1,961 participants**,** 47% were men (922)**.** The mean age was 57 years for men and 55 for women. 67% of men and 73% of women reported very good childhood health, 79% of men and 75% of women were born in South Africa, 74% of men and 69% of women had at least some formal education, and 80% of men and 70% of women were literate. On average, men were older at the birth of their last then women (39 vs 34). For men, with each additional year of age at birth of last child, memory scores were 0.018 SD units higher (95% CI: 0.009 – 0.026), but the slope of memory decline was steeper (b: -0.002, 95% CI: -0.0030 to -0.0003). For women, age at birth of last child was not associated with memory function or memory decline.

Conclusion: Older age at the last birth was associated with greater memory function but faster decline in men but not women. In this sample, the relationship between reproductive life history and cognition may be shaped by gendered experiences and biological factors. However, the generalizability of these findings may be limited. These results suggest that, highlighting the importance of considering these differences in future work investigating the relationship between reproductive life history and cognition.

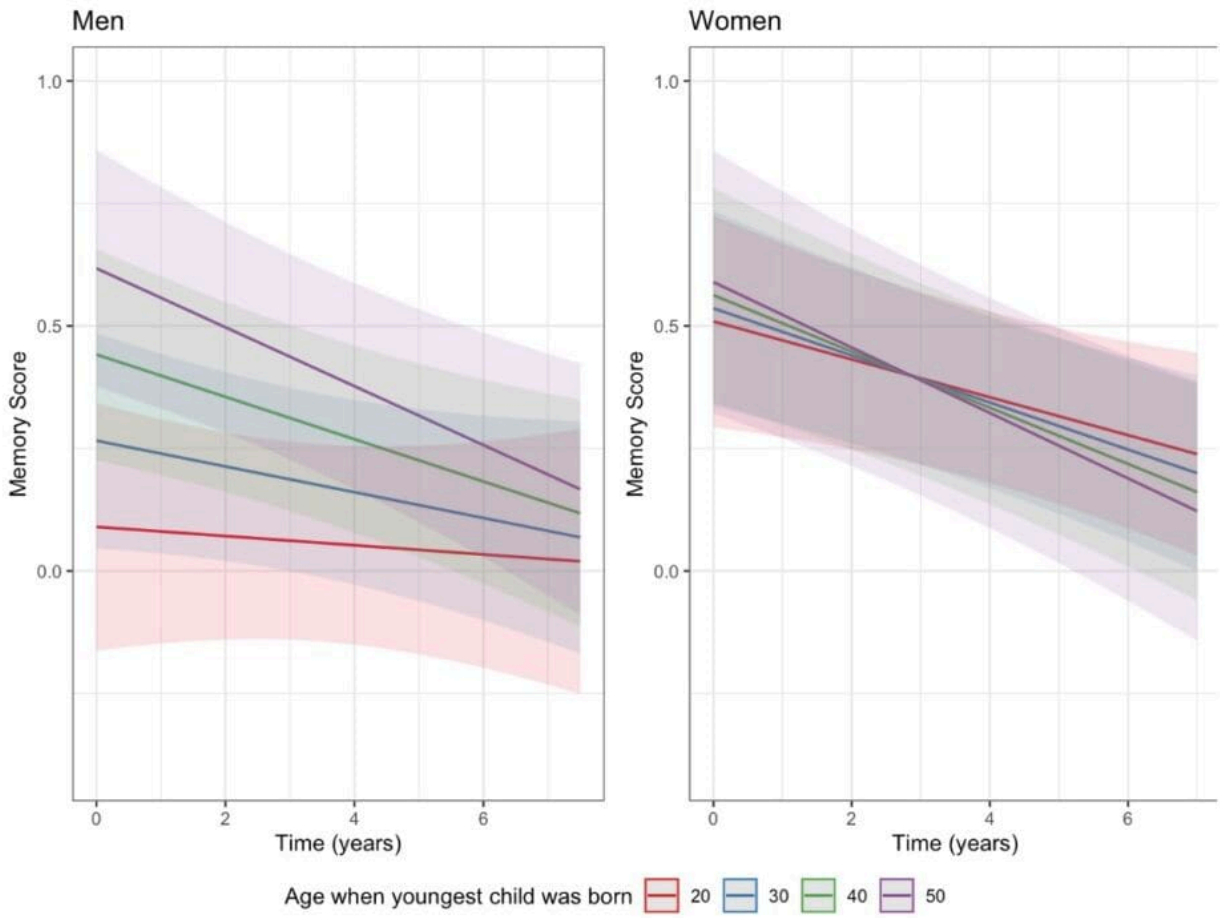


Figure: Predicted values from the fully adjusted mixed effects models for memory scores over time by age at the birth of the last child in men and women, 2014-2022, HAALSI, Agincourt, South Africa
All continous covariates are held constant at their means and categorical covariates at their reference levels.
(Age: Men: 57, women: 56; education: no formal education; literacy: illiterate; childhood health: very good; country of birth: South Africa; father's occupational skill level during childhood: Level 1; and household asset-based wealth index: 3; number of children:1)

Aging

Double Risk: How Diabetes and Hypertension Impact Disability in Non- Institutionalized Brazilian Older Adults – Evidence from Two Population-Based Studies Rafaela Gonçalves Ribeiro Lucas* Rafaela Gonçalves Ribeiro Lucas Bárbara Niegia Garcia de Goulart Patricia Klarmann Ziegelmann

Introduction: Diabetes and hypertension are prevalent global comorbidities, particularly among older populations in low- to middle-income countries. Their complications increase mortality and impair quality of life and functional capacity, significantly affecting basic (ADL) and instrumental (IADL) activities of daily living. This study examines the impact of these conditions on moderate and severe disability among Brazilian older adults, using data from the 2013 and 2019 National Health Surveys.

Methods: Individuals aged ≥60 years were analyzed using Poisson regression with robust variance, adjusted for sampling design and confounding factors. Disability was assessed with the Katz and Lawton scales, categorized as moderate or severe. Prevalence ratios (PR) and 95% confidence intervals (CI) were calculated separately for ADL and IADL.

Results: In 2013 and 2019, participant characteristics are: age 60–80 years (86.6%; 86.7%), women (59.3%; 55.1%), black/brown ethnicity (51.0%; 54.8%), and incomplete elementary education (69.2%; 65.4%). The prevalences were: severe ADL (5.3; 7.0) and IADL (17.7; 23.3); moderate ADL (10.3, 13.6) and IADL (14.0; 64.5). In 2013, diabetes and hypertension increased moderate ADL (PR=1.9; CI 1.4–2.6) and severe ADL disability (PR=2.0; CI 1.4–2.7). By 2019, the impact on moderate ADL disability decreased (PR=1.6; CI 1.4–1.8) but remained similar for severe ADL (PR=1.9; CI 1.7–2.3). In IADL, these conditions were associated with severe disability in 2013 (PR=1.4; CI 1.2–1.7) and with the moderate (PR=1.2; CI 1.19–1.22) and severe disability (PR=1.66; CI 1.6–1.7) in 2019.

Conclusion: From 2013 to 2019, the coexistence of diabetes and hypertension significantly impacted moderate and severe disability, particularly in IADL, with progression linked to aging. These findings emphasize the need for public policies targeting disease management and functional support for older adults, especially in the Americas.

Aging

Widowhood, Immunosenescence, and Mortality in Older American: Evidence from the Health and Retirement Study Youngjoon Bae* Youngjoon Bae Yuan Zhang Jaydon Jun Yu Chin Grace A. Noppert Rebecca Stebbins Daniel W. Belsky Allison E. Aiello

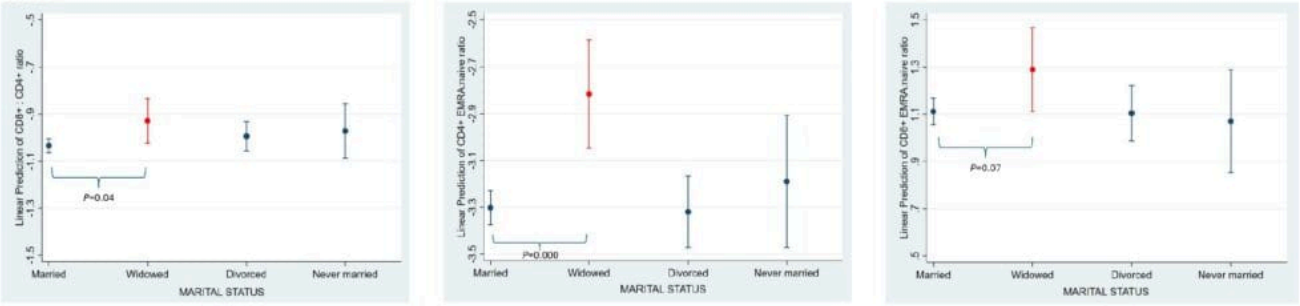
Widowhood is linked to an increased risk of mortality, particularly among men. Studies examining biomarkers related to the loss of a loved one have identified changes in the immune system as a potential mechanism behind this risk. However, most research has focused on general indicators of inflammation. Another immune pathway related to the stress of widowhood is immunosenescence, which refers to the gradual decline of the immune system associated with aging.

We analyzed data derived from flow cytometry analysis of blood samples from 8,136 US adults aged 50 and older, participants in the Health and Retirement Study (HRS). We first explored the associations between widowhood and measures of immunosenescence through linear regression models. Specifically, Immunosenescence was assessed using three log-transformed T-cell aging markers, including the CD4+:CD8+ T-cell ratio, EMRA CD4+: Naïve CD4+ Ratio, and EMRA CD8+: Naïve CD8+ Ratio. Next, we examined whether widowhood was linked to increased mortality rates by employing Cox proportional hazard models, taking immunosenescence into account. In both analyses, we adjusted for age, race, ethnicity, education, depression, and recent spousal loss (<= 5 years).

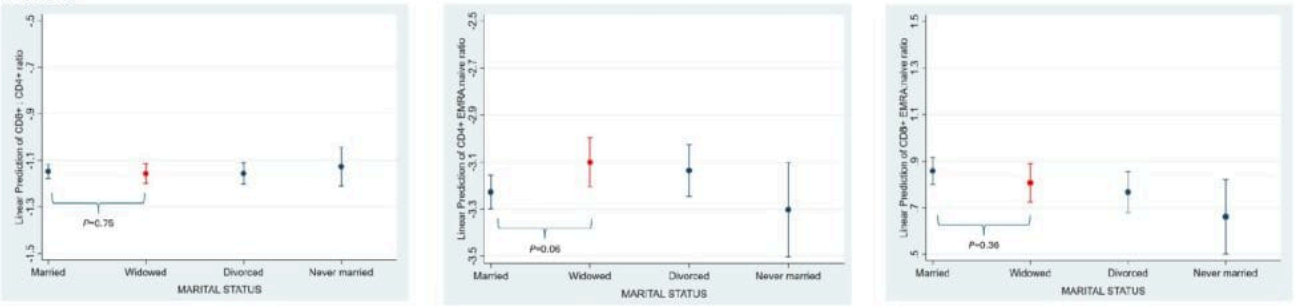
We observed that widowhood was associated with significantly higher levels of T-cell aging markers in men but not women, in fully adjusted models (see Figure 1 for details). The survival analysis results indicated that elevated levels of T-cell aging markers were risk factors for mortality in both men and women—however, the small impact of these T-cell markers on the relationship between widowhood and mortality was found only in men. These findings suggest that widowers have a more aged immune profile than married men, and the relationship between widowhood and mortality among men may be partially explained by immunosenescence. Men may be at greater risk for poor health outcomes and mortality upon widowhood suggesting the need for early intervention and prevention.

Figure 1. Linear prediction of T-cell aging markers for marital status categories by gender

Men



Women



Note. Age, race, ethnicity, education, depression, and spousal loss within the past 5 years were adjusted.

Aging

Adverse Socioeconomic Changes and Mental Health in Older Age: Results from the Lebanon Study on Ageing and Health Martine Elbejjani* Martine Elbejjani Aya El Sammak Carlos Mendes de Leon Abla Mehio Sibai Stephen McCall Sawsan Abdulrahim Adina Zeki Al Hazzouri Monique Chaaya

Background

Socioeconomic disadvantage is a key determinant of mental health across the lifecourse. Less is known about the impact of socioeconomic changes in older age and current evidence come from higher-income countries where retirement and welfare support can help withstand adverse changes. We assessed how socioeconomic adversities experienced during a recent record economic crisis relate to mental health among older adults in Lebanon.

Methods

We used data from the population-based Lebanon Study on Ageing and Heath (LSAHA, n=3,027, mean age=70.55±7.89; 37% men). The relation of self-reported ability to secure basic needs (e.g., food, electricity, heat) during the recent crisis with elevated depression (Center for Epidemiologic Studies Depression Scale (CESD-8) and anxiety (Generalized Anxiety Disorder (GAD-7)) symptoms was assessed using logistic regression models adjusted for age, gender, education, mental health history, and wealth index.

Results

Around 57% and 43% of participants had elevated depressive and anxiety symptoms; 63% reported being unable to purchase basic needs since the crisis. This adverse change was associated with 1.42 (95% CI= 1.29, 1.57) and 1.38 (95% CI= 1.24, 1.54) higher odds of elevated depressive and anxiety symptoms, respectively. Associations were more substantial in rural settings and further analyses will examine potential gender and socioeconomic disparities.

Conclusion

Results show a significant mental health burden among older adults in Lebanon and a large-magnitude association with hardship due to the recent economic crisis. Results emphasize the importance of monitoring the health impact of socioeconomic changes in older age, particularly in settings with limited resources to mitigate such changes.

Aging

Comparing major comorbidity indices as predictors of all-cause mortality in the Veterans Affairs healthcare system Hind A. Beydoun* Hind Beydoun Dorota Szymkowiak May A. Beydoun Neil Nixdorff Robert Brunner Jack Tsai

Background: The Charlson Comorbidity Index (CCI), the Elixhauser Comorbidity Index (ECI), and the Functional Comorbidity Index (FCI) are validated clinical measures of comorbidity, but direct comparisons between these measures have rarely been studied especially in high-risk patient populations, such as homeless individuals. The U.S. Department of Veterans Affairs (VA) offers large patient samples to compare these comorbidity measures as predictors of mortality using administrative and clinical records. **Objectives:** To examine CCI, ECI, and FCI scores among veterans seeking VA healthcare services, including those experiencing homelessness, and compare their predictive value in relation to all-cause mortality risk. **Research Design, Subjects, Measures:** Several VA databases from 2017–2021 were retrospectively linked and 4,701,711 U.S. veterans [308,553 with homelessness and 4,393,158 without homelessness] were evaluated over a median follow-up of 4.1 years, yielding 917,921 recorded deaths. Regression models were constructed, and Harrell's Concordance Statistic (HCS) was calculated that assessed the ability of z-transformed comorbidity scores to discriminate 'high-risk' vs. 'low-risk' groups of patients for mortality risk, after adjustment for demographic and clinical characteristics. **Results:** In adjusted models, ECI (HCS=0.76) and CCI (HCS=0.76) were better able to discriminate 'high-risk' vs. 'low-risk' groups than FCI (HCS=0.74). Compared to ECI and CCI, FCI was more strongly associated with homelessness, whereas ECI and CCI were more strongly related to all-cause mortality risk among non-homeless than homeless patients. **Conclusions:** CCI and ECI may be more predictive of all-cause mortality risk than FCI, although FCI may be a useful measure of functioning in homeless populations.

Aging

Cardiovascular disease, bone fracture, and all-cause mortality risks among postmenopausal women by arthritis and veteran status: A multistate Markov transition analysis Hind A. Beydoun* Hind Beydoun May A. Beydoun Jordan Weiss Robert Brunner Nishant K. Mishra Ming Ding Jean Wactawski-Wende Philippe Jean-Luc Gradidge Simin Liu Jack Tsai

Arthritis, a chronic inflammatory condition linked to cardiovascular disease (CVD) and bone fracture, is more frequent among military veterans and postmenopausal women. This study examined correlates of arthritis and relationships of arthritis with risks of developing CVD, bone fractures, and mortality among postmenopausal veteran and non-veteran women. We analyzed longitudinal data on 135,790 (3,436 veteran and 132,354 non-veteran) postmenopausal women from the Women's Health Initiative who were followed-up for an average of 16 years between enrollment (1993–1998) and February 17, 2024. Regression and multistate Markov modeling were applied to meet study objectives. The prevalence of arthritis at enrollment (1993–1998) did not differ by veteran status in a fully adjusted logistic model. Variable selection yielded 5 key predictors of prevalent arthritis among veterans and 15 key predictors among non-veterans. In fully-adjusted Cox models, prevalent arthritis was associated with CVD (hazard ratio [HR]=1.08, 95% confidence interval [CI]: 1.05, 1.10) and all-cause mortality (HR=1.03, 95% CI: 1.01, 1.05) risks among non-veterans only, but was not associated with bone fracture risk irrespective of veteran status. Transition probabilities between health and CVD and between bone fracture and death were higher among women with vs. without arthritis. The latter transition was more strongly related to arthritis among non-veteran vs. veteran women. In conclusion, among postmenopausal women, prevalent arthritis was associated with greater probabilities of transitioning from a healthy state to CVD and from bone fracture to death, with worse prognosis after bone fracture among those who did not serve in the military.

Aging

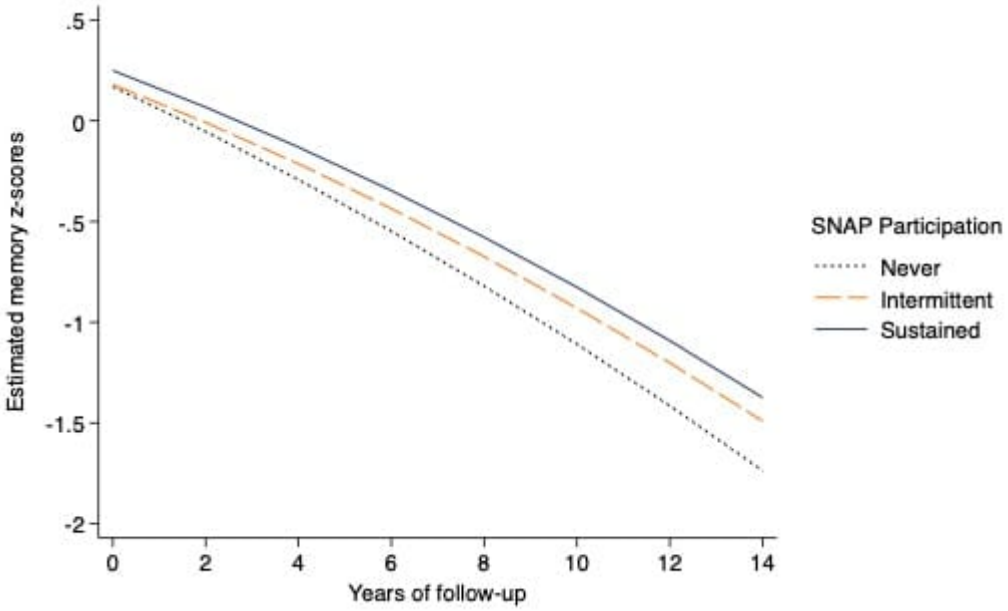
Cumulative Supplemental Nutrition Assistance Program Participation and Memory Aging among US Older Adults, 1996-2018 Xuexin Yu* Xuexin Yu Katrina L Kezios Peiyi Lu Samuel L Swift Adina Zeki Al Hazzouri

Introduction: Supplemental Nutrition Assistance Program (SNAP) has been shown to effectively reduce food insecurity and improve health outcomes among low-income populations. Limited research has assessed the health effects of cumulative SNAP participation in later life, even though fluctuations or churn episodes in SNAP participation are common. We aimed to investigate the association between cumulative SNAP participation and subsequent memory function and decline among US older adults.

Methods: This prospective cohort study used data from US Health and Retirement Study 1996-2018. We included 2,633 adults aged 65 and over who were eligible for SNAP in at least one survey year between 1996-2004 (Cohort A) or 1998-2006 (Cohort B). We calculated the percentage of the time individuals participated in SNAP relative to the number of times they were eligible to participate over the 8-year period. We operationalized cumulative SNAP participation as never, intermittent (less than two-thirds of the time), and sustained (two-thirds or more of the time). We used composite memory z-scores that incorporated direct and proxy memory assessments as the outcome measure. We fit a mixed-effects linear regression model to investigate the association between SNAP participation and subsequent memory function and decline.

Results: Mean (SD) age at baseline was 74 (5.95), and 66.4% were women. A total of 2,257 (85.7%) participants never used SNAP, 219 (8.4%) participated in SNAP less than two-thirds of their eligible period, and 157 (6.0%) participated in SNAP two thirds or more of their eligible period. Compared to those who never participated in SNAP, individuals with intermittent (0.017 SD units; 95% CI: -0.002 to 0.036) and sustained SNAP participation (0.020 SD units; 95% CI: 0.001 to 0.040) experienced a slower rate of memory decline. The observed effect size was equivalent to delaying memory decline by 1.87 and 2.24 years per decade for SNAP intermittent and sustained participants.

Conclusions: Cumulative SNAP participation may help to preserve memory health among low-income older adults in the United States. Policy interventions are warranted to promote continuous SNAP enrollment among eligible individuals.

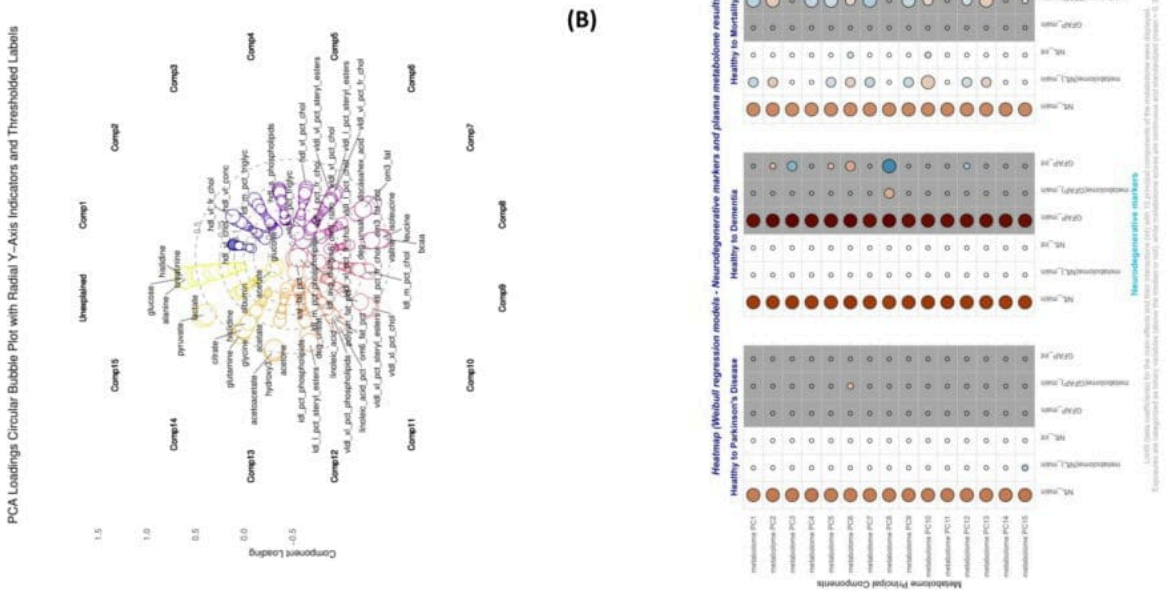

.5
0
-.5
-1
-1.5
-2
Estimated memory z-scores
0
2
4
6
8
10
12
14
Years of follow-up
SNAP Participation
Never
Intermittent
Sustained

Aging

The interplay of air pollution with plasma neurodegenerative markers and metabolome for dementia, Parkinson's Disease and all-cause mortality risks and transitions: the UK Biobank study May A. Beydoun* May Beydoun Tianyi Huang Yi-Han Hu Jordan Weiss Michael F. Georgescu Nicole Noren Hooten Marie T. Fanelli-Kuczmarski Hind A. Beydoun Minkyo Song Lenore J. Launer Michele K. Evans Alan B. Zonderman

Interactions between two important neurodegeneration exposures [Neurofilament Light (NfL), and Glial Fibrillary Acidic Protein (GFAP)], air pollution and the plasma metabolome, in relation to transitions from healthy to neurodegenerative phenotypes [dementia, Parkinson's Disease (PD)] and mortality were examined. Data were extracted from 19,645 UK Biobank participants (mean baseline age=61y, follow-up:2006-2023). Parametric Weibull models were conducted within a multistate framework, including two-way interactions among three groups of exposures (i.e. NfL/GFAP, air pollution and plasma metabolome). Healthy–>PD; Healthy–>Dementia; and Healthy–>Death transitions were directly associated with elevated NfL, while only Healthy–>Dementia was positively and strongly linked to elevated GFAP (fully-adjusted hazard ratio, above vs. below median GFAP, HR=2.65, 95% CI: 2.17-3.25, PDeath transition, while nitric oxide exposures (NO2 and NOx) attenuated the association between GFAP for this same transition. Synergism between PM2.5 and several metabolomic clusters was detected for Healthy–>Dementia and Healthy–>PD transitions, pertaining mainly to cholesteryl esters in very low-density lipoproteins (VLDL) for dementia, cholesterol/cholesteryl esters in chylomicrons/extremely large VLDL, and acetone/acetoacetate/3-hydroxybutyrate for PD. Metabolomic markers also interacted with NfL/GFAP to increase Healthy–>mortality and Healthy–>dementia transition risk, while branched-chain amino acids and omega-3 fatty acids as main effects were among metabolites to be inversely related to Healthy–>dementia transition. In conclusion, NfL and GFAP consistently predicted dementia risk, while air pollution modified their associations with mortality risk. The metabolome interacted with neurodegenerative and air pollution markers, including PM2.5, in relation to PD, dementia and mortality risk.

FIGURE 1. Blood markers of neurodegeneration, plasma metabolome And their interactive association with transitions from healthy to PD, Dementia and death, UK Biobank 2006-2023



Aging

The Role of DNA methylation-based Biological Aging, Immunity and Inflammation Biomarkers in the Relationship between Stroke, Short- and Long-term Cognition. Reem Waziry* Reem Waziry

Objective. To determine indirect effects of stroke on short- and long-term cognition in relation to inflammation, immunity and aging.

Methods. The study population included individuals who consented for blood draw in the Health and Retirement 2016 Venous blood study. 3, 467 individuals were included. Indirect effects of stroke on short- and long-term cognition with respect to select biological biomarkers with a focus on inflammation, immunity and DNA methylation based biological aging were assessed using four-way decomposition models. Direct and indirect effects of APOE 4 carriership, as a risk factor gene, on cognition in relation to stroke were also assessed.

Results. Pure natural indirect effects of stroke on short-term cognition in relation to key biological biomarkers were as follows: inflammatory biomarkers: beta=-0.01 (P value=0.250), immunity biomarkers: -0.04 (P value =0.002), White Blood Cells: -0.04 (P value= 0.016), DNA methylation-based biological aging: -0.41 (P value < 0.001), and all biomarkers jointly: -0.38 (P value < 0.001).

Reference interaction effects of stroke on short-term cognition in relation to key biological biomarkers were as follows: TGF-beta: beta= -2.13 (P value <0.001); immunity: 3.51 (P value=0.260); White Blood Cells: 0.04 (P value= 0.910); DNA methylation-based biological age:-0.25 (P value < 0.01), and all biomarkers jointly: 11.98 (P value= 0.01).

Conclusions. Stroke effects on cognition are partially through mediation and interaction with key inflammatory, immunity and biological aging biomarker pathways. Therapeutics targeting joint pathways are likely essential to optimize cognitive resilience especially in stroke survivors.

Aging

Associations Between Birthweight and Preterm Birth and the Risk of Alzheimer's in Women from the Women's Health Initiative Emily A. Nyhan* Emily Nyhan Christian Daniele Rachel E. Wacks Cassandra N. Spracklen Ramon Cassanova Sabiha Nasrin Leslie V. Farland Bernhard Haring Su Yon Jung Longjian Liu JoAnn E. Manson Nazmus Saquib Jean Wactawski-Wende Robert B. Wallace Brian W. Whitcomb

ABSTRACT

Associations Between Birthweight and Preterm Birth and Risk of Alzheimer's Disease in Women from the Women's Health Initiative

Emily A. Nyhan, B.S., UNIVERSITY OF MASSACHUSETTS AMHERST

M.S., UNIVERSITY OF MASSACHUSETTS AMHERST

Directed by: Dr. Cassandra N. Spracklen

Alzheimer's Disease is known as the most common type of dementia, currently affecting 5.8 million Americans. Dementia is an increasingly prevalent brain disease known for the loss of cognitive functioning and behavioral abilities that results in the inability to complete basic life tasks. The Developmental Origins of Adult Disease (DOAD) hypothesis states that exposures *in utero* and in early life can increase the risk of developing chronic disease decades later. The study aimed to investigate the potential associations between birthweight, preterm birth status, and the risk of Alzheimer's disease in women from the Women's Health Initiative (WHI). The WHI is a large prospective cohort study, made up of women from various demographic backgrounds. At baseline, women self-reported their birthweight and preterm birth category (<6lbs., 6-7lbs 15 oz., 8-9lbs 15 oz., or ≥10 lbs.; ≥4 weeks premature or full term). Data on incident Alzheimer's Disease were obtained through self-administered questionnaires during the Main and Extension phases of the study, as well as from death certificate data. During the follow-up periods, participants were asked to report if a doctor had ever told them they had "moderate or severe memory problems" and/or "Dementia or Alzheimer's" (yes/no). Cox-proportional hazards regression models were used to generate hazards ratios.

After adjusting for demographic and lifestyle factors, we found no association between low or high birthweights or preterm birth and Alzheimer's disease. Individuals reportedly born weighing (8-9 lbs. 15 oz.) had a slight protective factor of developing Alzheimer's Disease. Further research in the area is warranted to confirm our findings.

Aging

Healthcare Costs and Utilization Patterns Before and After Dementia Onset With and Without Clinical Recognition by the Healthcare System Bryan James* Ziwei Song Annie Chen Joya Bhattacharyya Yi Chen Francine Grodstein Bryan D. James Emma K. Stapp Melinda C. Power Ali Moghtaderi

Background: Prior research has shown substantial underdiagnosis of dementia in healthcare settings, as well as an increase in healthcare utilization and costs around the time of clinical dementia diagnosis. However, patterns around the onset of dementia—independent of clinical dementia diagnosis—remain poorly understood. This study examines healthcare utilization and costs around dementia onset among those with and without clinical recognition. Methods: Participants were from five Rush Alzheimer's Disease Center (RADC) cohorts. Healthcare costs and utilization data were extracted from linkage to Medicare fee-for-service claims, covering the period from three years before to one year after cohort-determined dementia onset. Outcomes include total and category-specific Medicare payments (Parts A and B), emergency department (ED) visits, outpatient provider interactions, and hospitalizations. We analysed four-year healthcare utilization trajectories, from before to after dementia onset. We also identified whether persons with cohort-determined dementia had a dementia diagnosis recorded in Medicare claims within the four-year window and examined differences in healthcare utilization and cost according to clinical recognition of dementia. Results: Among 557 participants, the median age at dementia onset was 87 years, 26% were female, and 88% identified as non-Hispanic White. Inpatient and outpatient costs, ED visits, and hospitalizations increased leading up to and during the year of dementia onset, then declined in the year after. Although the overall patterns were similar irrespective of clinical recognition of dementia, the 54% of persons with clinical recognition had consistently higher costs and ED/hospitalization utilization. Conclusions: Healthcare utilization peaks at the time of dementia onset irrespective of clinical recognition of dementia. What drives this pattern and whether observed declines after dementia onset reflect improvement in care remains unclear.

Aging

The association between frailty and incident dementia among older adults in the National Health and Aging Trends Study (NHATS) Bailey Reutinger* Bailey Reutinger Allison Musty Hannah Lee Anna Kuzma Emilie D Duchesneau

Background

Frailty, an age-related syndrome characterized by reduced physiologic reserve, is a risk factor for adverse health outcomes including cognitive decline. We quantified the association between frailty and 5-year dementia risk in older adults.

Methods

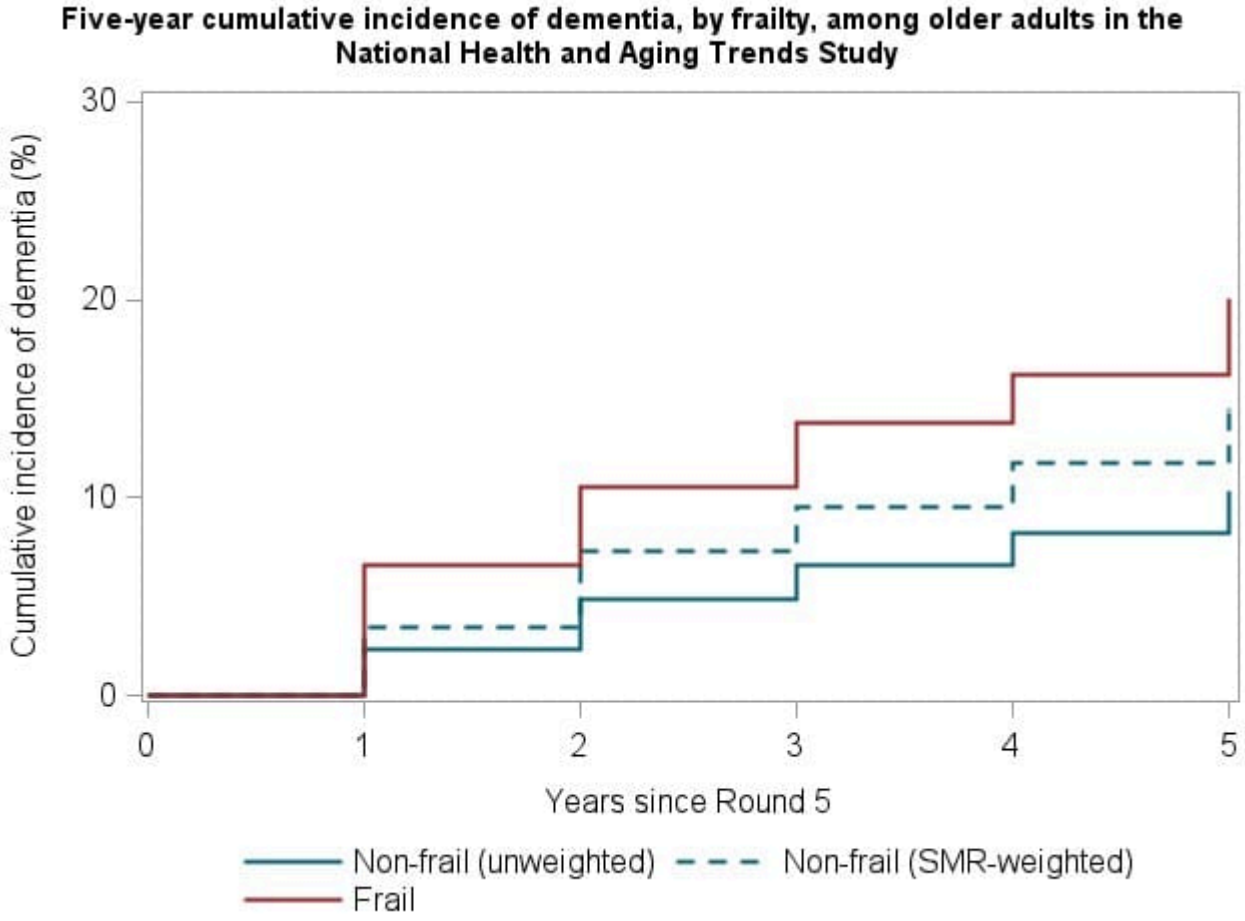
We used Rounds 5-10 (2015-2020) of NHATS, a nationally-representative longitudinal cohort of older adults (≥65 years) with annual assessments of age-related conditions. We included community and non-nursing home residential care dwelling older adults without dementia in Round 5 (baseline). Frailty was assessed using the Fried frailty phenotype, which characterizes frailty as having 3-5 symptoms (exhaustion, low physical activity, shrinking, slowness, weakness). Dementia was assessed using a validated measure based on self-reported diagnoses, the AD8 screening tool, and assessments of memory, orientation, and executive function. Multiple imputation accounted for missing data. Standardized mortality ratio (SMR) weights standardized the age, gender, and race distributions for frail and non-frail individuals. We used crude and SMR-weighted Aalen-Johansen estimators to compare 5-year dementia risk between frail and non-frail individuals, accounting for death as a competing risk. 95% CIs were estimated using bootstrapping.

Results

Among 6204 older adults, 16% were frail and 84% were non-frail. Frail participants were more likely to be older, female, and have diabetes than non-frail older adults. The crude 5-year incidence of dementia was higher in frail vs. non-frail older adults (**Figure;** 20% vs. 10%; difference=10%, 95% CI 7-12%). Differences attenuated slightly after standardization (20% vs. 14%; difference=6%, 95% CI 3-8%).

Conclusions

After standardizing demographic factors, frail older adults are at higher risk of dementia compared to non-frail counterparts. Targeted interventions, such as physical activity programs or nutritional support, may help mitigate dementia and frailty risk in this vulnerable population.


Five-year cumulative incidence of dementia, by frailty, among older adults in the National Health and Aging Trends Study
Cumulative incidence of dementia (%)
30
20
10
0
0
1
2
3
4
5
Years since Round 5
Non-frail (unweighted)
Non-frail (SMR-weighted)
Frail

Aging

Associations of Everyday and Lifetime Discrimination with Hippocampal and White Matter Hyperintensity Volumes among Older Black Adults Yodit Goshu* Yodit Goshu Joseph Fong L. Paloma Rojas-Saunero Eleanor Hayes-Larson Maria Glymour Paola Gilsanz Rachel Whitmer Pauline Maillard Kacie Deters Katelyn Mooney Laura Zahodne Ruijia Chen Tanisha G. Hill-Jarrett Courtney Thomas Tobin Elizabeth Rose Mayeda

Discrimination is linked to poor health outcomes, especially for people racialized as Black in the U.S. Few studies have assessed links between discrimination and dementia neuroimaging biomarkers. We aimed to evaluate the effects of discrimination on hippocampal volume and white matter hyperintensity (WMH) volume among older adults racialized as Black. We used data from the Kaiser Healthy Aging and Diverse Life Experiences (KHANDLE) and Study of Healthy Aging in African Americans (STAR) cohorts (n=308). Discrimination was measured using the Everyday Discrimination Scale, a 6-item questionnaire with sum of scores ranging from 0-45, and Major Experiences of Discrimination Scale, a questionnaire with 9 binary items (range 0-9). Scores were reverse coded, summed, and categorized (everyday low 0-9, moderate 10-18, high 19+; major experiences low 0-1, moderate 2, high 3+). We fit linear regression models to relate each discrimination measure with hippocampal volume and log-transformed WMH volume, adjusting for age at scan, educational attainment, sex/gender, parental education, southern birth, and total cranial volume. Mean hippocampal volume was 5.9 cm^3 and mean WMH volume was 6.0 cm^3. Everyday and major experiences of discrimination were not associated with hippocampal volumes (everyday high vs. low b = 0.00, 95% CI: -0.21, 0.22; everyday moderate vs. low b = -0.03, 95% CI: -0.18, 0.12; major experiences high vs. low b = -0.05, 95% CI: -0.20, 0.10; major experiences moderate vs. low b = 0.05, 95% CI: -0.14, 0.24). Everyday discrimination, but not major experiences of discrimination, was associated with higher WMH volume (everyday high vs. low b = 0.64, 95% CI: 0.10, 1.18; everyday moderate vs. low b = 0.28, 95% CI: -0.10, 0.66; major experiences high vs. low b = 0.08, 95% CI: -0.30, 0.48; major experiences moderate vs. low b = -0.15, 95% CI: -0.63, 0.34). Our findings suggest that discrimination may contribute to higher WMH volume among Black older adults in the U.S.

Aging

Quantifying the Population Attributable Fraction of Dementia from Insomnia among Older Adults in the United States Ruijia Chen* Yuqian Lin Fei Wu Yuhan Wu Wanru Liu Goodarz Danaei Ruijia Chen

Background: Insomnia has been identified as a plausible modifiable risk factor for dementia in prior research, and yet no studies have quantified its population-level impact on dementia risk in the United States. This study estimated the proportion of dementia cases attributable to insomnia among U.S. adults aged 65 and older, overall and stratified by age and sex.

Methods: We analyzed data from the 2022 National Health and Aging Trends Study (NHATS), a nationally representative longitudinal cohort of Medicare population aged 65 and older in the U.S. We estimated the prevalence of insomnia and dementia using the NHATS data and derived the relative risk of dementia associated with insomnia from a published meta-analysis to obtain the population attributable fraction (PAF).

Results: Among 5899 participants (44.7% aged ≥80 years; 57.9% female), 12.1% experienced only sleep-onset insomnia, 6.6% had only sleep-maintenance insomnia, and 10.0% reported both. The prevalence of probable dementia was 6.6%, with prevalence increasing with age for both sexes. The estimated PAF of probable dementia due to any type of insomnia was 12.8%, with higher estimates for females (13.4%) than males (12.0%). Among females, insomnia had the largest contribution to dementia in the youngest age group (ages 65–69, 14.4%). For males, the greatest contribution was observed in the 70–74 age group (12.8%). An estimated 471,229 dementia cases in the U.S. in 2022 could have been prevented if insomnia had been eliminated among adults aged 65 and older.

Conclusion: Approximately 13% of probable dementia cases, almost half a million cases per year, among older adults in U.S. could be attributable to having any types of insomnia, an estimate comparable to the well-established risk factors such as hearing loss. These findings underscore the potential for interventions aimed at addressing insomnia to reduce dementia risk.

Table Population Attributable Fraction of dementia from insomnia and attributable number of cases

Sex	Age	Weighted Prevalence of Insomnia %	RR	PAF (%)	Weighted Number of Dementia Cases	AtD
Male	65 to 69	27.8	1.51	12.4	218,285	27,120
	70 to 74	28.7	1.51	12.8	218,322	27,877
	75 to 79	24.5	1.51	11.1	208,319	23,167
	80 to 84	22.7	1.51	10.4	298,902	31,020
	85+	26.2	1.51	11.8	438,942	51,661
	Subtotal	26.6	1.51	12.0	1,398,554	167,335
Female	65 to 69	33.1	1.51	14.4	235,280	33,978
	70 to 74	29.1	1.51	12.9	244,469	31,623
	75 to 79	31.2	1.51	13.7	406,453	55,721
	80 to 84	28.9	1.51	12.8	454,571	58,371
	85+	28.1	1.51	12.5	867,170	108,532
	Subtotal	30.4	1.51	13.4	2,287,786	307,165
Total	Total	28.7	1.51	12.8	3,688,583	471,229

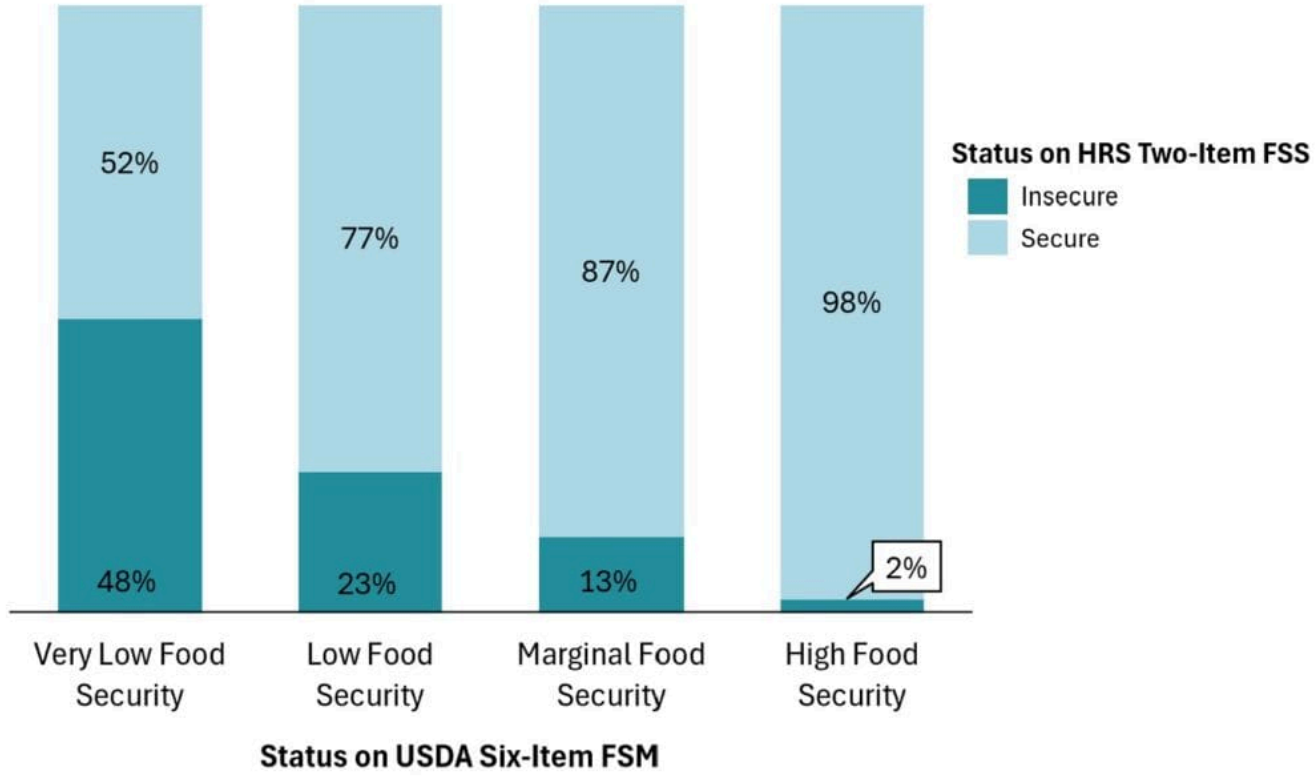
RR: risk ratio. PAF: population attributable fraction. AtD: attributable number of dementia cases.

Aging

Do We Need Better National Data on Food Insecurity in Older Adults? A Validation Study of the Health and Retirement Study's 2-Item Food Security Screener Kelley Akiya* Kelley Akiya Suzanna Martinez Anusha Vable

Background: One in 11 older adults experience food insecurity, a modifiable social condition associated with greater mortality and multiple barriers to healthy aging. An important source of national health data among older adults comes from the Health and Retirement Study (HRS), a nationally representative longitudinal study that surveys community-dwelling adults ages 50 and older. The purpose of this study was to examine whether the ongoing biennial 2-item food security screener (FSS), implemented since 1996 prior to the development of the U.S. Department of Agriculture's (USDA) food security modules, is a valid assessment of food insecurity. **Methods:** The current study used a subsample of HRS participants (n=7,067) who responded to the FSS (about the past 2 years) in the 2014 biennial survey and the USDA's validated 6-item food security module (FSM, about the past 12 months) in an ancillary study (the Health Care and Nutrition Study) conducted from November 2013-May 2014. We defined food insecurity as low or very low security and, using the FSM as the gold standard, calculated the FSS's sensitivity, specificity, and Area Under the Receiver Operating Characteristic Curve (AUC). Next, we calculated the same measures separately for respondents reporting very low, low, marginal, and high security on the FSM. **Results:** The FSS had low sensitivity (0.34), high specificity (0.97), and inadequate discriminant validity (AUC = 0.66 vs. a null value of 0.50). Importantly, the FSS only identified food insecurity in 48% of those reporting very low security on the FSM and 23% of those reporting low security. The FSS more accurately identified those reporting food security (marginal, 87%; high, 98%) on the FSM. **Discussion**: In comparison to the FSM, the FSS inadequately detects food insecurity in older adults. The HRS could benefit from adding the FSM to its biennial surveys for a more valid assessment of food insecurity and examination of related health outcomes.

Figure 1. Status on the USDA Six-Item Food Security Module (FSM) vs. the HRS Two-Item Food Security Screener (FSS)



Notes: HRS = Health and Retirement Study, USDA = United States Department of Agriculture

Aging

Socioeconomic and Gender-Based Disparities in Admissions to Long-Term Care Facilities in Quebec, Canada Clara Bolster-Foucault* Clara Bolster-Foucault Isabelle Vedel Nadia Sourial Claire Godard-Sebillotte Amélie Quesnel-Vallée

An overwhelming majority of older adults wish to remain in their homes and communities as they age. Despite the near-universal preference for aging in place, health inequities across the lifespan and gaps in publicly-funded home- and community-based services to support aging in place may create disparities in the ability to do so. Our objective was to examine socioeconomic and gender-based inequities in the age at long-term care (LTC) admissions in Quebec.

Using the TorSaDE Cohort, which contains linked Canadian Community Health Survey data from 2007-2016 and longitudinal provincial health administrative data from 1996-2016, we created a representative sample of community-dwelling Quebec residents aged 65 and older (n=24,269). We used Cox proportional hazards models to measure disparities in the hazard of admission to LTC by educational attainment (having a high school diploma or not) and gender, modelling intersectional effects using statistical interaction. We used the Fine-Gray subdistribution hazard approach to account for competing risk of death and accounted for time-fixed (self-rated health, racialization, rurality, marital status, household size) and time-varying (age, comorbidity score) covariates.

The average length of follow-up was 4.25 years. Among men, lower educational attainment was associated with a higher rate of admission to LTC (sHR=1.34, 95%CI: 1.12-1.60). However, among women, lower educational attainment was associated with a lower rate of admission to LTC (sHR=0.82, 95%CI: 0.65-1.04). Among older adults with higher educational attainment, women were at a higher rate of admission to LTC than men (sHR=1.22, 95%CI: 1.02-1.46).

Our results reveal meaningful socioeconomic and gender-based disparities in admissions to LTC among older adults in Quebec. The effect of education differs qualitatively among men and women, indicating an important intersectional effect. These results can inform efforts to equitably support aging in place.

Aging

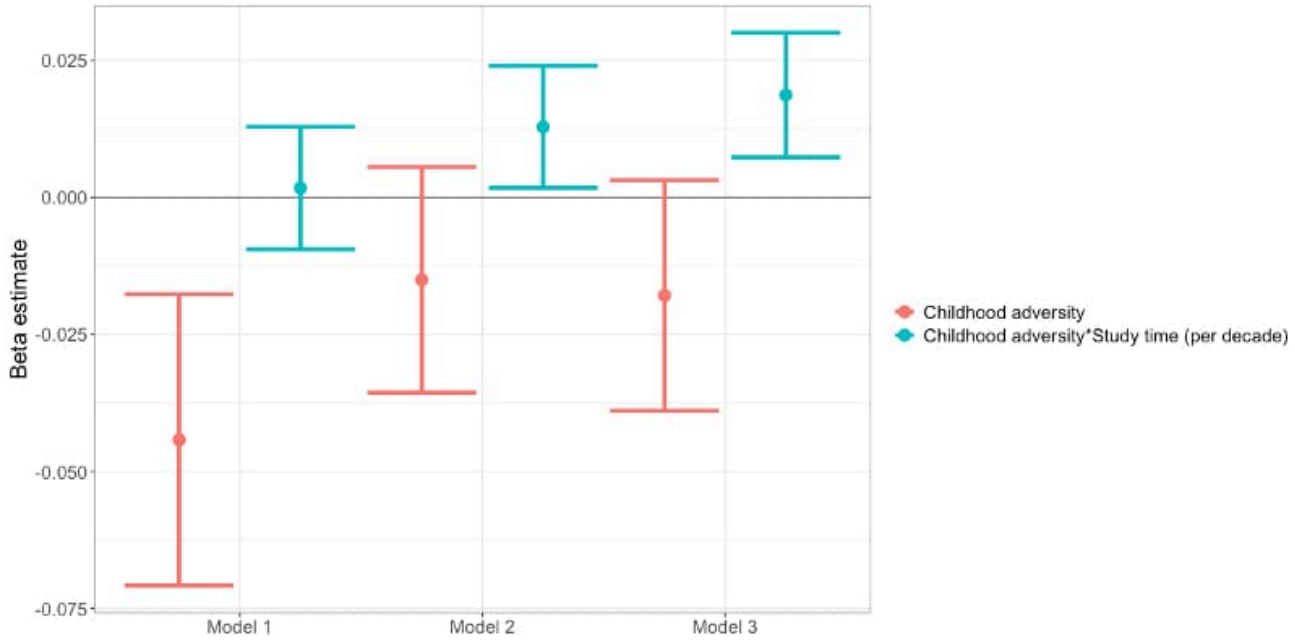
Estimating the effect of childhood adversity on mid- and late-life memory decline in a nationally representative sample Eleanor Hayes-Larson* Eleanor Hayes-Larson Taylor M Mobley Karestan C Koenen

Introduction: Evidence on the relationship between childhood adversity and cognitive decline is inconsistent. We aimed to estimate the effect of childhood adversity on mid- and late-life memory decline in a national population-based sample.

Methods: We used data from Health and Retirement Study participants aged 50+ with complete exposure and covariate data (n=6,208). Childhood adversity factor z-scores were constructed with confirmatory factor analysis of 6 self-reported items: trouble with the police, parental drug or alcohol problems, parental abuse, lived in an orphanage, lived in a foster home, and parental separation/divorce. Imputed memory scores (Wu et al., z-scored to baseline sample) were defined biennially 1995-2020 using direct and proxy assessments. We estimated associations between childhood adversity and baseline memory function and memory decline using nested multivariate linear mixed effect models with random intercepts adjusted for study time (in decades) as the timescale, practice effects, confounders (Model 1: practice effect, baseline age; Model 2: Model 1 + sex/gender, race/ethnicity, parental education, Southern US birth; Model 3: Model 2 + childhood financial capital), and interactions between study time and childhood adversity factor scores and study time and confounders.

Results: The analytic sample was 57% female and 85% non-Hispanic White. Childhood adversity item prevalence ranged from 1.5% (lived in a foster home) to 16% (parental drug or alcohol problems). In the fully-adjusted model (Model 3), childhood adversity was associated with lower baseline memory function (beta=-0.02, 95% CI: -0.04, 0.00) but slower memory decline (beta=0.02, 95% CI: 0.01, 0.03).

Conclusions: Consistent with some existing literature, childhood adversity was associated with lower baseline memory function but slower memory decline; resilience mechanisms and selective survival may contribute to these findings and inconsistencies in the larger literature.



Model 1: adjusted for practice effects, baseline age and baseline age*study time
Model 2: adjusted for M1 covariates + sex/gender + race and ethnicity + parental education + Southern birth + interactions between covariates and study time
Model 3: adjusted for M2 covariates + childhood financial capital + childhood financial capital*study time

Behavior

Exploring the mediating effect of life satisfaction on psychological distress and eating behavior association in students from economically disadvantaged regions. Kliver Antonio Marin* Kliver Marin Barbara Saldanha Lima Lorrane Cristine Conceição da Silva Jose Guilherme dos Santos Neto Luiz Fernando Oliveira Barbosa Izabela de Melo Valadares Silva Liz Mendes de Almeida Kaike da Costa Rodrigues Rhavenna Thais Silva Oliveira Shirley Cunha Feuerstein Augusto Cesar Ferreira De Moraes Marcus Vinicius Nascimento-Ferreira

Abstract
Aim: To investigate the mediating effect of life satisfaction on the association between psychological distress and eating behavior in students from economically disadvantaged regions. Methods: We analyzed self-reported data from 485 students (65.6% aged ≤20 years; 70.4% female; 71.6% non-White; 43.6% with monthly household income below a minimum wage) from two Brazilian cities (Gini indices ≤0.56). We consider psychological distress (somatization, depression, and anxiety symptoms) as the exposure and eating behaviors (emotional, external, and restrained eating) as the outcome. Life satisfaction was assessed both as an exposure and a mediator. Data analysis included multilevel linear regression models with random effects, canonical correlation analysis to create synthetic variables for key exposures and outcomes, and structural equation modeling to evaluate the indirect effects of life satisfaction.
Results: Life satisfaction was negatively associated with emotional eating (β = -0.021; 95% CI: -0.035, -0.007). Conversely, psychological distress was positively associated with eating behaviors, including emotional (β = 0.018; 95% CI: 0.011, 0.023), external (β = 0.010; 95% CI: 0.006, 0.013), and restrained eating (β = 0.010; 95% CI: 0.004, 0.016). A pair of canonical variables—psychological distress ('u1') and eating behaviors ('v1')—was statistically significant (r1 = 0.41; Wilks's λ, p < 0.0001) associated, explaining 16.5% of the variance. The total effect of u1 on v1 was significant (β = 0.372; 95% CI: 0.285, 0.458), with both indirect (β = 0.048; 95% CI: 0.010, 0.086) and direct (β = 0.323; 95% CI: 0.230, 0.417) effects contributing to this relationship. Mediation by life satisfaction accounted for 13.9% of the total effect.
Conclusion: Life satisfaction mediates the association between psychological distress and eating behaviors in students from economically disadvantaged areas.
Keywords: Life Satisfaction, psychological distress, eating behavior, students.

Behavior

Association between cadence (steps/min) and intensity during treadmill activity among 18–20 year olds: the SKyRoCKeT study Tahmina Begum* Tahmina Begum Laura H. Gunn Catrine Tudor-Locke Cayla R. McAvoy Agnes Bucko Mariya Boikova Trudy Moore-Harrison Michael Dulin Daheia J. Barr-Anderson Leah Patterson Spencer Ingoglia Maha Raya Sicong Ren

Background: Physical activity studies often use treadmill protocols to assess cadence (steps/minute) as an indicator of ambulatory intensity. Accurately quantifying intensity is essential for surveillance, research, and clinical/public health applications. This study aimed to determine cadence-intensity thresholds that reliably translate to predictable metabolic equivalents (METs) during treadmill activity.

Methods: Participants ages 18-20 years (n=72) completed up to 12 5-minute bouts on a treadmill incrementally from 0.5–6.0 miles/hour. Steps were visually counted (video validated) and intensity was objectively measured using a portable metabolic system. MET thresholds were defined for moderate (≥3 to <6 METs) and vigorous (≥6 METs) intensities. Optimal cadence thresholds for moderate and vigorous intensity were identified using a segmented log-level regression model and receiver operating characteristic (ROC) curve. Age, sex, race/ethnicity, body mass index (BMI), body fat %, and leg length were also explored.

Results: A total of 670 bouts were collected. Participants' (51.4% female; 41.7% non-Hispanic white) mean values were: age 19.0 (SD 0.8) years; BMI 23.9 (SD 4.7) kg/m2; body fat 20.6% (SD 9.8%); and leg length 81.0 (SD 7.7) cm. In the segmented regression model, with a breakpoint of 81 steps/minute, moderate and vigorous intensity thresholds were 73.0 (99% CI 67.5, 79.8) [and via ROC analysis 83.1; 99% CI 77.9, 92.5] and 118.2 (99% CI 115.5, 121.0) [112.5; 99% CI 107.1, 118.9] steps/minute, respectively. The segmented regression R2 value was 0.87, thus supporting a good fit. The ROC area under the curve (AUC) values were ≥0.95, indicating excellent classification accuracy. Other variables were non-significant (p≥0.094).

Conclusions: Cadence-intensity thresholds can be used to accurately assess cadence-intensity/METs during treadmill walking and running. Accounting for cadence, other variables were not associated with intensity.

Funding: NICHD-R01HD105768

Behavior

Replacing Sedentary Behavior with Physical Activity: A 15-Minute Strategy to Alleviate Psychological Distress in College Students from Economically Disadvantaged Regions

Marcus Vinícius Nascimento-Ferreira* Marcus Vinicius Nascimento Ferreira Antonio Gibran de Almeida Cardoso Benjamin Baird Evillyn Ravena da Silva Gomes Marina Lira da Silva Helen Ferreira de Brito Souza Jacqueline Fernandes de Sá Xavier Ladislau Ribeiro do Nascimento Tiago Almeida de Oliveira Shirley Cunha Feuerstein Kliver Antonio Marin Augusto César F. De Moraes

Aim: To examine psychological distress predictions using compositional data analysis of time reallocations among daily movement behaviors in undergraduate students from economically disadvantaged regions.

Methods: 405 students from two Brazilian cities (Gini indices up to 0.56) participated: 67.9% were female, 65.1% under 20 years old, 71.8% identified as non-white, and 86.7% reported a monthly household income below USD 260.15. The exposures were self-reported 24-hour movement behaviors: sedentary behavior (SED), light physical activity (LPA), moderate-to-vigorous physical activity (MVPA), and sleep. Psychological distress, the outcome, was measured using a scale for somatization, depression and anxiety symptoms. Covariates included biological sex, age, race/ethnicity, household income, academic course, semester and shift. Movement behaviors were expressed as isometric log-ratio (ILR) coordinates: ILR1 (sleep relative to SED, LPA, and MVPA), ILR2 (SED relative to LPA and MVPA), and ILR3 (LPA relative to MVPA). Log-ratio multiple linear regression predicted psychological distress for the mean movement behavior composition and for new compositions reflecting 15-, 30-, 45-, and 60-minute time reallocations between behaviors.

Results: In the original model, only IRL1 was significantly associated with psychological distress (β= -5.41, 95% CI: -9.07 to -1.75). Neither IRL2 (β= 2.07, 95% CI: -0.12 to 4.26) nor IRL3 (β = 0.51, 95% CI: -1.38 to 2.40) showed significant associations. Replacing SED with MVPA resulted in the following IRL2 estimates: 15 minutes (β= 2.20, 95% CI: 0.23 to 4.19), 30 minutes (β= 2.06, 95% CI: 0.03 to 4.08), 45 minutes (β= 1.88, 95% CI: -0.18 to 3.94), and 60 minutes (β= 1.66, 95% CI: -0.40 to 3.73). Reallocating 15 and 30 minutes from SED to MVPA predicted reductions in psychological distress scores of 0.38 and 0.59 units, respectively.

Conclusions: Replacing as little as 15 minutes of sedentary behavior with moderate-to-vigorous physical activity is a promising approach to reducing psychological distress in college students from disadvantaged regions.

Behavior

Emotional, Cognitive, and Behavioral Self-Regulation in Early Childhood and Premature All-Cause Mortality Decades Later Jing Yu* Jing Yu Denise L. Haynie Rajeshwari Sundaram Stephen E. Gilman

Self-regulation characterizes a child's ability to manage emotions, direct cognition, and control behavior across various contexts. Greater ability to self-regulate may confer long-term benefits for social and health outcomes. While the importance of early self-regulation in psychosocial adjustment and educational success is well established, its potential influence on health outcomes including life expectancy is less understood.

We investigated this question using data from 49,853 offspring of women enrolled in the Collaborative Perinatal Project. At ages 4 and 7, children's emotional, cognitive, and behavioral self-regulation was assessed through psychologist ratings of behavioral profiles during standardized testing. Offspring's vital status through mid-adulthood was tracked through the National Death Index up to 2016.

Cox regression results of age-adjusted associations between early self-regulation and premature mortality are presented in Figure 1. After adjusting for potential confounders (e.g., childhood adversity), high emotion reactivity, hostility, and separation anxiety, and low frustration tolerance at age 7 remained associated with 24% to 39% increased hazard of premature mortality by mid-adulthood. Too little emotion reactivity, separation anxiety, or fear at 7 were also associated with elevated, though smaller, mortality risk (Hazard Ratios=1.11 to 1.14). Those with a short attention span, little effort to achieve a goal, overactivity, and rigid or impulsive behavior at 7 had 17% to 24% higher mortality risk. Shyness and compliance to directions were not associated with risk of premature death.

Poorer childhood self-regulatory skills, particularly emotion regulation, were associated with a higher risk of premature mortality by mid-adulthood. Self-regulation capacities may influence mortality risk by shaping key risk factors later in life, including adult socioeconomic status, mental illnesses, health-related behaviors, and chronic health conditions.

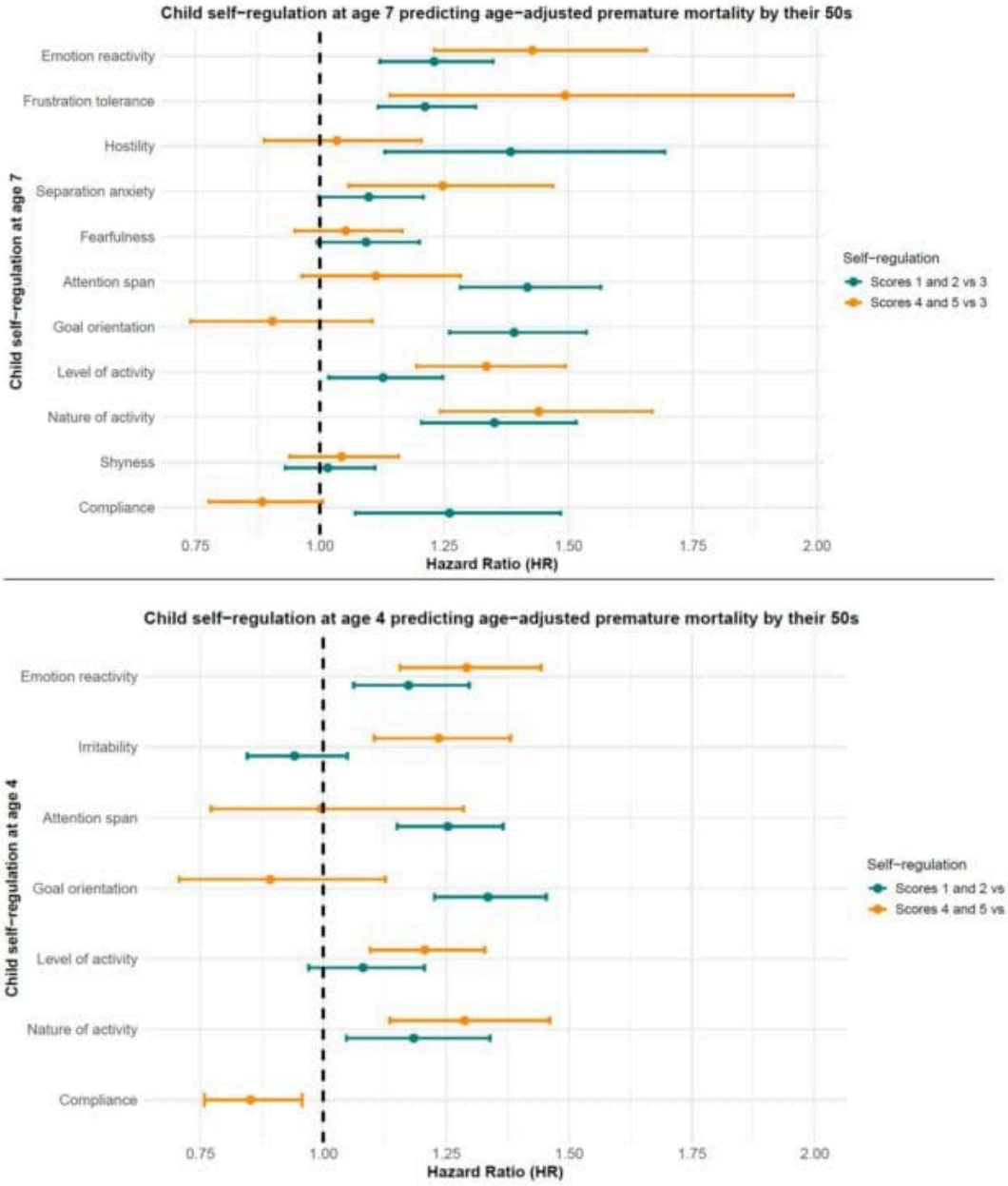


Figure 1. Hazard ratios for child self-regulation at ages 7 and 4 predicting mortality from Cox regression models adjusting for age. For some (e.g., emotional reactivity), scores 1 and 2 reflect overcontrol (e.g., little change in emotional tone), and scores 4 and 5 reflect lack of control (e.g., marked emotional lability). For others (e.g., attention span), scores 1 and 2 reflect lack of control (short time with task) and scores of 4 and 5 reflect overcontrol (e.g., high perseverative).

LATEBREAKER

Behavior

Changes in parental feeding practices and association with children's dietary habits in the implementation study of the Healthy School Start program in 5-7-year-old Swedish children Sara Raposo* Sara Raposo Emelie Nacksten Zoë Morris Emma Patterson Mahnoush Etminan Malek Liselotte Schäfer Elinder Kristi Sidney Annerstedt

Background:

The increasing prevalence of childhood overweight and obesity in Sweden poses a major public health challenge. Parental feeding practices (PFPs) are behaviors and interactions that influence children's dietary habits and can thereby also have effects on children's weight. The IMPROVE study is a parallel cluster randomized hybrid type 3 implementation effectiveness trial of the Healthy School Start intervention program in 5-7-year-old Swedish children with primary aim to compare two bundles of implementation strategies. The purpose of this study is to perform a pre-post evaluation of the intervention program on the entire cohort.

Objective:

To study changes in parental feeding practices and their association with children's dietary habits after one year in the Healthy School Start intervention program.

Methods:

In total, 45 schools residing in three municipalities with high rates of child obesity in Stockholm participated in the 1-year intervention, enrolling in 2021 and ending in 2024. Parental socio-demographic data was collected at recruitment. Self-reported parental data on PFPs and children's dietary habits was collected through validated questionnaires at baseline and end of intervention. The PFPs studied were monitoring, pressure to eat, restriction of food, use of food for emotional regulation, and healthy eating guidance measured on a 5-point Likert scale. Children's dietary habits was assessed using eight questions on portions consumed the previous day, categorized into low and high consumption of unhealthy drinks, unhealthy foods and healthy foods. Changes in PFPs and children's dietary habits were evaluated using one-sample t-tests and logistic regression was used to study the association between PFPs and children's dietary habits, adjusting for parental education, BMI and type-2 diabetes risk score.

Results:

In total, 915 parents and 668 children participated in the intervention. A majority of the parents had a university degree (55%) and were of Nordic origin (64%). Self-reported parental overweight/obesity was 44 % and 7% reported a moderate to high type-2 diabetes risk. At 1 year, there was a decrease in pressure to eat ($p<0.001$) and emotional regulation ($p<0.05$), however no changes were seen for monitoring, restriction or healthy eating guidance. Differences in PFPs between mothers and fathers was found for pressure to eat ($p<0.05$) and for restriction ($p<0.05$), where fathers were more likely to use these PFPs than mothers. No changes between mothers and fathers was found for monitoring, emotional regulation or healthy eating guidance. For children's dietary habits there was an increase in consumption of unhealthy drinks ($p<0.05$) and unhealthy foods ($p<0.001$), but no changes in intake of healthy foods ($p=0.29$). Monitoring and healthy eating

guidance were associated with a lower consumption of unhealthy drinks ($p<0.05$), while pressure to eat, restriction and emotional regulation were associated with a higher consumption of unhealthy drinks ($p<0.05$). Monitoring, pressure to eat, restriction and emotional regulation were associated with unhealthy foods and healthy eating guidance was associated with healthy eating in crude models, however not when adjusting for parental socio-demographic variables.

Conclusions:

This study shows effects in changes in PFPs after one year of the Healthy School Start intervention program. There were also differences in PFPs between mothers and fathers. Some PFPs were associated with children's dietary habits after intervention. Further investigation into how PFPs can mediate children's dietary habits are needed.

Behavior

The relationship of perceived stress between 24-hour movement behaviors and psychological distress among undergraduate students from low-income regions Shirley Cunha Feuerstein* Shirley Cunha Feuerstein Maria Isabela Alves de Almeida Silva Benjamin Baird Ana Clara Arrais Rosa Barbara Saldanha Lima Andrea Ramirez Varela Leticia Ribeiro Borges Armando Rodrigues de Alencar Santos Marcia Ferreira Sales Kliver Antonio Marin Augusto Cesar Ferreira De Moraes Marcus Vinícius Nascimento-Ferreira

Aim: To investigate the mediating effect of perceived stress on the association between 24-hour movement behavior and psychological distress among undergraduate students from low-income regions.

Methods: We assessed a total of 507 students from two Brazilian cities (Gini indices up to 0.56): 68.7% female, age up to 20 years (68.7%), 71.9% non-white, and 43.6% with a monthly household income below US$260.15. We assessed perceived stress using the Perceived Stress Scale (PSS) and psychological distress using the Brief Symptom Inventory 18 (BSI-18). The exposure was perceived stress and adherence to 24-hour movement guidelines, while the outcome was psychological distress (somatization, depression, anxiety), assessed using multilevel linear regression. The associations were expressed as beta (β) coefficients with 95% CIs. Perceived stress served as exposure and mediator, assessed through self-efficacy and helplessness. Confounding variables retained in the adjusted multilevel model were included as covariates. We assessed model fit using root mean square error of approximation (RMSEA) and standardized root mean square residual (SRMR). A good fit was defined as RMSEA ≤ 0.06 and SRMR ≤ 0.0838.

Results: Our multilevel linear regression analysis revealed that 24-hour movement behaviors (β = -1.3, 95% CI: -2.4 to -0.3) and self-efficacy (β = -0.3, 95% CI: -0.5 to -0.1) were negatively associated with psychological distress, while helplessness showed a positive association (β = 1.8, 95% CI: 1.6 to 1.8). Structural equation modeling indicated significant indirect effects for self-efficacy (β = -0.8, 95% CI: -1.3 to -0.2) and helplessness (β = -1.5, 95% CI: -2.5 to -0.5), mediating 25.1% and 51.4% of the total effect, respectively.

Conclusions: Healthy daily movement behaviors are inversely associated with psychological distress among undergraduate students from economically disadvantaged regions, with perceived stress serving as a mediating mechanism through self-efficacy and helplessness pathways.

Big Data/Machine Learning/AI

Geospatial clustering of physician age in the US physician workforce Jag Lally* Jag Lally Ryan Crowley David M Kline Amanda Bunting

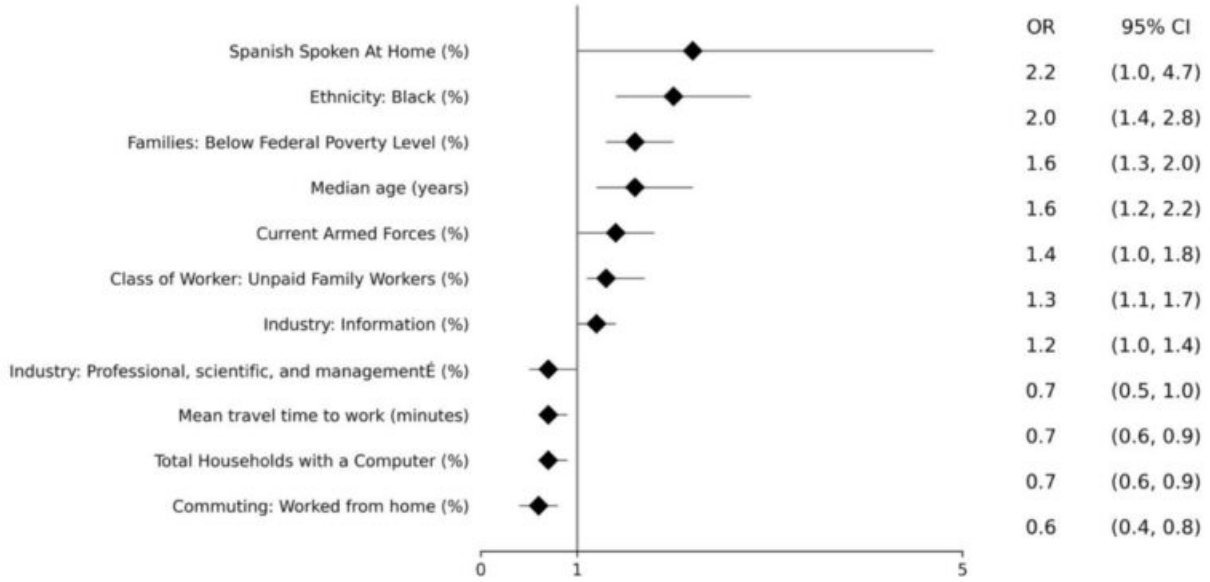
Background: We investigated geospatial clustering of physician age among physicians in 2024, focusing on how regional characteristics influence areas of high or low physician age.

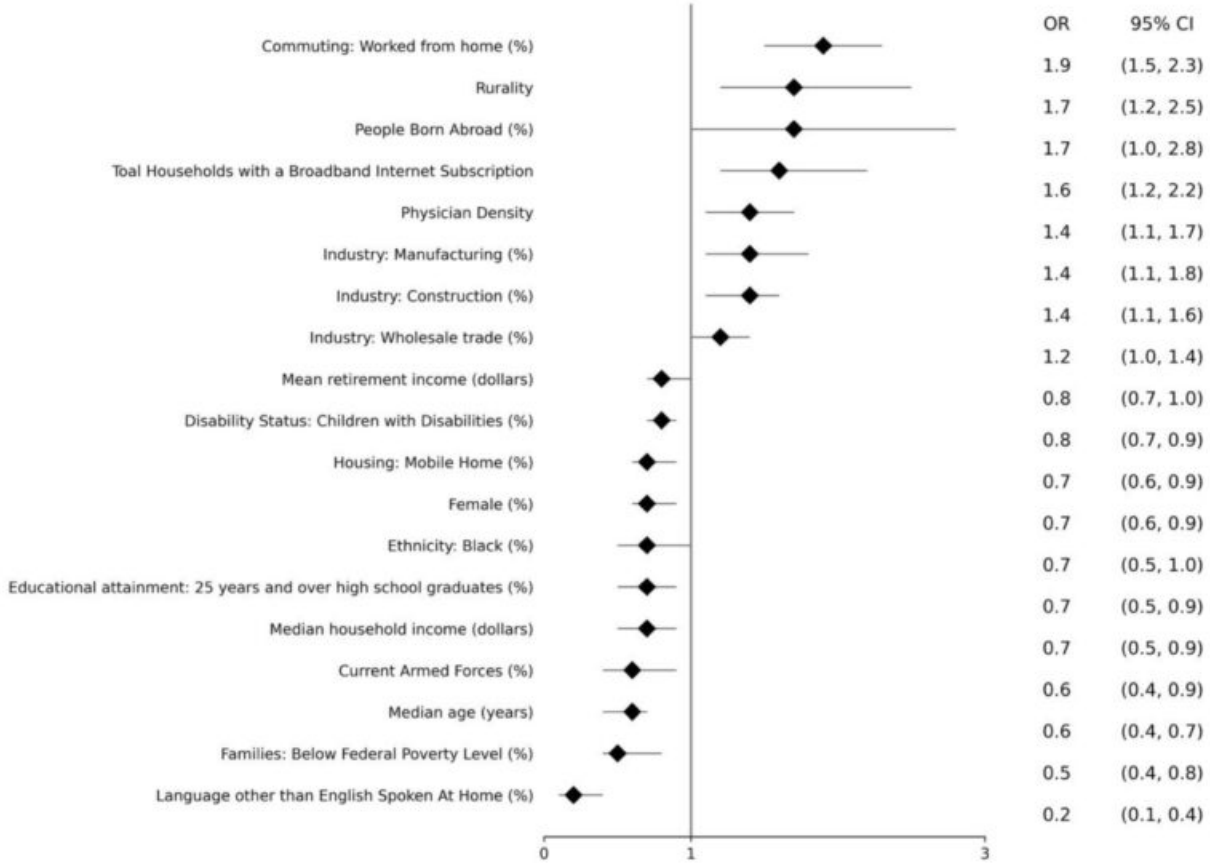
Methods: We linked the 2008-2021 Medicare Data on Provider Practice and Specialty (MD-PPAS) dataset with the 2024 Centers for Medicare and Medicaid Services (CMS) Doctors and Clinicians national downloadable file. All US physician providers with valid National Provider Identifiers (NPIs), zip code, and age data were included. We used Rural-Urban Continuum Codes (RUCCs) to measure rurality. We performed Local Indicators of Spatial Association mapping of counties which identified clusters of counties with physician ages above and below the median. Multivariate regression analyses using county-level demographic, socioeconomic, and healthcare variables from the American Community Survey (ACS) data were performed to identify factors associated with regions of older and younger physicians.

Results: The mean physician age was 52.6 years. There were clusters of high physician age in Wyoming, North Dakota, Texas, Alabama, Mississippi, and Georgia and clusters of low physician age in Washington, Utah, Colorado, Kansas, and Illinois. Most of the high age clusters were in rural counties. Counties with higher levels of Spanish spoken at home (OR: 2.2, 95% Cl: 10-4.7) and with a greater prevalence of Black residents (OR 2.0, 95% CI: 1.4-2.8) were most strongly associated with high physician ages. Counties with more individuals working from home (OR 1.9, 95% CI: 1.5–2.3) and more rural counties (OR 1.7 95% CI: 1.2–2.5) were strongly associated with low physician ages.

Conclusions: Distinct geographic clusters of older physician ages in certain counties could exacerbate healthcare access disparities as these providers age and retire. Socioeconomic and infrastructural factors may shape physician demographic patterns, and targeted interventions could aid efforts to achieve greater healthcare equity.

Figure: Multivariate Regression Analysis: Statistically Significant Covariates for Older Physician Clusters (Top) and Younger Physician Clusters (Bottom)





Big Data/Machine Learning/AI

Error Patterns in Machine Learning Algorithms for Healthcare: a Multicohort Study Across Brazil's Five Regions Júlia Neuenschwander* Júlia Neuenschwander Alexandre Chiavegatto Filho

Machine learning (ML) algorithms are increasingly used in healthcare, yet studies examining their error patterns remain limited. Understanding whether misclassified patients share common traits, and how algorithmic architecture influences error profiles, is essential to improving diagnostic accuracy and fairness. Thus, this study aimed to assess the error patterns in ML models predicting COVID-19 mortality, exploring the relationship between algorithmic architecture, error profiles, and dataset characteristics. Data were sourced from the IACOV-BR initiative, which includes 15,598 adult patients with RT-PCR-confirmed COVID-19 across 21 hospitals in Brazil. The multicohort design, spanning Brazil's vast geographical area and diverse population, enhances the generalizability of the findings. Five models—Random Forest, XGBoost, Catboost, LightGBM, and TabPFN—were evaluated using demographic and laboratory data. The performance was assessed using the area under the receiver operating characteristic curve (AUROC), and Shapley values were used to determine variable importance. The results revealed that TabPFN exhibited the best overall predictive performance, particularly in smaller datasets, which further supports its utility in resource-limited settings. Approximately 10% of patients were misclassified by all models, and 54% were correctly classified by all of them. Key predictors of misclassification included age, platelet count, and C-reactive protein. Strong error correlation was observed between gradient boosting models (XGBoost and LightGBM: $R2 = 0.85$), while Random Forest showed moderate correlation with both boosting models and TabPFN. Performance validation across hospitals demonstrated improved outcomes with larger datasets, with hospital-specific factors influencing variability. In conclusion, this study highlights shared error patterns across ML models and the influence of specific predictors on misclassification. Additionally, it suggests that no single algorithm consistently outperforms others, emphasizing the need for hospitals to select ML models tailored to their specific contexts. These insights can guide the development of diagnostic tools and strategies to mitigate errors, enhancing the robustness and equity of ML applications in healthcare.

LATEBREAKER

Big Data/Machine Learning/AI

Assessing Community Alerts for Increased HIV Risk on HIV Risk Behavior in a Network of People who Inject Drugs: An Application of Network Targeted Maximum Likelihood Estimation Natallia Katenka* Ashley Buchanan Ke Zhang

We employed the network targeted maximum likelihood estimation (TMLE) evaluate the direct and spillover effects of community alerts on self-reported HIV risk behavior at 6-month among people who inject drugs (PWID) and their contacts in the Transmission Reduction Intervention Project (TRIP) from 2013 to 2015 in Athens, Greece. PWID often participate in HIV risk behaviors that comprise HIV risk networks. Previous work found evidence of a possibly meaningful spillover effect of community alerts on HIV risk behavior in TRIP; however, the prior study made parametric modeling assumptions for the exposure model, and used inverse probability weighted estimators that are known to not be the most efficient. By using network TMLE in combination with the SuperLearner with highly adaptive lasso (HAL) as one of the algorithms, we can allow the data to determine the best fitting model or algorithm for the data while also using a doubly-robust estimator.

Big Data/Machine Learning/AI

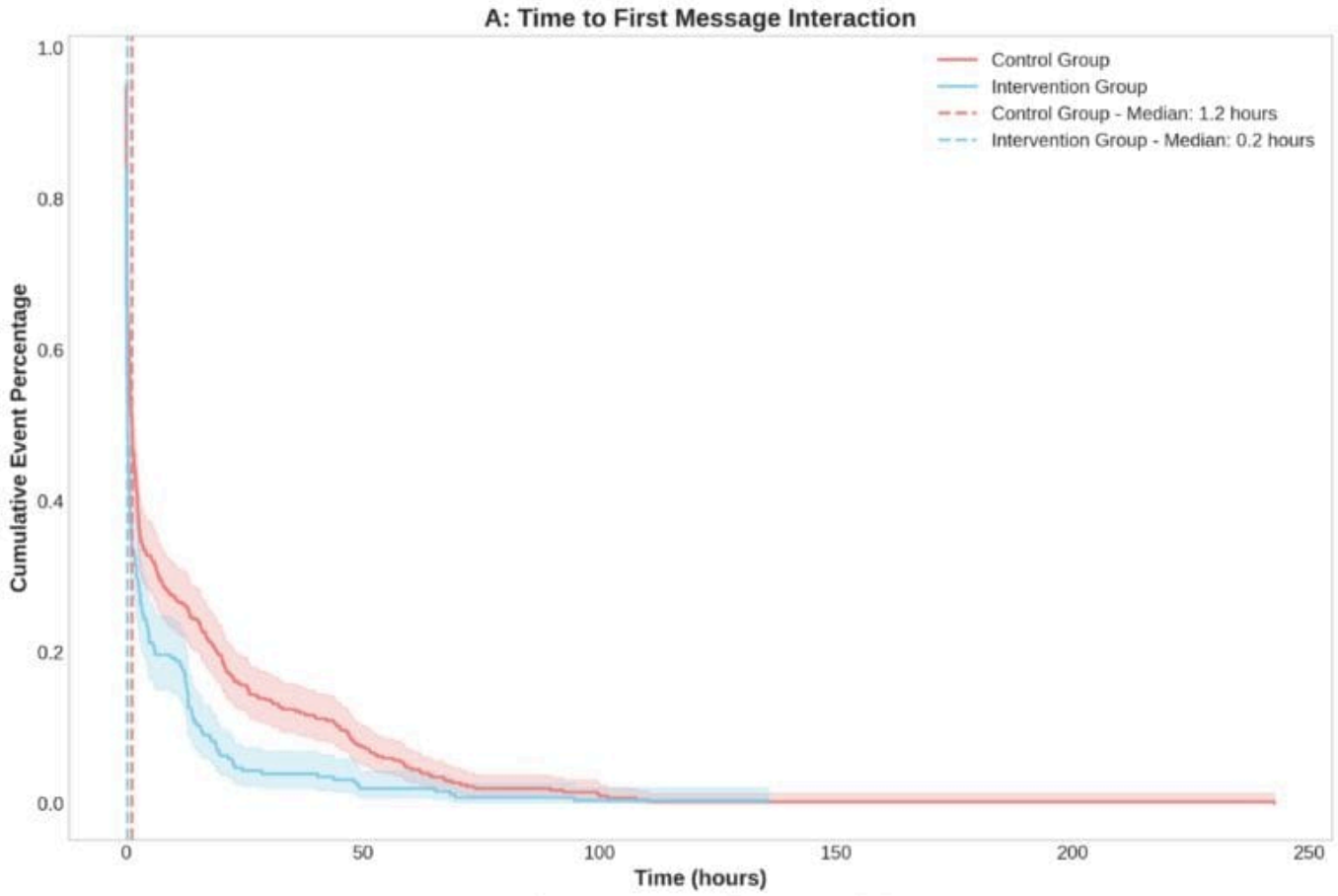
Development and Real-World Evaluation of a ClinicianTrained Model for Managing Patient Portal Messages Muhammad Zia ul Haq* Muhammad Zia ul Haq Blake J. Anderson Yuanda Zhu Andrew Hornback Alison D. Cowan Bradley Gallaher Arash Harzand

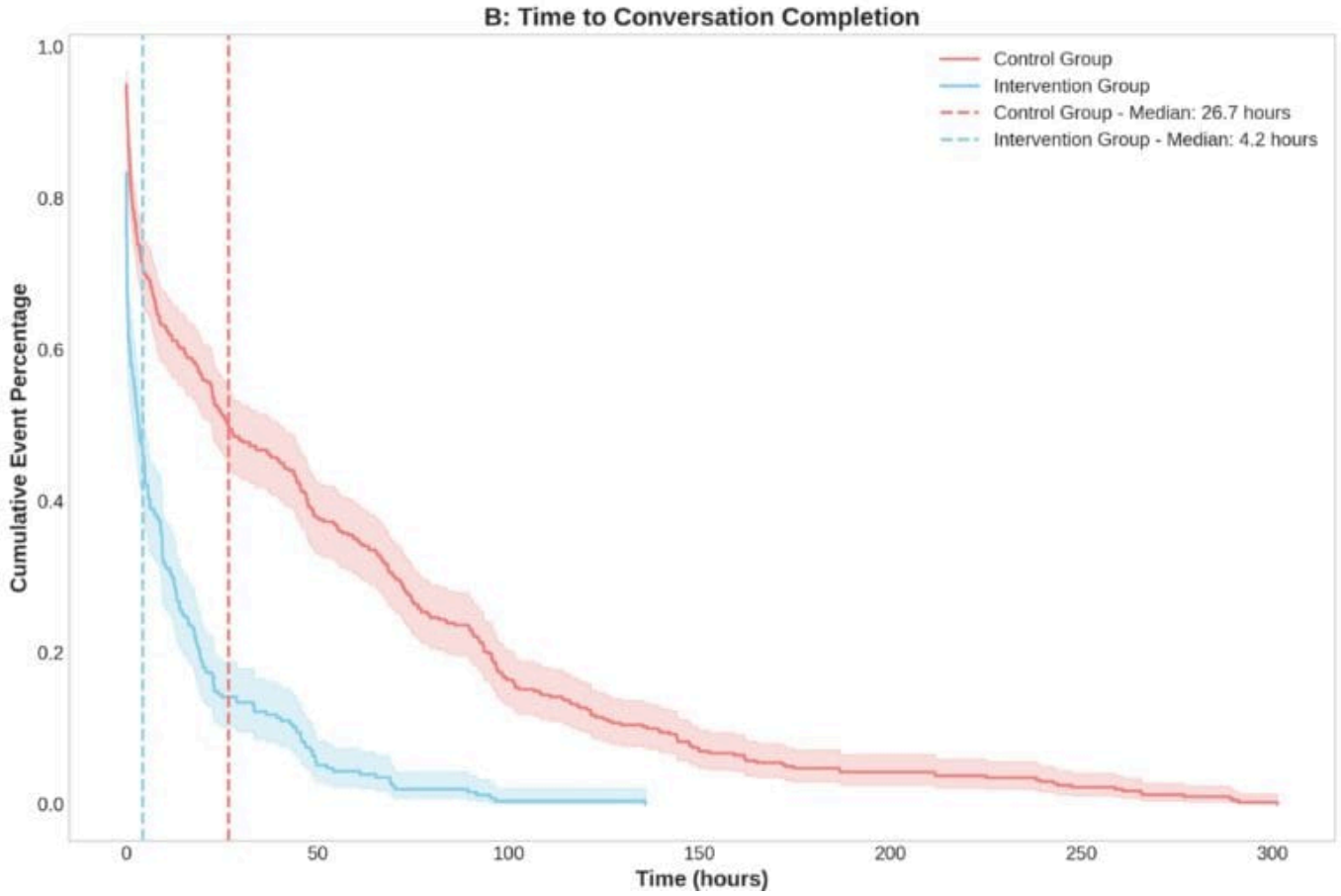
BACKGROUND: While patient-portal messages in the electronic health record (EHR) provide convenience and enhance patient and provider communications, their rapidly increasing volume reveals challenges in clinical practice, including delays in timely response, staff shortages, and even provider burnout. We evaluated the impact of a natural language processing (NLP) algorithm for intelligent message routing in clinical practice.

METHODS: We developed an NLP model to accurately label and route inbound patient messages using a pretrained classifier that was fine-tuned using clinician feedback. The model was prospectively deployed in an outpatient clinic environment for real-world validation. A parallel group of unrouted messages was generated for comparative analysis. The primary endpoints used to assess model performance included time to first message interaction, time to conversation resolution, and the total number of message interactions by healthcare staff, compared with the control group. Secondary endpoints were the precision, recall, F1 score (a measure of positive predictive value and sensitivity), and accuracy for correct message classification.

RESULTS: The model prospectively labeled and routed 469 unique conversations over 14 days. Compared to a control group of 402 unrouted conversations from the same period, staff in the routed message group used less time to initially address a new patient message (difference in medians, -1 hour; 95% CI 1.42 to -0.5; P<0.001) and to complete a conversation (difference in medians, -22.5 hours; 95% CI 36.3 to -17.7; P<0.001); routed group staff also had a significantly fewer number of total message interactions (difference of medians, -2.0 interactions; 95% CI –2.9 to –1.4; P<0.001). The model demonstrated high precision (>97.6%), recall (>95%), and F1 scores (>96.5%) for accurate prediction of all five message classes, with a total accuracy of 97.8%.

CONCLUSIONS: Real-time message routing using advanced NLP was associated with significantly reduced message response and resolution times and fewer overall message interactions among clinic staff.


A: Time to First Message Interaction
Control Group
Intervention Group
Control Group - Median: 1.2 hours
Intervention Group - Median: 0.2 hours
Cumulative Event Percentage
Time (hours)


B: Time to Conversation Completion
Control Group
Intervention Group
Control Group - Median: 26.7 hours
Intervention Group - Median: 4.2 hours
Cumulative Event Percentage
Time (hours)

Big Data/Machine Learning/AI

Application of data imputation using a generative adversarial network Hayden L. Smith*
Hayden Smith

Background: Data missingness is a common occurrence in medical research. Imputation is the process of filling in missing values using substitution. These values can be estimated with statistical models. Advances in generative machine learning provide additional methods, such as generative adversarial networks (GANs). These networks use two competing models (e.g., neural networks) to uncover underlying data structures and generate synthetic data. Objective: to present a basic process for imputing missing data using GAN architecture.

Methods: A version of the Framingham Heart Study dataset was used in this example and included age, sex, weight, diastolic BP, systolic BP, cholesterol, cigarettes per day, and mortality. A GAN was fit to create synthetic values for randomly removed data, using functions from Generative Adversarial Imputation Nets and PyTorch. Next, missing rates, sample sizes, and hyperparameters (i.e., alpha and learning rates) were varied to explore limits of the approach. Lastly, a mortality classification model was fit with varied amounts of imputed covariate data.

Results: The sample included 5000 complete case observations. After randomly removing data from the sample, GAN-based imputation was performed with results and model specifics presented in the Figure. When varying sample size from 0.1 to 0.7, RMSE changed from 0.26 to 0.23. When altering missing rate from 0.2 to 0.8, RMSE changed from 0.25 to 0.30. Adjusting alpha from 0 to 15, RMSE reduced from 0.45 to 0.25 and changing learning rate from 0.1 to 0.01 resulted in a RMSE change from 0.28 to 0.24. Lastly, when altering missingness from 0.0 to 0.9, the mortality classification AUROC went from 0.66 to 0.58.

Conclusions: The presented process can be used to impute synthetic data and repeated to conduct multiple imputation. The process can be computationally intensive. Further analyses should examine GAN utility in different scenarios and include comparative analytics with other approaches.

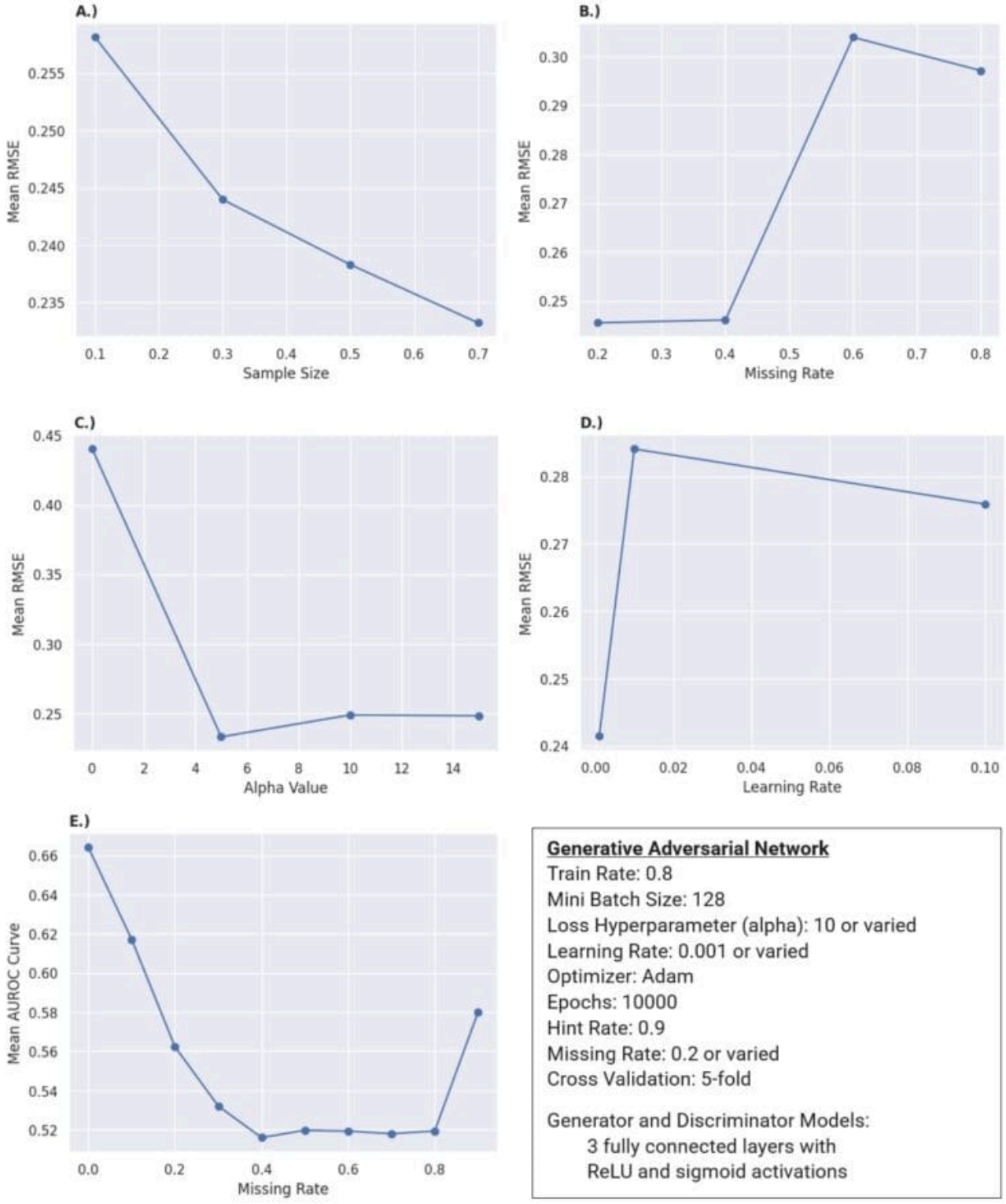


Figure. Plots present average root mean squared errors (RMSE) from 5-fold splits for imputed values versus true values or mean area under the receiver operating characteristic (AUROC) curve for the classification model. A.) RMSE values against sample size; B.) RMSE values against amount of random missing data; C.) RMSE against increasing alpha; D.) RMSE against learning rate; and E.) AUROC curve for a logistic regression model classifying mortality status versus amount of randomly missing data. Last pane provides model details.

Big Data/Machine Learning/AI

A Comparison of Deep Neural Network Compression for Citizen-Driven Tick Surveillance

Yichao Liu* Yichao Liu Emmanuel Dufourq Joacim Rockloev

Vector-borne diseases, like Crimean-Congo hemorrhagic fever (CCHF) from ticks, pose global health risks. Citizen science initiatives use web and mobile apps to enable public reporting of vector sightings, enhancing data collection for monitoring populations and disease spread. Machine learning can automate species identification, improving surveillance and reducing manual effort. However, deploying these models on mobile devices is challenging due to their over-parameterized nature, requiring significant storage, computation, and energy—constraints for battery-limited devices. Effective model compression is essential for practical deployment in citizen science applications.

In this study, mainstream model compression techniques like pruning and quantization were evaluated to reduce the size of object detection models, as object detection acts as the first step in identification and has a strong impact on overall performance. Pruning removes non-essential parameters to lower computational demands and improve speed. Two types of pruning were tested: structured, which removes entire model sections, and unstructured, which selectively removes individual elements.

Quantization reduces model size by using lower-bit formats (e.g., 8-bit, 4-bit) instead of 32-bit floating-point numbers. Dynamic quantization adjusts precision during processing, while static quantization converts parameters to lower precision before deployment, ensuring consistent size and speed improvements.

The impact of compression techniques was evaluated on mobile devices by comparing the runtime performance of compressed and original models under identical conditions. Combining structured and unstructured pruning reduced model size by up to 60% with minimal performance loss, addressing limitations of each method alone. Quantization also proved effective, significantly reducing size and runtime with negligible performance impact.

Effective model compression techniques enable real-time, automated identification of disease vectors on mobile devices. This study’s findings could enhance public participation in vector surveillance, aiding in the control of vector-borne diseases.

Table 1: model compression comparison for tick dataset

method	mAP50	parameters/M	MACs/G	time/ms	RAM/MB
original model	77.15	3.0	4.07	148	214
unstructure pruning (20% prune)	76.3	3.0	4.07	133	193
unstructure pruning (40% prune)	74.9	3.0	4.07	139	190
structure pruning (20% prune)	72.8	2.12	1.55	106	152
structure pruning (40% prune)	73.3	1.39	1.07	82	167
dynamic quantization	77.8	3.0	4.07	104	150
static quantization	74.2	3.00	4.07	56	141

Big Data/Machine Learning/AI

Predictive Modeling of Gestational Weight Gain: A Machine Learning Multiclass Classification Study Audêncio Victor* Audêncio Victor Fabiano Barcellos Filho Liania A. Luzia Alexandre Dias Porto Chiavegatto Filho Patricia Helen Rondó Gabriel Ferreira dos Santos Silva Alexandre de Fátima Cobre

Background: Gestational weight gain (GWG) is a critical factor influencing maternal and fetal health. Excessive or insufficient GWG can lead to various complications, including gestational diabetes, hypertension, cesarean delivery, low birth weight, and preterm birth. This study aims to develop and evaluate machine learning models to predict GWG categories (below, within, or above recommended guidelines)

Methods: We analyzed data from the Araraquara Cohort, Brazil comprising 1557 pregnant women with a gestational age of 19 weeks or less. Predictors included socioeconomic, demographic, lifestyle, morbidity, and anthropometric factors. Five machine learning algorithms (Random Forest, LightGBM, AdaBoost, CatBoost, and XGBoost) were employed for model development. The models were trained and evaluated using a multiclass classification approach. Model performance was assessed using metrics such as area under the ROC curve (AUC-ROC), F1 score and Matthews correlation coefficient (MCC).

Results: The outcome were categorized as follows: GWG within recommendations (28.7%), GWG below (32.5%), and GWG above recommendations (38.7%). The LightGBM model presented the best overall performance with an AUC-ROC of 0.79 for predicting GWG within recommendations, 0.756 for GWG below recommendations, and 0.624 for GWG above recommendations. The Random Forest model also performed well, achieving an AUC-ROC of 0.774 for GWG within recommendations, 0.732 for GWG below recommendations, and 0.593 for GWG above recommendations. The most importante were predictors of GWG were pre-gestational BMI, maternal age, glycemic profile, hemoglobin levels, and arm circumference.

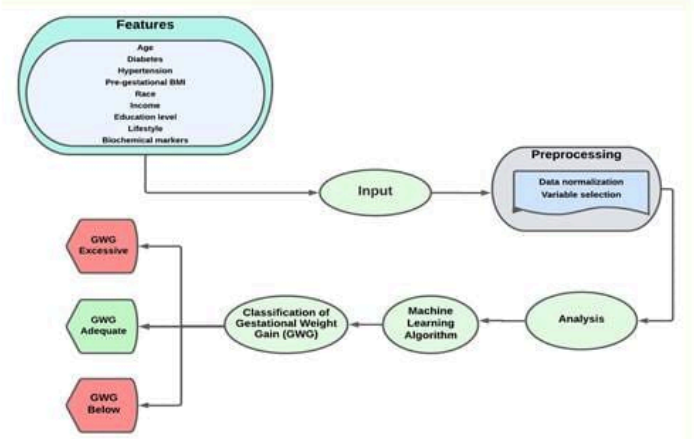
Conclusion: Machine learning models can effectively predict GWG categories, providing a valuable tool for early identification of at-risk pregnancies. This approach can enhance personalized prenatal care and interventions to promote optimal pregnancy outcomes.

Keywords: Gestational weight gain, machine learning, prediction models, maternal health, fetal health, Araraquara Cohort.

Predictive performance on test data of the best algorithm for each outcome with hyperparameter tuning

odel + Class	Hyperparameter Tuning	AUC-ROC	Acuracy	Recall	Specificity	Precision	F1	MCC
I (GWG Within)	{'num_leaves': 31, 'learning_rate': 0.1}	0.79	0.75	0.58	0.83	0.62	0.60	0.42
GWG Within)	{'n_estimators': 200, 'max_depth': 3, 'learning_rate': 0.1}	0.79	0.74	0.59	0.82	0.60	0.60	0.41
orest (GWG Within)	{'n_estimators': 100, 'max_depth': 10}	0.77	0.76	0.58	0.82	0.60	0.59	0.41
GWG Within)	{'learning_rate': 0.1, 'iterations': 100, 'depth': 6}	0.77	0.75	0.60	0.82	0.61	0.61	0.42
I (GWG Below)	{'num_leaves': 31, 'learning_rate': 0.1}	0.76	0.68	0.74	0.64	0.57	0.64	0.37
GWG Below)	{'n_estimators': 200, 'max_depth': 3, 'learning_rate': 0.1}	0.76	0.68	0.69	0.68	0.58	0.63	0.36
GWG Below)	{'learning_rate': 0.1, 'iterations': 100, 'depth': 6}	0.75	0.68	0.69	0.67	0.58	0.63	0.36
orest (GWG Below)	{'n_estimators': 100, 'max_depth': 10}	0.73	0.68	0.77	0.59	0.55	0.64	0.35
(GWG Below)	{'n_estimators': 200, 'learning_rate': 0.1}	0.71	0.66	0.77	0.60	0.55	0.64	0.36
(GWG Within)	{'n_estimators': 200, 'learning_rate': 0.1}	0.71	0.72	0.55	0.80	0.57	0.56	0.35
GWG Above)	{'learning_rate': 0.1, 'iterations': 100, 'depth': 6}	0.61	0.69	0.36	0.85	0.49	0.42	0.23
GWG Above)	{'n_estimators': 200, 'max_depth': 3, 'learning_rate': 0.1}	0.65	0.65	0.36	0.84	0.47	0.40	0.21
I (GWG Above)	{'num_leaves': 31, 'learning_rate': 0.1}	0.62	0.62	0.30	0.85	0.44	0.36	0.17
(GWG Above)	{'n_estimators': 200, 'learning_rate': 0.1}	0.57	0.57	0.22	0.89	0.43	0.29	0.13
orest (GWG Above)	{'n_estimators': 100, 'max_depth': 10}	0.60	0.59	0.24	0.89	0.47	0.32	0.17

Workflow diagram for classifying GWG adequacy



Big Data/Machine Learning/AI

Improving Fairness in Predictive Models: A Multicalibration Analysis Across Brazilian Hospitals Fabiano Barcellos Filho* Fabiano Barcellos Filho Carine Savalli Alexandre Chiavegatto

Accurate mortality prediction is essential for improving patient care and optimizing resource allocation. This study evaluated the performance of machine learning models, such as XGBoost, CatBoost, and LightGBM, for mortality prediction in COVID-19 across Brazilian regions. A key focus was the impact of isotonic calibration on model fairness. Models were tuned with randomized search using AUC-ROC as the performance metric. The dataset was stratified by mortality outcome and systematically partitioned into training, validation, and test subsets.

Pre-calibration analysis revealed significant subgroup disparities. Males and younger patients (<65) consistently outperformed females and older adults (≥65). In the Northeast region, younger adults outperformed older adults (AUC of 0.9663 vs. 0.7735), while in the North, males outperformed females (0.9735 vs. 0.8250). These disparities highlighted the importance for calibration techniques to enhance model fairness and ensure equitable performance across diverse demographic groups.

After isotonic calibration, fairness improved across all regions. In the North, female AUC increased from 0.8250 to 0.9042, and older adults maintained exceptional performance, improving from 0.9886 to 0.9943. The Northeast showed improvements for older adults (AUC = 0.7735 to 0.7989) and males (AUC = 0.8848 to 0.9067), reducing gaps with younger adults. In the Southeast, disparities lessened, with male AUC rising from 0.8256 to 0.8421 and elderly AUC from 0.7734 to 0.7959. The South exhibited the most significant improvements, with older adults increasing its AUC from 0.7723 to 0.8348 while maintaining high male performance (0.9183 to 0.9422).

We conclude that isotonic calibration, while slightly reducing AUC in some regions, consistently enhanced fairness across age and gender groups. This demonstrates its utility in promoting equity in predictive healthcare, striking a balance between performance and fairness to better serve diverse populations.

Big Data/Machine Learning/AI

Leveraging artificial intelligence to gather epidemiologic data on infectious diseases: the Global Repository of Epidemiological Parameters (GREP) project Melanie Sterian* Melanie Sterian Kusala Pussegoda Tricia Corrin Bing Hu Emmalie Tomini Nauman Shakeel Lizaveta Vasileuskaya Stephanie Brazeau Lisa Waddell

Background:

The emergence of new infectious diseases and the increasing threat of epidemics and pandemics highlight the importance of improving efficiencies in acquiring and analyzing epidemiological parameter data to inform public health response.

Objective:

The Global Repository of Epidemiological Parameters (GREP) project, developed within the World Health Organization Collaboratory, aims to create an accessible, living database of epidemiological parameters on priority infectious diseases to serve as a global public health resource.

Methods:

Several projects are underway to progress on GREP's five workstreams: prioritization of pathogens and key parameters; standardized data extraction methods; tools for storage and use of data; data validation and continuous maintenance of the database; and scientific recognition of contributors to the database. The data pipeline under development leverages artificial intelligence (AI) technologies to automate the maintenance of GREP in real-time.

Results:

Extraction of over 25 parameters for diseases such as measles is underway using systematic review methodology. In tandem, large language models are being used to automate literature searches and deduplication of search results, relevance screening, obtaining full texts, data extraction of parameters and data validation. Data storage and analyses are also being developed by other collaborators. The presentation will focus on specific approaches and performance related to automation of the data pipeline.

Discussion:

Using AI to modernize the way parameter data is gathered and synthesized will reduce the burden of repetitive tasks in the identification and extraction of data from the literature and allow human resources to be focused on assessment and analysis. GREP will be a centralized resource that helps to reduce global duplication of effort in curating evidence and facilitate faster evidence-based decision-making for better public health outcomes and epidemic preparedness.

Big Data/Machine Learning/AI

The contribution of global climatic patterns to forecasting dengue cases in Colombia Adrien Saucier* Adrien Saucier Katia Charland Lais Picinini Freitas Jan Saynisch-Wagner Ying Liu Bertha Restrepo Cesar Garcia Gloria Jaramillo Mabel Carabali Kate Zinszer

Dengue incidence is widely associated with global weather patterns. Certain global climate dynamics, such as El Niño Southern oscillation, influences the living conditions of the disease vectors (Aedes aegypti and Aedes albopictus mosquitoes), which in turn, influences dengue incidence. These climatic patterns could provide valuable lead time in dengue forecasting and enhance early warning systems. The objective of our study was to quantify the contributions of El Niño Southern oscillation and Indian Ocean sea surface temperature in dengue forecasting models for Colombia. For this work, we compared different machine algorithms including support vector machine and extreme gradient boosting machine, and selected the best performing algorithms based on different metrics. Using Shapley Additive explanations method, we measured predictor importance at various lead time horizons. Our preliminary results demonstrate the importance of El Niño Southern oscillation (ENSO) and Indian Ocean sea surface temperatures (IOBW) in predicting dengue incidence, with IOBW outperforming ENSO for longer terms forecasts. Longer term forecasting (-12 and -16 weeks ahead) for all locations varied between a mean scaled absolute error of 0.7 and 1.1, indicating good forecasting potential. Early warning systems could benefit from the consideration of IOSS and ENSO in dengue forecasting to improve lead time for outbreak response efforts.

Cancer

Association Between Travel Distance to Treatment Facilities and Survival Among Children with Cancer in Louisiana Emma Hymel* Emma Hymel Kendra Ratnapradipa Edward Peters Cheng Zheng Jenna Allison Mei-Chin Hsieh Shinobu Watanabe-Galloway

Background: Treatment for pediatric cancer generally occurs in specialized tertiary care centers found in large urban areas, resulting in a significant travel burden for pediatric cancer patients. The effects of travel burden on pediatric cancer patients has primarily been examined with qualitative studies, and the few existing quantitative studies have observed mixed results.

Methods: We conducted a population-based longitudinal study using data from the Louisiana Tumor Registry. This study included all children with cancer diagnosed at age 0-19 from 2000 to 2020. Multiple imputation with chained equations was used to handle missing data. Travel distance was reported as the distance between patients' homes and treatment facilities in miles using the great circle distance method. Cox proportional hazards regression models were used to compute the association between distance to treatment (in quartiles) and cancer-specific survival. A directed acyclic graph was used to identify the variables needed to control for confounding.

Results: Our study included 2,720 children with cancer in Louisiana. Overall, 458 (16.84%) of the children died during follow-up and over 15% of the children lived over 100 miles from their treatment facility, with a median distance of 21.58 miles. Travel distance was significantly associated with survival; compared to those living closest to their treatment center, those living furthest from their treatment center were 61% more likely to die from their cancer (95% CI: 1.22-2.11). The effect of travel distance was strongest for children with extracranial solid tumors (Q3 vs. Q1: aHR=2.00, 95% CI: 1.29-3.11; Q4 vs. Q1: aHR=2.40, 95% CI: 1.56-3.68).

Conclusion: In our study, we observed that travel distance was associated with pediatric cancer survival. The effect of distance on survival varied by cancer type. In future studies, we will explore differences in the effect of estimated travel time and accessibility rather than travel distance.

Cancer

UGT2B10 haplotypes within the substrate binding and enzyme activity functional pockets are associated with lung cancer Maher Alsaadi* Maher Alsaadi Mohammed S Orloff Heather Robeson

Background.

Smoking accounts for 80-90% of lung cancer cases, yet only 10-15% of smokers develop the disease, indicating the complexity of genetic factors involved. Smoking-related carcinogens can damage the lungs, but genetic mutations greatly increase lung cancer risk. The UDP glucuronosyltransferase 2B10 (UGT2B10) gene helps remove tobacco-specific carcinogens, and reduced activity of this gene raises serum nicotine levels in smokers. While associations between UGT2B10 SNPs and lung cancer have been reported, the full extent of genetic/allelic heterogeneity remains unexplained. Our goal was to investigate the relationship between UGT2B10 haplotype and lung cancer.

Methods.

A total of 154 tissue samples, including lung cancer and normal tissue, were genotyped for the exon 1 of UGT2B10. In this cohort 69 matched pairs of non-small cell lung cancer (NSCLC) tissues and their corresponding normal tissues, and 16 unmatched samples were analyzed. Allelic and genotypic association analyses were performed using PLINK 1.9 and Haploview 4.2. Linkage disequilibrium (LD) analysis and moving window haplotype analysis were used to assess haplotype structures and LD patterns. UGT2B10 protein stability and enzyme activity were studied for significant haplotypes containing relevant missense mutations by AlphaFold and Alpha Missense.

Results.

Twenty-one of the 26 SNPs that passed quality control spanned the UGT2B10 domain containing multiple structural pockets (P1–P20), which are critical for substrate binding and enzyme activity. The haplotype analysis revealed three significant haplotypes P= 0.01 to 0.04. These haplotypes contained alleles that mapped to multiple pockets including P1 (which affects substrate interactions), suggesting their role in substrate interactions and enzyme efficiency.

Conclusion.

These genetic variations may influence UGT2B10 function, affecting toxic/nicotine metabolism and NSCLC pathogenesis.

Cancer

Evaluating clinical factors implicated in racial differences in survival among patients with multiple myeloma Jade Mason* Malaika Jade Mason Bei Wang Andrew Yang Brian C. Chiu

Unlike the well-recognized two-fold higher incidence rate of multiple myeloma (MM) among African Americans (AA) than European Americans (EA), findings on racial differences in MM survival have been inconclusive. We investigated potential roles of well-recognized prognostic factors in racial disparities in MM overall survival (OS). 561 newly diagnosed MM patients at the University of Chicago Medical Center were prospectively enrolled between 2010-2019 and followed until February 2022. Vital status was ascertained using the National Death Index. OS was defined as time from diagnosis until death from any cause. Baseline sociodemographic and clinical information were collected from electronic medical records and a self-administered questionnaire. We evaluated the associations of race with demographic and prognostic factors using chi-square test for categorical variables and T-test for continuous variables. Of the 561 patients, 151 (27%) were AA and 410 (73%) were EA. Compared with EAs, AAs were significantly older (EAs=61.8 years, AAs=64.0 years, p=0.03), more likely to be obese (EAs vs AA=30.7% vs 43%), and had lower education levels (below college EAs vs AAs=17% vs 22%). AAs had worse age-adjusted OS (HR=1.4; 95% CI=1.0-2.4), compared with EAs. Among the prognostic factors, we found significant racial differences in lactic dehydrogenase (LDH) levels (elevated LDH: 28.5% AAs vs 19.3% EAs, p=0.03) and insurance types (50.2% of EAs had private insurance, 48.3% of AAs had Medicare, p<0.001). There were no racial differences in stage at diagnosis, induction therapy type (i.e., triplets or doublets), and glomerular filtration rate. Multivariate Cox models controlling for confounders and prognostic factors are ongoing and will be presented at the meeting. In the cohort of 561 MM patients, we found significant racial differences in LDH levels and insurance type at time of diagnosis that could potentially explain the racial differences in overall survival amongst MM patients.

Table 1. Characteristics of participants with multiple myeloma by race, N=561

	White (N=410)	Black/African-American (N=151)	P-value
Age at enrollment (years)			
Mean (SD)	61.8 (9.80)	64.0 (11.0)	0.0292
Median [Min, Max]	62.0 [31.0, 88.0]	64.0 [38.0, 99.0]	
Sex			
F	162 (39.5%)	93 (61.6%)	<0.001
M	248 (60.5%)	58 (38.4%)	
BMI			
normal	111 (27.1%)	32 (21.2%)	0.0641
underweight	7 (1.7%)	2 (1.3%)	
overweight	151 (36.8%)	48 (31.8%)	
obese	126 (30.7%)	65 (43.0%)	
Missing	15 (3.7%)	4 (2.6%)	
Education level			
below college	70 (17.1%)	33 (21.9%)	0.00748
some college or completed college	142 (34.6%)	38 (25.2%)	
graduate or professional degree	86 (21.0%)	14 (9.3%)	
Missing	112 (27.3%)	66 (43.7%)	
International Staging System (ISS)			
1	192 (46.8%)	65 (43.0%)	0.53
2/3	107 (26.1%)	43 (28.5%)	
Missing	111 (27.1%)	43 (28.5%)	
Induction therapy type			
doub	47 (11.5%)	20 (13.2%)	0.901
trip	125 (30.5%)	58 (38.4%)	
Missing	238 (58.0%)	73 (48.3%)	
Lactic Dehydrogenase U/L			
Elevated (>240)	79 (19.3%)	43 (28.5%)	0.0335
Normal (<=240)	248 (60.5%)	81 (53.6%)	
Missing	83 (20.2%)	27 (17.9%)	
Estimated glomerular filtration rate (eGFR)(mL/Min)			
<60	121 (29.5%)	48 (31.8%)	0.81
>=60	268 (65.4%)	99 (65.6%)	
Missing	21 (5.1%)	4 (2.6%)	
Insurance type			
medicaid	6 (1.5%)	17 (11.3%)	<0.001
medicare	155 (37.8%)	73 (48.3%)	
private	206 (50.2%)	53 (35.1%)	
Missing	43 (10.5%)	8 (5.3%)	

Cancer

Impact of Regional Factors on Breast Cancer Stage at diagnosis: Exploring Age-Specific Differences Around Korea's National Cancer Screening Policy Eunhye Park* Eunhye Park

Background: Breast cancer incidence is rising in South Korea, with widening regional disparities in outcomes. The national breast cancer screening program targets women aged 40 and over. However, the influence of regional factors, such as the Area Deprivation Index (ADI), on breast cancer stage at diagnosis remain underexplored, particularly with limited studies considering screening age.

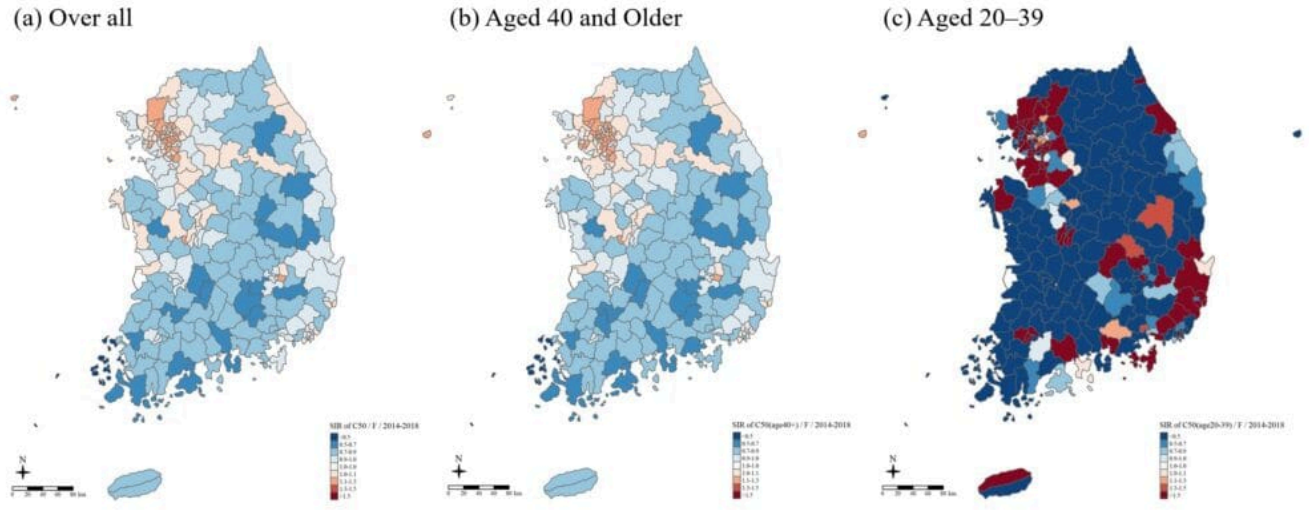
Objective: To examine the impact of regional factors, including ADI and other risk factors, on breast cancer stage at diagnosis in women under and over 40 years of age.

Methods: The Korea National Cancer Incidence Database (2014–2018) were analyzed at 250 administrative municipal levels. Breast cancer stages were classified using SEER summary stages. Bayesian hierarchical models evaluated associations between breast cancer incidence and regional factors.

Results: Among 105,755 breast cancer cases, 10,748 were aged 20–39 years, and 95,007 were aged 40 and older. Overall, lower ADI (β = -0.033, 95% Credible Interval [CrI] = -0.052, -0.014), lower obesity rates, higher alcohol consumption, and greater mammography availability were associated with higher breast cancer incidence. Localized breast cancer negatively associated with ADI overall, while distant-stage cancer showed a positive association. In women aged 40 and older, localized breast cancer was negatively associated with ADI (β = -0.046, 95% CrI = -0.073, -0.019), reflecting early detection benefits. Conversely, women aged 20–39, localized breast cancer was positively associated with ADI (β = 0.059, 95% CrI = 0.008, 0.111), suggesting that breast cancer risk factors are more prevalent in deprived areas within this age group.

Conclusions: ADI has opposing effects on breast cancer incidence by summary stage. Efforts to reduce regional disparities in breast cancer incidence should focus on age-specific regional risk factors and improving early detection.

Figure 1. Geographic Distribution of Breast Cancer Incidence in South Korea (2014–2018): Overall, Aged 20–39, and Aged 40 and Older



Cancer

Measuring completeness of reporting of US cancer registries Lindsay J Collin* Lindsay Collin Richard F. MacLehose Thomas P. Ahern Rebecca Nash James Baurley Kevin C. Ward Timothy L. Lash

Background: Cancer surveillance is crucial for cancer control and research. Cancer registry completeness is a measure of the proportion of true cases captured by a registry. Gold star certification of a registry requires a completeness estimate of ≥95%. When completeness is less than 100%, the incident cancer rates are underestimated. If completeness is differential by demographic groups, then information on cancer health disparities will be biased. Current methods for measuring completeness do not include data from the most common cancers, all racial and ethnic groups, or account for regional variability. We propose a new, comprehensive method to assess completeness.

Methods: We obtained county-level cancer incidence and mortality data by sex, age, and race from the California Cancer Registry. We fit Bayesian joint hierarchical Poisson models for county-level incidence and mortality rates with a shared conditional autoregressive error structure, which allowed information borrowing across counties. Predicted incidence and mortality rates were estimated for each county to generate county-specific Incidence-to-Mortality Rate Ratios (IMRRs). We decomposed the overall registry completeness estimate into geographic and demographic completeness estimates.

Results and Future Directions: Completeness estimates were assessed by region (Northern, Central, and Southern California), county, race (Black, White) and natal sex. Region-specific completeness IMRRs were 99%, 103%, and 94% for Southern, Central, and Northern regions, respectively. Figure 1 highlights county-specific estimates below 95% completeness. In both the Southern and Central regions, Black women had substantially lower levels of completeness than any other group, falling below the gold certification threshold. Our method highlights differential completeness, which allows registries to target efforts for improvement. Future work will assess completeness for the entire US and across demographic groups.


Figure 3: Model-estimated completeness rates for 58 counties in California
Completeness
<95%
>95%

Cancer

Implications of neighborhood socioeconomic status on work ability among cancer survivors in the UNC Cancer Survivorship Cohort Yung-Fang Deng* Yung-Fang Deng Mu Jin Brent J. Small Laura Farnan Tzy-Mey Kuo Hazel B. Nichols

Background: Work ability is critical for cancer survivors due to its connections to cancer-related financial hardship and quality of life. We examined the association between neighborhood socioeconomic status (SES) and work ability among cancer survivors.

Methods: Among cancer survivors in the UNC Cancer Survivorship Cohort (2010-2016), neighborhood SES was assessed using the census-tract level Yost index (state-based quintiles, Q1-Q5) linked to residential addresses at enrollment, where lower quintiles represent lower SES areas. Participants completed the modified Work Ability Index, including a general score (0-10), composite physical/mental score (2-10), and number of annual missed days of work. We estimated mean differences (β) and 95% confidence intervals (CI) in work ability across Yost quintiles using multivariable linear regression, overall and in subgroup analyses stratified by cancer type, chemotherapy status, time since diagnosis, and rurality.

Results: Among 1,326 currently working participants in the cohort, mean age was 54.4 at survey and 53.1 at diagnosis; 11.1% of the cohort lived in the lowest SES quintile. We observed higher general work ability (β= 0.68, 95% CI: 0.13, 1.22) and composite physical/mental ability (β= 0.38, 95% CI: 0.05, 0.71) scores in Q5 vs. Q1 of the Yost index. In subgroup analyses, we observed fewer annual missed days in Q5 vs. Q1 of the Yost index among survivors who did not receive chemotherapy (N=1,006; β= -13.70, 95% CI: -22.26, -5.14); prostate cancer survivors (N=134; β= -26.71, 95% CI: -42.62, -10.81); those diagnosed within a year (N=995; β= -11.50, 95% CI: -21.32, -1.68); and those in urban areas (N=1,017; β= -16.48, 95% CI: -29.14, -3.82).

Conclusion: Our findings suggest that disparities in work ability exist across neighborhood SES, with those in higher SES areas reporting better work ability. These contribute to the evidence supporting interventions to rebuild or protect work ability among cancer survivors.

Cancer

Associations between a posteriori dietary patterns and prostate cancer risk: results from the BIOCaPPE prospective cohort study Farah Ben Souilah* Farah Ben Souilah Caroline Diorio Jean Philippe Drouin-Chartier Benoît Lamarche Fred Saad Michel Carmel Armen Aprikian Réseau BIOCaPPE Vincent Fradet

In Canada, 1 in 8 men will develop prostate cancer (PCa) during their lifetime, with 25% of cases being potentially preventable. Age, ethnicity and family history are established risk factors for PCa. Lifestyle habits such as diet are suspected to impact PCa development and progression. Although studies have suggested an association between diet and PCa, evidence remains insufficient for diet-based prevention strategy, likely due to inadequate study designs and the complexity of diet as an exposure. Our approach is to study the associations between a posteriori dietary patterns and PCa risk in a large prospective cohort study.

BIOCaPPE (BIOmarqueurs, Cancer de la Prostate: Prévention et Environnement) is a multicentric prospective cohort study conducted in Canada between 2013 and 2022. Men at risk of PCa were eligible by either a 1st negative biopsy 6 months prior to enrollment or a prostate-specific antigen ranging between 2.5-10 ng/ml with no prior biopsy. At study baseline, a web-based food frequency questionnaire was completed to assess dietary intake. Dietary patterns were identified using principal component analysis. The association between dietary patterns and PCa incidence was assessed using adjusted Cox proportional hazard regression after a minimum two-year follow up and adjusted on confounders identified by directed acyclic graphs.

Three dietary patterns were identified: Prudent (high in fruits, vegetables, fish, seafood, and olive oil), Western (high in red/processed meats, processed foods, and butter), and Sweet & Dairy (high in cookies, dairy, and some fruits). For the highest versus the lowest quintiles, the hazard ratio for the Prudent pattern was 0.70 [0.47-1.05, adjusted p-trend=0.03]. No association was found for the two other dietary patterns.

These results allow for a thorough description of diets among men at risk of PCa. A better characterization of this population-specific Prudent diet may reveal additional protective effects against PCa

Cancer

Personal Talc Use and Incident Lung Cancer Maya Deshmukh* Katie O'Brien Maya Deshmukh Kaitlyn Lawrence Dale Sandler

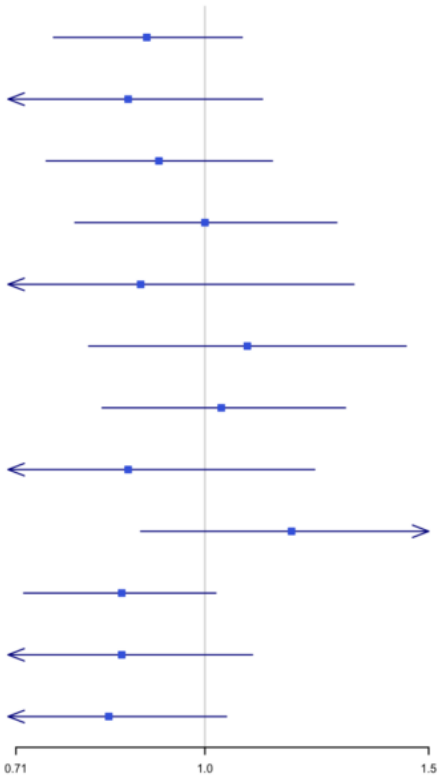
Background: Talc is a known risk factor for lung disease due to its small particle size and commonly aerosolized form. Further, talc may contain asbestos, a known lung carcinogen. Studies on talc exposure and lung cancer have largely been conducted among men in occupational settings. Personal use of talc-based powders is common among U.S. women. The association of talc in personal care products with lung cancer is not well studied.

Methods: We studied the association of self-reported talc use and incident lung or bronchus cancer in the Sister Study. Participants reported talc use in the 12 months prior to enrollment, including frequency of use on the underarms, genitals, or other sites. Measures of lifetime talc use also incorporated data on use at ages 10-13 and ever genital talc use. We used Cox proportional hazards models to estimate covariate-adjusted hazards ratios (HRs) and 95% confidence intervals (CIs) for the associations between talc use and incident lung cancer.

Results: Among 49,499 eligible women, 571 lung cancer cases were identified. The average enrollment age was 56 years, with a median follow-up of 12.5 years. Overall, 41% of women reported using talc on any site in the last 12 months, with an HR for ever versus never use of 0.90 (CI: 0.76-1.07). HRs were similar across application sites, with no evidence of dose-response trends (**Figure**). Frequent use of underarm talc was positively associated with adenocarcinoma (HR=1.52, CI: 0.99-2.31). Ever lifetime use at any site was not strongly associated with lung cancer (HR=1.00, CI: 0.84-1.21 overall, HR=1.13, CI: 0.82-1.56 for adenocarcinoma).

Conclusions: Personal talc use was not consistently associated with incident lung cancer. This novel investigation of the association between talc-based body powders and lung cancer incidence in women contributes to a better understanding of the potential health effects of personal care products, which may contain asbestos or other harmful substances.

Talc Use in Last Year	Cases (%)	HR (95% CI) vs. No Use
Any talc use (all sites)	**229 (41%)**	**0.90 (0.76-1.07)**
<1 time/month	88 (16%)	0.87 (0.69-1.11)
≥1 time/month	141 (25%)	0.92 (0.75-1.13)
Any genital talc use	**82 (15%)**	**1.00 (0.79-1.27)**
<1 time/month	29 (5%)	0.89 (0.61-1.31)
≥1 time/month	53 (9%)	1.08 (0.81-1.44)
Any underarm talc use	**100 (18%)**	**1.03 (0.83-1.29)**
<1 time/month	38 (7%)	0.87 (0.62-1.22)
≥1 time/month	62 (11%)	1.17 (0.89-1.53)
Any talc use other areas	**203 (36%)**	**0.86 (0.72-1.02)**
<1 time/month	84 (15%)	0.86 (0.67-1.09)
≥1 time/month	119 (21%)	0.84 (0.68-1.04)



Cancer

Sodium-glucose cotransporter 2 inhibitors and prostate cancer among type 2 diabetes patients: observational evidence from All of US Yangbo Sun* Yangbo Sun Qian Yang Jay H. Fowke Feng Liu-Smith Jie Zheng

Sodium-glucose cotransporter 2 inhibitors and prostate cancer among type 2 diabetes patients: observational evidence from All of US

Qian Yang, Jay H. Fowke, Feng Liu-Smith, Jie Zheng, Yangbo Sun

Background

A large randomized controlled trial of sodium-glucose cotransporter 2 inhibitor (SGLT2-i) provided suggestive but inconclusive evidence on reducing prostate cancer (PCa) risk. A more recent study triangulated Mendelian randomization analyses in Europeans against electronic health records (EHR) data from Shanghai, China, and also suggested a potential protective association. Our goal is to clarify whether glucose control via SGLT2-I among type 2 diabetes (T2D) patients may reduce PCa risk.

Methods

The All of Us study is a large-scale, longitudinal precision medicine initiative aiming to link EHR data from 453,000 participants across the U.S. We conducted real-world data analyses to estimate the association between SGLT2-i and PCa incidence among T2D patients. Our controls used dipeptidyl peptidase-4 inhibitors (DPP4-i) to control glucose. Analyses included 4,059 men without PCa at baseline and who have initiated either SGLT2-i or DPP4- i. Logistic regression was used to estimate the association between SGLT2-i and PCa risk.

Results

Among 2,225 SGLT2-i users, 1.7 % (n=38) developed PCa. Among 1,834 DPP4-i users, 3.7 % (n=67) developed PCa. After adjusting for age, race/ethnicity, education, income levels, smoking status, alcohol use, self-reported health status, and BMI, SGLT2-i use was significantly associated with a lower risk of PCa (OR 0.50, 95% CI: 0.33 to 0.76) compared to diabetic men taking DPP4-i.

Conclusion

Consistent with prior suggestive analyses, our study found that T2D patients taking SGLT2-i had a lower risk of PCa compared to DPP4-1 users. The differences in T2D treatments on PCa pathophysiology remain uninvestigated. Further studies are warranted to validate our findings.

Cancer

Young Women are at Increasing Risk for Cancers, Including Colorectal Cancer (CRC) Ella Sukup* Ella Sukup David

Since the inception of the US “war on cancer” in 1971, the incidence rate of cancer in the US (using NCI SEER Data, 1975-2021 for all cancer sites combined) has continued to gradually increase. Among females, annual incidence rates of cancer (NCI SEER data, all sites combined) have risen from 366.9 (95% CI 362.5 – 371.3) per 100,000 in 1975 to 431.5 (95% CI 428.2 – 434.7) per 100,000 in 2021. For males, annual incidence rates of cancer have risen more gradually from 466.4 (95% CI 460.5 – 472.4) per 100,000 in 1975 to 479.2 (95% CI 475.7 – 482.7) per 100,000 in 2021.

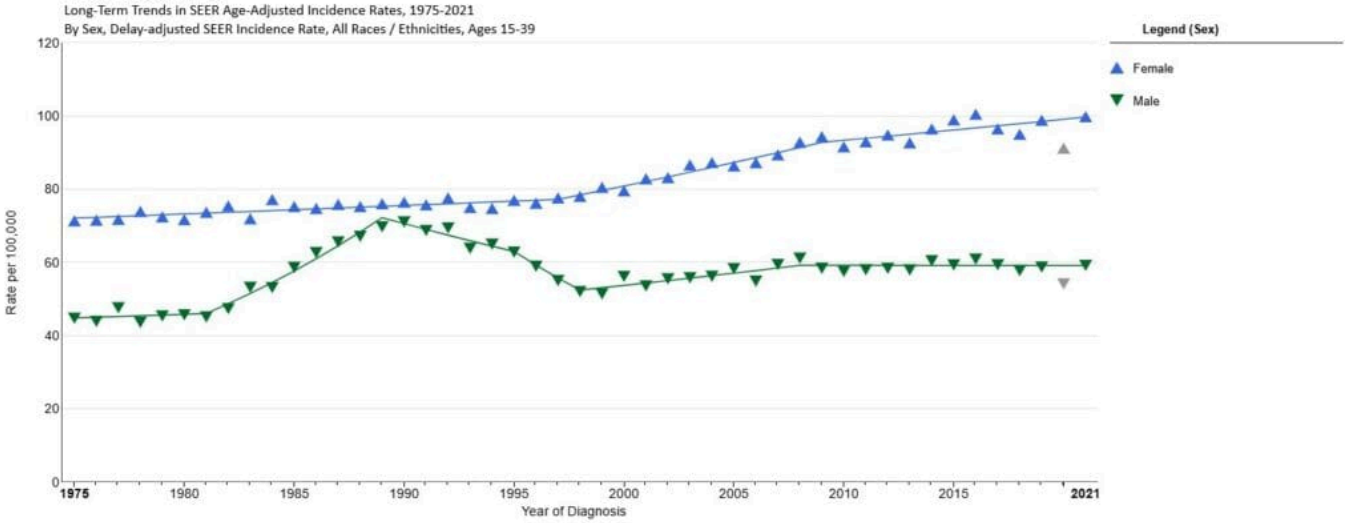
Strikingly, the incidence rate of cancer (any sites combined) among young women (ages 15-39 years) has risen from 71.3 (95% CI 68.0 – 74.5) to 99.7 (95% CI 96.8 – 102.7) between 1975 and 2021, a cumulative increase of 40%. As illustrated in Figure 1, this increase is significantly larger than that observed in males in the same age group over the same period of time.

Looking at specific sites, a concerning rise in the incidence of colorectal cancer (CRC) can be seen in both males and females aged 15-39 years. In the two decades leading to 2021, the annual percentage change (APC) in the incidence of CRC was 3.3% for both sexes combined. Notably, the incidence of colorectal cancer grew more quickly during this time period for females. By 2021, the annual incidence of CRC was 6.3 (95% CI 5.6 – 7.1) per 100,000 females ages 15-39 and 5.4 (95% CI 4.8 – 6.1) per 100,000 males in the same age group. Indeed, in 2021, the annual incidence of CRC in young women (6.2 per 100,000; 95% CI 5.5 – 7.0) exceeded the annual incidence of cervical cancer (5.4 per 100,000; 95% CI 4.6 – 6.2) in this same group.

Using NCI SEER data, the authors will present additional analyses highlighting the rise of cancer in young people, specifically young women, hypotheses of risk factors contributing to the elevated incidence of cancer in these groups, and proposed public health approaches focusing on cancer in young people in the US.

Figure 1.

All Cancer Sites Combined
Long-Term Trends in SEER Age-Adjusted Incidence Rates, 1975-2021
By Sex, Delay-adjusted SEER Incidence Rate, All Races / Ethnicities, Ages 15-39



Data Source:
• SEER Incidence Data, November 2023 Submission (1975-2021), SEER 8 registries [https://seer.cancer.gov/registries/terms.html].
Methodology:
• Rates are per 100,000 and are age-adjusted to the 2000 US Std Population (19 age groups - Census P25-1130).
• The Annual Percent Change (APC) and Average Annual Percent Change (AAPC) estimates were calculated from the underlying rates using the Joinpoint Trend Analysis Software [https://surveillance.cancer.gov/joinpoint], Version 5.1, April 2024, National Cancer Institute using the default settings.
• The APC's/AAPC's direction is "Rising" (↑) when the entire 95% confidence interval (C.I.) is above 0, "Falling" (↓) when the entire 95% C.I. is lower than 0, otherwise, the trend is considered "Not Significant".
• The 2020 incidence rate(s) were not used in the fit of the trend line(s) and are displayed on the graph as gray data points. Impact of COVID on SEER Cancer Incidence 2020 data [https://seer.cancer.gov/data/covid-impact.html]
Race/Ethnicity Coding:
• For years prior to 1990, the Census Bureau has only provided county-level population estimates for White, Black, and Other races.
Cancer Site Coding:
• See SEER*Explorer Cancer Site Definitions [https://seer.cancer.gov/statistics-network/explorer/cancer-sites.html] for details about the cancer site coding used for SEER Incidence data.
Created by https://seer.cancer.gov/statistics-network/explorer on Thu Jan 09 2025.

Cancer

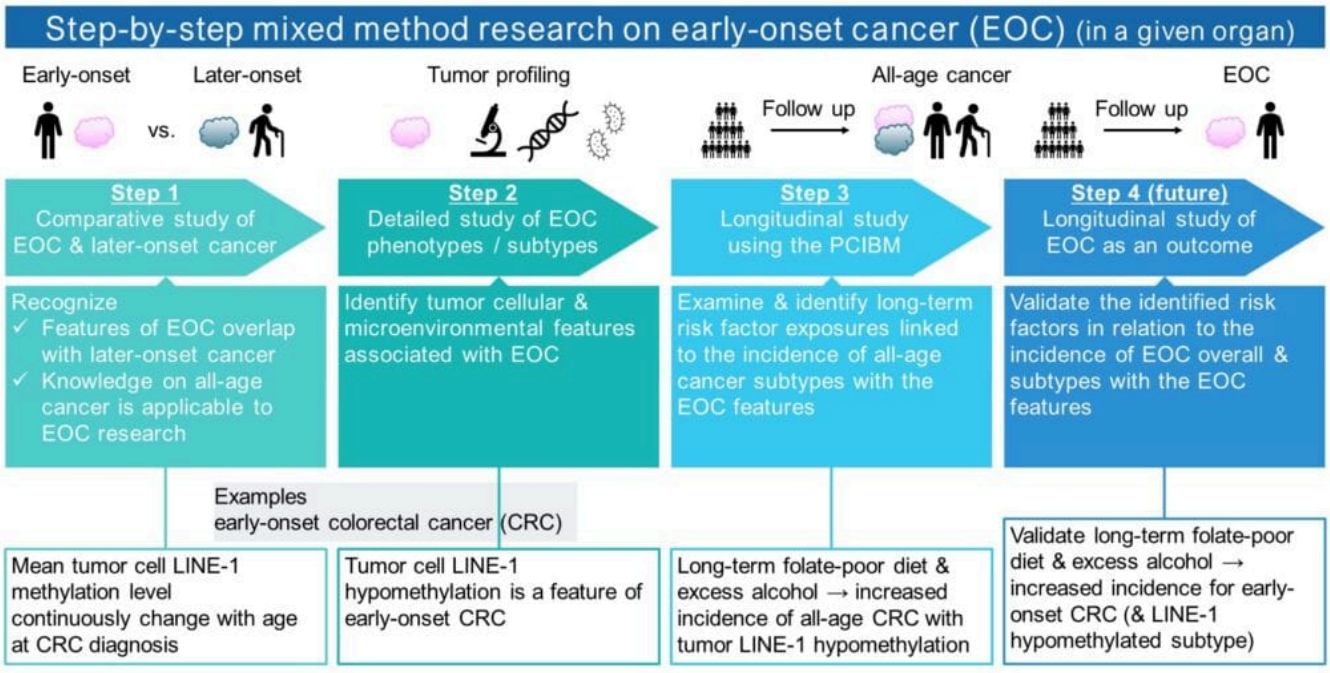
Tobacco-related urinary biomarkers and lung cancer risk in women, a case-cohort analysis
Mahdi Nalini* Mahdi Nalini Arash Etemadi Christian C Abnet Katie O'Brien Dale Sandler Cindy Chang Benjamin C. Blount Lanqing Wang Antonia M Calafat Deepak Bhandari Neal D. Freedman

Background: Carcinogenic components of tobacco smoke, particularly those contributing to the lung cancer risk among women, have yet to be clearly identified. We assessed associations between biomarkers of polycyclic aromatic hydrocarbons (PAHs), tobacco-specific nitrosamines (TSNAs), and volatile organic compounds (VOCs) and lung cancer incidence among women across the United States.
Methods: In a case-cohort analysis within the Sister Study cohort (50,884 women, 35-74 years, enrolled 2003-2009), data were obtained for all incident lung cancers through September 15, 2017, and a random subcohort stratified by ethnicity (non-Hispanic White, non-Hispanic Black, Hispanic, others) and smoking status (current, past, never). We measured 30 biomarkers in baseline urine samples and calculated hazard ratios (HRs) for the associations between a one-unit increase in the natural logarithm of biomarker concentrations and lung cancer incidence using weighted Cox regression models adjusted for potential confounders.
Results: Our sample included 356 cases and 433 non-case participants during a follow-up of 9.6 years. Among current smokers, associations were observed for biomarkers of PAHs (naphthalene, phenanthrene, pyrene, fluorene; HRs:1.4-5.3), TSNAs (N'-nitrosoanabasine, N'-nitrosoanatabine, 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNAL);HRs:1.3-2.5), and VOCs (xylene, acrylamide, acrylonitrile, 1,2-dibromoethane/vinyl-chloride/ethylene-oxide/acrylonitrile, acrolein, styrene/ethylbenzene, benzene, dimethylformamide/methylisocyanate, 1,3-butadiene, crotonaldehyde, isoprene;HRs:1.6-4.4). The associations for most PAH biomarkers were independent of nicotine metabolites, NNAL, and smoking frequency and duration. In women who did not smoke at baseline, associations were observed for styrene/ethylbenzene and dimethylformamide/methylisocyanate biomarkers.
Conclusion: We found direct evidence of associations between several PAH, TSNA, and VOC biomarkers and lung cancer risk in women.

Cancer

The early-onset cancer epidemics: novel role of mixed methods research using the prospective cohort incident-tumor biobank method Shuji Ogino* Shuji Ogino Satoko Ugai Tsuyoshi Hamada Tomotaka Ugai

Early-onset cancer (EOC), generally defined as cancer diagnosed in adults under the age of 50 years, has shown increasing incidence in many parts of the world since the 1990s. Influences of decades-long risk factor exposures are suspected to contribute to the widespread rise of EOC in many organ systems. Current EOC research has a substantial gap between long-term exposure assessments and tumoral molecular/microenvironmental profiling. This is because a prospective cohort study, which typically enrolled middle-aged participants to have enough incident cancer cases during follow-up, may lack enough incident EOC cases in a given organ for tumor tissue profiling. To address this gap, we have developed a step-by-step “mixed-methods” approach, leveraging the prospective cohort incident-tumor biobank method (PCIBM) (Figure). The Figure also provides a proof-of-principle study example, using tumor cell LINE-1 DNA hypomethylation as a feature of early-onset colorectal cancer (CRC). The first step is to recognize that features of EOC in a given organ overlap with a later-onset cancer counterpart and that existing knowledge and new research on all-age cancers are useful for a better understanding of EOC. Second, EOC tumoral features are discovered and replicated. Third, the PCIBM examines long-term exposure variables and the incidence of all-age cancer (in a given organ) subtypes that possess tumoral features of EOC in the organ. Fourth, possibly in the future, identified putative risk factors will be tested for the incidence of EOC (in that organ) overall and subtypes that possess EOC tumoral features. This step-by-step mixed methods approach (even only up to the third step) enables us to better understand EOC etiologies when there are not enough incident EOC cases in a given organ with tumor profiling data in a prospective cohort study that has precious data on long-term exposure variables.



Cancer

Epidemiological trends of synovial sarcoma by primary tumor sites in the US from 2000 to 2020 Dejka M. Araujo* Riddhi R. Patel George L. Delclos Stacia M. DeSantis Michael B. Cannell Philip J. Lupo Patrick P. Lin

Background: Synovial sarcoma (SS) is a rare soft-tissue cancer. Existing literature encompasses Surveillance, Epidemiology, and End Results (SEER) data-based research on SS explaining the incidence-prevalence in general, by subtypes, and by age at diagnosis. Therefore, this study aimed to fill in the gap of knowledge about measures of disease occurrence and burden of SS by tumor site using the SEER database.

Methods: In this cross-sectional study, primary SS patients were selected from SEER 17 Registries, Nov. 2021 (2000-2020) using ICD-O-3 codes 9040, 9041, 9042, and 9043. Patients with additional cancers were excluded. The primary tumor site was categorized into (1) head/neck, (2) internal thorax, (3) abdomen/pelvis, (4) upper extremity, and (5) lower extremity using ICD-10CM codes. Five outcomes were analyzed: age-adjusted incidence rate, 5-year limited-duration prevalence rate, incidence-based mortality, case-fatality rate, and overall survival.

Results: From 2000-2020, the overall age-adjusted incidence rate was 0.15 per 100,000; the 5-year limited duration prevalence rate was 0.56 per 100,000; and the incidence-based mortality rate was 0.06 per 100,000 people. The case-fatality and 5-year OS rates were 39.2 % and 62.9 %, respectively. Lower extremity had the highest incidence of 0.07 (estimated 1166 cases), prevalence of 0.36 (estimated 224 cases), and mortality rate of 0.025 (estimated 429 deaths) per 100,000. The other four locations had much closer rates with each other. Intrathoracic SS had the highest case-fatality rate of 71.5 % (148/207) and lowest 5-year OS of 26.0 % (95 % CI: 19.6 %, 32.9 %) than other sites.

Conclusion: Based on the measures of disease frequency, the most common primary tumor site is the lower extremity, followed by the upper extremity, abdomen/pelvis, internal thorax, and head/neck. The least favorable primary location is the internal thorax. Those with a primary location of the upper extremity have the longest overall survival, followed by the head/neck, lower extremity, abdomen/pelvis, and internal thorax.

Cancer

Air pollution is associated with cardiovascular and respiratory healthcare encounters among testicular cancer survivors Judy Ou* Judy Ou Joemy M Ramsay Heydon K Kaddas Jim VanDerslice Brock O Neil Sarah M Garcia Heidi Hanson Anne Kirchhoff

Aim: Chemotherapy for testicular cancer is highly effective but contributes to long-term risks for heart and lung problems. Air pollution leads to and worsens heart and lung conditions, but its impact on the health of testicular cancer survivors is unknown. We assessed associations between exposure to nitrogen dioxide (NO2) and ozone (O3) and health events with a cardiovascular or respiratory diagnosis among survivors of adolescent and young adult (AYA) testicular cancer.

Methods: This Utah-based case-crossover study included 385 survivors, diagnosed 2000-2016 at age 15-39 years and living 2 years after diagnosis, who had emergency department/urgent care [ED/UC] or inpatient admissions with a cardiovascular (nevent=257) and/or respiratory (nevent=685) diagnosis. Conditional logistic regression with robust standard errors estimated associations while controlling for temperature and humidity. Continuous and dichotomous (≥moderate Air Quality Index (AQI)) measures were included for NO2 and O3 for the 1-4 days before events (lag days). We conducted subgroup analysis according to cancer treatments.

Results: Exposure to NO2 ≥moderate AQI on lag day 1 increased odds for any cardiovascular event (OR=1.97, 95% CI=1.08-3.59) and cardiovascular inpatient admission (OR=2.48, 95% CI=1.21-5.10). Survivors treated with chemotherapy and exposed to NO2 ≥moderate AQI on lag day 1 had increased odds for cardiovascular inpatient admission (OR=3.00, 95% CI=1.29-7.00). O3 ≥moderate AQI on lag day 4 also increased odds for respiratory ED/UC visit (OR=1.34, 95% CI=1.00-1.79). O3 on lag day 4 was associated with any cardiovascular event (OR=1.02/1-ppb, 95% CI=1.00-1.03) and cardiovascular inpatient admission (OR=1.03/1-ppb, 95% CI=1.00-1.05).

Conclusions: Air pollution may worsen long-term outcomes among AYA testicular cancer survivors. This information can improve survivorship care plan for testicular cancer by addressing air pollution as a risk factor for exacerbation of these conditions.

Cancer

Changes in frailty among older adults with chronic lymphocytic leukemia/small lymphocytic lymphoma Vanessa Siebert* Vanessa Slater Ryan Carnahan Brian Smith Michael O'Rorke Christopher Strouse Elizabeth Chrischilles

Background: Chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) predominantly impacts older adults and many have comorbidities at diagnosis. Comorbidities and frailty are associated with inferior clinical outcomes; however, it is not known how a CLL/SLL diagnosis impacts the trajectory of patients' frailty. We sought to assess how frailty changes after diagnosis for patients with CLL/SLL in comparison to people without cancer and to patients with follicular lymphoma (FL).

Methods: Using the Surveillance, Epidemiology, and End Results-Medicare data, we identified 36,775 patients with CLL/SLL, 220,643 people without cancer, and 20,874 patients with FL. Frailty was measured using Medicare claims to calculate a total score from the 16 Function-Related Indicators. Logistic regressions computed ORs and corresponding 95% CIs for baseline frailty and worsening of frailty in the 12-months after diagnosis and linear mixed effects models assessed change in frailty.

Results: Patients with CLL/SLL had higher baseline frailty compared to people without cancer (adjusted OR=1.20, 95% CI: 1.17-1.22) and patients with FL (adjusted OR=1.06, 95% CI: 1.03-1.10). Patients with CLL/SLL were more likely to have worsening of frailty in the 12-months after diagnosis (adjusted OR=2.21, 95% CI: 2.15-2.27) and had a higher rate of increase in frailty (adjusted βinteraction=0.02, 95% CI: 0.01-0.02) compared to people without cancer. In contrast, patients with CLL/SLL were less likely to have worsening of frailty in the 12-months after diagnosis (adjusted OR=0.75, 95% CI: 0.73-0.78), but had a higher rate of frailty development (adjusted βinteraction=0.02, 95% CI: 0.02-0.03) compared to patients with FL.

Conclusions: Patients with CLL/SLL and patients with FL experienced worsening frailty after diagnosis. Our study results support the continued need for clinical assessments for frailty and consideration of ways to mitigate worsening of frailty after a diagnosis of CLL/SLL or FL.

Cancer

Inflammatory and insulinemic dietary patterns during adolescence and risk of invasive breast cancer among US women Andrea Romanos-Nanclares* Phuong Anh Le Walter C. Willett Bernard Rosner Wendy Y. Chen Michelle D. Holmes Andrea Romanos-Nanclares A. Heather Eliassen

Adolescence is marked by the rapid proliferation of breast tissue and hormonal changes, presenting a susceptible window for breast carcinogenesis. Exposures during this period, including diet, could influence breast cancer risk. Chronic inflammation and hyperinsulinemia are thought to be important underlying mechanisms for several chronic diseases, including breast cancer. This study examines the association between inflammatory and insulinemic dietary patterns during adolescence and invasive breast cancer risk in adulthood. We analyzed data from 47,355 women aged 33-52 years old in the Nurses' Health Study II (NHSII) who reported their adolescent diet using a food frequency questionnaire in 1998. We calculated the empirical dietary inflammatory pattern (EDIP) and empirical dietary index for hyperinsulinemia (EDIH) scores, which reflect the diet's potential to modulate circulating inflammatory biomarkers and C-peptide, respectively. Participants were followed from 1998 until the occurrence of breast or other cancer, death, loss to follow-up, or study end in 2019, whichever occurred first. Multivariable Cox Proportional Hazards models were used to estimate hazard ratios (HR) and 95% confidence intervals (CI). During 896,647 person-years of follow-up, we documented 1,945 invasive breast cancer cases. We observed no association between EDIP or EDIH and breast cancer risk. The HRs (highest vs. lowest quintile) were 1.10 (95%CI: 0.94, 1.29) for EDIP and 0.95 (95%CI: 0.80, 1.13) for EDIH. Results did not differ by estrogen receptor status, menopausal status, or body mass index at age 18. In conclusion, adolescent dietary patterns with high inflammatory or insulinemic potential were not associated with increased breast cancer risk.

LATEBREAKER

Cancer

Cardiovascular disease mortality among women diagnosed with metastatic breast cancer in the United States, 2000-2020 Cody Ramin* Cody Ramin Jessica Li Gillian Gresham Katelyn Atkins Andriana Nikolova Mia Hashibe

Background: Although patients with metastatic breast cancer (MBC) are living longer due to advances in treatment, risk of cardiovascular disease (CVD) remains understudied in this patient population.

Methods: We identified 33,239 women, aged 20-84, who were diagnosed with MBC between 2000-2020 and survived ≥1 year after diagnosis from 17 Surveillance, Epidemiology, and End Results Program registries. We estimated standardized mortality ratios (SMRs) and 95% confidence intervals (CIs) for CVD mortality overall and by age, year, and time since MBC diagnosis. We calculated cumulative incidence and 95% CIs for CVD mortality overall and by age at MBC diagnosis accounting for competing risks (e.g., breast cancer mortality).

Results: Over 3.1 median years of follow-up, 724 MBC patients died of CVD (554 heart disease; 127 cerebrovascular disease; 43 other CVD). Overall patients with MBC had an elevated risk of CVD mortality compared to women in the general population accounting for age, year, race, and ethnicity (SMR=1.45, 95%CI=1.34-1.55). SMRs were further elevated among patients aged <50 years at MBC diagnosis (SMR=3.48; 95%CI=2.67-4.46) but decreased with increasing age (p-trend<0.001). Risk of CVD mortality was higher among more recently diagnosed patients (SMR2015-2020=1.57, 95%CI=1.32-1.86), those diagnosed with triple negative tumors (SMR=2.51, 95%CI=1.71-3.57), and within the first four years since diagnosis (SMR=1.62; 95%CI=1.48-1.77). Among patients with MBC aged <50 years, risks were further elevated among those recently diagnosed (SMR2015-2020=5.44, 95%CI=2.90-9.31) and within the first four years of diagnosis (SMR=5.09, 95%CI=3.68-6.86). Approximately 1 in 60 patients died from CVD within five years following their MBC diagnosis (5-year cumulative incidence: 1.73%, 95%CI=1.58-1.88%) with the highest cumulative incidence among women aged 50 years or older (5-year cumulative incidence: 2.13%, 95%CI=1.95-2.33%).

Conclusions: Patients with MBC have significantly elevated CVD mortality, especially among those diagnosed before age 50, in more recent years, and within the first few years following diagnosis. Further research is warranted to address the heightened risk of CVD in patients with MBC, including the relationship between cardiotoxic cancer therapies and baseline CVD risk.

LATEBREAKER

Cancer

Association of Smoking and Bladder Cancer among adults in the United States Manali Desai* Manali Desai Dhvani Parikh Dhawal Bandrey

Association of Smoking and Bladder Cancer among adults in the United States

Manali Desai, Dhvani Parikh, Dhawal Bandrey

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Background: In United States, bladder cancer is sixth most common cancer. Smoking is the highest risk factor for bladder cancer. According to the American Cancer Society (ACS), individuals who smoke have three times higher risk of developing the disease than individuals who do not smoke.

Objective: This study aimed to examine the association between bladder cancer and smoking controlling for other sociodemographic variables.

Methods: A total of 27651 participants were analyzed from National Health Interview Survey (NHIS) 2022 for this cross-sectional study. The outcome variable was defined as ever diagnosed with bladder cancer. The independent variable was smoking status and covariates included race/ethnicity, sex, marital status, place of usual care, general health status, US born, insurance, location of residence. Weighted bivariate and multivariable logistic regression was performed.

Results: Approximately (104) 3.10% of participants were diagnosed with bladder cancer, and (3252) 96.90% were not diagnosed with bladder cancer. There were 76 (0.83%) smokers whereas 28 (2.27%) were non-smokers. In bivariate analysis, smoking was associated with higher odds of having diagnosed with bladder cancer (crude OR = 3.22, 95% CI: 1.97-5.26) compared to non-smokers. In the multivariable analysis, smoking was associated with higher odds of having bladder cancer (aOR = 2.607 95% CI: 1.64-4.38) compared to non-smokers. Compared to males, females had 24% (95%CI:0.14-0.41) lower odds of being diagnosed with bladder cancer.

Conclusion: The study found an association between bladder cancer and smoking. Therefore, targeted smoking cessation programs are crucial to decrease the prevalence of bladder cancer among adults in the US.

LATEBREAKER

Cancer

The impact of the number of chronic health conditions on cancer screening: results from a 2016-2022 U.S. national study Sarala Pandey* Sarala Pandey S. Cristina Oancea

Chronic health conditions (CHC) and cancer screening (CS) are key public health concerns, impacting healthcare access and outcomes. While CS is vital for early cancer detection, individuals with multiple CHC may encounter challenges or enablers influencing CS adherence. There is limited research describing the impact of the number of CHC on CS in U.S. adults. Examining this relationship is essential for improving preventive health care strategies. This study analyzes the nationally representative 2016-2022 BRFSS data to explore the association between the number of CHC and CS among U.S. adults based on specific sex and age-group standard recommendations for CS. Weighted and adjusted multivariable logistic regression models were used to perform analyses. CHC accounted for in this study were coronary heart disease, asthma, chronic obstructive pulmonary disease, arthritis, depression, kidney disease, diabetes, and obesity. On average, 15.12 % of the study participants had ≥ 3 CHC, whereas 35.08 % of the study participants had no CHC. The weighted and adjusted odds (WAO) of breast (N= 260,567 ages 50-74 years old YO), cervical (N= 313,511 ages 21-65 YO) and colorectal (N= 267,948 ages 50-75 YO) CS among females with ≥3 CHC were 122% (95%CI:1.95,2.54), 15% (95%CI:1.06,1.25), and 126% (95%CI:2.10,2.43) significantly greater, respectively, than the WAO of corresponding CS among females who had no CHC. The WAO of prostate (N= 118,889 ages 55-69 YO), and colorectal (N= 241,077 ages 50-75 YO) CS among males with ≥3 CHC, were 39% (95%CI:1.27,1.51), and 116% (95%CI:1.99,2.35) significantly greater, respectively, than the WAO of corresponding CS among males who had no CHC. These results indicate that the prevalence of multiple CHC, particularly ≥3 CHC, is significantly associated with greater odds of cancer screening. These findings underscore the importance of healthcare providers actively encouraging CS among patients with CHC as a preventive healthcare strategy.

LATEBREAKER

Cancer

Impact of COVID-19 on area-based socioeconomic inequalities in cancer mortality in Japan: 2017-19 and 2020-22 Yuri Ito* Yuri Ito Aoi Kataoka Keisuke Fukui Tomoki Nakaya

Background

An important highlight of the 4th National Cancer Plan in Japan was Socioeconomic inequalities in cancer. The COVID-19 pandemic influenced cancer control activities at the community level, such as screening programs and treatment. However, the impact of COVID-19 on socioeconomic inequalities in cancer mortality in Japan has not been evaluated. We aim to estimate changes in socioeconomic inequalities in cancer mortality before/after the onset of COVID-19 pandemic.

Method

We used the areal deprivation index (ADI) to establish an area-based socioeconomic position. We categorized municipalities into ADI quintiles weighted by population size; Q1 is the least deprived, and Q100 the most deprived group. We obtained annual mortality data from vital statistics from 2017 to 2022. Annual population data was obtained from the National Census data from 2015 and 2020 with linear inter/extrapolation. The age-standardized mortality rate (ASMR) was calculated using the direct method based on the standard population of 1985. We estimated the Slope Index of Inequalities (SII) and the Relative Index of Inequalities (RII) as the absolute and relative index of inequalities in ASMR, respectively; by for two periods 2017-2019 and 2020-2022, as before and after the onset of COVID-19 pandemic (hereafter referred as before/after COVID-19), respectively.

Results

The SII of ASMR for all site cancer before COVID-19 was 65.9 in men and 24.4 in women per 100,000; these gaps increased to 72.7 and 28.4 after COVID-19. By cancer site, the largest SII was observed in lung cancer in men and colorectal cancer in women. SII of male lung cancer increased from 16.8 to 20.7 per 100,000. SII of pancreatic cancer has also widened before/after COVID-19. For women, cervical, breast and corpus uteri cancer also showed a widening gap. The largest RII was observed in liver cancer in both sexes, but in most of cancer sites did not show large change before/after COVID-19.

Discussion

We observed changes in SII and RII of ASMR before/after the onset of COVID-19 pandemic by cancer site. We need to consider the reasons for the change in sites with widening gaps such as lung and pancreatic cancer based on the change of lifestyle including risk factors, screening participation and accessibility of treatment during COVID-19 pandemic. Further analysis is needed to consider how the severity of the COVID-19 pandemic by area level influenced inequalities in cancer mortality.

LATEBREAKER

Cancer

Investigating the Effect of Alcohol Consumption Intensity on Gastric Cancer Risk Using Targeted Maximum Likelihood Estimation chungho kim* BOMI PARK Byungmi Kim

Investigating the Effect of Alcohol Consumption Intensity on Gastric Cancer Risk Using Targeted Maximum Likelihood Estimation

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Background

Gastric cancer is a leading cause of cancer-related deaths worldwide, influenced by environmental and lifestyle factors. While alcohol consumption is a potential risk factor, its causal relationship with gastric cancer remains unclear. This study evaluates the causal impact of alcohol consumption on gastric cancer incidence using a large-scale cohort and advanced causal inference methods.

Methods

We analyzed the Korean National Health Insurance Service (KNHIS) database, including individuals aged 50–69 who underwent general health check-ups in 2010–2011. Participants with a history of cancer, deaths within 5 or 10 years, or missing confounder variables were excluded. The final study population consisted of 5,909,463 individuals (37,622 gastric cancer cases) for the 5-year follow-up and 5,747,743 individuals (72,651 cases) for the 10-year follow-up. Alcohol consumption intensity was calculated as “(weekly drinking frequency ÷ 7) × daily drinking amount × 8g of pure alcohol per drink” and categorized into non-drinkers (0 g/day), light drinkers (0.01–12.4 g/day), moderate drinkers (12.5–24.9 g/day), heavy drinkers (25.0–49.9 g/day), and high-risk drinkers (≥50.0 g/day). A Directed Acyclic Graph (DAG) identified confounders, including sex, age, income, smoking, physical activity, family history of gastric cancer, and cancers other than gastric cancer. To estimate the causal relative risk of alcohol consumption on gastric cancer, we applied Targeted Maximum Likelihood Estimation (TMLE) and improved model performance using the SuperLearner algorithm, incorporating Generalized Linear Models (GLM) and XGBoost.

Results

After adjusting for confounders, light drinkers showed no significant risk increase at 5 years (RR: 1.01, 95% CI: 0.97–1.03) but had a significant increase at 10 years (RR: 1.02, 95% CI: 1.00–1.05). Moderate drinkers exhibited increased risks at 5 years (RR: 1.07, 95% CI: 1.02–1.12) and 10 years (RR: 1.09, 95% CI: 1.03–1.18). Heavy drinkers had elevated risks at 5 years (RR: 1.21, 95% CI: 1.16–1.25) and 10 years (RR: 1.33, 95% CI: 1.26–1.39), while high-risk drinkers had the highest risks at 5 years (RR: 1.36, 95% CI: 1.31–1.41) and 10 years (RR: 1.41, 95% CI: 1.37–1.52). These findings suggest higher alcohol consumption significantly increases gastric cancer risk.

LATEBREAKER

Cancer

Depressive symptoms in relation to breast cancer mortality: findings from the Black Women's Health Study Nuo Xu* Nuo Xu Mollie E. Barnard Etienne X. Holder Julie R. Palmer

Although breast cancer incidence rates are similar for Black women and White women in the U.S., breast cancer mortality is about 40% higher in Black women. Depression is a common comorbidity among breast cancer patients and has been linked to poorer survival, yet data from Black women are limited. To address this gap, we used data from the Black Women's Health Study, a cohort of 59,000 Black women followed by biennial questionnaires since enrollment in 1995, to assess the relation of depressive symptoms to breast cancer mortality. The Center for Epidemiologic Studies Depression Scale (CES-D) is a widely used self-report tool for assessing depressive symptoms across diverse populations, with a score of 16 or higher considered the cutoff for identifying individuals at risk for clinical depression. The CES-D scale was included as part of the 1999, 2005, and 2019 questionnaires. Deaths and cause of death were identified through linkage with the National Death Index. Hazard ratios (HR) and 95% confidence intervals (CI) for high versus low CES-D score in relation to breast cancer death were estimated by Cox proportional hazards models, with adjustment for age and stage at diagnosis. A total of 1,157 women with invasive breast cancer diagnosed at stages I-III completed the CES-D close to the time of diagnosis. Over a median follow-up of 15 years, 168 breast cancer-specific deaths occurred. The HR for a CES-D score of ≥16 relative to <16 was 1.39 (95% CI 1.00, 1.94). The association was consistent across stage at diagnosis and was somewhat stronger among women aged 55 and older (HR 1.84, 95% CI 1.07, 3.14). Next steps in this analysis include investigating possible mediators and modifiers of the association. The findings suggest that early depression screening of breast cancer patients with tools like the CES-D to identify at-risk individuals and offer supportive interventions may be warranted.

Cancer

Physical activity and risk of liver cancer in the NIH-AARP Diet and Health Study Frances Albers* Frances Albers Ghazaleh Dashti Charles Matthews Lin Yang Darren Brenner Roger Milne Dallas English Brigid Lynch Katherine McGlynn

Background: Physical activity reduces the risk of several cancers; however, evidence is less established for liver cancer, and the competing risk of death must be carefully considered. We estimated the effect of physical activity on risk of primary liver cancer using a formal causal inference framework for competing risks.

Methods: This analysis included data for 263,184 participants (870 liver cancers) in the NIH-AARP Diet and Health Study. The total effect of physical activity on risk of primary liver cancer was defined by conceptualizing competing death as a mediator on the causal pathway with a deterministic relationship with the outcome, such that if competing death = 1, primary liver cancer = 0. Risk differences (RDs) for the total effect were estimated as the differences in standardized, cause-specific cumulative incidence functions of primary liver cancer under exposure (≥ 4 hours/week of recreational moderate- to vigorous-intensity physical activity [MVPA]) versus no exposure (< 4 hours/week of MVPA). 95% confidence intervals (CIs) were obtained via the delta method. A sensitivity analysis was conducted for hepatocellular carcinoma (HCC), the most common histological subtype of primary liver cancer.

Results: RDs for the total effect of physical activity on risk of primary liver cancer at the average age of diagnosis (67 years) and average life expectancy (78 years) in the United States were estimated to be -18.1 (95% CI: -29.9, -6.2) and -58.4 (95% CI: -95.8, -21.1) cases per 100,000 persons, respectively. The magnitude of the RD increased from age 55 (RD per 100,000 persons = -2.0, 95% CI: -4.5, 0.6) to 85 years (RD per 100,000 persons = -79.0, 95% CI: -133.4, -24.7). Results for HCC were attenuated.

Conclusion: Physical activity may have a protective effect on primary liver cancer that increases with age.

Cancer

Racial Disparities and the Impact of Physical Activity on Mortality in the Pathways Study, A Prospective Cohort Study of Breast Cancer Survivors Tanvi Srivastava* Tanvi Srivastava Lia L D'addario Lawrence Kushi Janise M Roh

Physical activity (PA) is widely recognized for its numerous health benefits, including improved survival rates and quality of life for breast cancer (BCa) survivors. However, disparities in PA levels among different racial and ethnic groups have been documented. Understanding these disparities among BCa survivors is crucial for developing targeted interventions to promote PA among underserved populations. The diverse prospective cohort of BCa survivors in the Pathways study at Kaiser Permanente Northern California provides a unique opportunity to explore these disparities in a comprehensive manner. A cohort of 4,504 women was enrolled between Jan 2006 and May 2013 with data collected through surveys, EHR linkage, and other sources. As part of the cohort, self-reported PA data was collected at baseline (~2 months post-diagnosis). Follow-up surveys were collected at around 6 months and 24 months after baseline. The cohort is currently being followed for BCa outcomes including recurrence, overall mortality, and cause-specific mortality. PA levels were categorized as low, medium, and high based on MET-hour tertiles. Among 4,386 survivors, 21% were foreign-born. Asian Americans (AA) had the highest percentage (48%) of college-educated patients. AA survivors reported the highest household incomes, with 41% earning $90,000+, while Non-Hispanic Blacks (NHB) had the lowest incomes, with 38% earning <$50,000. Using Poisson regression, we found that AA and NHB survivors were more likely to have lower PA levels (adj. RR for AA = 1.69 (1.42, 2.01), $p<0.01$; adj. RR for NHB = 1.24 (1.02, 1.51), $p=0.03$) compared to NHW patients. AA survivors were less likely to have higher PA levels (adj. RR = 0.64 (0.53, 0.77), $p<0.01$) compared to NHW patients. The next objective of this project is to investigate the impact of PA on BCa recurrence, BCa mortality, and mortality due to cardiovascular disease amongst BCa survivors in the Pathways cohort across different racial/ethnic groups.

Cardiovascular

Advancing Applicability and Effectiveness of Cardiovascular Disease Prevention Education Programs Through Culture-Specific Designs Alina* Alina Yang

Background: Cardiovascular disease (CVD) disparities among adolescents are pronounced across racial and ethnic groups and exacerbated by cultural factors often overlooked by standard health education, prompting an evaluation of the effectiveness of culturally tailored versus standard prevention programs.

Methods: Utilizing a tripartite randomized design, 615 secondary school students (33% Hispanic, 29% White, 18% Asian, 12% Black, 8% Indigenous; ages 14-18) were allocated to: culturally tailored intervention (n=205), standardized intervention (n=205), or control cohorts (n=205). The culturally tailored protocol incorporated ethnically specific dietary and physical activity modifications over nine months. Qualitative data collection comprised 25 focus groups, analyzed through open, axial, and selective coding procedures to evaluate cultural congruence, knowledge acquisition, attitudinal modifications, and behavioral adaptations.

Results: Students in the culturally tailored group reported substantial increases in CVD knowledge and exhibited greater confidence in applying prevention strategies, with many integrating these changes into daily routines, such as adopting culturally adjusted dietary practices and participating in culturally specific exercises. They also expressed a heightened sense of personal responsibility for their health and a proactive stance in disseminating knowledge within their communities. Conversely, among the standard intervention group, students discussed challenges in relating the uniform content to their personal and cultural practices, leading to limited integration into their daily lives. The control group exhibited negligible changes in knowledge, attitudes, and behaviors.

Conclusion: The study demonstrates that culturally tailored CVD prevention programs significantly improve knowledge and attitudes toward cardiovascular health, supporting their broader adoption to address disparities and promote long-term health equity.

Cardiovascular

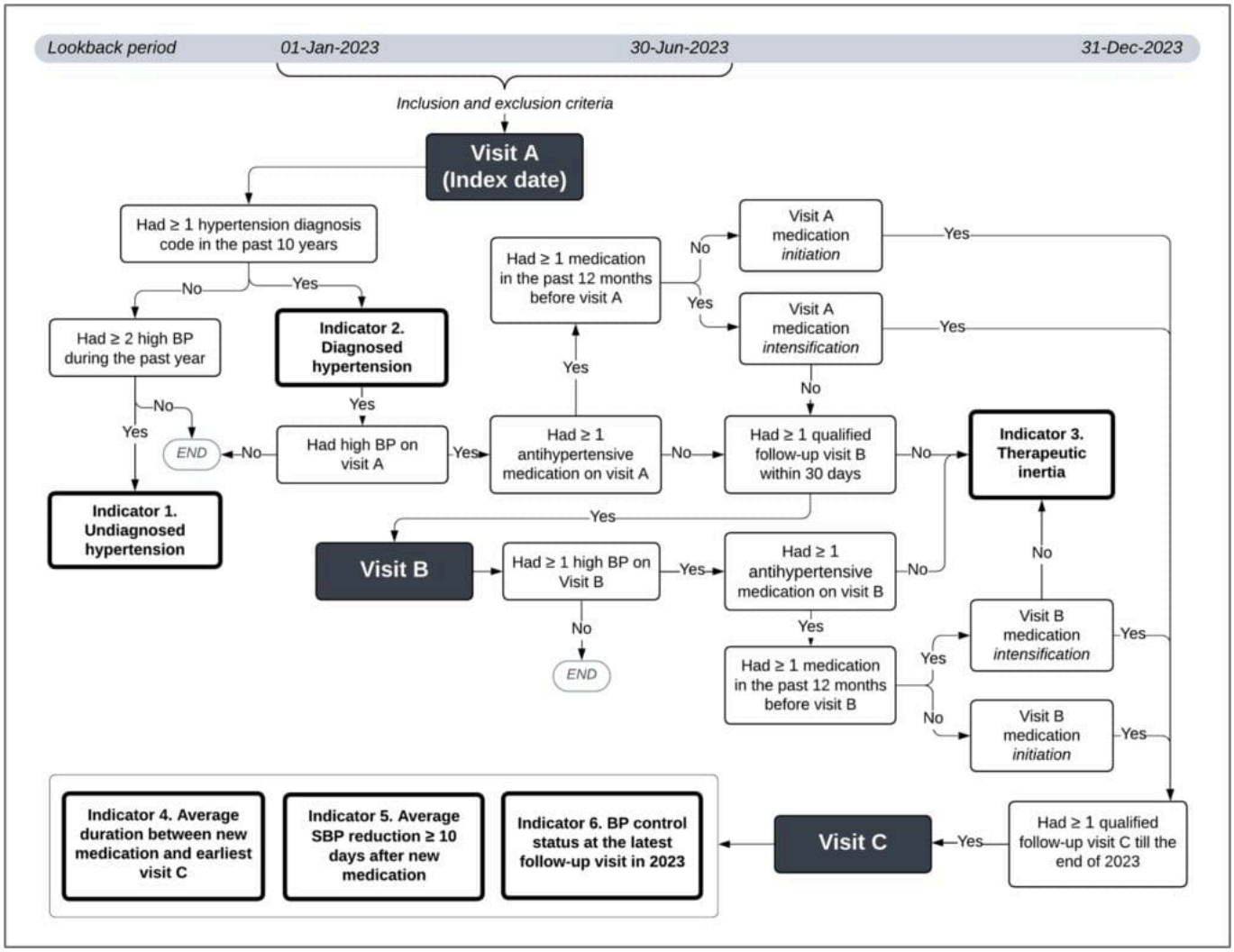
Healthcare quality, therapeutic inertia, and blood pressure control among patients with hypertension Sandra Jackson* Sandra Jackson Siran He Omoye Imoisili Elizabeth Lundeen Greg Wozniak Stavros Tsipas Nicole Therrien Elena Kuklina

Purpose: To assess hypertension-related healthcare quality metrics.

Methods: 3,410,800 patients aged ≥18 yrs with ≥1 primary or hypertension-related encounter and ≥1 blood pressure (BP) measurement between January–June 2023 were identified from the IQVIA Ambulatory Electronic Medical Records-United States, a nationwide dataset of over 100,000 outpatient providers. Adapting American Medical Association metrics (Figure), potential therapeutic inertia was defined as uncontrolled BP ≥140/90 mmHg and no medication intensification at the index visit or a subsequent visit within 30 days. Among patients receiving medication intensification [≥1 new antihypertensive medication class(es)], we assessed: duration to earliest follow-up, subsequent systolic BP (SBP) reduction, and subsequent BP control. Demographic and clinical characteristics associated with quality metrics were analysed using logistic regression.

Results: Of 1,585,894 patients with diagnosed hypertension, 469,904 (29.6%) had uncontrolled BP at the index visit. Among these patients, 317,675 (67.6%) experienced potential therapeutic inertia. For patients receiving medication intensification, median duration to follow-up was 68 days, mean SBP reduction was 12.6 mmHg, and 55.6% achieved subsequent BP control. Older patients (aged ≥65 yrs) were more likely to experience potential therapeutic inertia (aOR 1.16, 95% CI 1.14–1.18). Among those receiving medication intensification, Black (vs. White) patients (0.66, 0.63–0.70) and those seeing hypertension specialists (vs. family medicine) (0.77, 0.73–0.81) were less likely to achieve subsequent BP control.

Conclusion: Potential therapeutic inertia affected two-thirds of patients with diagnosed hypertension and uncontrolled BP, and was more likely among older adults. Among patients receiving medication intensification, only half achieved subsequent BP control. Clinicians and health systems can implement evidenced-based strategies to improve hypertension management.


Lookback period
01-Jan-2023
30-Jun-2023
31-Dec-2023
Inclusion and exclusion criteria
Visit A (Index date)
Had ≥ 1 hypertension diagnosis code in the past 10 years
No
Yes
Had ≥ 2 high BP during the past year
Indicator 2. Diagnosed hypertension
No
Yes
END
No
Had high BP on visit A
Yes
Had ≥ 1 antihypertensive medication on visit A
Yes
No
Had ≥ 1 medication in the past 12 months before visit A
No
Visit A medication initiation
Yes
Yes
Visit A medication intensification
Yes
No
Had ≥ 1 qualified follow-up visit B within 30 days
No
Indicator 3. Therapeutic inertia
Yes
Indicator 1. Undiagnosed hypertension
Visit B
Had ≥ 1 high BP on Visit B
Yes
Had ≥ 1 antihypertensive medication on visit B
No
No
END
Yes
Had ≥ 1 medication in the past 12 months before visit B
Yes
Visit B medication intensification
Yes
No
Visit B medication initiation
Yes
Indicator 4. Average duration between new medication and earliest visit C
Indicator 5. Average SBP reduction ≥ 10 days after new medication
Indicator 6. BP control status at the latest follow-up visit in 2023
Visit C
Yes
Had ≥ 1 qualified follow-up visit C till the end of 2023

Cardiovascular

Cardiovascular Disease and Post-traumatic Stress Disorder in World Trade Center Exposed Firefighters Madeline Cannon* Madeline Cannon Hillel W. Cohen Charles B. Hall Nadia Jaber David Prezant Rachel Zeig-Owens

Background: World Trade Center (WTC) exposure is associated with cardiovascular disease (CVD) in firefighters, other first responders, and survivors. However, the extent to which this is caused by particulate matter or post-traumatic stress disorder (PTSD) is unclear.

Aim: To assess if PTSD is a mediator of the association between WTC exposure and CVD in male firefighters.

Methods: We prospectively followed 9,758 male WTC-exposed firefighters from 9/11/01 (9/11) to 9/11/22. Cox regression models analyzed WTC exposure and CVD, adjusted for race/ethnicity and age and positive screen for PTSD symptoms (y/n) at first exam. CVD included electronic medical record of myocardial infarction, stroke, angina, coronary artery surgery, angioplasty, transient ischemic attack, cardiomyopathy, aortic aneurysm, peripheral arterial vascular intervention, carotid artery surgery, or CVD death. Age and PTSD were also modeled as time-dependent covariates, including all exams with complete data. A causal mediation analysis assessed PTSD as a mediator of the association between WTC exposure and CVD.

Results: 1,027 participants had a CVD event. Compared to firefighters who arrived at the WTC site from 9/12/01 to 9/24/01, those who arrived in the morning on 9/11 had a 34% increased hazard of CVD (95% CI=1.11-1.62), while those arriving in the afternoon had a 20% increased hazard (CI=1.04-1.38). PTSD at first exam was not associated with CVD (HR=1.02, CI=0.84-1.25). In the time-dependent analysis, arrival in the morning of 9/11 (HR=1.30, CI=1.08-1.57), arrival in the afternoon of 9/11 (HR=1.18, CI=1.02-1.36), and PTSD (HR=1.38, CI=1.14-1.68) were all associated with CVD. PTSD symptoms mediated 10% of the association between arrival in the morning of 9/11 and CVD, with a controlled direct effect of 1.30 (CI=1.08-1.57) and a natural indirect effect of 1.03 (CI=1.01-1.04).

Conclusion: PTSD symptoms partially mediate, albeit minimally, the association between WTC exposure and CVD among firefighters.

Cardiovascular

The Impact of Life’s Essential 8 on Metabolic Syndrome Development in Adolescents: A Longitudinal Study Jyun-Hao Guan* Jyun-Hao Guan Pei-Wen Wu Yu-Ting Chin Pei-Tung Lin Sheng-Hung Chu Chien-Hung Lee

Background: Cardiovascular health (CVH) and metabolic syndrome (MetS) during adolescence significantly influence the development of cardiovascular disease in adulthood. The American Heart Association’s Life’s Essential 8 (LE8) outlines eight metrics for assessing CVH across the life course, which may substantially impact adolescent MetS. This longitudinal study aimed to investigate the associations between CVH scores and the transition of MetS in adolescents over a follow-up period of 2.1 years.

Methods: This ongoing prospective cohort study was initiated in 2020. We have examined 729 adolescents aged 15-19 years, randomly selected from 10 senior high schools in Taiwan. Data were collected on LE8 health behaviors and factors, including diet, physical activity, nicotine exposure, body mass index (BMI), blood lipid, blood pressure, blood glucose, and sleep health. Adolescent MetS was defined using combined criteria from the International Diabetes Federation and the Taiwan Pediatric Association. We used Cox proportional hazards models to analyze the relationship between changes in LE8 components and transitions in MetS.

Results: The incidence of MetS at follow-up among adolescents without MetS at baseline was 3.7%. Among those with MetS, the proportions of persistent and remitted MetS were 65.2% and 34.8%, respectively. After adjusting for covariates, an increased number of abnormal LE8 components was associated with a 1.4-fold higher hazard ratio (HR) for incident MetS. Compared to adolescents with moderate-to-high levels of LE8, those with low LE8 levels had a 13.1-fold HR for persistent MetS. Additionally, abnormal BMI and blood lipid levels were the major contributors to the occurrence of MetS after 2.1 years of follow-up.

Conclusion: This study demonstrates the impact of cardiovascular health, as measured by LE8, on the development and persistence of MetS in adolescents, underscoring the importance of early interventions to enhance cardiovascular health.

Cardiovascular

Differences in cardiovascular disease, mortality in high income countries are too large to be explained by health system quality alone – using the normalized mortality index can help to clear the mist Bernd Kowall* Susanne Stolpe

Background

Age-standardised mortality (ASM) from cardiovascular diseases (CVD), especially from ischemic heart disease (IHD), is used to assess the quality of health systems. IHD mortality in high-income countries is very diverse. In 2019, ASM for IHD in Germany (44.7/100.000) was much higher than in the neighbour countries Netherlands (NL, 18.2/100.000) and Denmark (DK, 23.2), but lower than in the USA (53.9). CVD mortality is affected by national preferences in cause of death (CoD) selection, not necessarily reflecting population morbidity: in 2019, IHD was selected as CoD in NL in 5.4% of all deaths, in DK in 6.2%, but twice as often in DE and USA. Therefore, it is questionable if conclusions on health care quality are reliable.

Aim

To develop a measure to compare disease-specific mortality that more reliably reflects differences without being affected by different preferences in CoD selection.

Methods

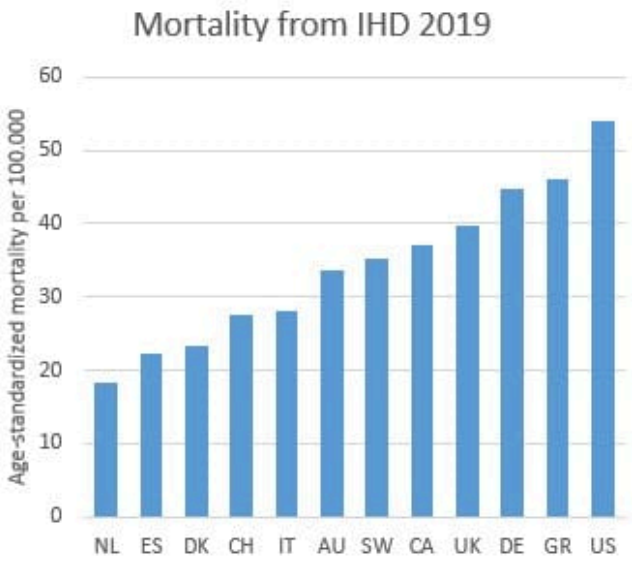
WHO data on all deaths, CVD and IHD deaths, and ASMs for CVD and IHD for West-European countries, USA, Australia and Canada for 2019 was used. The normalized mortality index was calculated by dividing the ASM by the proportion of IHD and CVD resp. among all CoD, then multiplying by 10. This normalizes the ASM to reflect a CoD proportion of 10% of all deaths.

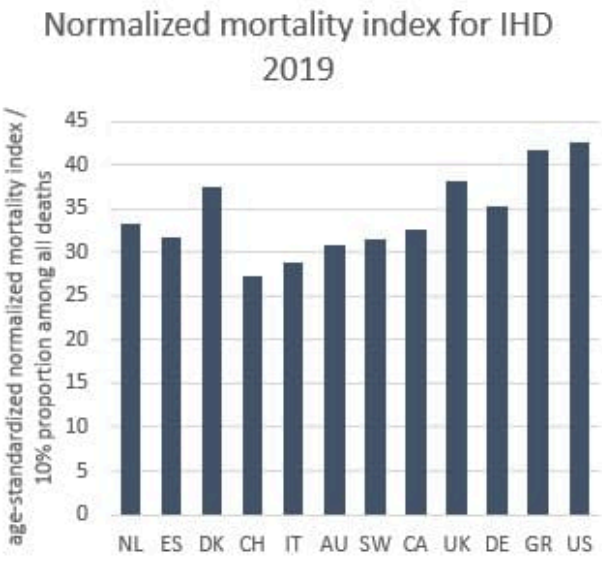
Results

The normalized mortality index for IHD in 2019 was similar for NL (33.4), DE (35.3) and DK (37.4), but higher for the USA (42.6) – plausibly indicating comparable or lower (USA) health system quality. For CVD, equally assuming a 10% share as CoD, the normalized mortality index was slightly lower (NL: 30.4, DE: 33.8, DK: 35.8, US: 41.9).

Conclusion

The normalized mortality index is easy to calculate. Normalizing the disease-specific ASM to a proportion of 10% as CoD among all deaths avoids distortions by nationally preferential CoD selection and enables more reliable conclusions on health system quality and population health. We recommend to include the normalized mortality index in health reporting.


Mortality from IHD 2019
Age-standardized mortality per 100.000
60
50
40
30
20
10
0
NL ES DK CH IT AU SW CA UK DE GR US


Normalized mortality index for IHD 2019
age-standardized normalized mortality index / 10% proportion among all deaths
45
40
35
30
25
20
15
10
5
0
NL ES DK CH IT AU SW CA UK DE GR US

Cardiovascular

Neighborhood Physical Disorder and Stroke: Findings from the Health and Retirement Study Mohammad Moniruzzaman* Mohammad Moniruzzaman Yangyang Deng Breanna Rogers Ram Jagannathan Lu Hu Kosuke Tamura

PURPOSE: Stroke is the fifth leading cause of death in the United States. Neighborhood physical disorder may contribute to an elevated risk of stroke; however, this relationship remains understudied. We investigated whether higher levels of neighborhood physical disorder are associated with an increased risk of stroke and examined potential variations by age, sex, and race.

METHODS: Data came from the 2022 Health and Retirement Study, the most recent available data (n=3754; females=54.1%; mean age=69.1 years; non-White adults=15.4%). Stroke status was assessed by self-reported physician diagnosis (yes/no). Perceived neighborhood physical disorder was assessed using a scale measuring physical features of neighborhoods (e.g., vandalism, vacant houses); higher scores indicate greater physical disorder and were expressed as a 1-SD increase. Weighted generalized logistic regression was used to evaluate the association between neighborhood physical disorder and stroke, adjusted for age, sex, race, marital status, education, employment, smoking, alcohol drinking, and hypertension. Analyses were stratified by sex (male, female), age groups (<69, ≥69 years), and racial groups (White, non-White).

RESULTS: Stroke occurred in 251 participants. Each 1 SD increase in neighborhood physical disorder was significantly associated with 27% higher odds of stroke in the overall sample (OR: 1.27, 95% CI 1.06–1.51), 38% higher odds in females (OR:1.38, 95% CI 1.12–1.69), and 30% higher odds in White adults (OR:1.30, 95% CI 1.05–1.61). No significant association was observed among males, non-White adults, or across age groups.

CONCLUSION: Higher neighborhood physical disorder was associated with an increased risk of stroke, particularly among females and White adults. Targeting specific aspects of neighborhood physical disorder may mitigate stroke risk and reduce disparities. Future research is needed to further explore the observed differences and mechanisms underlying these relationships.

Keywords: physical disorder, neighborhood environment, stroke, adults, disparities

Cardiovascular

Cardiac Rehabilitation Participation Association with Blood Pressure Trajectories in UCSF Health Patients Joan Shim* Joan Shim Alexis

Importance: Blood pressure (BP) trajectories, or patterns of BP over time, are can identify cardiovascular disease risk. Cardiac rehabilitation (CR) may help improve BP control.

Objective: The main objective of this study is to identify subgroups of individuals with similar BP trajectories and to determine the relationship of BP trajectories with CR among patients at UCSF Health eligible for CR.

Design, Study, and Participants: We analyzed electronic medical records from UCSF Health in this retrospective cohort study, in which participants discharged from UCSF hospitals were selected based on eligibility of CR from September 2019 to January 2023. Group based trajectory modeling was used to determine BP trajectory groups, and we used logistic regression to assess the association between CR participation and BP trajectories, adjusting for age, gender, race/ethnicity, marital status, smoking, and socioeconomic status.

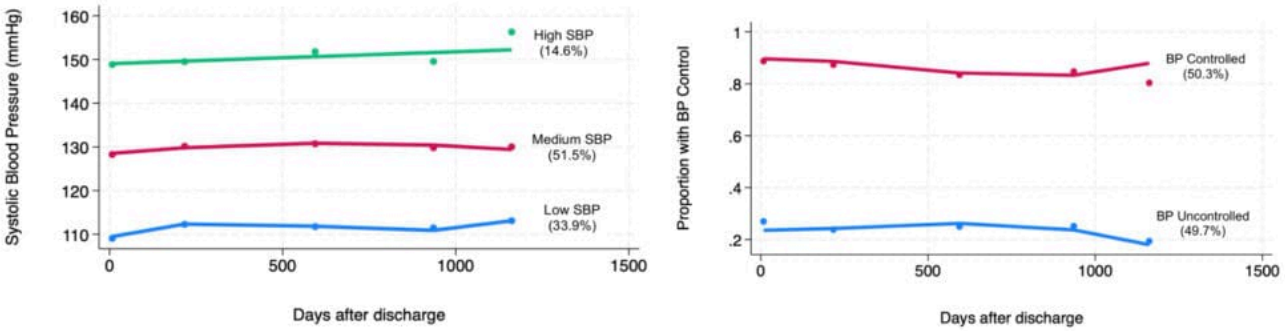
Main Outcomes and Measures: Two or more measurements of systolic BP (SBP) and diastolic BP (DBP) were clinically recorded at least one year after hospital discharge. BP control was defined by BP measurements averaging less than 130/80. CR participation was identified through CPT Code 93797 or 93798.

Results: In 3,282 patients (37% female;mean age 68 years[SD=15];7% CR participation), there were three SBP (Low SBP, Medium SBP, High SBP) and two BP control trajectories (BP Controlled, BP Uncontrolled). Participating in CR was associated with a lower odds of high SBP versus the middle and low SBP trajectories (adjusted OR=0.65;95%CI=0.50,0.85). Participating in CR was associated with a higher odds of controlled BP versus uncontrolled BP trajectory (adjusted OR=1.68;95%CI=1.25,2.25).

Conclusions and Relevance:

Participation in CR has a protective association against high BP and is associated with increased odds of a controlled BP. Future research should focus on how to best incorporate this knowledge into clinical care to reduce the burden of hypertension.

Figure 1. Trajectories in Systolic Blood Pressure and Blood Pressure Control in UCSF Health Patients (N=3,282)



Trajectory classes identified for systolic blood pressure and blood pressure control; their pattern by number of days after being discharged from the hospital, and number of UCSF Health patients in each group.

LATEBREAKER

Cardiovascular

6 years of ARNI use in Israel – effectiveness analysis in real world data Bracha Erlich* Bracha Erlich Ronen Arbel Talish Raz Benita Jean-Marc Weinstein Arie Ben-Yehuda Zaza Iakobishvili Ronit Calderon-Margalit

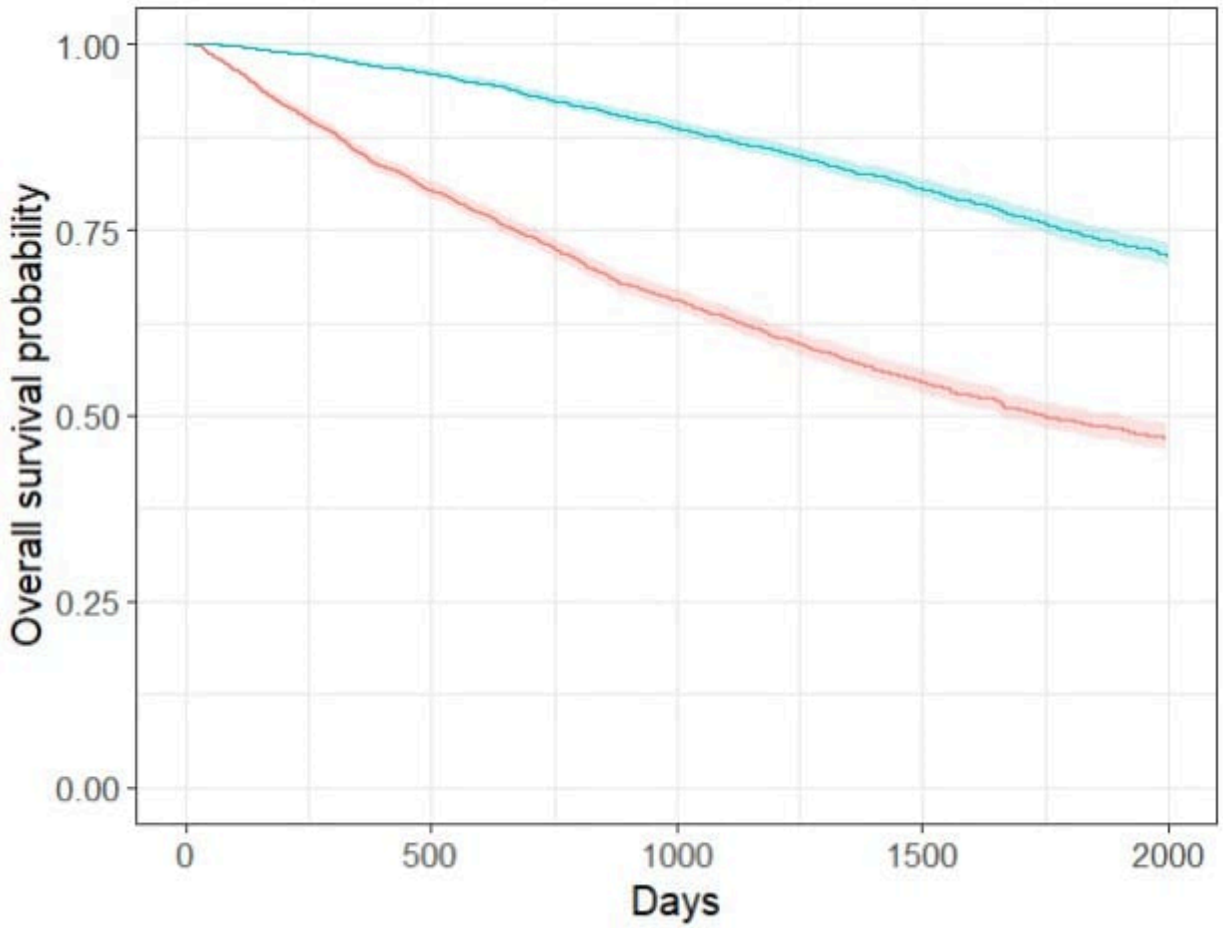
Background: Heart failure with reduced ejection fraction (HFrEF) is a chronic condition associated with high mortality, frequent hospitalizations, reduced quality of life, and significant healthcare costs. Angiotensin receptor-neprilysin inhibitors (ARNI) have shown efficacy in improving outcomes in HFrEF patients. However, only few studies were conducted using real-world data, and long-term associations with mortality and hospitalizations remain to be studied.

Objective: To study the effectiveness of ARNI treatment in HFrEF patients in reducing mortality and hospitalizations over six-years follow-up.

Methods: We conducted a historical cohort study, using data from Clalit Health Services, Israel's largest healthcare provider. We included HFrEF patients aged≥40 years, followed from the date ARNI treatments were available in Israel (1/2017) until death, hospitalizations, or 5/2023. ARNI users (n=3,017) were matched 1:1 to non-users using nearest neighbor propensity score, based on sex, age, registry entry, diabetes, and medications. Sensitivity analyses included a whole cohort analysis with time dependent models; 1:1 exact matching based on sex, birth year, and registry entry date; and stratifying the analysis by ACEi/ARB history. Kaplan-Meier survival analyses and Cox models (with and without time varying covariates) were used to compare the risk for death or hospitalizations, yielding HR and 95% CI.

Results: The cohort consisted of 79% men aged 72.4±11.4 years. ARNI treatment was associated with a 26% reduction in mortality risk (HR:0.74, 95%CI:0.66–0.82). No significant reduction was observed in hospitalization rates (HR:0.95, 95% CI:0.85–1.02). Sensitivity analyses yielded similar results with HR for mortality ranging 0.62-0.87.

Conclusion: In this real-world study, ARNI treatment significantly reduced mortality but did not lower hospitalization rates in HFrEF patients. These findings align with clinical trials, and sensitivity analyses confirmed their robustness.


1.00
0.75
0.50
0.25
0.00
Overall survival probability
0
500
1000
1500
2000
Days

LATEBREAKER

Cardiovascular

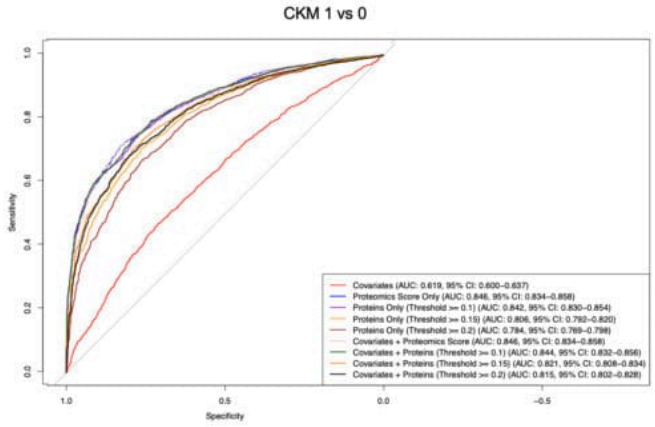
Associations of plasma proteomic signatures of cardiovascular-kidney-metabolic syndrome with incident cardiovascular disease Tong Xia* Tong Xia Liming Liang Jie Hu Meir Stampfer Frank B Hu Danielle E. Haslam Samia Mora Shilpa N Bhupathiraju

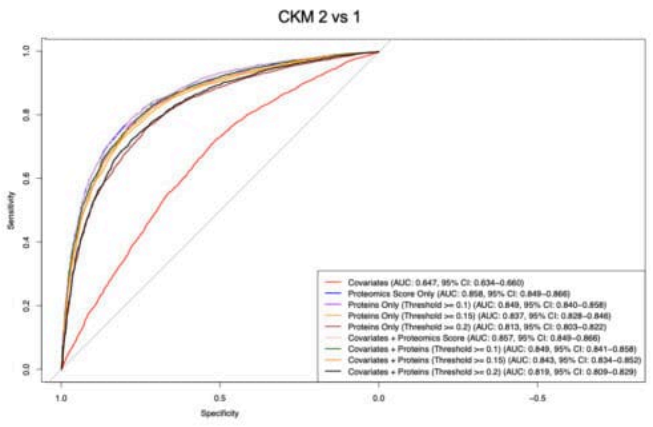
Introduction: Cardiovascular-kidney-metabolic (CKM) syndrome is associated with high cardiovascular disease (CVD) risk. High-throughput proteomics profiling enhances mechanistic understanding and CKM risk stratification.

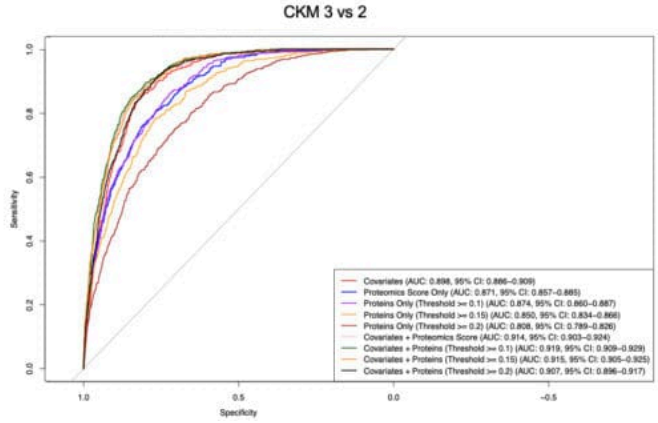
Methods: We analyzed 2,922 plasma proteins (Olink) in 43,254 UK Biobank participants (39–73 y). Participants were classified into CKM stages at baseline: 0 (healthy), 1 (adiposity), 2 (metabolic/kidney risk), 3 (subclinical CVD/kidney disease), and 4 (CVD). Proteomic signatures of CKM (stages 1 vs. 0, 2 vs. 1, 3 vs. 2, and 4 vs. 3) were identified via elastic net regression. Protein-protein interaction network analyses followed. ROC curves compared traditional risk models (age, sex, race, deprivation index, alcohol, physical activity; excluding other risk factors which were in CKM definition) with predictive models incorporating proteomics. Cox regression examined associations of proteomic signatures and network clusters with incident CVD. Bonferroni correction set statistical significance at $P < 0.05$.

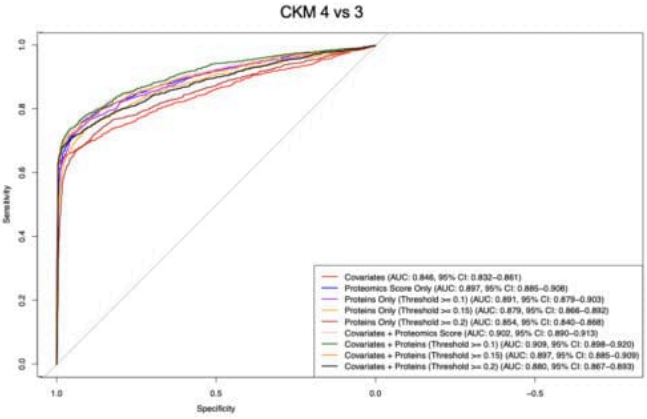
Results: We identified four CKM proteomic signatures with 99, 159, 42, 109 proteins for CKM stages 1 to 4. Key pathways included adipocytokine signaling (CKM 1 vs. 0), renin-angiotensin/angiogenesis (CKM 2 vs. 1), coagulation (CKM 3 vs. 2), and lysosomal function (CKM 4 vs. 3). Integrating 4 proteomic signatures with traditional covariates improved CKM prediction over covariates alone. All 4 proteomic signatures [HR (95% CI) CKM 1 vs. 0: 1.39 (1.07–1.80); CKM 2 vs. 1: 1.43 (1.28–1.61); CKM 3 vs. 2: 1.96 (1.72–2.25); CKM 4 vs. 3: 3.02 (2.39–3.80)] were linked to higher incident CVD risk. Among 33 network clusters, 13 were associated with CVD, with top clusters in immune surveillance [1.55 (1.37–1.74)], extracellular matrix-immune remodeling [1.50 (1.30–1.73], and renin-angiotensin [1.48 (1.23–1.79)].

Conclusions: We identified 4 CKM proteomic signatures and 13 clusters of CKM linked to CVD risk, improving CKM prediction beyond traditional risk factors.


CKM 1 vs 0
Sensitivity
Specificity
Covariates (AUC: 0.619, 95% CI: 0.600–0.637)
Proteomics Score Only (AUC: 0.846, 95% CI: 0.834–0.858)
Proteins Only (Threshold >= 0.1) (AUC: 0.842, 95% CI: 0.830–0.854)
Proteins Only (Threshold >= 0.15) (AUC: 0.806, 95% CI: 0.792–0.820)
Proteins Only (Threshold >= 0.2) (AUC: 0.784, 95% CI: 0.769–0.798)
Covariates + Proteomics Score (AUC: 0.846, 95% CI: 0.834–0.858)
Covariates + Proteins (Threshold >= 0.1) (AUC: 0.844, 95% CI: 0.832–0.856)
Covariates + Proteins (Threshold >= 0.15) (AUC: 0.821, 95% CI: 0.808–0.834)
Covariates + Proteins (Threshold >= 0.2) (AUC: 0.815, 95% CI: 0.802–0.829)


CKM 2 vs 1
Sensitivity
Specificity
Covariates (AUC: 0.647, 95% CI: 0.634–0.660)
Proteomics Score Only (AUC: 0.858, 95% CI: 0.849–0.866)
Proteins Only (Threshold >= 0.1) (AUC: 0.849, 95% CI: 0.840–0.858)
Proteins Only (Threshold >= 0.15) (AUC: 0.837, 95% CI: 0.828–0.846)
Proteins Only (Threshold >= 0.2) (AUC: 0.813, 95% CI: 0.803–0.822)
Covariates + Proteomics Score (AUC: 0.857, 95% CI: 0.849–0.866)
Covariates + Proteins (Threshold >= 0.1) (AUC: 0.849, 95% CI: 0.841–0.858)
Covariates + Proteins (Threshold >= 0.15) (AUC: 0.843, 95% CI: 0.834–0.852)
Covariates + Proteins (Threshold >= 0.2) (AUC: 0.819, 95% CI: 0.809–0.829)


CKM 3 vs 2
Sensitivity
Specificity
Covariates (AUC: 0.898, 95% CI: 0.886–0.909)
Proteomics Score Only (AUC: 0.871, 95% CI: 0.857–0.885)
Proteins Only (Threshold >= 0.1) (AUC: 0.874, 95% CI: 0.860–0.887)
Proteins Only (Threshold >= 0.15) (AUC: 0.850, 95% CI: 0.834–0.866)
Proteins Only (Threshold >= 0.2) (AUC: 0.808, 95% CI: 0.789–0.826)
Covariates + Proteomics Score (AUC: 0.914, 95% CI: 0.903–0.924)
Covariates + Proteins (Threshold >= 0.1) (AUC: 0.919, 95% CI: 0.909–0.929)
Covariates + Proteins (Threshold >= 0.15) (AUC: 0.915, 95% CI: 0.905–0.925)
Covariates + Proteins (Threshold >= 0.2) (AUC: 0.907, 95% CI: 0.896–0.917)


CKM 4 vs 3
Sensitivity
Specificity
Covariates (AUC: 0.846, 95% CI: 0.832–0.861)
Proteomics Score Only (AUC: 0.897, 95% CI: 0.885–0.908)
Proteins Only (Threshold >= 0.1) (AUC: 0.891, 95% CI: 0.879–0.903)
Proteins Only (Threshold >= 0.15) (AUC: 0.879, 95% CI: 0.866–0.892)
Proteins Only (Threshold >= 0.2) (AUC: 0.854, 95% CI: 0.840–0.868)
Covariates + Proteomics Score (AUC: 0.902, 95% CI: 0.890–0.913)
Covariates + Proteins (Threshold >= 0.1) (AUC: 0.909, 95% CI: 0.898–0.920)
Covariates + Proteins (Threshold >= 0.15) (AUC: 0.897, 95% CI: 0.885–0.909)
Covariates + Proteins (Threshold >= 0.2) (AUC: 0.880, 95% CI: 0.867–0.893)

LATEBREAKER

Cardiovascular

Adverse Pregnancy Outcomes and Lifetime CVD Risks in Nurses' Health Study II Tiange Liu* Tiange Liu Hanne Vonen Kathryn Rexrode Janet Rich-Edwards

Background: Adverse pregnancy outcomes (APOs), including gestational diabetes (GDM), gestational hypertension (GHTN), preeclampsia (PE), preterm delivery (PTD), and low birth weight (LBW) are linked to higher cardiovascular disease (CVD) risks. However, studies examining multiple APOs in the same population are limited.

Methods: We examined associations between APOs and lifetime CVD risk, including myocardial infarction, fatal coronary heart disease, stroke, and cardiovascular revascularization in Nurses' Health Study II (1989-2017). Cox proportional hazard models adjusted for pre-pregnancy sociodemographic, lifestyle, and clinical factors. Additionally, we assessed if APOs improved lifetime CVD risk prediction beyond established risk factors (race, systolic blood pressure, hypertensive medication use, cholesterol, high density lipoprotein cholesterol, smoking and diabetes) when predicting from age 30 or 40.

Results: Among 59,154 parous women (26.6±4.6 years at first delivery, 94.1% white), 29.4% had ≥1 APO, with 1,524 incident CVD events over 35.6±7.4 years. Each APO was associated with higher lifetime CVD risk: GDM (HR: 1.27 [95% CI:1.03, 1.56]), GHTN (1.84 [1.57, 2.15]), PE (1.60 [1.37, 1.87)), PTD 35-37 weeks (1.18 [1.00, 1.38]), PTD <35 weeks (1.38 [1.09, 1.75]), and LBW (1.31 [1.21, 1.54]). When modeled together, only GHTN (1.62 [1.36, 1.93]) and PE (1.31 [1.11, 1.55]) remained independently associated with CVD. More APO episodes were associated with higher risk: 1.27 (1.11, 1.46), 1.47 (1.25, 1.73), 1.92 (1.60, 2.31) for 1, 2, and ≥3 episodes, respectively. GHTN and PE improved risk discrimination (C-difference: 0.006 [0.002, 0.011]) and re-classification (net reclassification index: 0.034 [0.015, 0.053]), though small in magnitude, when predicting from age 30 but not 40.

Conclusions: Although all APOs individually contributed to higher CVD risk, only hypertensive disorders of pregnancy improved early risk stratification and only among younger women.

LATEBREAKER

Causal Inference

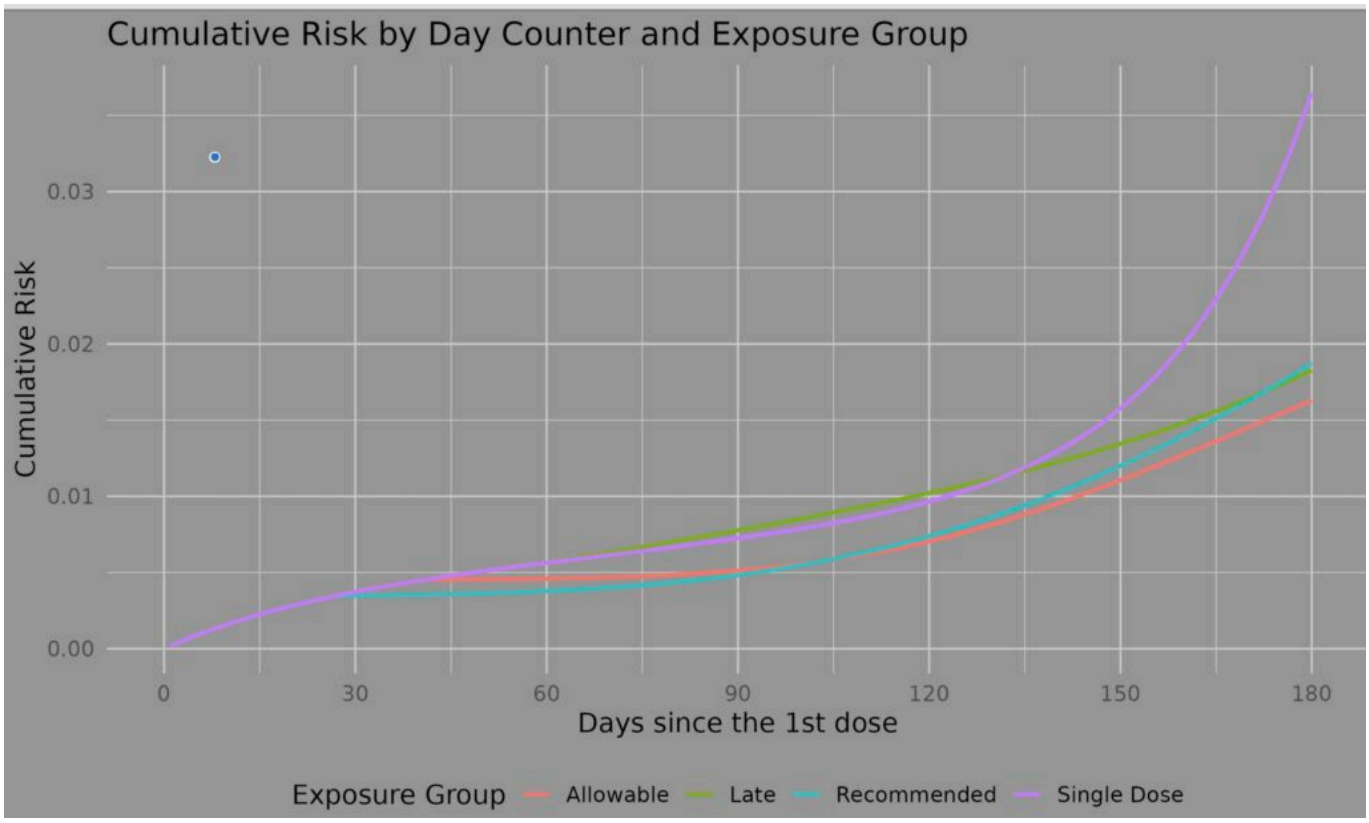
G-computation for the Optimal Timing of the Second Dose Administration of mRNA COVID-19 Vaccines in Georgia in 2020-2022 Heavenlight A Paulo* Heavenlight Paulo Margaret Lind Kayoko Shioda

Background: Interdose intervals between the first and second doses of the primary series of the mRNA COVID-19 vaccines affect effectiveness. Our previous study used clone-censor weight (CCW) analysis within a target trial emulation framework to compare the timing of the second dose administration and found that delaying it by 1-2 weeks would have offered stronger long-term protection. In this study, we applied an alternative method, G-computation, to estimate the comparative effectiveness of dosing schedules using the same dataset.

Method: We analyzed data from the statewide COVID-19 vaccine registry and surveillance from 6110381 individuals in Georgia, USA who received at least one vaccine dose between December 13, 2020 and March 16, 2022. We assessed SARS-CoV-2 infection risk under three timings of the second dose: FDA-recommended (17–25 days after the first dose for Pfizer, 24–32 days for Moderna), late-but-allowable (26–42 days for Pfizer, 33–49 days for Moderna), and late (≥43 days for Pfizer, ≥50 days for Moderna). We estimated optimal timing and reported cumulative risk at 90 and 180 days.

Results: Mirroring the findings from our CCW analysis, the cumulative risk of SARS-CoV-2 infection at 90 days was lowest under the recommended interval protocol (0.5%), followed by the late-but-allowable (0.6%) and late interval protocols (0.7%). By 180 days, the late-but-allowable protocol generated the lowest cumulative risk (1.5%), followed by the recommended (1.8%) and late interval protocols (1.8 %).

Discussion: The alignment of the findings from our analysis using G-computation and CCW highlights the ability of G-computation to serve as an alternative for vaccine dosing schedule evaluation. Evaluating dosing schedules using observational data presents various analytical challenges, including the need to address design biases, and applying multiple approaches may help us enhance the robustness of the conclusions.


Cumulative Risk by Day Counter and Exposure Group
Cumulative Risk
0.03
0.02
0.01
0.00
0
30
60
90
120
150
180
Days since the 1st dose
Exposure Group
Allowable
Late
Recommended
Single Dose

Causal Inference

Comparative effects of generalized time-varying treatment strategies with repeatedly measured outcomes in EHR data Sean McGrath* Sean McGrath Jason P. Block Jessica G. Young

We consider the problem of estimating comparative effects of adhering to certain medication strategies on future weight gain based on electronic health records data. This problem presents several methodological challenges. First, this setting involves time-varying treatment strategies with treatment-confounder feedback. Second, the treatment strategies involve dynamic and non-deterministic elements, including grace periods. Third, the outcome is repeatedly measured (e.g., at each follow-up interval) with substantial missingness that follows a nonmonotonic pattern. Fourth, individuals may die during follow-up, in which case weight gain is undefined after death. In this talk, we describe approaches to estimate comparative effects that address the aforementioned challenges in our setting, which we refer to as time-smoothed inverse probability weighted (IPW) approaches. We conducted simulation studies that illustrate efficiency gains of the time-smoothed IPW approach over a more conventional IPW approach that does not leverage the repeated outcome measurements. We then applied the time-smoothed IPW approaches to estimate effects of adhering to antidepressant medication strategies on future weight gain.

Causal Inference

Analysis of the long-term incidence trend of hypothyroidism with Oral Lichen Planus in Taiwan Yu-Ching Chou* Shih-yi CHen Fu-Huang Lin Chien-An Sun

Chen-Shih Yi1, Fu-Huang Lin1, Chien-An Sun2, Yu-Ching Chou1*

1School of Public Health, National Defense Medical Center, Taipei, 2Department of Public Health, College of Medicine, Fu-Jen Catholic University, New Taipei City, Taiwan
*Corresponding author: trishow@mail.ndmctsgh.edu.tw

Background: Hypothyroidism is a common endocrine disorder characterized by insufficient thyroid hormone secretion, impacting multiple systemic functions. Oral lichen planus (OLP) is a chronic immune-mediated oral mucosal disease potentially associated with thyroid dysfunction. Immune dysregulation is hypothesized to connect these conditions. However, large-scale evidence on their relationship and the role of comorbidities remains limited.
Methods: This descriptive study utilized data from the Taiwan National Health Insurance Research Database (NHIRD) between 2000 and 2013. Approximately 30,260 newly diagnosed cases of hypothyroidism (ICD-9: 2449, 2452) and subsequent occurrences of OLP (ICD-9: 697) were identified. Individuals aged >20 years were included in the analysis, with data stratified by age, sex, and healthcare utilization patterns.Annual incidence rates of hypothyroidism and OLP were calculated per 10,000 individuals. Long-term trends in incidence rates were analyzed using linear trend analysis to assess changes over the 14-year period.
Results: The incidence rate of hypothyroidism among the general population decreased from 11.74 per 10,000 individuals in 2000 to 9.97 in 2013. Conversely, the incidence rate of oral lichen planus (OLP) among hypothyroidism patients increased from 0.71 per 10,000 individuals in 2000 to a peak of 6.30 in 2012 before slightly declining to 5.85 in 2013.Age-specific incidence rates of OLP rose across all age groups from 2000 to 2013, with the highest increase observed among patients aged ≥60 years. The incidence rate among this group showed a steeper rise compared to younger age groups.
Regarding healthcare utilization, patients with more frequent clinical visits for hypothyroidism exhibited higher OLP incidence rates. Specifically, the incidence rates were 6.32 per 10,000 individuals for those with ≤3 visits, 8.44 for 4–37 visits, and 7.62 for ≥38 visits. These findings suggest that higher healthcare utilization may be associated with increased detection of OLP cases..
Conclusion: Over the past 14 years, the incidence of OLP among hypothyroidism patients has increased, particularly in older age groups and those with higher healthcare utilization. These findings emphasize the need for further research to explore the mechanisms linking hypothyroidism and OLP, aiding in the development of prevention and intervention strategies.

Keywords: Hypothyroidism, Oral Lichen Planus, Comorbidity, Immune Regulation.

Causal Inference

Herpes Zoster Vaccine for the Prevention of Dementia: A Target Trial Emulation Using Electronic Health Records Guilin Li* Guilin Li Michael J. Figueroa Muñiz Hanna Gerlovin William Robb Alejandro Szmulewicz Miguel A. Hernán Barbra A. Dickerman

Several observational studies have reported a lower risk of dementia among recipients of the herpes zoster (shingles) vaccine compared with non-recipients. Although the prospect of preventing dementia with a vaccine already recommended for use among adults aged ≥60 years for the prevention of herpes zoster is very appealing, observational studies are susceptible to selection bias (when restricting the analysis to persons who sought health care during follow-up) and confounding due to insufficient adjustment (e.g., for health care-seeking behaviors). As an alternative approach to confounding adjustment, some observational studies have implemented a regression discontinuity design (based on a birth date threshold), but the generalizability of these findings to broader age ranges is unclear.

In this study, we used nationwide electronic health records from the Department of Veterans Affairs, the largest integrated healthcare system in the United States, to emulate a target trial of Zostavax (zoster vaccine live) vaccination and dementia among ~2.5 million eligible individuals (median age 65 years, IQR 12 years) over up to 10 years of follow-up. First, we used inverse-probability weighted pooled logistic regression models to estimate dementia risks, adjusting for baseline and time-varying confounders. Second, we explored the influence of closely matching individuals in each vaccine group according to key confounders. We also evaluated the potential for residual or unmeasured confounding using negative controls and by benchmarking against a randomized trial.

Causal Inference

Standardized Tools for Constructing DAGs: Advancing Causal Inference and Risk Assessment in Pharmaceutical Studies Sherrine Eid* Laura Watson Sherrine Eid

Causal inference and directed acyclic graphs (DAGs) are powerful tools in pharmaceutical research, facilitating analysis of critical questions and decision-making. By visualizing causal relationships, DAGs help identify confounders, mediators, and colliders, guiding the selection of covariates to control confounding and improve causal estimates. They play a role in detecting and mitigating biases, thus improving study design and analysis robustness. For comparative effectiveness research, DAGs clarify causal pathways, supporting the evaluation of treatment effects and drug efficacy and safety. They inform and optimize study designs for randomized controlled trials and observational studies. DAGs support risk assessments by analyzing real-world data for adverse drug reactions and long-term safety. They also support data integration by identifying compatible datasets and combining findings while preserving causal interpretability. Beyond analysis, DAGs are educational tools for communicating causal relationships and informing regulatory decisions and healthcare policies.

Specifically in bias detection, DAGs provide a framework for visualizing relationships among variables to assess potential biases in causal inference. Bias typically arises from three sources: data source (e.g., systematic inclusion/exclusion of subjects or stakeholder influence), study design, and analysis methods. While SAS procedures like PROC ASSESSBIAS address biases from analysis, they overlook biases from data sources and study design. DAGs bridge this gap by identifying biases from all sources, offering a broader understanding of causal inference.

Standardized tools for constructing DAGs would ensure consistency in analysis, enabling reproducible and comparable results across studies. SAS Viya, SAS 9, R, and Python offer strengths and limitations for conducting causal inference and leveraging DAGs in pharmaceutical research. We explore these comparative strength and limitations in this work.

COVID-19 Pandemic

Comparison of survey questions to define Long COVID: implications for prevalence and disparities Jana L. Hirschtick* Jana Hirschtick Nancy L. Fleischer

Background: Survey-based Long COVID estimates vary widely. Although survey mode, sampling approach, setting, and pandemic phase contribute to this variation, how and when the survey questions are asked may also impact Long COVID estimates.
Methods: Using a population-based cohort of adults with confirmed SARS-CoV-2, we compared Long COVID estimates from baseline and follow-up surveys (median of 4 and 18 months after COVID-19 onset, respectively) overall and by race, ethnicity, and sex. We defined Long COVID as: 1) 90-day symptoms at baseline; 2) ever Long COVID at follow-up; 3) current Long COVID at follow-up; and 4) diagnosed Long COVID at follow-up.
Results: In our sample (n=3,826), 17.0% reported 90-day symptoms at baseline. At follow-up, 24.5% reported ever Long COVID, 16.9% reported current Long COVID, and 10.8% reported diagnosed Long COVID. Among adults without 90-day symptoms at baseline, 17.3% reported ever Long COVID at follow-up. Relatedly, among adults with 90-day symptoms at baseline, 31.1% reported they never had Long COVID at follow-up. Further, the use of different survey questions had implications for Long COVID disparities. Although American Indian/Alaskan Native adults had the highest prevalence of 90-day symptoms at baseline (24.5%, 95% CI 16.7-34.4%), Black adults had the highest prevalence of ever Long COVID at follow-up (33.6%, 28.8-38.9%). Also, while Black females and males did not have a statistically different prevalence of 90-day symptoms at baseline (23.9% vs. 21.4%, p=0.607), Black females (vs. males) had a statistically higher prevalence of current Long COVID at follow-up (33.4% vs. 14.7%, p<0.001).
Conclusion: Surveys should employ several questions to define Long COVID and interpret findings within the context of factors that may impact responses, including Long COVID symptom fluctuation, reinfection, awareness, and potential stigma.

COVID-19 Pandemic

Heterogeneity and Duplication in Common Data Elements for the Study of COVID-19 Megan M. Chenoweth* Megan Chenoweth Chloe A. Perry John T. Kubale

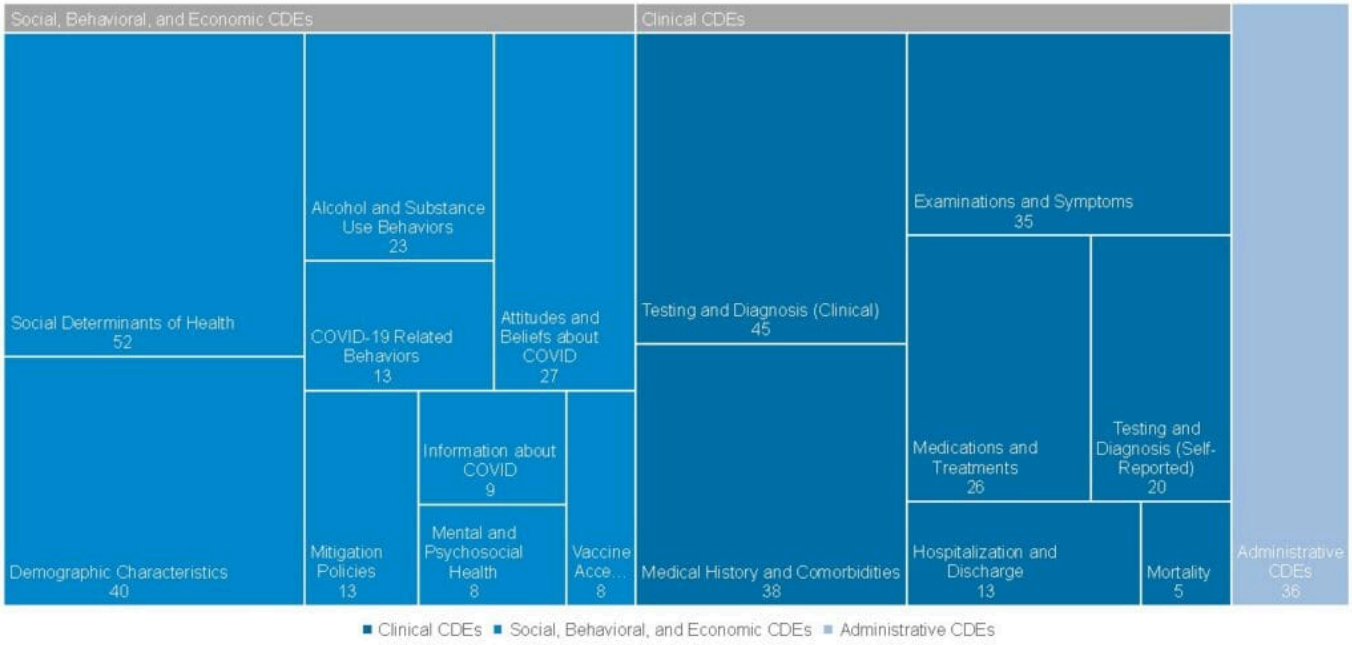
INTRODUCTION: The COVID-19 pandemic has highlighted the importance of consistent shared measures to support comparability of findings across studies. Common Data Elements (CDEs)—standardized questions, variables, or measures with specific sets of responses that are common across multiple studies—are an important tool for this. Since March 2020, researchers have worked to define CDEs related to COVID-19, add them to the National Library of Medicine (NLM) CDE repository, and endorse them according to criteria set forth by the NIH Scientific Data Council. Our aim is to examine CDEs related to COVID, categorize them by topic, and note duplication across sources.

METHODS: We inventoried COVID-related CDEs in the NLM CDE repository, characterizing them by source, endorsement status, and topic. We used topics to identify duplication and heterogeneity across sources. We then manually grouped topics into categories and subcategories that will be validated using textual analysis so that similarities could easily be identified.

RESULTS: We identified 411 COVID-related CDEs from four sources in the NLM CDE repository. CDEs from only two sources (n=138, 33.6%) are endorsed. We noted 80 topics in three categories: clinical (n=182, 29 topics); social, behavioral, and economic (SBE, n=193, 50 topics); and administrative (n=36, not categorized by topic). In 17 cases, there were CDEs from 2-3 sources covering the same topic: two clinical, 15 SBE.

DISCUSSION: Our inventory is the first step toward describing the extent of existing COVID CDEs, as well as the first attempt to demonstrate duplication within topics. The heterogeneity we see suggests a lack of agreement on which CDEs are optimal in which contexts, especially in the SBE domain. This is exacerbated by some CDEs not undergoing endorsement and changes to the endorsement process itself over time. Improved guidance on selecting CDEs could reduce heterogeneity and increase harmonization across studies.

NLM COVID CDEs by Category



LATEBREAKER

COVID-19 Pandemic

Effectiveness of Omicron JN.1 vaccination against SARS-CoV-2 infection in a prospective cohort study in the Netherlands, September 2024 to February 2025 Anne Huiberts* Anne Huiberts Dirk Eggink Hester de Melker Susan van den Hof Mirjam Knol

Introduction: We estimated vaccine effectiveness (VE) of JN.1 vaccination against self-reported SARS-CoV-2 infection between 23 September 2024 and 23 February 2025 among adults who had previously received primary vaccination and at least one booster vaccination.

Methods: JN.1 vaccine-eligible participants (aged ≥60 years, with a medical risk condition and healthcare workers) of an ongoing prospective cohort study (VAccine Study COvid-19; VASCO) were included in the analysis. In VASCO, questionnaire and serology data are collected and self-tests are provided to participants. VE against self-reported SARS-CoV-2 infection was estimated using Cox regression with JN.1-vaccination as time-varying exposure and adjustment for age group, sex, education level, medical risk condition and SARS-CoV-2 infection history. SARS-CoV-2 infection history concerned infections before 23 September 2024 and was based on self-reported positive tests and anti-nucleoprotein antibodies. To compare protection against Omicron variants KP.3.1.1 and XEC, we analyzed whether there was an association between JN.1 vaccination and the variant of infection using logistic regression. The variant of infection was determined by WGS of viral genetic material in positive self-tests.

Results: Of 19,422 included participants who reported to (almost) always test in case of COVID-19-like symptoms, 12,710 reported to have received JN.1 vaccination. During the study period 1,282 infections were reported. VE was 32% (95%CI:2-52) in 18-59-year-olds and 22% (10-33) in 60-85-year-olds. We found no significant difference in protection against KP.3.1.1 (n=250) and XEC (n=187) variants (OR: 1.2; 0.7-2.0).

Conclusion: We showed that, during a study period with low incidence, JN.1 vaccination provided limited added protection in preventing SARS-CoV-2 infection. We found no difference in protection against KP.3.1.1 and XEC variants, which is in line with expectations as variants are closely related to each other.

COVID-19 Pandemic

COVID-19 and maternal substance use during pregnancy Xiaozhong Wen* Xiaozhong Wen Minseon V. Chung Haeni Lee Nayoung Kwak

Objectives. We examined whether e-cigarette, combustible cigarette, marijuana, and alcohol use among U.S. pregnant women were affected by the COVID-19 pandemic.
Methods. In Phase 8 of the U.S. Pregnancy Risk Assessment Monitoring System, we included mothers who gave birth between June 2016 and December 2021 and had data on e-cigarette (N=141,199), cigarette (N=141,466), marijuana (N=51,532), and/or alcohol (N=51,642) use during pregnancy. Logistic regression was used to fit the pre-COVID trend of each substance use from June to September (Jun-Sep) and October to December (Oct-Dec) during 2016-2019. The expected prevalence during the pandemic (2020-2021) was estimated from models and compared with the observed prevalence.
Results. The observed (Obs) prevalence of e-cigarette use was similar to the expected (Exp) prevalence in Jun-Sep (Obs 1.48% vs. Exp 1.50%) and in Oct-Dec (1.93% vs. 1.56%) in 2020, but significantly higher in Jun-Sep (2.27% vs. 1.63% [95% CI: 1.24-2.13%]) and in Oct-Dec (2.51% vs. 1.69% [1.24-2.30%]) of 2021. The observed prevalence of cigarette use was similar to the expected prevalence in Jun-Sep of 2020 (6.29% vs. 5.47%) but significantly higher in Oct-Dec (6.65% vs. 4.60% [3.61-5.84%]) of 2020, Jun-Sep (5.28% vs. 3.74% [2.65-5.25%]) and Oct-Dec (5.15% vs. 2.94% [1.85-4.65%]) of 2021. The observed and expected prevalence of Marijuana use was similar during the pandemic: 4.81% vs. 4.49% in Jun-Sep of 2020, 4.69% vs. 4.47% in Oct-Dec 2020, 4.69% vs. 4.45% in Jun-Spe 2021, and 3.95% vs. 4.43% in Oct-Dec of 2021. The observed prevalence of alcohol use was similar to the expected prevalence in Jun-Sep of 2020 (11.27% vs. 10.48%), Jun-Sep of 2021 (9.96% vs. 10.02%), and Oct-Dec of 2021 (8.54% vs. 9.80%), but significantly higher in Oct-Dec of 2020 (12.44% vs. 10.25% [9.05-11.58%]).
Conclusion. U.S. pregnant women were more likely to use e-cigarettes, cigarettes, and alcohol during the early stage of the COVID-19 pandemic than expected trends.

COVID-19 Pandemic

Exploring the Nutritional Impact of India's First COVID-19 Lockdown: Was it equitable?
Anushka Reddy Marri* Anushka Reddy Marri Madolyn Dauphinais Leonardo Martinez C. Finn McQuaid Pranay Sinha

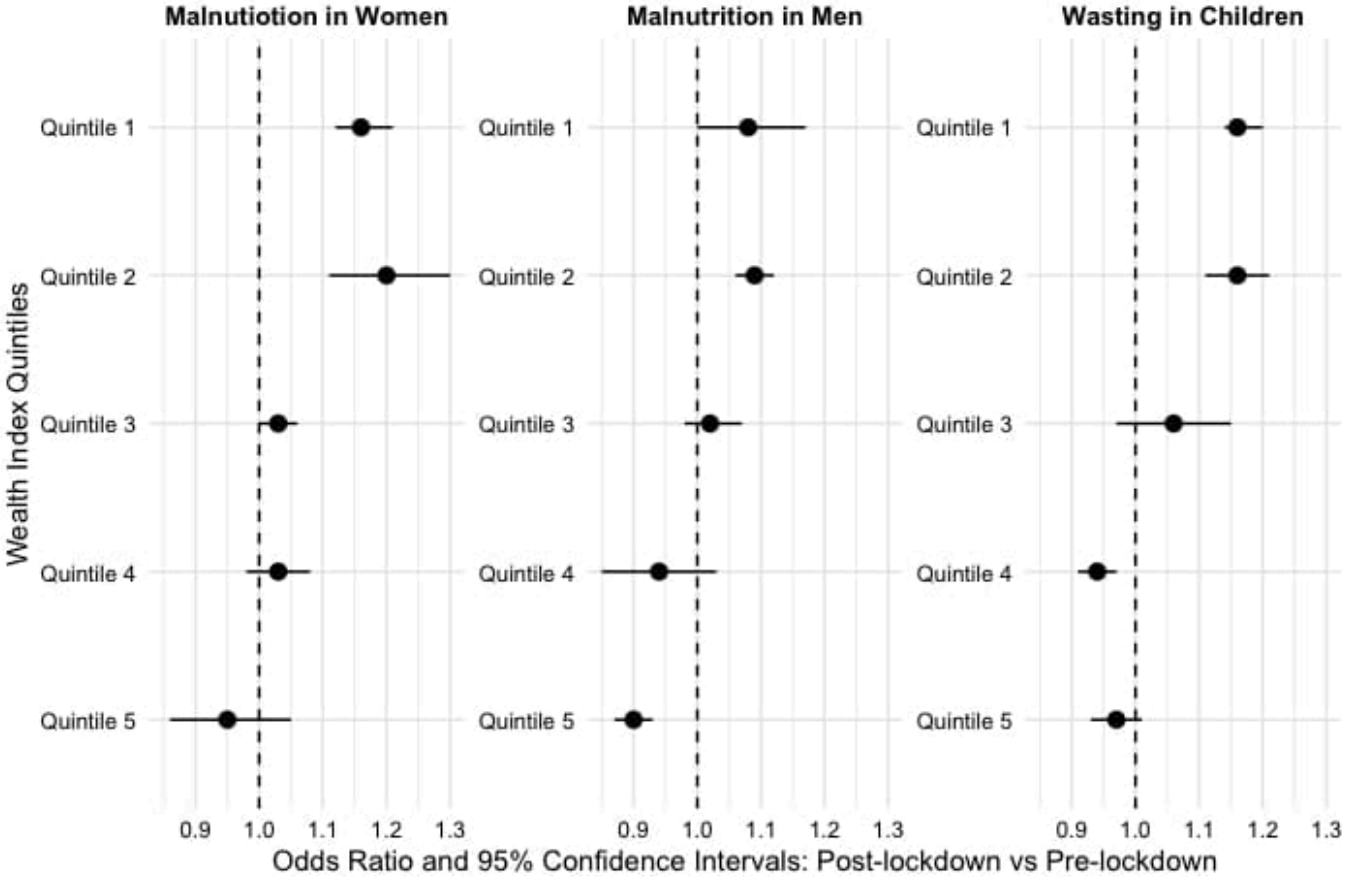
Introduction: The COVID-19 pandemic likely exacerbated nutritional disparities in India. Using data from the 5th National Family Health Survey, we explored the equity impact of the first COVID-19 lockdown on nutritional indicators.

Methods: After stratifying the data into pre-lockdown (June 2019–March 2020) and post-lockdown (June 2020–April 2021) periods, we used logistic regression models to evaluate changes in nutritional indicators (undernutrition, anemia, and wasting) across wealth index quintiles for women, men, and children. We further analyzed these indicators using concentration curves and indices.

Results: Post-lockdown, there was an increase in the prevalence of undernutrition in women (OR 1.05; 95% CI 1.04–1.07) and men (OR 1.07; 95% CI 1.03–1.11) and wasting in children (OR 1.06; 95% CI 1.04–1.09). Stratifying by wealth quintiles, undernutrition increased disproportionately in lower quintiles for women (OR (95% CI): 1.17 (1.14-1.20) in Quintile 1 (Q1); 0.90 (0.87-0.93) in Quintile 5 (Q5)) and men (OR (95% CI): 1.08 (1.01-1.17) in Q1; 0.95 (0.86-1.05) in Q5), as well as wasting in children (OR (95% CI): 1.16 (1.12-1.21) in Q1; 0.97 (0.93-1.01) in Q5) (see figure 1). Anemia prevalence decreased overall, with smaller reductions in Q1 and Q5. The discrepancies by wealth quintiles were evident in concentration curves and indices, highlighting the unequal burden across socioeconomic groups.

Discussion: Our findings highlight increased disparities in nutritional indicators during the COVID-19 pandemic in India, disproportionately affecting the economically disadvantaged. These inequities reflect immediate food insecurity impacts and signal long-term risks for diseases like TB, HIV, and pneumonia, that are worsened by malnutrition. Addressing nutritional inequalities through equitable resource distribution and targeted interventions is critical now, more than ever, to protect vulnerable populations from the ongoing health effects.

Figure 1: Changes in Malnutrition and Wasting by Quintile



Diabetes

Psychosocial Stressors at Work and Type 2 Diabetes Risk in Women and men: 18-Year Prospective Cohort Study of Combined Exposures Mathilde Lavigne-Robichaud* Mathilde Lavigne-Robichaud Mylene Miamdjo Alain Milot Denis Talbot Chantal Brisson Mahée Gilbert-Ouimet Xavier Trudel

Context:

Type 2 diabetes mellitus (T2DM) is increasingly prevalent globally, influenced by traditional risk factors like obesity, hypertension, as well as psychosocial stressors at work (PSW), such as job strain and effort-reward imbalance (ERI).

Methods:

This study analyzed data from 5,915 white-collar workers in the Prospective Quebec (PROQ) cohort, all free of T2DM at baseline and followed for 18 years. Job strain and ERI were measured using validated tools, and T2DM cases were identified via medico-administrative records. Cox proportional hazards models assessed the relationship between PSW and T2DM, adjusting for sociodemographic and clinical factors.

Results:

During the follow-up, 526 new T2DM cases were recorded. ERI was linked to a 30% increased risk of T2DM (HR 1.30, 95% CI 1.07–1.57), while combined exposure to high job strain and ERI raised the risk by 33% (HR 1.33, 95% CI 1.00–1.73). These associations remained significant after adjusting for traditional risk factors.

Conclusion:

ERI separately and in combination with high job strain exposures significantly contribute to T2DM risk. Reducing PSW through workplace interventions could offer substantial public health benefits, improving outcomes beyond T2DM prevention by addressing related health issues.

Diabetes

Association of Hyperinsulinemia and Insulin Resistance with All-cause, Cardiovascular, and Cancer Mortality Among Non-diabetic Americans: The US National Health and Nutrition Examination Survey 1999-2018 Yixun Ke* Yixun Ke Roch A. Nianogo Chuyue Wu

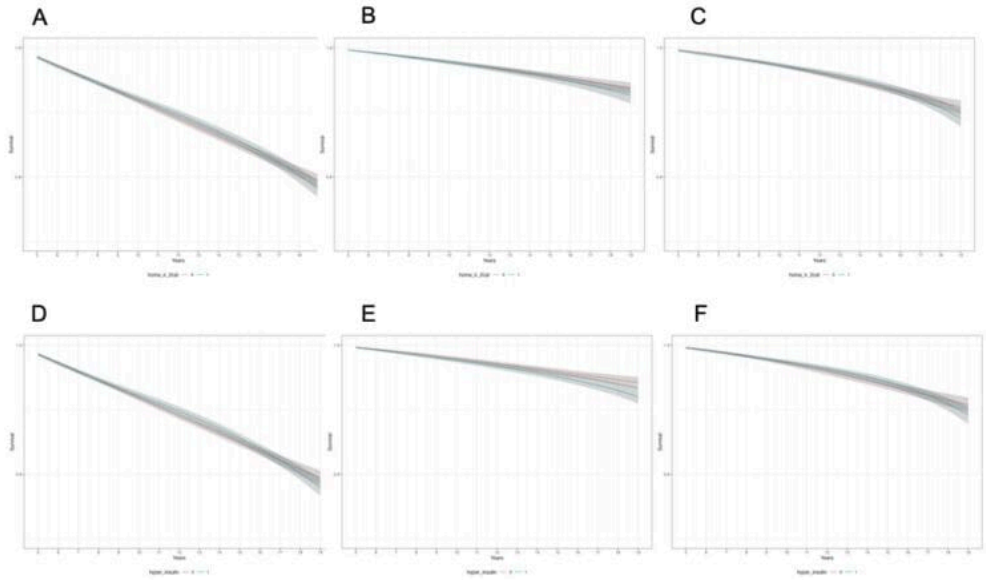
ABSTRACT

Background: The effect of hyperinsulinemia and insulin resistance (HOMA-IR) on mortality outcomes, including all-cause mortality, cancer mortality, and cardiovascular disease (CVD) mortality, remains a topic of interest among non-diabetic Americans with and without obesity. This study examines the impact of hyperinsulinemia and insulin resistance (HOMA-IR) on mortality risks, including all-cause mortality, cardiovascular mortality and cancer mortality in the American population, utilizing NHANES data from 1999-2018.

Methods: This study includes 16,567 individuals from NHANES from 1999 to 2018, involving non-diabetic Americans with and without obesity. Mortality outcomes were ascertained by linkage to the National Center for Health Statistic Survey Data (NCHS). We employed the parametric g-formula to estimate the cumulative incidence of death for participants followed for at least 5 years and 10 years with and without hyperinsulinemia, and each HOMA-IR category. Pooled logistic regression models were used to calculate the HR and 95% confidence intervals (CIs) for all-cause mortality, cancer-cause mortality, and cardiovascular disease (CVD) cause mortality in individuals. We also performed stratified analyses based on age, gender and obesity subgroups.

Results: During a mean follow-up 143 months, a total of 2,316 deaths were documented, of which 711 were due to cardiovascular disease and 574 were due to cancer. Study outcomes reveal a significant relationship between hyperinsulinemia and increased cancer mortality (HR 1.92, 95% CI:1.27-2.88), notably more marked in nonobese subjects (HR 2.03, 95% CI: 1.24- 3.30), without corresponding elevations found in all-cause mortality or cardiovascular disease (CVD) cause mortality. The elevated risks noted in nonobese participants were not mirrored in the obese group across all mortality types.

Conclusion: The insights derived from NHANES data (1999-2018) enhance the understanding of hyperinsulinemia’s and insulin resistance’s role in mortality risks. These patterns highlight the critical role of metabolic health among nondiabetic individuals in mortality risk, emphasizing the importance of personalized interventions on hyperinsulinemia and insulin resistance regardless the presence or absence of obesity.



Adjusted Survival Probability for Mortality With and Without Insulin Resistance/Hyperinsulinemia Among All Participants - Adjusted survival probabilities for all-cause, cancer-cause, and CVD-cause mortality among all participants, highlighting the impact of insulin resistance and hyperinsulinemia: (A) shows survival probability for all-cause mortality with insulin resistance, (B) for cancer-cause mortality with insulin resistance, (C) for CVD-cause mortality with insulin resistance, (D) for all-cause mortality with hyperinsulinemia, (E) for cancer-cause mortality with hyperinsulinemia, and (F) for CVD-cause mortality with hyperinsulinemia.

Diabetes

Diabetes Identification in Self-Reported Population-Based Survey Data Versus Health Administrative Data Divine-Favour Chichenim Ofili* Divine-Favour Chichenim Ofili Amélie Quesnel-Vallée

Background: In the absence of clinical diagnoses, diabetes is identified through self-reported data or algorithmic diagnoses from health administrative data (HAD). Understanding the diagnostic agreement and uniqueness of these sources is key for guiding data selection.

Aim: To evaluate diabetes diagnosis concordance across data sources in Quebec, Canada, and explore sociodemographic and health variations among individuals identified by each source.

Methods: This study used the Care Trajectories-Enriched Dataset (TorSaDE), linking the Canadian Community Health Survey to Quebec's HAD. Individuals aged ≥20 years in the survey and who completed at least one survey wave were included. Those with missing diabetes diagnosis survey responses or suspected gestational diabetes were excluded. Diabetes presence or absence was assessed using both self-reported data and HAD. Group characteristics were compared with ANOVA, chi-square, and post-hoc tests. Age and sex effects were adjusted for using linear and logistic regression.

Results: From 101150 individuals, 10740 (10.6%) were diagnosed with diabetes. Diagnosis concordance was high, as ~65% of individuals with diabetes were found in both sources. In fact, ~90% of those self-reporting diabetes were also algorithmically diagnosed. Individuals with diabetes were generally older, of lower educational status, poorer health, and lower household income than those without diabetes. Significant differences in age, sex, residence, health and healthcare use were found between individuals diagnosed exclusively in each source and those with concordant diagnoses, but their educational and economic status were comparable.

Conclusion: Despite a high concordance between the two data sources, each identifies distinct subpopulations in terms of social and health characteristics. It is best to combine both sources for more comprehensive studies, but if only one is available, results should be interpreted based on the population it best represents

Table 1
Diabetes in self-reported population-based survey versus health administrative data (algorithmic diagnosis)

		Self-reported Diagnosis		Total
		Diabetes absent	**Diabetes present**	
Algorithmic Diagnosis	**Diabetes absent**	90,410 (99.1) (96.8)	782 (0.9) (10.1)	91,192 (90.2)
	Diabetes present	2,998 (30.1) (3.2)	6,960 (69.9) (89.9)	9,958 (9.8)
Total		93,408 (92.3)	7,742 (7.7)	101,150 (100)

Note: Information in each cell follows this order: frequency, row percentage, and column percentage.

Disaster Epidemiology

World Trade Center (WTC) dust exposure and risk of breast cancer among female WTC survivors Ashley Geczik* Ashley Geczik Julia Sisti Mst Afroza Parvin James Cone Janna Metzler Jiehui Li

World Trade Center (WTC) dust from the 9/11 attacks contained many carcinogens, such as polycyclic aromatic hydrocarbons (PAHs), which have been reported to be associated with breast cancer risk. We examined associations between WTC dust exposure and first primary invasive breast cancer among WTC-exposed female survivors who lived, worked, attended school in the exposure area or who were passersby on 9/11, were enrolled in the WTC Health Registry in 2003-2004, and ever lived in New York State (NYS) since the exposure. Breast cancer cases were identified through linkage with the NYS Cancer Registry. WTC dust exposure was assessed with a composite score that accounted for location on 9/11, dust cloud exposure, and exposure to smoke and debris during clean-up. Follow-up began at study enrollment (2003-2004) and ended on the earliest date of first breast cancer diagnosis, death, or 12/31/2020. Multivariable Cox proportional hazards models adjusted for age, race/ethnicity, education, smoking history, and prior medical conditions were used to estimate HRs and 95% CI for associations of quartiles of WTC dust scores and breast cancer. Among 17,434 female survivors in our study sample, 554 were diagnosed with invasive breast cancer over an average of 16 years of follow-up. The median age on 9/11 was 42 years old. The associations between breast cancer and WTC dust exposure were not statistically significant (adjusted HR_Q2: 0.85, 95% CI: 0.64-1.13; HR_Q3: 0.95, 95% CI:0.72-1.26; HR_Q4 0.88, 95% CI:0.66-1.17) when compared to relatively lower level of exposure (Q1). Our findings do not support evidence for a link between WTC dust exposure and breast cancer among female survivors. Surveillance for this and other cancers among survivors is continuing.

Environment/Climate Change

Air pollution and migraine: Same-day and lagged associations of smartphone app attack records following environmental exposures Andrea Portt* Andrea Portt Erjia Ge Christine Lay Hong Chen Peter Smith

Background and aims: Although migraine affects over 1 billion people worldwide, little is known about its environmental triggers. While some research has observed an association between ambient air pollution and migraine events, most studies have been limited to single pollutants and/or relied on emergency-department visit data. Our objective was to estimate the associations between environmental exposures and migraine events captured using a smartphone app in the province of Ontario, Canada.

Materials and methods: Migraine Buddy is a well-established smartphone app with approximately 3 million users worldwide. Environment and Climate Change Canada provided exposure estimates for 2017-2019.

Previous work used statistical methods with pooled data. The case time series is a newly developed modeling technique that harnesses longitudinal individual-level data in relation to multiple environmental exposures Associations between environmental exposures and migraine events were estimated using the case time series method with lagged multi-pollutant models, accounting for demographic covariates.

Results: There were 14,526 migraine attacks reported by 2,989 research-consenting Migraine Buddy participants. On average, participants were more likely to report new migraine attacks on days with relatively higher temperatures or ozone, and on days with relatively large increases in barometric pressure. In contrast, participants were more likely to report new migraine attacks the day after relatively large negative changes in barometric pressure, and the day after relatively high nitrogen dioxide or particulate matter 2.5 exposure.

Conclusion: This is the first study to estimate associations of environmental exposures and migraine using smartphone data and the case time series. Our results demonstrate the application of smartphone data in epidemiologic research, and suggest that this neurologic health outcome may occur with different time lags depending on the exposure.

Environment/Climate Change

Spatial Patterns and Predictors of Illegal Dumping in Mississippi Nina Franzen Lee* Nina Lee Marcos Luna Sarah Kountouris Cristina Nica Erica Walker

Background Illegal dumping of waste is an increasingly difficult problem to solve and persists despite strategies to curb the prevalence. Dumping sites can contaminate soil and water, increase health risks for neighboring communities, and dampen economic investment in already vulnerable areas through visual pollution. Mississippi is an understudied area with a long history of environmental health challenges and injustices that routinely appears at the bottom of state health and economic rankings. **Aim** To identify patterns and drivers of uncontrolled illegal dumping sites across MS at the neighborhood level to better understand this exposure and provide foundational data for future epidemiologic analyses and interventions. **Methods** Publicly available data on illegal dumping sites were combined with sociodemographic and spatial predictors at the site and census block group level. Sites were mapped, and a clustering analysis was performed. Descriptive statistics explore key predictors and outcomes. A negative binomial model was employed to account for the excess variance in the count data. Model selection was guided by AIC, Moran's I, and LRT (p-value: 0.952) and a standard model was used with no spatial lags. **Results** The model has a pseudo R2 of 0.64. Significant predictors include proximity to hazardous waste facilities (positive), number of wood and paper manufacturing facilities (positive), presence of Environmental Justice categories exceeded (positive), higher percentage of group quarters populations (positive), and support from waste tire assistance grants (negative). **Conclusion** There are spatial patterns of illegal dumping in MS potentially aligning with industry, existing policy interventions, and environmental vulnerability. These results suggest that with improvements in illegal dumping data, higher resolution vulnerability predictions can be made, with potential for making progress on much-needed epidemiological studies and assessing policy interventions.

Environment/Climate Change

Temperature and emergency police calls in Phoenix, Arizona Veronica A. Wang* Veronica Wang Ernani Choma Barrak Alahmad John D. Spengler Antonella Zanobetti

Despite mounting evidence of temperature effects on human health, few studies have quantified the impact on municipal emergency services. Even fewer have examined the potential burden on police departments. As part of the Smart Surfaces Coalition program, we investigated whether hotter temperatures measured from weather stations increased police calls in the city of Phoenix, Arizona. Quasi-Poisson regression models, adjusted for seasonality and long-term trends, were fitted separately for the total number of calls. Using police calls data across eight years from 2016 to 2023, we examined calls for violent crimes, nonviolent crimes, car accidents, health, domestic emergencies, and sexual-based emergencies. We considered average day of and prior-day maximum and minimum temperature to gain insight into daytime and overnight conditions, respectively. We found a higher demand for police services during hotter periods. A 5˚C increase in maximum temperature was associated with a 1.1% (95% CI: 0.9%, 1.5%) increase in police calls overall. Higher temperatures were also associated with a greater number of calls related to violent crimes (2.6% [95% CI: 2.0, 3.2%]), health (4.2% [95% CI: 3.3%, 5.0%]), and domestic emergencies (3.1% [95% CI: 2.1%, 4.0%]). Results were similar and oftentimes stronger for minimum temperature, with the addition of elevated calls for nonviolent and sexual-based emergencies. Even in Phoenix, where the climate is hot and dry and residents are presumably well adapted to heat, the number of police calls increased with temperature, and differentiating by call reasons allowed us to also gain insight into the potential drivers. Furthermore, our findings suggest that the inability to cool down overnight should be taken into consideration when allocating resources to emergency police services and for the well-being of the individuals who live, work, and play in Phoenix.

Environment/Climate Change

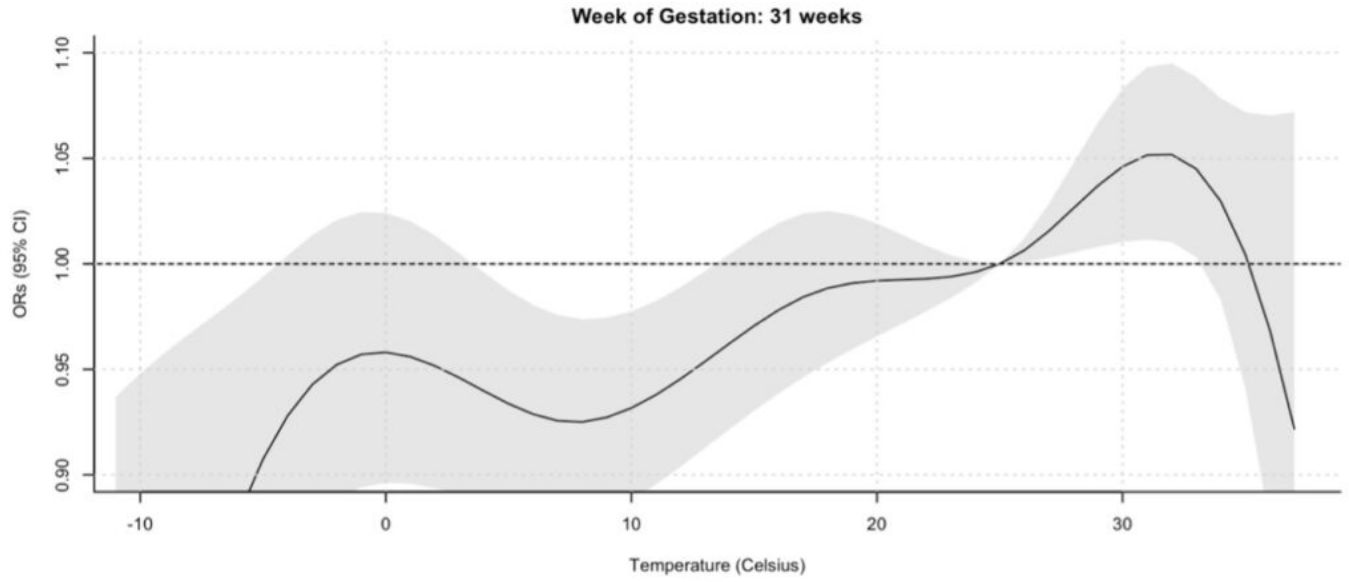
Estimate Joint Effects of Time-varying Air Pollutant Mixtures on Mortality in Canada Using a Novel Methodologic Approach Juwel Rana* Juwel Rana Alexander P. Keil Hong Chen Tarik Benmarhnia Scott Weichenthal Jay S. Kaufman

Background and Objective: Studies have established the association between total PM2.5 mass and mortality in Canada. However, no research has specifically investigated the joint effects of PM2.5 constituents on mortality in the Canadian context. This study examines the joint effects of time-varying PM2.5 constituent mixtures on nonaccidental all-cause and cardiovascular disease (CVD)-related mortality in Canada. Methods and Materials: We developed a novel approach: time-varying quantile g-computation (tvcQGcomp), which estimates the joint effects of increasing all exposures in a quantile across all time points. To evaluate tvcQGcomp, we conducted simulations involving nonaccidental deaths; time-varying black carbon (BC), sulfate (SO_4^{2-}), ammonium (NH_4^+), nitrate (NO_3^-), and organic matter (OM), and both time-fixed and time-varying confounders. We then constructed a population-based cohort involving approximately 3 million adults (ages 25 to 89) from the Canadian Census Health and Environment Cohort (CanCHEC, comprising 3,070,547 observations followed from 2007 to 2019. We estimated annual mean concentrations of BC, SO_4^{2-}, NH_4^+, NO_3^-, and OM using satellite data and a global atmospheric chemistry transport model, assigned by annual postal code. Results: Simulation results show that tvcQGcomp yields unbiased joint effect estimates for time-varying mixtures, with ~95% confidence interval coverage and acceptable type I error rates (5–7%). The correlation among these five PM2.5 constituents ranged from 0.20 to 0.91. We will apply tvcQGcomp to estimate 13-year nonaccidental all-cause and CVD-related mortality risks associated with the time-varying PM2.5 constituents. Conclusion: Our novel approach can elucidate dose-response relationships and effect estimates to better inform composition-specific targeted public health policies across Canada.

Environment/Climate Change

Evaluating the Association Between Ambient Temperature and Small for Gestational Age Outcomes in Pennsylvania Births in 2010 and 2011 Jennifer Ko* Jennifer Ko Jagadeesh Puvvula Kyle Jackson Angela Aherrera Heather Burris Aimin Chen

Heat exposure can trigger adverse health outcomes in pregnant women, increasing dehydration risk and reducing appetite, which may impair fetal blood flow and nutrition. Prior studies often used city, ZIP code, census tract, and 4km/1km resolution temperature data from urban settings. This study used the Pennsylvania state birth registry to examine the association between gestational ambient temperature exposures and small-for-gestational-age (SGA). This study includes 178,428 live births between 2010-2011, with a gestational age of 32-42 weeks, to ensure an adequate sample size within each week. We assigned ambient temperature exposures on a weekly scale from 2 weeks before the mother's last menstrual period until delivery. The exposure assessment was based on the study participants' complete geocoded addresses during pregnancy and ambient temperatures at an 800m resolution from the PRISM climate group. We defined SGA as newborns with birthweight below the 10th percentile stratified by sex and week of gestation. Exposure-outcome associations are modeled using logistic regression within a distributed lag non-linear framework. These associations were adjusted for maternal race/ethnicity, education, marital status, birth year, and maternal smoking. We observed a non-linear association between ambient temperature and SGA during the third trimester. Notably, at 31 weeks of gestation, compared to the reference average weekly Tmax of 25°C, colder temperatures (-10 to -3°C and 3 to 13°C) were linked to lower odds of SGA, while 13 to 25°C showed lower non-significant odds and 25-33°C showed higher odds. Temperatures exceeding 33°C were associated with non-significant odds, with a declining trend potentially explained by protective measures such as spending more time indoors. These measures may reflect risk perception and adaptive behaviors in response to higher temperatures. Future analyses will integrate additional years to improve sample size and precision estimation.



Environment/Climate Change

Early Life Neighborhood Built Environment and Late Life Cognition Justin Farmer* Justin Farmer Peter James Laura D. Kubzansky Rajarshi Mukherjee Ian W. Tang William Kessler Laura T. Germine Marc. G. Weisskopf

Background: Studies suggest living in areas with high walkability and access to greenspace promotes healthier cognition in older adults. However, most studies only consider current exposure to these factors. It is largely unknown if early life exposures are associated with late life cognition. **Methods:** We geocoded childhood (mean age=7) residences of participants in the St. Louis Baby Tooth Study (n = 2,956). Walkability was measured as a composite of mean Z-scores of intersection density and point of interest density from a 1968 street map, and population density from 1960 U.S. Census. Greenspace was measured as mean Z-scores of park density, proportion of census tract composed of parks, and distance to nearest park from the 1968 street map. Higher scores indicated greater walkability and more greenspace. Late life (mean age=63) cognition was measured via a battery of online cognitive tests (TestMyBrain). Linear mixed effects models estimated associations between greenspace/walkability, their components, and cognition, with random intercepts to account for individual and neighborhood clustering. **Results:** Neither composite score (early-life walkability, greenspace) was associated with late life cognition. Models separately looking at each exposure component found intersection density was positively (0.04, 95% CI: 0.00, 0.08) and population density was negatively (-0.06, 95% CI: -0.11, -0.00) associated with late life cognition. **Discussion:** While composites of early life greenspace and walkability were unassociated with late life cognition, two walkability components, intersection and population density, appeared suggestive, but in opposite directions. The nature of the component associations may be why the composite appears unassociated. **Conclusion:** Components of early-life walkability may be relevant for late life cognitive health. While often measured as a composite, it may be important to evaluate associations with individual aspects of this metric.

Table 1: Early-life Neighborhood Resources and Late Life Cognition

Difference in Standardized Global Cognition per SD (95% CI)			
Walkability	**Intersection**	**Population**	**Point of Interest**
0.01	0.04*	-0.06*	0.01
(-0.03, 0.05)	(0.00, 0.08)	(-0.11, -0.00)	(-0.02, 0.05)
Greenspace	**Distance**	**Density**	**Proportion**
0.01	-0.00	0.01	-0.00
(-0.04, 0.05)	(-0.03, 0.02)	(-0.02, 0.04)	(-0.03, 0.03)

Environment/Climate Change

The Association Between Temperature and Cardiovascular Death by Housing Type in a Japanese Large City Akihiko Narisada* Akihiko Narisada Tomohiro Umemura Nauta Yamanaka Kohta Suzuki

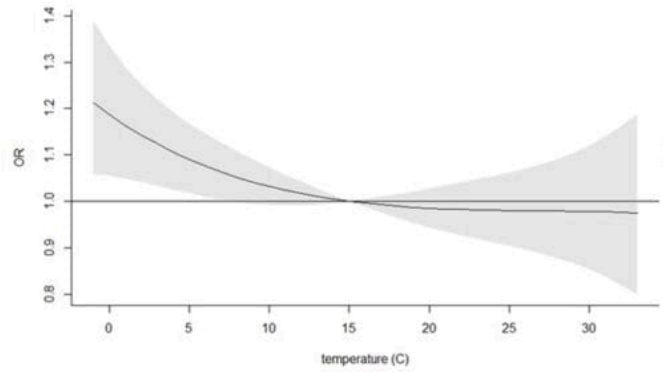
Background: The relationship between temperature and risk of cardiovascular disease death is nonlinear, with risk increasing both in cold and hot temperatures. In the “HOUSING AND HEALTH GUIDELINES”, the World Health Organization recommends improving the insulation performance of houses and using air conditioners appropriately to maintain appropriate indoor temperatures. However, in Japan, many houses, especially detached houses, still have poor insulation performance. In addition, it is thought that some people, especially those living in apartment buildings, are unable to use air conditioners appropriately for economic reasons. Therefore, it is possible that the risk of cardiovascular death due to temperature differs depending on the type of house. The aim of this study is to examine the relationship between temperature and emergency transport for cardiovascular disease by housing type in a Japanese large city.

Methods: The study included cases in which patients were transported by ambulance from houses due to cardiovascular disease or death between April 2016 and March 2022 in Nagoya city, a city with a population of 2 million located in central Japan. Using a time-stratified case-crossover design, we calculated the risk of transport due to cardiovascular disease using a nonlinear model (distributed lag nonlinear model) with a mean temperature of 15°C as the reference.

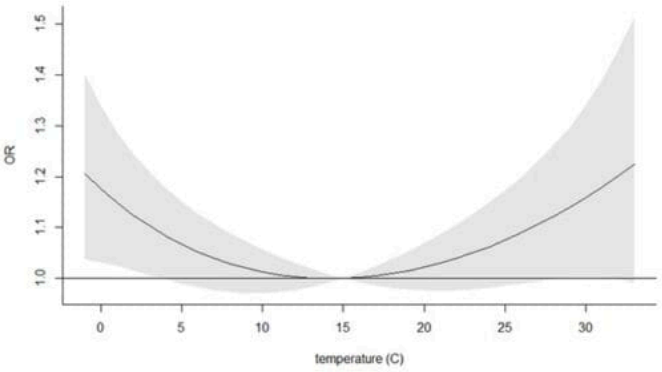
Results: There were 31,047 cases (16,926 in detached houses and 14,121 in apartment buildings). Regarding cold, the risk of emergency transport due to cardiovascular disease increased significantly with decreasing temperature in both detached houses (risk of 3℃: RR: 1.12, 95% CI: 1.03-1.21) and apartment buildings (RR: 1.10, 95% CI: 1.01-1.21). On the other hand, regarding heat, no increase in risk was observed in ordinary houses (risk of 30°C : RR: 0.98, 95% CI: 0.85-1.12), but the risk increased significantly in apartment buildings (RR: 1.16, 95% CI: 1.00-1.34).

Conclusions: We examined the relationship between temperature and emergency transport due to cardiovascular disease by housing type in Nagoya City. The risk of cold exposure was elevated in both types, whereas the risk of heat exposure differed by housing type: it was not elevated in detached houses but was elevated in apartment buildings.

The Risk for Temperature



Detached Houses



Apartment Buildings

Environment/Climate Change

The association between hydrogen sulfide exposure and blood pressure in Carson, CA Arbor Quist* Arbor Quist Alexander Silverman Jerry Yuxuan Wu Meredith Franklin Jill Johnston

Hydrogen sulfide (H2S) is a toxic, colorless, odorous, gas known for its “rotten egg” smell. H2S exposure at moderate levels can harm the respiratory, neurological, and cardiovascular systems, and high-level exposure can result in death. Literature on the health effects of low-level H2S exposure is mixed, including literature on the association between low-level H2S exposure and blood pressure (BP). No studies to our knowledge have examined this association using modeled H2S. For this study, we partnered with community organizations in Carson, California, where residents have been concerned about odors and where elevated levels of H2S have been measured. Carson was also the location of a H2S crisis (concentrations reached 7000 ppb) in October 2021. We recruited 265 participants from the Carson area and collected 3 BP measurements for each participant ~1 year post-disaster. We averaged the BP measurements and defined hypertension as >130 mmHg systolic or >80 mmHg diastolic. We modeled H2S across time and space using Extreme Gradient Boosting, incorporating H2S concentrations from 13 ambient stationary monitors, wind speed, wind direction, and distance to refinery, among other variables. Participants were assigned the maximum H2S concentration at their home during the 30 days prior to their study visit. We conducted multivariable linear regression to examine the association between modeled H2S exposure (split into tertiles) and hypertension, adjusting for BMI, smoking status, distance to freeway, sex, age, and use of antihypertension medications. We observed higher odds of hypertension among participants exposed to the highest tertile of H2S (0.6-2.1 ppb) compared to the lowest tertile (0.1-0.5 ppb; OR=1.23, 95% CI: 1.09, 1.39). The association was stronger when restricted to participants who were exposed to >5 ppb H2S during the 2021 H2S crisis (OR=1.38, 95% CI: 1.17, 1.63, N=143). H2S exposure, even at relatively low levels, can increase odds of hypertension.

Environment/Climate Change

Short term fine particulate matter (PM2.5) exposure and "deaths of despair" in Michigan: 2006-2016: a case crossover study Peter S. Larson* Peter Larson Rachel Bergmans Leon Espira

Introduction: Ecological analyses indicate associations of PM2.5 exposure and specific mental health outcomes, but the impacts of individual exposure to air pollutants and broad mental health related mortality are not well understood. This research uses public death records with a case crossover design to assess associations between short term lag exposure to particulate matter 2.5 (PM2.5) and mortality from suicide, alcohol related liver failure and opioid drug overdose.
Methods: Records for all deaths from suicide, alcohol related liver failure, and overdose from 2006 to 2016 were obtained from the State of Michigan. Residential addresses were geocoded, and locations were added to the database. Raster data of daily PM2.5 concentrations at 1km resolution were obtained from the National Aeronautics and Space Administration's (NASA) Socio-economic Data and Applications Center (SEDAC). We extracted PM2.5 measures for 21 days before the date of death. We used a case crossover design, where everyone serves as their own control. Lag associations of PM2.5 and mortality were then tested using stratified regression models within a directed non-linear modelling framework.
Results: There were 49,031 relevant deaths between 2006 and 2016. There were 19,100 suicides, 8,657 deaths from alcohol related liver failure and 21,374 overdose deaths. Patterns of association of exposure to PM2.5 differed between the types of mortality. Risk of suicide had a positive association with PM2.5 exposure, significantly peaking at lag day 7. For alcohol related liver failure, increased exposure to PM2.5 follow non-significant positive associations with mortality. We found no association of PM2.5 exposure with overdose.
Conclusions: Exposure to extreme levels of PM2.5 at 7-10 days is associated with elevated risk for suicide. Future work should work to explore the exact links between air pollution exposure and develop pro-active means to limit exposure or target at risk persons

Environment/Climate Change

Heatwaves and Health System Burden in Santiago: Disparities in Exposure Across Urban Zones (1992 – 2019). Estela Blanco* José Daniel Conejeros Estela Blanco Rayana Palharini Eduardo Undurraga

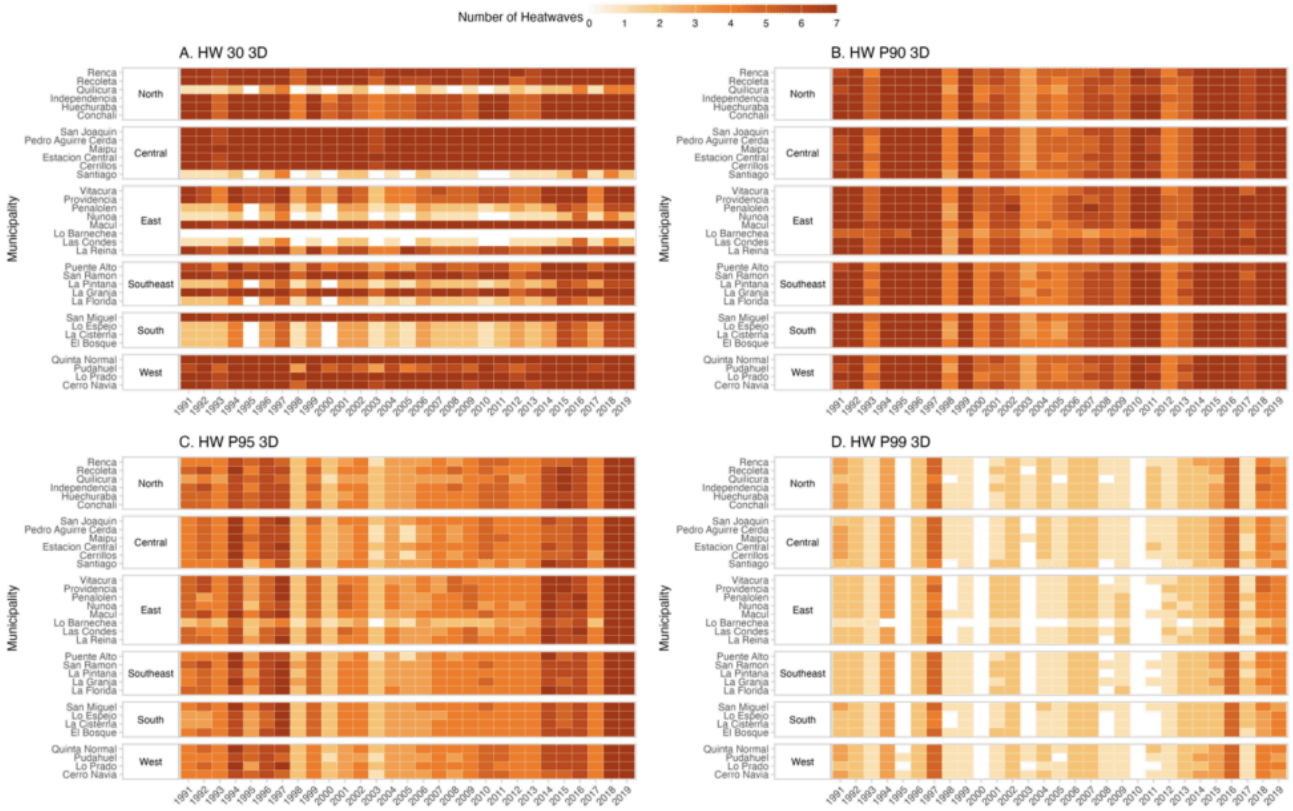
Background: Heatwaves (HWs) have become increasingly frequent and severe due to climate change, posing significant risks to urban populations and health systems. While studies globally have associated HWs with increased hospital admissions and emergency visits, the evidence from South America, particularly urban areas, remains limited. Furthermore, little is known about disparities in HW exposure across health zones within Latin America's major urban centers.

Methods: This study examines the evolution of the health system burden from HWs in Santiago, Chile (1992–2019), and identifies disparities across health zones. Daily maximum air temperature was used to calculate HW metrics: 3 consecutive days exceeding 30°C, 90th, 95th, and 99th percentiles, and the Excess Heat Factor (EHF). Emergency visit data from the Chilean Ministry of Health (DEIS) were aggregated by municipality and year. Distributed lag linear models were applied to assess delayed HW effects.

Results: Preliminary results show temporal and spatial variability in HW exposure, with more frequent events in eastern and southern Santiago. Municipalities like Quilicura, Estación Central, and Cerrillos experienced up to 3 consecutive days above the 95th percentile (Figure 1). These vulnerable zones faced higher burdens during HWs, especially using EHF metrics, and showed the largest increases in emergency visits, with an RR of 1.21 (95% CI: 1.05–1.37). Findings highlight inequities in exposure and health outcomes, urging targeted interventions.

Conclusions: Our findings underscore the need for targeted public health interventions to mitigate the impacts of HWs, particularly in socioeconomically vulnerable areas. Incorporating diverse HW metrics, including air and land temperatures and radiation, provides a more comprehensive understanding impacts of extreme events on urban populations. This study highlights the importance of addressing climate-related health disparities as cities face increasing HW frequency.

Figure 1. Heatwave Exposure across municipalities and by heatwave definition and Year in Santiago, Summer 1992-2019.



Abbreviations: HW=heatwave. The summer period corresponds to November and December of the current year, combined with January, February, and March of the following year. Heatwave metrics (HW) correspond to the number of heatwaves lasting at least 3 consecutive days by four definitions: 30º celsius, temperature maximum centile 90th, 95th, 99th.

Environment/Climate Change

Air pollution and postpartum psychological dysfunction symptoms: the interplay with prenatal stress. Gary Joseph* Gary Joseph Megan Niedzwiecki Itai Kloog Allan C. Just Rosalind J. Wright Ivan.Gutierrez-Avila Elena Colicino Martha María Téllez Rojo Robert O. Wright Lauren M. Petrick

Background: Postpartum depression (PPD) is a global health issue that impairs a mother's ability to care for herself or her baby. Ambient air pollution (PM2.5) has been associated with PPD in Hispanic women, but the modifying role of psychosocial stress on this relationship is unclear. We also assessed the modifying role of prenatal stress in this relationship.

Methods: We assessed the association between prenatal PM2.5 exposure and psychological dysfunction (PPD, anhedonia, anxiety, and depression) at 6 months postpartum using PROGRESS cohort data (n=457 mothers). Daily residence level PM2.5 estimates were generated from our hybrid satellite-based machine learning model, and averaged over pregnancy. Psychological dysfunction was assessed using the Edinburgh Postnatal Depression Scale (EPDS) at 6 months postpartum. Modified Poisson regression evaluated the association between PM2.5 and PPD (EPDS≥13), stratified by negative life events (NLEs) and perceived stress score (PSS), dichotomized around the median (low/high). Negative binomial regression was used for EPDS subscales (anhedonia, anxiety, and depression).

Results: A 5-µg/m3 increase in average prenatal PM2.5 exposure was associated with an increased risk of overall PPD (RR: 1.48, 95%CI: 1.02-2.17), and new onset of PPD (RR: 2.55, 95%CI: 1.27-5.12) at 6 months. Stratifying PPD risk by NLE and PSS scores showed increased overall PPD risk per unit increase in PM2.5 in low-PSS subgroups and new-onset PPD in high-NLE and low-PSS subgroups. PM2.5 was positively associated with EPDS subscales of anhedonia and depression, with greater risk in low-PSS subgroups.

Conclusion: Prenatal PM2.5 exposure is associated with an increased risk of postpartum psychological dysfunction symptoms, especially in those with low-PSS or high-NLE scores. These findings highlight the need for interventions addressing both air pollution and prenatal stress to prevent adverse postpartum mental health outcomes.

LATEBREAKER

Environment/Climate Change

The role of particulate radioactivity on the impacts of PM2.5 and its long-term effects on hospitalizations related to neurodegenerative disorders with causal mediation analysis: a national retrospective cohort study in the USA Shuxin Dong* Shuxin Dong Shuxin Dong Marc Weisskopf Petros Koutrakis Brent Coull Longxiang Li Antonella Zanobetti

Objective: Neurodegenerative disorders – particularly Alzheimer's Disease (AD) and Parkinson's Disease (PD) – pose a major global public health challenge. In the absence of effective treatments, identifying and mitigating modifiable risk factors, such as PM2.5 exposure, is crucial. Although PM2.5 has been linked to neurodegeneration, its toxic properties remain poorly understood. We propose that particulate radioactivity (PR), which primary source is radon gas and its decay products, may be a key contributor to PM2.5's neurotoxic effects. We also proposed that PR itself, as an environmental exposure, has effects on neurodegenerative disorders. In this study, we aim to (1) estimate the long-term effects of PR on Alzheimer's disease and related dementias (ADRD) and PD, and to (2) assess the extent to which PR contributes to PM2.5's toxicity on ADRD and PD.

Methods: We assembled a nationwide retrospective cohort of all Medicare fee-for-service beneficiaries aged ≥65 in the contiguous USA from 2000 to 2016, following individuals from enrollment until their first hospitalization with ADRD or PD. Annual average gross beta activity (as a proxy of ambient PR concentrations) was estimated at each individual's residential ZIP code, and annual average PM2.5 and radon levels were similarly calculated to control for confounding. We utilized time-varying Poisson survival analysis to estimate the long-term effects of PR on health outcomes. To assess the contribution to PM2.5's toxicity, we employed a causal mediation framework – first, we used a Poisson survival model with PR and PM2.5, adjusting for age, socioeconomic status, seasonal temperature, and relative humidity.Next, a linear mediator model was used to assess PR and PM2.5's relationship. Natural direct and indirect effects of PM2.5 were then calculated and reported as incidence rate ratios (IRRs) with bootstrap-derived standard errors.

Results: The cohort comprised 68,640,730 individuals, with 7,108,045 (10.4%) hospitalized for ADRD and 1,019,099 (1.5%) for PD during the study period. Average follow-up was 8.10 years (SD 5.00) for ADRD and 8.26 years (SD 5.03) for PD hospitalizations. A significant association was observed between PR and both outcomes; an interquartile range increase in PR (0.0025 mBq/m^3) corresponded to an IRR of 1.033 (95% CI 1.031–1.034) for ADRD and 1.030 (95% CI 1.027–1.034) for PD. For an interquartile range increase in PM2.5 (3.8 $\mu g/m^3$), the ADRD analysis yielded a natural direct effect IRR of 1.034 (95% CI: 1.032–1.035) and an indirect effect IRR of 1.008 (95% CI: 1.006–1.035), indicating that 19.7% of the effect was mediated by PR. In the PD analysis, the natural direct effect was 1.050 (95% CI: 1.048–1.052) and the natural indirect effect 1.005 (95% CI: 1.002–1.008), with 9.7% mediation.

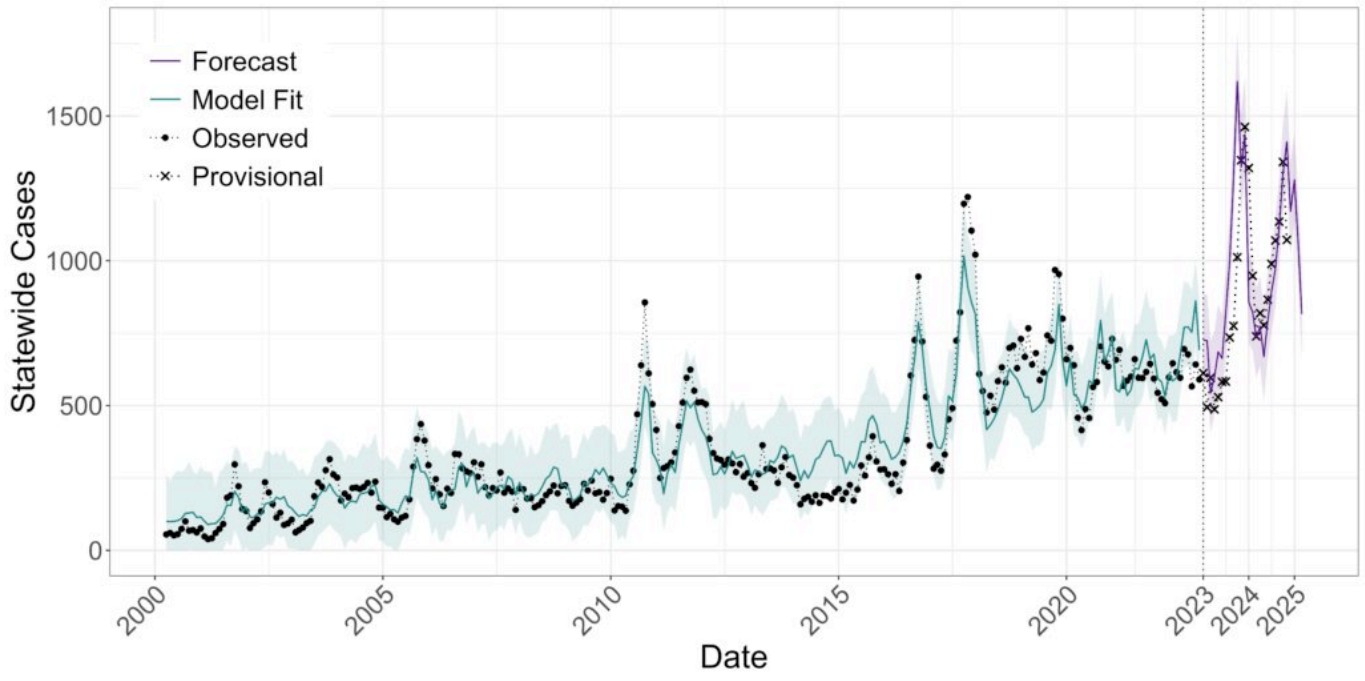
Conclusions: These findings provide novel evidence that long-term exposure to particulate radioactivity is associated with an increased risk of hospitalization for ADRD and PD, highlighting the role of environmental factors in neurodegenerative disease risk. Moreover, our results suggest that PR significantly contributes to PM2.5 toxicity, with a more pronounced mediating effect on ADRD than on PD.

LATEBREAKER

Environment/Climate Change

Forecasting the impact of hydroclimatic swings on coccidioidomycosis incidence in California Simon Camponuri* Simon Camponuri Alexandra Heaney Gail Sondermeyer-Cooksey Duc Vugia Seema Jain Daniel Swain John Balmes Justin Remais Jennifer Head

Coccidioidomycosis, or Valley fever, is an infectious disease caused by inhalation of Coccidioides spp., fungi found primarily in soils of the southwestern United States. Prior work showed that coccidioidomycosis cases in California sharply increase by nearly 2-fold following wet winters that occur one- and two-years following drought. Statewide drought between 2020-2022 followed by heavy precipitation during the 2022-2023 winter raised concerns over potential increases in coccidioidomycosis cases in the fall of 2023, prompting California Department of Public Health (CDPH) to issue public health alerts. As anticipated, California saw a near record number of cases in 2023, with 9,054 provisional cases reported. During the 2023-2024 California wet season, precipitation was 115% the long-term average, furthering concerns about continued high coccidioidomycosis risk. We developed an ensemble prediction model consisting of five candidate prediction algorithms relating monthly reported cases per census tract in California to climatological or environmental predictors. Using this model, we predicted a total of 11,846 cases (90% PI: 11,224–12,456) in California between April 1, 2023, and March 31, 2024, closely aligning with the preliminary state report of 10,519. Our model forecasted 12,244 cases (90% PI: 11,638–12,917) statewide between April 1, 2024, and March 31, 2025 — a 62% increase over the cases reported during the same period two years prior, and on par with the high incidence seen in 2023. Our model forecasts that disease incidence will exhibit pronounced seasonality with cases beginning to rise in June and peaking in November at 1,411 (90% PI: 1,076–1,396) cases statewide – 98% higher than the peak two years prior and nearly as high as the peak in 2023. Near-term forecasts have the potential to inform public health messaging to enhance provider and patient awareness, encourage risk reduction practices, and improve recognition and management of coccidioidomycosis.



LATEBREAKER

Environment/Climate Change

Ecological study Examining Correlations Between County-Level Days Flooded and Incidence of Flood-Related Diagnoses Dhitinut Ratnapradipa* Kevin Boes Jack H. Taylor Joy Doll Timothy Guetterman Dhitinut Ratnapradipa Lillia Cherkasskiy

Flood events have significant effects on community health. In addition to injuries in the immediate aftermath of a flood, environmental hazards such as drinking water contamination, compromised food storage, and decreased air quality can result in increased risk of flood-related illnesses such as gastrointestinal illness, respiratory infections, and COPD. While associations between such factors have been documented at the macro level, micro- or local associations have been less studied. To examine how flood events impact incidence of the above illnesses at such scales, we conducted analysis aiming to determine whether cross-correlation existed between trends in county-level daily flooding and incidence of the above illnesses. Data for diagnoses were obtained from the Nebraska Hospital Association for all inpatient and outpatient diagnoses in Nebraska hospitals from March 2018 to March 2023, and data for flood warnings were obtained from National Weather Service data processed into csv format by the Iowa Environmental Mesonet. Flood warning data were obtained for warnings occurring in Nebraska and its adjacent states from March 2018 to March 2023. Both diagnosis data and flood warning data were geocoded to a county and processed into a netCDF format for use in spatiotemporal analysis. Diagnoses were normalized against 2020 US Census population estimates to produce county-level incidence of each diagnosis. The resulting dataset was analyzed using time series cross-correlation analysis within ArcGIS Pro 3.4. The dependent variables are county-level incidence of inpatient and outpatient gastrointestinal illness, respiratory infections, and COPD. The explanatory variable is county-level daily flooding. Results include Pearson’s correlation coefficient for each county as well as lag measurements for time lags producing the strongest positive, negative, and absolute correlations between the trends in flooded days and incidence of diagnoses. These results have implications for prioritization of health education resources in preparation for flood events. Future research may include follow-up analyses investigating characteristics of counties with strong or weak correlations to determine local-level protective and risk factors.

Environment/Climate Change

Medium-term exposure to wildfire smoke PM2.5 and cardiorespiratory hospitalization risks

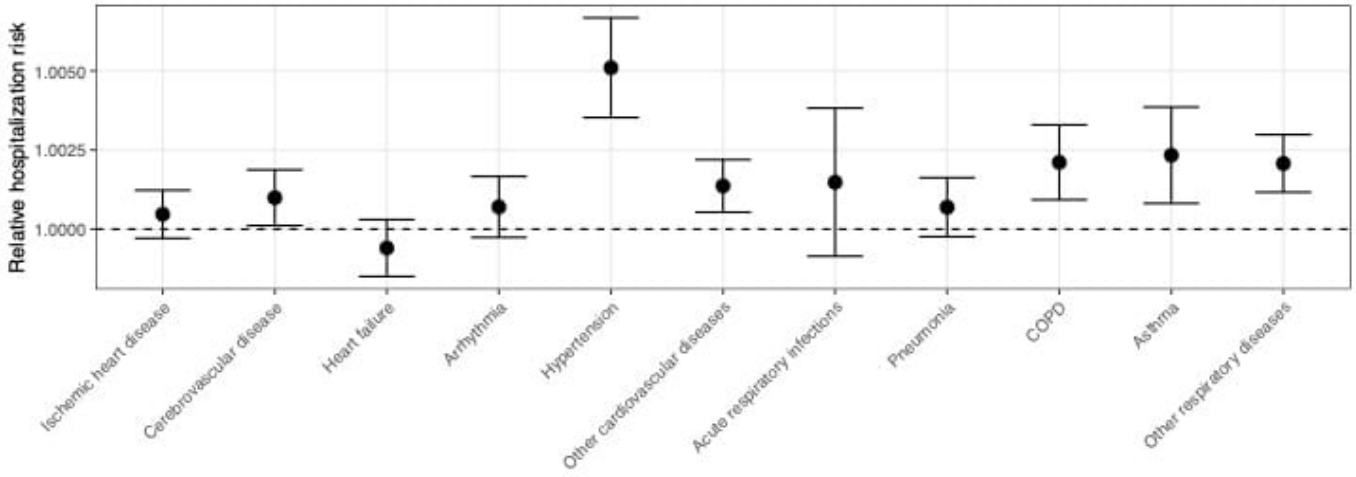
Yaguang Wei* Yaguang Wei Edgar Castro Kanhua Yin Alexandra Shtein Bryan N. Vu Mahdieh Danesh Yazdi Longxiang Li Yuxi Liu Adjani A. Peralta Joel Schwartz

Background: Wildfire activity in the US has increased significantly in recent decades. Smoke PM2.5, a primary wildfire emission, can spike for months after a wildfire begins, yet large-scale evidence of its health effects remains limited.

Methods: Hospitalization records for the residents of 16 US states between 2006–2016 were obtained from the State Inpatient Databases. Daily smoke PM2.5 at 10 km2 grid cells across the contiguous US were estimated using a machine learning model that incorporated ground, satellite, and reanalysis data, and were aggregated to ZIP codes to match the spatial resolution of the hospitalization records. We developed a novel self-controlled design, a case-crossover variant, to examine associations between 3-month average exposure to smoke PM2.5 and hospitalization risks for a comprehensive range of cardiovascular (ischemic heart disease, cerebrovascular disease, heart failure, arrhythmia, hypertension, other cardiovascular diseases) and respiratory diseases (acute respiratory infections, pneumonia, COPD, asthma, other respiratory diseases). We further assessed effects of single-month lagged exposures and explored subgroup differences based on neighborhood- and individual-level characteristics.

Results: We found that 3-month average exposure to smoke PM2.5 was associated or marginally associated with increased hospitalization risks for most cardiorespiratory diseases. Results for single-month lagged exposures suggested that these effects persisted up to 3 months after exposure. Subgroup analyses showed larger effects in neighborhoods with higher deprivation levels or greater vegetation, as well as among ever-smokers.

Conclusions: Our findings provided unique insights into the medium-term cardiorespiratory effects of smoke PM2.5, which can persist for months, even after a wildfire has ended.


Relative hospitalization risk
1.0050
1.0025
1.0000
Ischemic heart disease
Cerebrovascular disease
Heart failure
Arrhythmia
Hypertension
Other cardiovascular diseases
Acute respiratory infections
Pneumonia
COPD
Asthma
Other respiratory diseases

Environment/Climate Change

Maternal Early-pregnancy and Newborn Prenatal Exposure to Hg, Mn, Se and Zn and Child Neurodevelopment Development in the First 24 Months: A Prospective Cohort Study

Fengxiu Ouyang* Fengxiu Ouyang Ting Zhang Yichun Xuan Yanlin Li Jinqian Ma Junxia Liu Chong-Huai Yan Jun Zhang

There is limited information on the joint effect of multiple-metal(loid)s on infant development. This study aimed to investigate the joint impact of early pregnancy and newborn exposures to mercury (Hg), selenium (Se), manganese (Mn) and zinc (Zn) on child neurodevelopment in the first 24 months. Included were 2771 mother-infant pairs from the Shanghai Birth cohort who had Hg, Mn, Se and Zn measured in early pregnancy maternal and cord blood samples. These elements were analyzed as both categorical in tertiles and log-transformed continious variables. Neurobehavior was assessed using the Ages and Stages Questionnaire, 3rd edition (ASQ-3) and the ASQ: Social-Emotional (SE) instrument at the age of 6 months, and Bayley Scales of Infant & Toddler Development, 3rd edition (BSID-III) at the age of 24 months. Using multiple linear regression, maternal blood Hg levels > 2.09μg/L were associated with 1.78 points higher ASQ:SE scores (95%CI: 0.22, 3.33; P < 0.05), and 1.20 points lower ASQ-3 communication scores (95%CI: -2.06, -0.35; P 5.62μg/L was associated with 2.74 points higher cognition score (95%CI 0.53, 4.94; p<0.05) at age 24 months. Similar results were observed by using Bayesian kernel machine regression (BKMR) with the four elements adjusted for each other. Overall, the maternal blood metal mixture was negatively associated with infant ASQ-3 communication scores at the age of 6 months, with Mn being identified as the dominant (cond PIP = 0.998) element with an inverse “U” shape association. Associations between maternal blood metal mixtures of Hg, Mn, Se and Zn with infant 24 months outcomes were found not significant. Our study findings suggest that maternal blood Hg concentrations, and the metal mixture in early pregnancy adversely impact infant neurobehavior development at the age of 6 months.

Environment/Climate Change

The Influence of Temperature in Age-Specific Mortality Associated with Ozone Exposure

Satbyul Estella Kim* Satbyul Estella Kim

The convergence of rising temperatures, increasing ozone levels, and a significantly aging population presents multiple threats to public health in Japan. Thus, this study investigated the influence of temperature on the mortality effects associated with ozone exposure across all regions in Japan (Hokkaido, Tohoku, Kanto, Chubu, Kansai, Chugoku, Shikoku, and Kyushu and Okinawa) and age groups (0–65, 65–75, and 75 years and above). We performed a two-stage analysis to examine the short-term associations between ozone exposure and mortality at different temperature levels across 47 prefectures, with a focus on the warmer months (June–September) from 2009 to 2019. First, we estimated the prefecture-specific associations using a comprehensive nationwide time-series dataset with a distributed lag nonlinear model. Subsequently, we used a multivariate meta-regression model to determine regional and national associations. A 10-ppb rise in ozone levels nationwide was significantly associated with a 0.44% (95% confidence interval [CI]: 0.26, 0.62) increase in all-cause mortality during the warmer months. Despite the heterogeneity in the degree of estimates, we observed an increasing trend in ozone-related mortality with higher temperature levels in all regions. Our findings from the age group stratification analysis imply that individuals aged 65 and older are more susceptible to ozone exposure with increasing temperature, as evidenced by a statistically significant increase in ozone-related mortality when the temperature reaches the 60th percentile, whereas individuals under 65 years of age show a significant increase at the 70th percentile. The study findings provide an avenue for future research to mitigate the adverse health effects of climate change and air pollution by developing targeted interventions that address the compounded risks of high temperatures and elevated ozone levels, particularly for vulnerable populations such as the elderly, in order to reduce the burden of ozone-related mortality in the context of global climate change.

Environment/Climate Change

Impact of arsenic exposure on glucose metabolism phenotypes among children in rural Bangladesh Margaret Quaid* Margaret Quaid Syed Emdadul Haque Tariqul Islam Mohammad Hasan Shahriar Golam Sarwar Alauddin Ahmed Farzana Jasmine Muhammad G Kibriya Habibul Ahsan Maria Argos

Children residing in rural Bangladesh have known exposure to arsenic through diet and water consumption. Arsenic exposure is associated with several adverse health outcomes, including cardiovascular disease, cancer, and metabolic disorders. To further evaluate the relationship between arsenic exposure and glucose metabolism phenotypes in children, we investigated the cross-sectional relationship between arsenic exposure, assessed in toenail clippings and spot urine samples, with glucose metabolism biomarkers (fasting glucose, fasting insulin, ratio of fasting glucose to fasting insulin, and various homeostasis model assessment metrics) among 500 children, aged 5-7 years, participating in the Bangladesh Environmental Research in Children's Health (BiRCH) cohort. We derived effect estimates and 95% confidence intervals from linear regression models evaluating associations with arsenic exposure tertiles, adjusted for potential confounding by sex, age, father's smoking status, and body mass index. Urinary creatinine was additionally included in the urinary arsenic exposure models. A positive association of urinary arsenic exposure was observed with fasting glucose (tertile 2 vs. 1 β=4.16 pg/mL; 95% CI: 0.81, 7.51 and tertile 3 vs. 1 β=1.47; 95% CI: -2.13, 5.07). We additionally observed an inverse association of urinary arsenic with fasting insulin (tertile 2 vs. 1 β=1.01; 95% CI: -32.4, 34.4 and tertile 3 vs. 1 β=-16.1, 95% CI: -51.8, 19.6). Findings with toenail arsenic exposure were similar. In conclusion, arsenic exposure appears to be associated with glucose metabolism in early life among healthy children, shedding light on the potential impact of early-life arsenic exposure on diabetes across the lifecourse. These results suggest the need to evaluate longitudinal trajectories and clinical outcomes to advance our understanding of the observed associations.

Environment/Climate Change

Investigating the Connection Between Green Spaces, Physical Activity, and Mental Health
Zoe Maxwell* Zoe Maxwell Aliana Rodriguez Acevedo Abby Katz Ugoji Nwanaji-Enwerem Brooke Ury Naomi Zeltzer Jue Yang Diana Grigsby-Toussaint Huy Tran Madelyn Dewitt Isha Thakkar

Investigating the Connection Between Green Spaces, Physical Activity, and Mental Health

Zoe Maxwell, MPH Candidate

Green spaces are widely recognized for their potential to enhance physical activity and mental health. However, their impact on elementary school-aged children remains relatively unexplored. This study addressed critical gaps by examining how green spaces, measured through the Normalized Difference Vegetation Index and tree equity, influence physical activity levels and mental health during school hours. The research focused on elementary school-aged children in Providence, Rhode Island, using data from Brown University's Project G-SPACE. The Normalized Difference Vegetation Index was computed using Sentinel-2 imagery, and tree equity data was gathered from American Forests' database. Using the Quantum Geographic Information System, 12 school polygons and their respective 50m, 100m, and 200m buffers were created. Associations between green space measures, physical activity, and mental health were then modeled via statistical regressions. Unexpectedly, an inverse relationship was found between the Normalized Difference Vegetation Index and physical activity at 50m, with marginal significance at 100m. Additionally, this study found a marginally significant positive association between the Normalized Difference Vegetation Index and negative mental health outcomes (stress, anxiety, fatigue) at 100m. Tree equity showed no significant effect on all variables. These findings highlight the complexity of green space impacts on children's health, specifically during school. As the Normalized Difference Vegetation Index is a metric solely quantifying the health and density of vegetation scaling -1 to 1, it's necessary to investigate the quality and accessibility of green spaces. Focus on these factors, rather than mere presence, is essential for guiding interventions utilizing green space as a tool to create and enhance active lifestyles and mental well-being.

Nature's Influence: Investigating the Connection Between Green Spaces, Physical Activity, and Mental Health

Zoe Maxwell, MPH Candidate

Introduction

- Utilizing data from Brown University's Project G-SPACE, this study explores the relationship between green space (NDVI and tree equity), physical activity (PA), and mental health among elementary school-aged children in Providence, Rhode Island [5].
- **Research question**: Does the availability of green spaces during school hours positively influence physical activity levels and mental health among elementary school- aged children in Providence, Rhode Island schools?

[4]

Background

- Project G-SPACE: a NIH funded study investigating the influence urban green space has on children's healthy habits, including physical activity, sleep, and mental health [5].
- Green space in this project is NDVI (measurement of visible and near-infrared light reflected by vegetation) and tree equity (tree canopy).
- Exposure to green space promotes mental restoration, enhancing positive emotions while reducing anxiety and rumination [1].
- Exposure to natural environments has been shown to improve memory, attention, and concentration among students [2].
- Prior research has found that those living in greener areas are more likely to achieve recommended physical activity [3].
- Green space encourages physical activities and can therefore tackle the issue of obesity, while fostering organic social interactions that lead to improved social skills, improved peer relationships, and increased opportunities for collaborative learning [2].
- Gap in literature: research supporting how green space influences children's health and well being at school.

Data and Methodology

Step	Description	Tool / Method Used	Output
1. Data Pre-Processing	Ensure consistent projections and data quality	QGIS (Set CRS, reproject)	All data layers aligned to a single projection
2. Merge Sentinel-2 Imagery	Merge band 4 (red) and band 8 (NIR) imagery to create a complete raster of Providence	QGIS (Merge tool)	Single, complete raster covering Providence
3. NDVI Calculation	1. Calculate NDVI for each summer month (June, July, August) from 2021 to 2024 2. Calculate average NDVI of those 4 layers	QGIS (Raster Calculator)	Average NDVI raster for 2021-2024
4. School Polygon Creation	Create polygons for 12 schools based on each participant data location	QGIS (Create Shapefile Layer)	Polygons for 12 schools
5. School Buffer Creation	Create 50m, 100m, and 200m buffers around each school	QGIS (Donut buffer tool)	School buffer polygons at 50m, 100m, and 200m
6. Zonal Statistics	Calculate mean NDVI within the 50m, 100m, and 200m buffers for each school	QGIS (Zonal Statistics tool)	Mean NDVI values for each buffer zone per school
7. Calculate Tree Equity	Calculate the average tree canopy within 50m, 100m, and 200m buffers around each school	QGIS (Join attributes by location)	Average tree equity (canopy) value for each buffer zone
8. Map Making	Mapped outdoor recreation, physical activity, mental health onto NDVI average layer	QGIS (Add vector layers, overlay)	Map with spatially distributions
9. Statistical Analysis	Regressions to assess relationships between NDVI, tree equity, physical activity, outdoor recreation, and mental health	STATA (regression)	Regression coefficients, p-values, and significance tests

Results

Relationship	Meaning	Significance (p-value)
NDVI and PA (50M buffer)	*Significant negative inverse relationship*	For every .01 increase in NDVI, PA decreases by 5.19 minutes (p-value: 0.047)
NDVI and PA (100M buffer)	*Marginal significance*	For every .01 increase in NDVI, PA decreases by 4.92 minutes (p-value: 0.055)
NDVI and PA (200M buffer)	Insignificant	No significant relationship
NDVI and Outdoor Recreation (50M and 100M buffer)	Insignificant	No significant relationship
NDVI and Outdoor Recreation (200m buffer)	*Significant positive relationship*	For every .01 increase in NDVI, the odds of having outdoor rec spots is 26% higher compared to when NDVI does not increase (p-value: 0.050)
PA and Outdoor Recreation (50m buffer)	Insignificant	No significant relationship
PA and Outdoor Recreation (100M buffer)	*Significant negative inverse relationship*	Outdoor rec spots within 100m buffer lower PA by 76.11 minutes (p-value: 0.026), and lower PA by 59.88 minutes within the 200m buffer (p-value: .042)
Outdoor Recreation as Mediator between NDVI and PA (50m, 100m, 200m buffers)	Insignificant	No significant mediation relationship
Stress/Anxiety/Fatigue and NDVI (50m, 200m buffers)	Insignificant	No significant relationship
Stress/Anxiety/Fatigue and NDVI (100m buffer)	*Marginally significant positive relationship*	For every .01 increase in NDVI, anxiety/stress/fatigue survey score increase by 0.93 units (p-value: 0.056)
Mental Health and PA	Insignificant	No significant relationship
Tree Equity and Mental Health, Outdoor Recreation, and PA (50m, 100m, 200m buffers)	Insignificant	No significant relationship

Significance based on .05 level

Conclusions

- **NDVI and Physical Activity:** A significant negative relationship was found between NDVI and physical activity at the 50m buffer, and was marginally significant at the 100m buffer. This suggests that while green space may typically encourage physical activity, it may also indicate that quality of green space does not support active recreation.
- **NDVI and Mental Health:** An unexpected marginally significant positive relationship was found between NDVI and mental health at the 100m buffer level, showing that when NDVI increases, negative mental health (stress, anxiety, fatigue) slightly increases. The effect is modest and may vary across different contexts or types of green spaces.
- **Tree Equity and Physical Activity:** Tree equity was not found to have a statistically significant impact on physical activity at any buffer level, suggesting tree canopy levels may not directly influence physical activity levels in this context. Other factors such as the accessibility or usability of the green space may be more important in promoting physical activity.
- **Outdoor Recreation and Physical Activity:** A significant inverse relationship was observed between physical activity and outdoor recreation spots within the 100m and 200m buffers, with physical activity decreasing when outdoor recreation spots were present. This counterintuitive result highlights the possibility of poorly maintained or unorganized spaces, which may not be conducive to physical activity, in addition to potential safety concerns or lack of proper infrastructure that could discourage children from utilizing these spaces for physical activity. Further research could investigate these environmental factors and their impact on children's physical activity.

Future Directions

- Further research needs to investigate quality and accessibility of green spaces, as NDVI and tree equity do not account for those factors.
- Additional efforts need to analyze physical activity levels in indoor facilities at schools and expand similar spatial analysis to neighboring cities.
- Intervention work in this field should target outdoor learning as a proxy for increasing green space exposure and outdoor play, while analyzing its impact on children's mental health.

References

Environment/Climate Change

Carbapenem-resistant Enterobacteriaceae infections associated with minimum temperature in South Korea from 2018 to 2021 Jeehyun Kim* Jeehyun Kim Mauricio Santillana

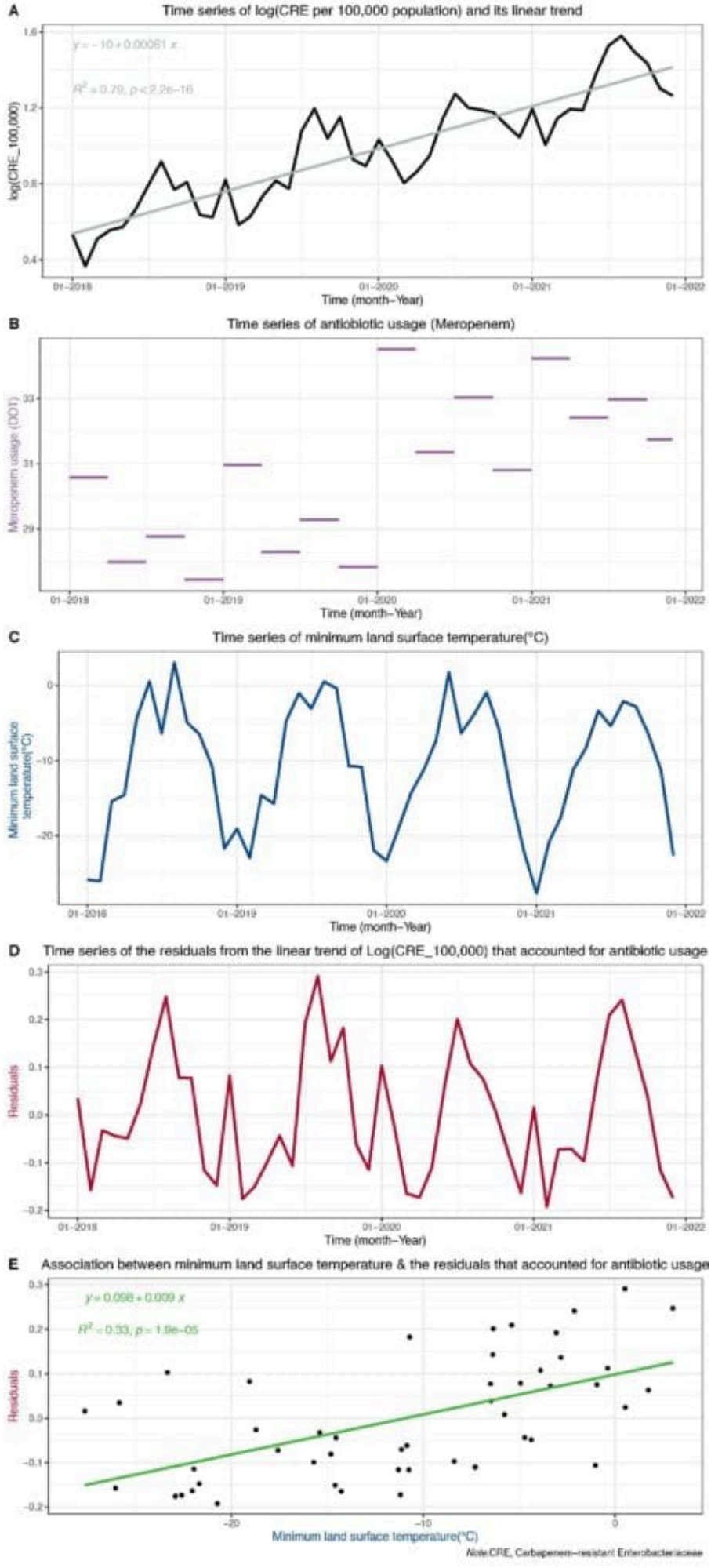
Background: Carbapenem-resistant Enterobacteriaceae (CRE) infections are a significant public health threat with limited treatments and high mortality. While antibiotic usage is a known driver of resistance, environmental factors such as temperature may also contribute to the spread of resistant infections. However, their role remains unclear.

Aim: To assess the association between minimum temperature and CRE infection cases in South Korea, accounting for antibiotic usage.

Methods: This retrospective time-series study analyzed CRE cases from national surveillance data in South Korea between January 2018 and December 2021. Monthly CRE infection cases were expressed as cases per 100,000 population and log-transformed for analysis. Minimum temperature was derived from MODIS satellite's daily land surface temperature data and summarized monthly. A multiple linear regression model evaluated the association between minimum temperature and residuals of log-transformed monthly CRE cases after accounting for antibiotic usage and overall temporal trend.

Results: A total of 68,747 CRE infection cases were reported, with a predominance among males (N=39,058, 56.8%) and individuals aged 70–79 years (N=19,252, 28.0%). CRE infections peaked seasonally from July to September. Residuals from the model of CRE infections, adjusted for time trends and meropenem usage, were significantly associated with minimum temperature ($\beta = 0.009$; 95% CI, 0.005–0.013; $P < 0.001$).

Conclusions: This study demonstrates a significant association between minimum temperature and unexplained variations in CRE infection cases, suggesting that higher ambient temperatures could contribute to a rise in antibiotic-resistance infections. Further research is needed to examine the long-term impacts of climate trends on resistance patterns.


A
Time series of log(CRE per 100,000 population) and its linear trend
y = −10 + 0.00061 x
R² = 0.79, p < 2.2e−16
log(CRE_100,000)
Time (month−Year)
B
Time series of antiobiotic usage (Meropenem)
Meropenem usage (DOT)
Time (month−Year)
C
Time series of minimum land surface temperature(°C)
Minimum land surface temperature(°C)
Time (month−Year)
D
Time series of the residuals from the linear trend of Log(CRE_100,000) that accounted for antibiotic usage
Residuals
Time (month−Year)
E
Association between minimum land surface temperature & the residuals that accounted for antibiotic usage
y = 0.098 + 0.009 x
R² = 0.33, p = 1.9e−05
Residuals
Minimum land surface temperature(°C)
Note:CRE, Carbapenem−resistant Enterobacteriaceae

Environment/Climate Change

From Opinion Polarization to Climate Action: A Socio-Climate Framework for Continuous Opinions Athira Satheesh Kumar* Athira Satheesh Kumar Krešimir Josić Chris T Bauch Madhur Anand

We developed a coupled socio-climate model with continuous opinions on climate change to investigate the interaction between public opinion and the climate system. Conventional models typically classify opinions into binary categories. However, human decision-making is much more intricate. We aim to explore the interactions between opinions in social networks and climate systems in shaping collective actions. Our analysis suggests that resistance to behavior change, elevated mitigation costs, and reduced response to climate events can result in irreversible climate outcomes due to warming beyond 2°C. Motivating at least 50% of the population to embrace mitigative practices, along with lowering the mitigation costs and improving social learning, could limit emissions and halt warming. Significantly, our model underscores how increased individual responses to climate events accelerate the adoption of mitigative practices. The socio-climate model indicates that frequent unexpected changes can slow mitigation. These insights emphasize the potential of targeted policies to leverage social influence, reduce mitigation barriers, and encourage lifestyle changes favorable to our climate goals. Our model offers a valuable framework for designing more inclusive and impactful climate mitigation strategies by integrating social dynamics and climate feedback.

Environment/Climate Change

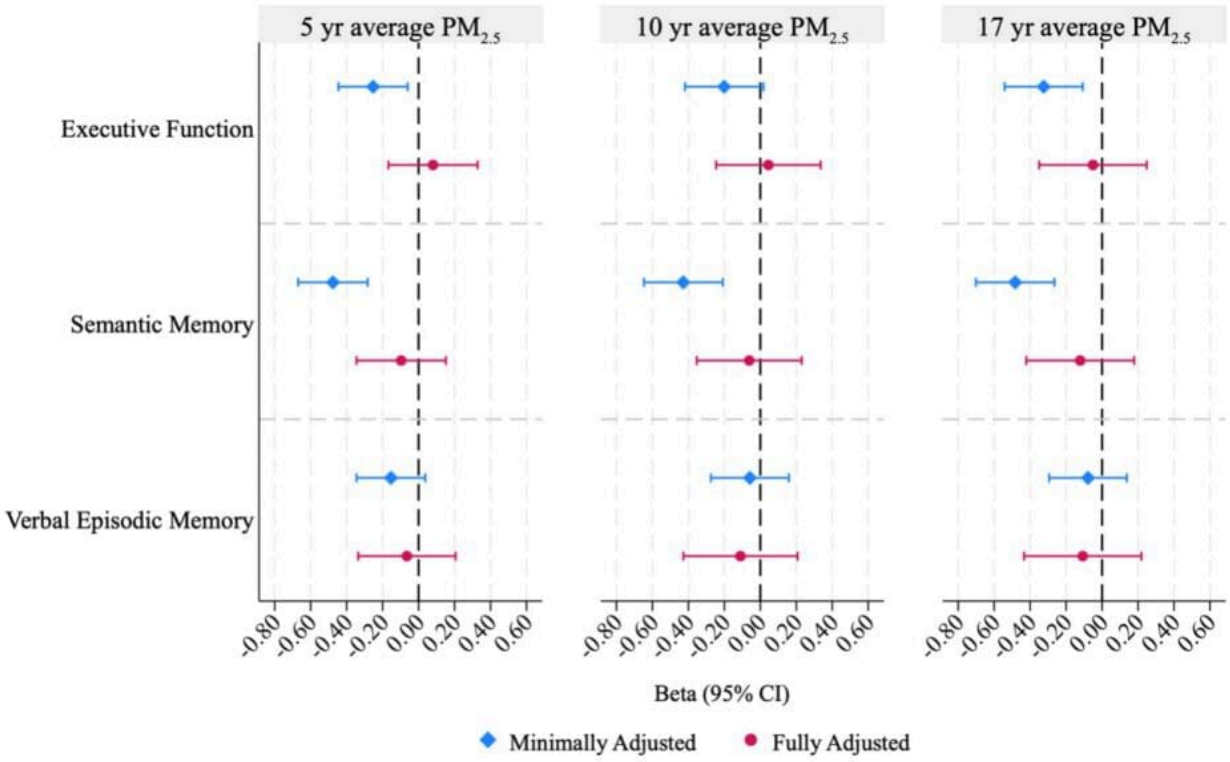
Fine particulate air pollution exposure and late-life cognitive function in the KHANDLE cohort Kathryn C. Conlon* Kathryn Conlon Stacey E. Alexeeff Chinomnso Okorie Paola Gilsanz Joel Schwartz Amanda Goodrich Rachel Whitmer

Background: Long-term exposure to fine particulate air pollution (PM<2.5μm in diameter, PM2.5) may be associated with cognitive function in older adults. However, most studies examining this question have lacked racial and ethnic diversity.

Methods: The study included data from N=1670 adults aged ≥65 in the ethnically diverse Kaiser Healthy Aging and Diverse Life Experiences (KHANDLE) study. Cognitive outcomes across three domains (semantic memory, verbal episodic memory, and executive function) were measured using the Spanish and English Neuropsychological Assessment Scales and standardized to Z-scores. PM2.5 exposures during 2000-2016 were generated at a high resolution of 1km using ensemble modeling that integrated three machine learning algorithms and linked to geocoded residential addresses. We examined the association between long-term exposure to PM2.5 (5-year, 10-year and 17-year averages) and each cognitive function outcome using linear regression models. Minimally adjusted models adjusted for age only and fully adjusted models adjusted for age, sex, race/ethnicity, marital status, education, and neighborhood income.

Results: Associations of long-term PM2.5 exposure with measures of cognition are shown in the Figure. In minimally adjusted models, a 5 μg/m3 increase in 17-year average PM2.5 exposure was associated with lower semantic memory (β = -0.48; 95% CI: [-0.70, -0.26]), and lower executive function (β = -0.32; 95% CI: [-0.54, -0.11]), but not associated with verbal episodic memory (β = -0.08; 95% CI: [-0.29, 0.14]). In fully adjusted models, 17-year average PM2.5 exposure was not associated with any cognitive function outcomes. Results were generally similar for 5-year average and 10-year average PM2.5 exposures.

Conclusion: Long-term PM2.5 exposure was not associated with cognitive function in this diverse cohort. Long-term PM2.5 exposure is a public health concern since it has been associated with adverse health outcomes in other studies.

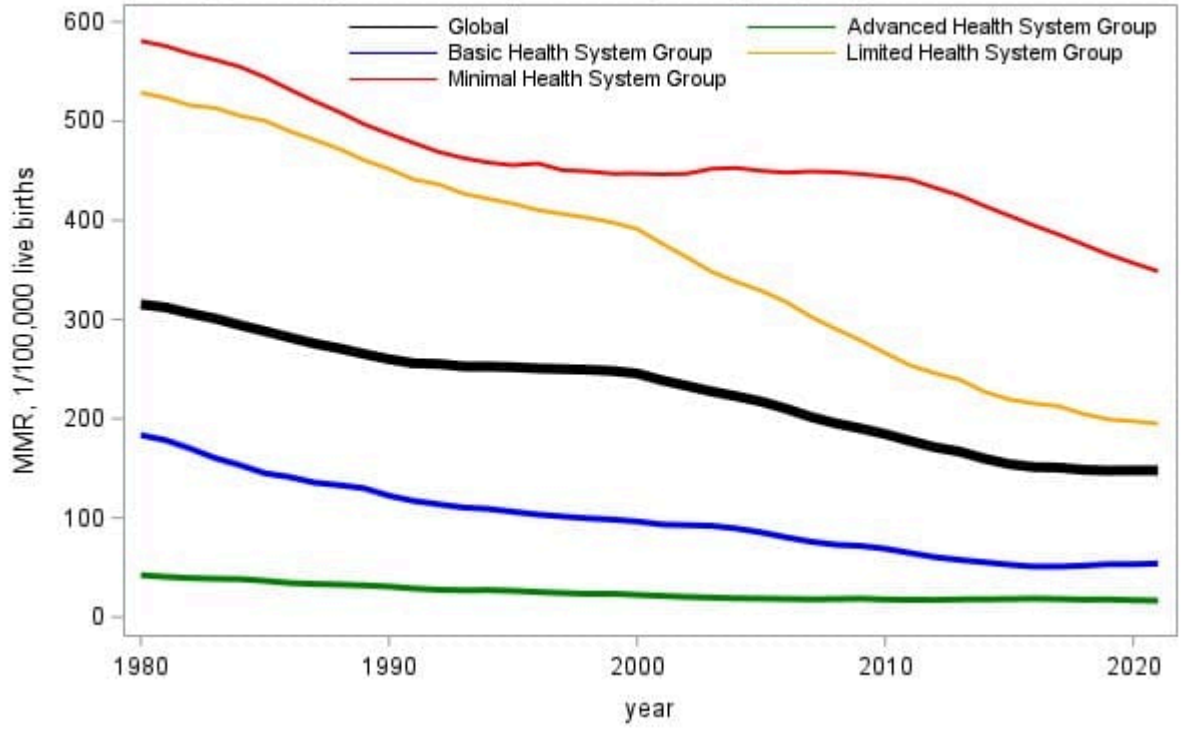

5 yr average PM2.5
10 yr average PM2.5
17 yr average PM2.5
Executive Function
Semantic Memory
Verbal Episodic Memory
-0.80
-0.60
-0.40
-0.20
0.00
0.20
0.40
0.60
Beta (95% CI)
Minimally Adjusted
Fully Adjusted

Global Health

Changes in Maternal Mortality Ratios According to Global Health System Levels Chaoyang Li* Chaoyang Li Endang Handzel Patricia Richter

Maternal mortality is the primary reason for death among women of reproductive age worldwide. Sustainable Development Goal 3 sets a 2030 deadline to reduce the global maternal mortality ratio (MMR) to less than 70 per 100,000 live births. This study aims to assess changes in MMRs using data from the 2021 Global Burden of Diseases Study. We included direct and indirect deaths during pregnancy, within 6 weeks of delivery, late maternal deaths up to 1 year after delivery, and HIV-related deaths aggravated by pregnancy in women of reproductive age (15-49 years). We first compared annual changes in overall and cause-specific MMRs between 1980-2000 (Period I) and 2001-2021 (Period II) and then compared the differences in two periods across four health system grouping levels (advanced, basic, limited, and minimal). We used a Generalized Estimating Equations model to account for the autocorrelation of the response variable and to test the differences in annual MMR changes between two periods across health system levels. Overall, MMR decreased by 22.1% in Period I and by 39.8% in Period II. The largest decreases were observed for maternal abortion and miscarriage (-35.2% in Period I, -56.5% in Period II) and maternal hemorrhage (-25.1% in Period I, -54.7% in Period II). Countries with advanced, basic, and minimal health systems experienced greater decreases in annual MMRs in Period I than Period II (all $P<0.001$). In contrast, countries with limited health systems exhibited greater progress during period II. Although other direct maternal disorders and indirect maternal deaths had increased across all health systems levels from 2000-2021, maternal hemorrhage remained the leading cause of maternal mortality globally. Despite significant improvement in MMRs, disparities persist with limited and minimal health systems exhibiting disproportionately high MMRs as of 2021. Health systems strengthening needs to be prioritized to combat maternal hemorrhage in resource-poor settings.

Fig. Changes in MMR by health system grouping levels, GBD 2021



LATEBREAKER

Global Health

Serological evaluation of the impact of mass drug administration on malaria transmission: results from a cluster randomized trial in Senegal Gloire Onya Mbaka* GLOIRE ONYA MBAKA Aminata Colle Lo Catriona Patterson Helena Brazal Monzo Elhadj KC Ba Abdoulaye Diallo Tidiane Gadiaga Amadou Seck Sylla Thiam Seynabou Gaye Ibrahima Diallo Pamela Gangar Elhadji Diouf Oumar Ba Ari Fogelson Xue Wu Paul Milligan Tabitha Kibuka Moustapha Hama Erin Eckert Adam Bennett Roly Gosling Doudou Sene Bayal Cissé Chris Drakeley Jean Louis Ndiaye Michelle E Roh Michelle S Hsiang

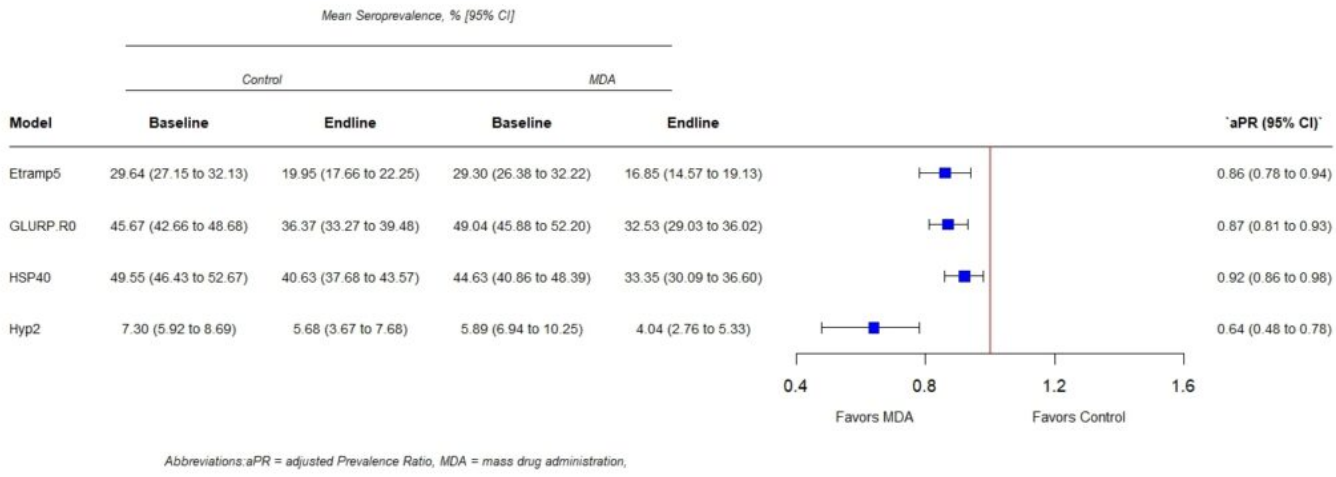
Background: Malaria incidence and parasite prevalence are standard measures to evaluate intervention impact on transmission. However, as transmission declines, more sensitive diagnostics, such as serological markers of recent exposure, are needed to capture longitudinal impacts on transmission.

Methods: We conducted a secondary analysis of a cluster randomized trial in a low-to-moderate transmission area in Senegal. Sixty villages were randomized to either three rounds of MDA with dihydroartemisinin-piperaquine + single low-dose primaquine (intervention) or standard-of-care—three rounds of seasonal malaria chemoprevention with sulfadoxine-pyrimethamine + amodiaquine for children 3-120 months (control). Blood from pre- and post-MDA cross-sectional surveys was analyzed using Luminex MAGPIX to assess serological markers of recent exposure (Etramp5, GLURP.R0, HSP40, Hyp2). To assess intervention impact on seroprevalence, we used mixed-effects Poisson regression models with village-level random intercepts and robust standard errors.

Results: Compared to control, MDA was associated with lower malaria incidence (aIRR: 0.45 [95% CI: 0.28-0.72]) and infection prevalence (aPR: 0.38 [0.20-0.78]), though effects were not sustained in the following year (aIRR: 0.74 [0.47-1.17]). Mean village-level seroprevalence ranged from 8% [0%-47%] (Hyp2) to 50% [35%-64%] (HSP40) at baseline and 6% [0%-40%] (Hyp2) to 40% [27%-54%] (HSP40) at endline. Across all markers, seroprevalence was lower in the MDA arm compared to control: Hyp2 (aPR=0.64 [0.48-0.80]), Etramp5 (aPR=0.86 [0.77-0.93]), GLURP.R0 (aPR=0.87 [0.81-0.93]), and HSP40 (aPR=0.92 [0.86-0.98]).

Conclusion: MDA reduced recent infection exposure, though the effect size was smaller compared to incidence and prevalence estimates. The high prevalence of markers of recent exposure suggest infections were persistent during the campaign, which may explain the lack of a sustained impact.

Figure1. Cluster-level seroprevalence by markers



Abbreviations:aPR = adjusted Prevalence Ratio, MDA = mass drug administration,

LATEBREAKER

Global Health

Evaluating interventions designed to expand access to medication abortion: a multi-country pre-post assessment Katherine Key* Katherine Key Heidi Moseson Chiara Bercu Ibtehal Jastaniah Jewelle Methazia Ika Ayu Kristianingrum Ijeoma Egwuatu Belén Grosso Sybil Nmezi Ruth Zurbriggen Ruvani Jayaweera

Across legal settings, people self-manage their abortions (SMA) – take action to end a pregnancy without clinical supervision. SMA with medication is safe and highly effective, especially with support from an accompaniment group (collectives of non-clinical abortion counsellors offering evidence-based information and non-judgmental support). People who self-manage abortions may engage with the formal health system for various reasons; however, healthcare providers often lack knowledge about the safety and effectiveness of SMA, and/or training on comprehensive, person-centered abortion care. This often leads to denial of care, mistreatment, or judgmental attitudes for those self-managing abortions. To increase knowledge about medication abortion among providers, and to shift abortion-related attitudes and practices, between 2022-2024, accompaniment groups in Argentina, Nigeria, and Indonesia led a series of trainings for medical students, pharmacists, community-health workers, and midwives. To measure the impact of the interventions on three domains (knowledge, attitudes, and intentions), we analyzed matched pre- and post- surveys from 29 workshops with 738 participants using paired t-tests. Survey questions were not standardized across sites. To account for these differences, we created standardized scores from 0 to 100 and reported the mean scores for each domain. Interventions had the greatest impact on knowledge and intentions. The average knowledge score increased from 43.9 to 81.0 ($p<0.001$) while the average intentions score increased from 49.4 to 80.9 ($p<0.001$). Although, changes in attitudes were more modest, the average attitude score increased from 60.7 to 77.2 ($p<0.001$). Accompaniment groups can play a vital role in training the formal healthcare workforce and, as more abortions take place outside the formal health system in the US and globally, attention to community-based initiatives is essential to ensure access to high-quality information and care.

Global Health

Burdens and risk factors for mortality in young people aged 10-24 years in Australia and comparison with OECD countries between 2000-2021: GBD 2021 Study Zahra Ali Padhani*
Zahra Ali Padhani Gizachew Jodie Salima Zohra

Background

Adolescents are considered the healthiest population of all age groups, yet they are vulnerable to illnesses and deaths from preventable causes. We aimed to systematically investigate the burden of morbidity, mortality, and risk factors for mortality among adolescents and young adults (10-24 years) in Australia compared to the Organisation for Economic Co-operation and Development (OECD) countries.

Methods

We retrieved the Global Burden of Disease (GBD) 2021 estimates on mortality and disease burden for Australia and compared them with those of 37 other OECD countries for the years 2000 and 2021. Country and age-specific estimates with 95% uncertainty intervals (UI) were obtained from the GBD Compare and Results Tool on all-cause mortality and 'disability-adjusted life-years (DALYs)' as an indicator of disability. The top 15 level-three risk factors of death were also investigated for adolescents and young adults. Causes of death by age groups, sex, and year for other diseases were measured using the Cause of Death Ensemble model (CODEm).

Findings

Since 2000, there has been a reduction in the mortality rate in Australia and across OECD regions on average, with substantial reductions in Australia (47.1 deaths/100,000 population; 95% UI: 46.6-47.5 to 27.9 deaths/100,000 population; 95% UI: 27.6-28.3 in 2021). We observed a very minimal decrease in DALYs among adolescents and young adults, with Australia ranked among the top eight countries for DALYs (10,363.9 DALYs/100,000 population) among young people.

Higher mortality rates and DALYs were observed among young adults (aged 20-24 years) compared to other age groups. In 2021, males in Australia (38.3 deaths/100,000 population; 95% UI: 37.8-38.8) and OECD regions (65.6 deaths/100,000 population; 95% UI: 64.3-67.1) had a higher mortality rate. In contrast, Australian females (10,748.3 DALYs/100,000 population; 95% UI: 8,126.1-13,670.2) had a higher rate of DALYs than males (9,999.3 DALYs/100,000 population; 95% UI: 8163.7-12079.4). The 10-14 age group had the lowest rates of both mortality and DALYs.

High alcohol and drug use were identified as the leading risk factors for death among young people, followed by metabolic risk factors. Environmental and occupational risks varied by age and country, and intimate partner violence emerged as a persistent concern, particularly among Australian females.

Interpretation

The mortality rate among adolescents and young adults has substantially reduced in Australia as compared to OECD countries, with only a minimal decrease in disease burden. However, the gap in mortality rates and disease burden continues to grow across countries, age groups, and genders. This widening gap may be largely attributed to the limited focus on males and young adults in health

strategies. Therefore, this study calls for comprehensive health strategies that address these disparities and aim to reduce the disease burden in young people, specifically among males.

Global Health

Intergenerational social mobility and mental health: evidence from a Filipino birth cohort

Lucy Barrass* Lucy Barrass Maria Theresa Redaniel Lucy Riglin Nanette R Lee Laura D Howe Duleeka Knipe

Evidence suggests that associations between educational attainment and mental health may vary according to social mobility i.e. changes in socioeconomic circumstances across the life course. This evidence is largely limited to high-income countries. We aimed to assess this relationship in the Philippines, a middle-income country. Using data from an ongoing birth cohort (Cebu Longitudinal Health and Nutrition Survey), we assessed the associations with mental health for both own educational attainment and intergenerational educational mobility (i.e. the difference in educational attainment between parents during pregnancy and in adulthood (age 18 and 35) in 2,038 Filipino individuals). Primary mental health outcomes were depressive symptoms, suicidal ideation and psychological distress at age 35 years, with the former two measures used as secondary outcomes at age 18. We used logistic regression models, adjusting for sex and urbanicity at birth. Individuals with lower levels of educational attainment were associated with higher odds of depressive symptoms (Odds Ratio (OR): 1.68; 95% CI: 1.11-2.52) and psychological distress (OR: 1.54; 95% CI: 1.09-2.17), but not suicidal ideation (OR: 1.43; 95% CI: 0.91-2.26), compared to those with higher educational attainment. Participants who had experienced downward educational mobility at age 35 had higher odds of depressive symptoms compared to participants remaining in higher levels of educational attainment (OR: 3.12; 95% CI: 1.46-6.66). There was no statistical evidence of this association for the other outcomes. We also did not find statistical evidence that upward social mobility was associated with mental health outcomes. Filipino individuals who were less educated than their parents had higher levels of depressive symptoms compared to those who remained in the higher education category. We found limited evidence of this associations for other measured mental health outcomes.

Global Health

Trends in the 14-Year Incidence of Fibromyalgia with Obstructive Sleep Apnea: A Nationwide Descriptive Study in Taiwan Yu-Lan Tsou* Yu-Lan Tsou Fu-Huang Lin Chien-An Sun Yu-Ching Chou

Trends in the 14-Year Incidence of Fibromyalgia with Obstructive Sleep Apnea: A Nationwide Descriptive Study in Taiwan

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Background: Obstructive sleep apnea (OSA) and fibromyalgia (FM) significantly affect quality of life. OSA involves sleep fragmentation, while FM is characterized by widespread pain and fatigue. Long-term studies on FM trends in OSA patients are scarce.This cohort study analyzed 14-year trends (2000–2013) in OSA and FM incidence using Taiwan's NHIRD.

Methods: This cohort study analyzed 14-year trends (2000–2013) in the incidence of OSA and FM using Taiwan's National Health Insurance Database (NHIRD). We identified 14,046 new OSA cases and evaluated incidence rates across sex, age groups, and time periods using chi-square tests and linear trend analysis.

Results: The incidence of OSA significantly increased from 4.42 to 17.34 per 100,000 men and from 1.57 to 7.26 per 100,000 women between 2000 and 2013, while its prevalence nearly tripled, rising from 2.85 to 7.73 per 100,000. Among OSA patients, the incidence of FM rose from 21.01 to 80.27 per 1,000 men and from 28.85 to 72.82 per 1,000 women, representing a 3.82-fold increase in men and a 2.52-fold increase in women. FM incidence peaked at 43.92 per 1,000 person-years in the 30–40 years age group (P trend < 0.001), with smaller variations in other age groups: 39.32 (20–30 years), 42.03 (40–50 years), 39.49 (50–60 years, lowest), and 40.72 (≥60 years). Additionally, FM incidence increased with the frequency of OSA visits, rising from 40.41 per 1,000 for ≤2 visits to 44.64 per 1,000 for ≥6 visits (P trend < 0.001).

Conclusion: Over 14 years, OSA incidence and prevalence grew significantly, with a notable increase in FM incidence among OSA patients, especially in younger groups and those with frequent healthcare visits. These findings call for further research on the OSA-FM relationship and integrated strategies to manage their co-occurrence.

Keywords: Obstructive Sleep Apnea (OSA), Fibromyalgia (FM),National Health Insurance Research Database (NHIRD), Incidence, prevalence.

Global Health

Structural racism and diminished health returns on education among Palestinian refugees in Lebanon Sawsan Abdulrahim* Sawsan Abdulrahim

Drawing on structural racism, we examined whether the association between education and health is diminished among Palestinian refugees in Lebanon (PRL) who live under conditions of structural gendered racism. The study utilized data from a national household survey of PRL conducted by a humanitarian organization in December 2022. In a subsample of 7,872 PRL 18 years and older, we assessed the association between education and diabetes, hypertension, and cardiovascular disease (CVD). Adjusted risk-ratios (aRR) were calculated to compare the proportions of the outcomes between each gender and education group of interest, adjusting for age, area of residence, and self-reported socioeconomic status. Analyses were conducted on the entire sample and a subsample of those 55 years and older.

Among PRL women, increasing education resulted in a sequential decrease in aRR for diabetes, hypertension, and CVD, although not all estimates were statistically significant. This pattern did not persist in the sub-sample of women 55 years or older. Conversely, increasing education level among men showed no differences in risk. For example, compared to men with elementary or less education, men with university education or higher have a higher aRR of 1.12 (95% C.I. 0.83-1.50) for the outcome of diabetes. This trend persisted when comparing outcome risk in the sub-sample of those 55 years of age and older.

The findings reveal a gendered association between education and chronic disease risk that is reflective of structural gendered racism. Whilst PRL women demonstrated a typical overall inverse association, PRL men exhibited a pattern of diminished health return on education. PRL men encounter racialized structures in the Lebanese mainstream economy, which stymies the health benefits they may accrue from education and access to other tangible resources.

Global Health

Persistent Health Challenges Among Post-TB and Post-Pregnancy Survivors with HIV in Uganda: A Case Series Asmith Joseph* Asmith Joseph Adenike McDonald

Introduction
Persons who experience tuberculosis (TB) while pregnant are likely to experience worse post-tb health outcomes. However, there is limited data to support this hypothesis. We identified a unique subgroup of five post-pregnant, post-TB survivors in our ongoing pilot cohort study that started in May 2024 in Kampala, Uganda. We describe their physical, functional, and psychosocial complications compared to age-matched non-post-pregnant controls.

Case Series Presentation

This case series includes five women treated for TB during pregnancy, between two to six months gestation. They were aged 22 to 37 years, had one to four children, 4/5 were HIV-positive, receiving antiretroviral therapy (ART) for 7 months to 8 years. Case 1 was a 22-year-old, para 1, HIV+, on ART for 8 months. Case 2 was a 30-year-old, para 2, HIV+, on ART for 7 months. Case 3 was a 34-year-old, parity unknown, HIV+ on ART for 12 months. Case 4 was a 37-year-old, para 4, HIV+, on ART for 8 years. Case 5 was a 36-year-old, para 1, HIV-. Participants underwent screening for respiratory symptoms, dyspnea using the modified Medical Research Council (mMRC) scale, functional capacity (6-Minute Walk Test), and disability (WHO Disability Assessment Schedule (WHODAS 2.0)).

Discussion
All cases reported some degree of morbidity, with 4 of 5 rating their overall health as moderate to very bad, experiencing productive or persistent cough and breathing difficulties, and 2 of 5 had moderate dyspnea with a score of 3 on the mMRC scale. The median (IQR) 6-minute Walking Distance was 360(357-418) meters versus 379(360-405) meters in the controls and a higher mean disability score of 19 versus 16 in the controls, indicating a worse overall quality of life in the post-TB and post-pregnant women. These findings highlight the post-pregnant TB survivors as a subgroup that needs further research and tailored interventions.

Global Health

Reduction of Child Mortality Rates following 10 years of a health system strengthening program in rural Madagascar: results from the Ifanadiana Health Outcomes and Prosperity longitudinal Evaluation (IHOPE) Ann C. Miller* Ann Miller Hobisoa Razanandranaivo Benedicte Razafinjato Sarah-Anne Barriault Marius Randriamanambintsoa Samuel Andrianambinina Andres Garchitorena Rado Rakotonahary Luc Rakotonirina Laura Cordier Karen Finnegan Matthew Bonds Andres Garchitorena

Background:Since 2014, the NGO Pivot and the Madagascar Ministry of Public Health collaborated on a health system strengthening(HSS) intervention in a low-resource District in eastern Madagascar (pop. 200,000). This study assessed HSS impact on child mortality at the population level over 10 years.

Methods: This population-representative longitudinal cohort study used a 2-stage cluster sample. 1600 households were randomly sampled from 80 randomly-selected clusters, half per each of 2 strata:Pivot's initial catchment(IC) and the rest of district(ROD). Professional data collectors conducted face-to-face interviews with women ages 15-49 repeatedly between 2014 and 2023. We provide 5-year weighted estimates of population-level mortality using synthetic life-table methods. We estimated absolute change from 2014 baseline for neonatal, infant and under-5 mortality(probability of death before 1, 12, and 60 months respectively per 1000 live births) comparing IC to ROD for each of the 5 waves of the cohort (2014, 2016, 2018, 2021, 2023), using 95% confidence intervals.

Results: 4380 children were included. Neonatal mortality dropped from 47.3/1000 [95%CI 26.9-67.7]live births to 30.7/1000 [4.5-56.8] in IC vs rising from 34.5/1000 [95%CI 18.4-50.6] to 64.4/1000 in ROD [37.5-91.3]. Infant mortality dropped from 66.1/1000 [40.4-91.9] in 2014 to 45.3/1000 [16.2-74.4] in 2023 (IC), while rising in ROD (64.3/1000 [45.6-82.9]to 88.2/1000 [60.4-116.4]). Under-5 mortality dropped for both strata from baseline; IC experienced greater reductions 104.1 [72.6-135.5] to 71.3/1000[36.1-106.5] vs ROD 168.6 [128.2-208.9]to153.3/1000[121.29-185.3]. Under-5 mortality was significantly different between strata in 2023.

Conclusions: In an area where health and economic indicators are not otherwise improving, these results provide evidence that strengthening health systems for universal care and access in low-resource settings can save lives.

Health Disparities

Socioeconomic Disparities in Temperature-related Illness Incidence: Evidence from Korea, 2014–2023 Soomin Kim* Jin Yong Lee Soomin Kim Bomi Lee Hyemin Jung

Introduction Climate change significantly impacts public health, with its effects being particularly pronounced among socioeconomically vulnerable populations. Korea's healthcare system offers a unique model for evaluating Socioeconomic health disparities, with National Health Insurance (NHI) covering high- and middle-income groups and Medical Aid (MA) targeting low-income populations. This study analyzed the incidence rates of heat- and cold-related illnesses in Korea from 2014 to 2023 to evaluate between NHI and MA.
Methods From 2014 to 2023, the National Health Insurance claims data were used to identify patients treated for heat-related illnesses (ICD-10: T67, T69.7) and cold-related illnesses (ICD-10: T33-T35, T68, T69.0-T69.1, T69.8-T69.9) under NHI and MA. Population data for NHI and MA were obtained from Statistics Korea to serve as denominators for calculating incidence rates. Differences in incidence rates between the two groups were analyzed using ANOVA, and trend in absolute disparities over time were assessed using simple linear regression.
Results There were 220,339 patients with heat-related illnesses from 2014 to 2023. The average incidence rate of heat-related illnesses was 27.9 per 100,000 population for NHI and 52.4 for MA, with a difference of 24.5 ($p<0.0001$). The absolute disparity in heat-related illness incidence rates decreased by an average of 3.4 per 100,000 annually ($p=0.0002$, adjusted R-square=0.8). There were 180,971 patients with cold-related illnesses over the past decade. The average incidence rate of cold-related illnesses was 34.2 per 100,000 population for NHI and 55.8 per 100,000 for MA, with a difference of 21.6 ($p=0.0005$). Although the absolute disparity in cold-related illness incidence rates showed a decreasing trend of 1.8 per 100,000 annually, it was not statistically significant ($p=0.2$, adjusted R-square=0.07). Throughout the study period, MA consistently higher incidence rates for both illnesses compared to NHI.
Conclusions Socioeconomic disparities in heat-related illnesses have significantly improved over time; however, the improvements in cold-related illnesses have been minimal and statistically insignificant. Moreover, MA remain at a higher risk of temperature-related illnesses, likely due to environmental vulnerabilities such as inadequate access to heating and cooling resources. This study highlights the need for tailored policies that integrate welfare and healthcare services, such as expanded support for heating and cooling resources for low-income populations and the establishment of community-based emergency response systems to address extreme weather events like heatwaves and cold waves, to mitigate health disparities caused by climate change.

Disclosure of Interest: None Declared
Keywords: Heat stress disorders, cold injury, climate change, health inequalities

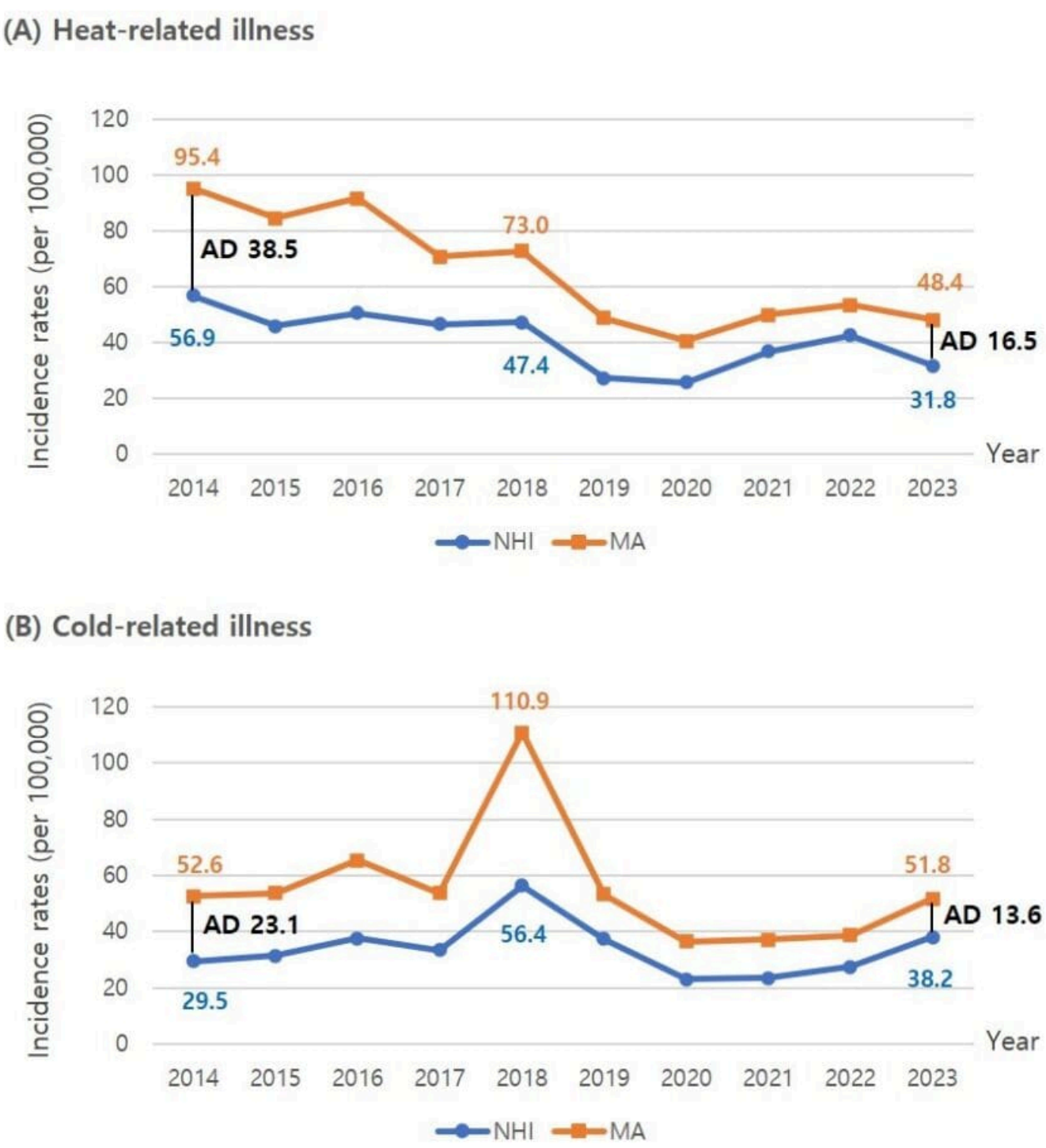


Fig. 1. Trend of temperature-related illness incidence, 2014–2023
NHI, National Health Insurance; MA, Medical Aid; AD, Absolute Disparity

Health Disparities

Prioritizing clinical utility in the association between allostatic load and the consequences of stress Zoe Walts* Zoe Walts Amy Cochran Mark Steinwandel Amy Trentham Dietz Nicci Owusu-Brackett Melissa Rosenkranz Anne Ersig Martha Shrubsole Shaneda Warren Andersen

Introduction: A chronic stress response harms diffuse bodily systems. Disproportionate stress exposure can thus cause downstream racial and socioeconomic cancer outcome disparities. Allostatic load measures the physiological consequences of stress and may identify cancer patients who will benefit from additional services. Currently, clinical use of allostatic load is limited, in part, because biomarkers used to calculate allostatic load are not regularly measured for most patients. We evaluated associations between depression with an established allostatic load index and an abbreviated index composed of a subset of biomarkers readily available in electronic medical records as co-occurring consequences of stress.

Methods: Data arise from a colorectal cancer study within the Southern Community Cohort Study (N=1010); 72% self-identified as Black, 63% reported income <$15,000. Participants completed epidemiologic surveys and provided blood samples which were analyzed for immune, metabolic, and cardiovascular biomarkers. To calculate allostatic load, the number of index biomarkers above standard clinical risk cutoffs were summed. Counts above median indicate high allostatic load. Age adjusted logistic models calculated associations between depression with allostatic load.

Results: Depression was positively associated with high allostatic load using full (OR: 1.64 95%CI: 1.23-2.18) and abbreviated indices (OR: 1.51; 95%CI: 1.16-1.97). Associations were similar in sex-stratified analyses. The association of depression with allostatic load was stronger among white (abbreviated index OR:1.92, 95%CI: 1.11-3.34) than Black (OR:1.37, 95%CI: 1.01-1.87) participants.

Conclusion: Robust relations of depression with allostatic load across indices strengthen its validity as a biomarker of stress-related outcomes. The abbreviated index is a clinically actionable biomarker which may be more easily integrated into patient care to identify high-risk patients and reduce outcome disparities.

Health Disparities

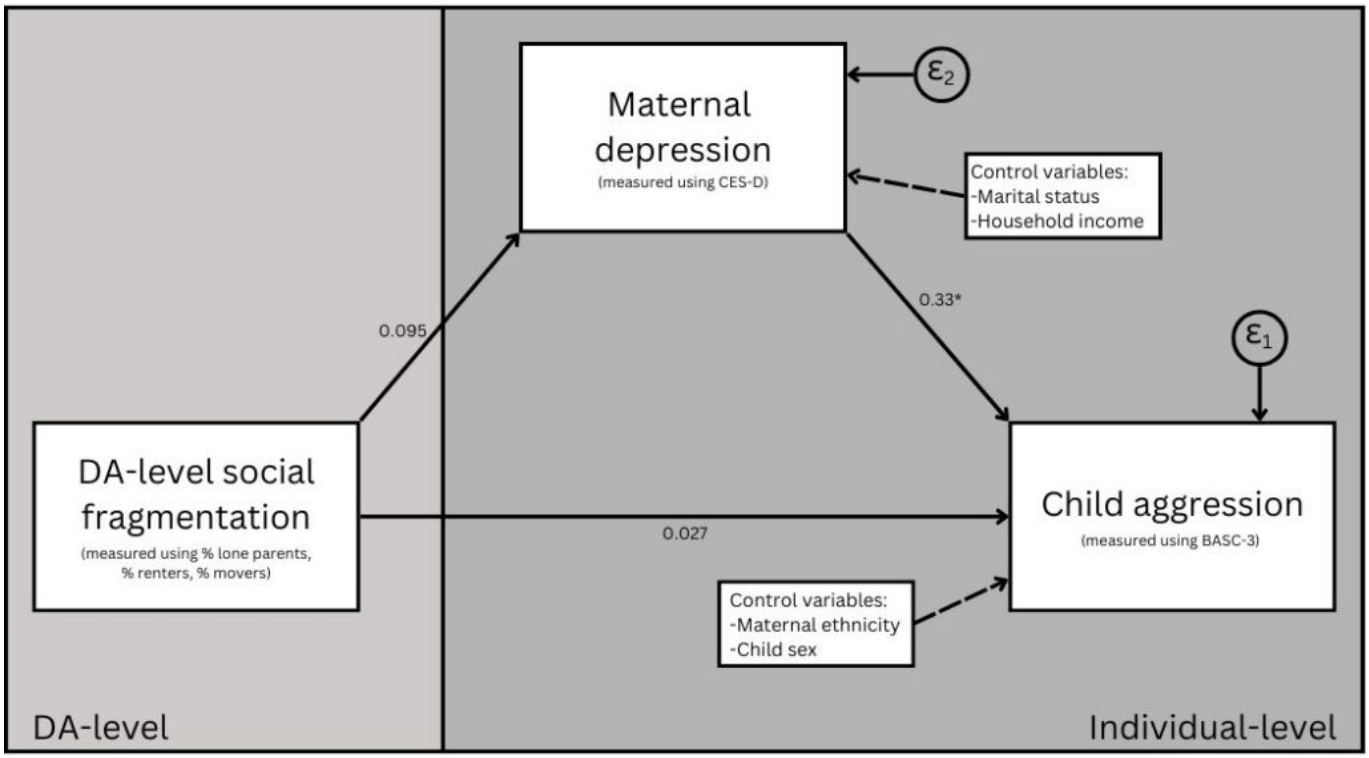
Fragile Ties: How Social Fragmentation and Maternal Mental Health Shape Childhood Aggression Kesia Muthuthotatil* Kesia Muthuthotatil Jason Mulimba Were Sheila McDonald Roman Pabayo

Objective: Childhood aggression, a significant public health issue, is influenced by individual, familial, and structural factors. Neighborhood social fragmentation, characterized by weakened social bonds and disrupted community networks, may foster environments contributing to aggressive behaviors in children. This study investigates whether maternal depression mediates the relationship between social fragmentation and child aggression among new mothers in Calgary, Alberta.

Method: Data from the All Our Families cohort among mothers and their infants, collected three years postpartum (2012–2015), were linked to neighborhood socioeconomic data from the 2006 Canadian Census. Social fragmentation was quantified using the Congdon Social Fragmentation Index, which combines variables such as lone-parent households, renter tenure, and residential mobility to reflect community instability. Generalized structural equation modeling assessed both direct and mediated associations between social fragmentation, maternal depressive symptoms, and child aggression.

Results: Maternal depressive symptoms were significantly associated with higher child aggression levels (ß = 0.33; 95 CI: 0.21, 0.45). However, no associations between social fragmentation and maternal depression (ß = 0.095; 95 CI: -0.12, 0.31) and between social fragmentation and child aggression (ß = 0.027; 95 CI: -0.38, 0.43) were observed, suggesting social fragmentation does not directly impact these outcomes within this sample.

Conclusion: Maternal mental health emerged as a critical factor shaping early childhood behavior independent of neighborhood social fragmentation. Targeted interventions, such as peer support programs and mental health services for new mothers, could mitigate childhood aggression by addressing maternal depressive symptoms. Future studies should prioritize diverse populations and longitudinal designs to identify how neighborhood and family-level factors influence childhood development over time.


Maternal depression
(measured using CES-D)
ε2
Control variables:
-Marital status
-Household income
0.33*
0.095
ε1
DA-level social fragmentation
(measured using % lone parents, % renters, % movers)
0.027
Child aggression
(measured using BASC-3)
Control variables:
-Maternal ethnicity
-Child sex
DA-level
Individual-level

Health Disparities

Trends in adult anxiety/depression by disability status, race/ethnicity, sex, and nativity in the US, 2019—2023 David Adzrago* David Adzrago Faustine Williams

Introduction: Mental health disorder symptoms, including anxiety and depression, have increased significantly with more pronounced burdens among individuals with disability, especially those with multiple minority identities. Nevertheless, trends in these symptoms based on the intersection of disability status, race/ethnicity, sex, and nativity are not examined. We assessed trends in anxiety/depression by disability status, race/ethnicity, sex, and nativity.

Methods: This national serial cross-sectional study included adults aged > 18 years (N= 150,220) from 2019 to 2023. We used Joinpoint regression to estimate trends in age-adjusted anxiety/depression and average annual percent change (AAPC) by functional disability status, race/ethnicity, sex, and nativity.

Results: From 2019 to 2023, age-adjusted anxiety/depression increased significantly among individuals without disability who identified as Black female (AAPC= 14.9%; 95% CI= 0.5%-31.4%) and male (AAPC= 8.3%; 95% CI= 3.5%-13.2%) foreign-born. Among those without disability, it increased among Hispanic male US-born (AAPC= 5.1%; 95% CI= 2.3%-7.9%) and foreign-born (AAPC= 5.3%; 95% CI= 3.4%-7.2%); White male US-born (AAPC= 4.4%; 95% CI= 1.02%-7.9%) and foreign-born (AAPC= 7.8%; 95% CI= 1.6%-14.3%); and White female US-born (AAPC= 3.4%; 95% CI= 2.1%-4.8%). No significant change was found by the intersection of race/ethnicity, sex, and nativity among persons with disability. Similarly, among persons without disability, no significant change was found among Black female and male US-born; Hispanic female US-born and foreign-born; or White female foreign-born.

Conclusions: Anxiety/depression increased among Black female and male foreign-born, Hispanic male US-born or foreign-born, and White male US-born and foreign-born or White female foreign-born without disability. These rising trends highlight the need for interventions and studies to consider unique differences in disability status, race/ethnicity, sex, and nativity.

Health Disparities

Developmental vulnerability in children from culturally and linguistically diverse backgrounds in Western Australia: a population-based study Kendalem Atalell* Kendalem Atalell Gavin Pereira Bereket Duko Sylvester Nyadanu Vegard Skirbekk Gizachew Tessema

Background: Early childhood developmental adversities have long-term effects on educational outcomes, overall health outcomes and well-being. However, the developmental outcomes of children from Culturally and Linguistically Diverse (CALD) backgrounds remain unclear. This study explores and compares these outcomes between CALD and non-CALD children in Australia.

Method: We conducted a retrospective population-based cohort study of 59,925 children using data from the 2009-2015 Australian Early Development Censuses (AEDC), Midwives Notification System (MNS), and Hospital Morbidity Data Collections (HMDC). Developmental vulnerability was defined as developmental domain scores <10th percentile across five AEDC domains such as physical health and well-being, social competence, emotional maturity, language and cognitive skills and communication skills and general knowledge. CALD status was defined using the following criteria: speaking English as a second language, using a language other than English at home, a child born outside Australia, or being born to a non-Caucasian mother. Logistic regression was used to investigate the association between CALD background and developmental vulnerability.

Result: Among 10,048 CALD and 49,877 non-CALD children, 23.7% of CALD children experienced vulnerability in at least one domain compared to 19.6% of non-CALD ($P < 0.001$). Adjusted analyses showed CALD children had 23% higher odds of vulnerability in at least one domain (OR: 1.23; 95% CI: 1.16–1.31) and DV2 (OR: 1.23; 95% CI: 1.13–1.33). CALD children had over twofold higher odds of vulnerability in communication skills and general knowledge (OR: 2.16; 95% CI: 1.99–2.34) and 37% higher odds in language and cognitive skills (OR: 1.37; 95% CI: 1.25–1.51).

Conclusion: This study found a higher developmental vulnerability burden among CALD children than their non-CALD counterparts, particularly in the communication skills and general knowledge domains. Strengthening culturally sensitive practices and providing additional resources to CALD families may help reduce developmental vulnerability disparities and promote equitable educational outcomes.

Health Disparities

Racial and Ethnic Disparities in Financial Toxicity among Adults with Early-Onset Cancer in the United States Jennifer S. Wang* Jennifer Wang Bijal A. Balasubramanian Qian Xiao Caitlin C. Murphy

Purpose: We examined racial and ethnic disparities in three aspects of financial toxicity—material hardships, coping behaviors, and psychological effects—among adults with early-onset cancer (diagnosed at age 18-49 years).

Methods: Adults with a self-reported history of early-onset cancer were identified from 2019-2023 National Health Interview Survey data. We used three distinct survey questions to measure each aspect of financial toxicity and estimated prevalence of each aspect, overall and by race and ethnicity. Separately for each aspect of financial toxicity, we used multivariable logistic regression models to estimate associations with race and ethnicity. Models were adjusted for age at diagnosis, sex, insurance, education, and health status.

Results: Among 3,394 adults with early-onset cancer (10.3% Hispanic, 78.6% White, 6.3% Black, 2.1% Asian, 2.9% Other or multiple race), common cancer types were skin (31.3%), breast (14.9%), and cervical (13.7%) cancer. Over half (53.8%) of adults experienced at least one aspect of financial toxicity: 17.7% experienced material hardships, 11.8% experienced coping behaviors, and 49.8% experienced psychological effects. By race and ethnicity, prevalence of material hardships, coping behaviors, and psychological effects was higher among Hispanic and non-Hispanic Black adults compared to all other racial and ethnic groups. For example, 26.4% of Hispanic adults and 26.2% of non-Hispanic Black adults had problems paying or were unable to pay medical bills compared to 16.4% of non-Hispanic White adults. In adjusted analyses, results followed similar patterns. For example, Hispanic and non-Hispanic Black adults had 2.17 (95% CI: 1.49, 3.15) and 1.45 (95% CI: 0.87, 2.43) times increased odds, respectively, of being very worried about medical bills compared to non-Hispanic White adults.

Discussion: Hispanic and non-Hispanic Black adults with early-onset cancer disproportionately experienced all three aspects of financial toxicity.

Health Disparities

Suicidal ideation, assets, and race in U.S. adults from 2023 to 2024 Catherine Ettman*
Catherine Ettman Rajesh Satpathy-Horton Priya Dohlman Sandro Galea

Limited evidence exists on whether race modifies the link between assets and suicidal ideation. Using longitudinal data on a nationally representative sample of U.S. adults collected in Spring 2023 and 2024 (CLIMB study, N=1,863), we used multiple logistic regression to estimate the 2023 predictors of suicidal ideation in 2024, adjusting for age, gender, and race and ethnicity. 2) We tested for effect modification by race by estimating the fully adjusted model stratified by each race/ethnicity group and models with interactions between race and financial, physical, and social assets. In survey-weighted logistic regressions, income was significantly associated with higher odds of suicidal ideation in the following year ($0-$45,000 income relative to $150,000+ income: OR=2.5 [95% CI 1.2, 4.9]), although all other financial and physical assets were non-significant for the overall group. Low social support was associated with higher odds of next year suicidal ideation [OR=3.0, (95% CI 2.3, 4.0). Models stratified by race showed a negative association between some financial (income, savings) and social (education) assets with suicidal ideation among White non-Hispanic participants but not among Black or Hispanic persons. While income was protective for White groups against suicidal ideation, income was not protective for Hispanic groups. We found no evidence of differences in the association between income and suicidal ideation for Black versus White groups in interaction terms. Some financial assets appeared to be protective against suicidal ideation for non-Hispanic White persons but not for non-Hispanic Black or Hispanic groups. Social support was consistently associated with reduced suicidal ideation with no significant difference in the protective effect across race groups. Financial assets may have different mental health protection for White versus Black or Hispanic populations. Social support is the most consistently protective asset across groups.

Health Disparities

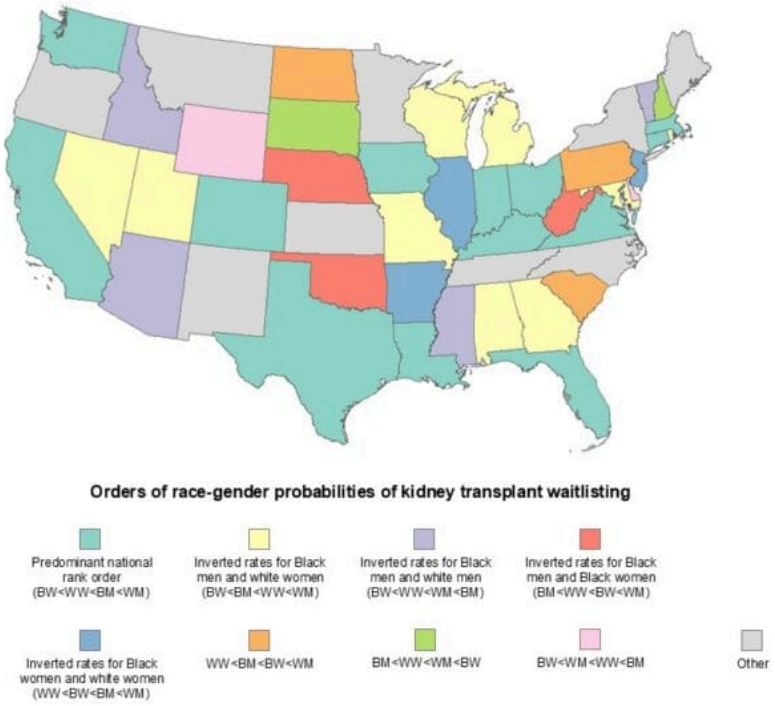
Geographic variation in intersectional racial and gender disparities in access to the kidney transplant waitlist in the US Annika Gompers* Annika Gompers Kaitlyn Stanhope Jessica Harding

Background: Kidney transplantation is lifesaving treatment for people living with kidney failure, however access is not equitable by race, gender, and their intersection. The objective of this study was to examine US state-level variation in intersectional racial and gender disparities in access to the kidney transplant waitlist.

Methods: We used the US Renal Data System to conduct a retrospective cohort study of all Black or white adults initiating kidney replacement therapy (KRT; dialysis or transplantation) in the US from 2015 through 2019, with follow-up through 2021. We estimated predicted probabilities of waitlisting in each race-gender group (Black women, Black men, white women, white men) and categorized their rank order. For US-wide estimates, we used generalized estimating equations to fit Cox proportional hazard models accounting for clustering by state. For state-specific estimates, we fit Cox proportional hazard models with an interaction term between race-gender group and state. We adjusted for individual clinical and social factors, dialysis facility characteristics, and neighborhood characteristics.

Results: Among 488,400 patients initiating KRT, the adjusted probability of waitlisting within 3 years was lowest among Black women (0.115 [95% CI 0.111-0.120]), followed by white women (0.123 [0.117-0.129]), Black men (0.128 [0.123-0.134]), then white men (0.141 [0.136-0.147]). There was heterogeneity in the rank order of waitlisting probabilities found in each US state (**Figure 1**). In 31 states the lowest probability was among Black women, in 11 states it was lowest among white women, and in 8 states it was lowest among Black men; white men did not have the lowest probability of waitlisting in any state.

Conclusion: Substantial geographic variation exists in intersectional racial and gender disparities kidney transplant access in the US, indicating that potentially intervenable state-level conditions may contribute to these disparities.


Orders of race-gender probabilities of kidney transplant waitlisting
Predominant national rank order (BW<WW<BM<WM)
Inverted rates for Black men and white women (BW<BM<WW<WM)
Inverted rates for Black men and white men (BW<WW<WM<BM)
Inverted rates for Black men and Black women (BM<WW<BW<WM)
Inverted rates for Black women and white women (WW<BW<BM<WM)
WW<BM<BW<WM
BM<WW<WM<BW
BW<WM<WW<BM
Other

Health Disparities

Association between neighborhood segregation and fecundability in a cohort of Black women Chen Sheng* Chen Sheng Yvette C. Cozier Sharonda M. Lovett Brittney Francis Mary D. Willis Wendy Kuohung Jacqueline Hicks Junenette L. Peters Lauren A. Wise Amelia K. Wesselink

Background: In the US, approximately 15% of couples experience infertility. Emerging research indicates that residential segregation can shape reproductive outcomes. However, there are few studies investigating the effects of residential segregation on fecundability (per-cycle probability of conception).

Methods: We used data collected during 1995-2011 from the Black Women's Health Study (BWHS), a prospective study of U.S. Black women who enrolled in 1995. Biennial health questionnaires from 1995-2011 contained questions on reproductive outcomes including births and miscarriages. A supplemental module in 2011 asked participants to report on each pregnancy resulting in a birth, including whether the pregnancy was planned and how many months it took to conceive. We collected additional data on unsuccessful pregnancy attempts. We used residential address data to calculate census tract level Index of Concentration at the Extremes (ICE). We defined ICErace+income, which reflects combined racial and economic segregation, as the number of non-Hispanic White individuals earning ≥$100,000/year to the number of non-Hispanic Black individuals earning <$25,000/year within a census tract. We implemented proportional probabilities regression models with generalized estimating equations to estimate fecundability ratios (FR) and 95% CI, adjusted for age, calendar year, geographic region, early life SES and educational attainment.

Result: The analysis included 2,857 planned pregnancy attempts from 2,183 participants. Compared with the highest quintile ICErace+income (most privileged), the adjusted FR (95% CI) for quintiles 1-4 were 0.93 (95% CI: 0.82-1.06), 0.93 (95% CI: 0.82-1.05), 1.02 (95% CI: 0.90-1.15), and 0.99 (95% CI: 0.88-1.11), respectively.

Conclusion: In this prospective cohort study, there was no strong association of combined racial and economic segregation with fecundability among Black women.

LATEBREAKER

Health Disparities

Transportation barriers to health care access: a scoping review of measurement approaches and associated health outcomes Josiane Kabayundo* Josiane Kabayundo Muskan Ahuja Snehal Jadhav Lisa C. Smith Farzana Bithi Shamim Shahi George Johnson Siddhi Munde Kendra L. Ratnapradipa

Background: Although transportation is acknowledged as a primary barrier, along with cost, to healthcare access; there is no standardized measure to assess transportation barriers to healthcare access. The lack of standardized measures limits the ability to compare findings across the study, hindering the identification of targeted transportation interventions.

Objectives: 1) To assess how transportation barriers to healthcare access and utilization are measured in U.S. studies, and 2) to describe the types of health outcomes examined in these studies. The review focuses on the constructs and operational definitions.

Methods: A systematic literature search of online databases identified articles published in English from 1 January 1991-10 February 2022 with a focus on articles assessing transportation as a means of accessing healthcare services or as a barrier to access/utilization of healthcare for a specified health outcome.

Results: Of 2,527 articles identified, 186 articles met our inclusion criteria and were descriptively summarized. Geographic specificity varied from point location to county. The most common transportation measures included estimated travel distance (n=95) and time (n=63), assessed as straight-line (n=48). Continuous results were further categorized (ordinal or dichotomous) for analysis in 21 studies. Eight studies assessed supply-demand density using a floating catchment area (FCA). Health measures could be generally categorized as service access (e.g., opioid treatment, cancer screening), healthcare utilization (e.g., missed appointments, hospital remissions), and disease-specific outcomes (e.g., all-cause or cancer mortality).

Conclusion: The study highlights the need for standardized measures and reporting to address transportation barriers across rural and urban settings, aiming to improve healthcare access and health equity. Included studies highlight the complex interactions between healthcare dynamics and transportation barriers.

LATEBREAKER

Health Disparities

Asian and Hispanic enclaves and hospitalizations with Parkinson's Disease in California Medicare beneficiaries Veronica A. Wang* Veronica A. Wang Scott Delaney Daniel Mork Michelle Audirac Danielle Braun Antonella Zanobetti

Aim: Living in ethnic enclaves may procure health benefits. We investigated whether residing in Asian and Hispanic enclaves was associated with fewer hospitalizations with PD (first hospitalization with a Parkinson's Disease diagnosis code) among California Medicare Fee-For-Service beneficiaries (2010-2016).

Methods: We considered three ethnic enclave binary exposure definitions using 2010 5-year American Community Survey variables: 1) cutoff (≥90th percentile % Asian/Hispanic residents), 2) spatial (local Moran's I to identify spatial clusters of Asian/Hispanic residents), and 3) dimension reduction (≥90th percentile composite score from principle component analysis on several acculturation variables). For each exposure definition and ethnic enclave, we fitted Poisson regressions adjusted for year, individual risk factors, atmospheric variables, with counts of hospitalizations with PD aggregated to the ZIP Code Tabulation Area level as the outcome. Subgroup analysis was conducted by fine particulate matter (9µg/m3 cutoff).

Results: Among 3+ million beneficiaries aged ≥65 years in our study, ~1% experienced a hospitalization with PD. Residing in an Asian enclave regardless of beneficiary race/ethnicity was associated with higher rates of the outcome (IRRs of 1.13 [95% CI: 1.10, 1.16] for cutoff, 1.11 [95% CI: 1.08, 1.15] for spatial, and 1.10 [95% CI: 1.06, 1.14] for dimension reduction), while Hispanic enclaves appeared protective (IRRs of 0.94 [95% CI: 0.91, 0.96] for cutoff, 0.92 [95% CI 0.88, 0.97] for spatial, and 0.86 [95% CI: 0.82, 0.90] for dimension reduction). Residing in a Hispanic enclave (but not an Asian enclave) was more beneficial in higher compared to lower air pollution settings.

Conclusion: A higher and lower rate of hospitalizations with PD was observed for residential Asian and Hispanic enclaves, respectively. Future work to clarify the multifaceted, context-dependent, and complex underlying mechanisms are needed to protect vulnerable populations.

LATEBREAKER

Health Disparities

Shared patient-provider demographics and risk for postpartum opioid dispensation among US military service members, 2017–2023 Celeste Romano* Celeste Romano Clinton Hall Gia Gumbs Ava Marie Conlin Marissa Seamans

Background: Undertreatment of women's pain, particularly Black women's pain, is prevalent, yet opioids can also be overprescribed, contributing to chronic misuse. This work aimed to assess the association between shared patient-provider race—a factor previously associated with health outcomes—and postpartum opioid dispensation.

Methods: Vaginal and low-risk cesarean deliveries among Black, Hispanic or Latino, and non-Hispanic White US service members at military hospitals, 2017–2023, were identified using TRICARE claims and military personnel records. Deliveries were quasi-randomly assigned an attending provider at time of admission. Eligible postpartum opioid dispensations were written within 1 day of discharge and dispensed within 7 days postpartum. Log-binomial regression was used to estimate crude risk ratios (RRs) and 95% confidence intervals (CIs) overall and by racial group.

Results: Postpartum opioid dispensation occurred among 2.6% (n=346), 2.2% (n=446), and 1.9% (n=190) of Black, non-Hispanic White, and Hispanic or Latino vaginal deliveries, respectively. In contrast, opioid dispensation ranged from 57.2% (n=1531) among non-Hispanic White low-risk cesarean deliveries to 59.2% among Black (n=1605) and Hispanic or Latino (n=1014) low-risk cesarean deliveries. Shared patient-provider race was not associated with opioid dispensation among vaginal deliveries, but risk was slightly attenuated among low-risk cesarean deliveries (RR=0.96, 95% CI: 0.91-1.01); stratified analyses revealed this association was unique to Black patients (RR=0.83, 95% CI: 0.71-0.96).

Conclusions: Postpartum opioid dispensation was rare for vaginal deliveries and occurred among <60% of low-risk cesarean deliveries. Dispensations were slightly more common among Black service members relative to other racial groups, but were less likely to occur if the attending provider also identified as Black. Follow up work is needed to identify possible reasons for differential dispensation patterns.

LATEBREAKER

Health Disparities

Mindfulness and Healthcare Spending Among Non-Hispanic Black Older Adults: A Stratified Analysis of the Health and Retirement Study Shilpa Patil* SHILPA PATIL RoiSan Nhpang Rohit Balsundaram Dr. Malinee Neelamegam

Mindfulness and Healthcare Spending Among Non-Hispanic Black Older Adults: A Stratified Analysis of the Health and Retirement Study

Background

Healthcare spending among older adults is influenced by various psychosocial and behavioral factors, including mindfulness practices. This study aimed to examine the association between mindfulness and healthcare spending among non-Hispanic Black older adults using data from the Health and Retirement Study (HRS). Specifically, we sought to determine whether those who engage in mindfulness practices spend less on healthcare compared to those who do not.

Methods

We conducted a cross-sectional analysis using data from the 2021 HRS Consumption and Activities Mail Survey (CAMS). The sample was stratified by race and ethnicity, focusing on non-Hispanic Black participants. Logistic regression models were used to assess the relationship between mindfulness (measured by the frequency of “often using the mind”) and healthcare spending, controlling for demographic variables such as age, gender, marital status, and income category. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated to quantify associations. The analysis included 267 individuals within the non-Hispanic Black subgroup.

Results

The logistic regression analysis revealed that non-Hispanic Black individuals who frequently engaged in mindfulness practices had significantly higher odds of reduced healthcare spending compared to their counterparts who did not. Specifically, the odds ratio for those who “often use mind” versus those who do not was 3.77 (95% CI: 1.314–10.859, p = 0.0137). This indicates that mindful individuals are nearly four times more likely to have lower healthcare expenditures. Other demographic factors, such as age, gender, marital status, and income category, did not show significant associations with healthcare spending in this subgroup.

The model’s fit statistics indicated moderate predictive power, with 52.1% concordance between predicted probabilities and observed responses. However, the overall likelihood ratio test for the model was not statistically significant (p = 0.2217), suggesting that other unmeasured factors may influence healthcare spending.

Conclusion

This study highlights the potential role of mindfulness in reducing healthcare spending among non-Hispanic Black older adults. Mindfulness practices may serve as a cost-effective strategy for managing healthcare utilization in this population. Future research should explore causal pathways and investigate additional psychosocial factors influencing healthcare spending. These findings

underscore the importance of culturally tailored interventions that promote mindfulness to improve health outcomes and reduce financial burdens among minority populations.

Health Disparities

Chronic Inflammation Management and Cardiovascular Disease Risk among Black Americans Olivia Affuso* Olivia Affuso Hoda Ahmed Kaylee Zettler Rodney Washington Harish Chander Xiaoqian Zhu

Background: Understanding the interplay of chronic inflammation and elevated cholesterol may be vitally important for screening in Black populations given the increased prevalence of elevated lipoprotein a, which has been characterized as proinflammatory. We hypothesize that measurement of chronic inflammatory may improve CVD risk stratification in this population.

Methods: We utilized data from the National Health and Nutrition Examination Survey (NHANES) 2017-2020 of Black Americans (aged 42.6±18.8 yrs, 45% male) with complete data (N=599). Elevated C-reactive protein (hsCRP) and low-density lipoprotein (LDL) were categorized using cutoffs of >3 mg/L and >100 mg/dL, respectively. Using generalized linear regression with a gamma distribution and log link, we examined the association between hsCRP-LDL groupings and 10-year total CVD Risk score estimated with the Predicting Risk of Incident CVD EVENTs (PREVENT) equation.

Results: The overall prevalence of elevated hsCRP and LDL was 39.8% and 49.1%, respectively. The mean PREVENT risk score was 4.1%[IQR:1.3-10]. Using low CRP/low LDL as the reference group, those in the high hsCRP/low LDL or high hsCRP/ high LDL had an increase in PREVENT risk score, with rate ratio (RR) of 1.354 (95% CI: 1.045,1.755) and 1.393 (95% CI:1.142, 1.700), respectively, after adjusting for age and sex. However, no statistically significant difference in PREVENT risk score was observed for individuals with low hsCRP/high LDL compared to those with low hsCRP/low LDL (RR: 1.114, 95% CI 0.881, 1.410).

Conclusion: These findings suggest that screening for chronic inflammation in addition to LDL cholesterol may be beneficial in identifying and better managing CVD risk via anti-inflammatory strategies such as improving diet quality in Black American populations.

Health Disparities

Uptake of the influenza and pneumococcal vaccines among immigrant and non-immigrant older adults in Canada: a cross-sectional analysis of data from the Canadian Longitudinal Study on Aging (CLSA) Ji Yoon Kim* Ji Yoon Kim Giorgia Sulis Alton Russell Seungmi Yang Jesse Papenburg Ananya Banerjee Patricia Li

Background: In Canada, influenza and pneumococcal vaccination rates in older adults fall below the national target of 80%. Immigrant status may be associated with lower uptake of both vaccines, but limited efforts have been made to explore such disparities. Therefore, we examined the association between immigrant status and uptake of influenza and pneumococcal vaccines among older adults as well as the relative importance of immigrant status in predicting uptake of both vaccines.

Methods: We conducted a cross-sectional secondary analysis of the Canadian Longitudinal Study on Aging data. We descriptively analyzed uptake of the vaccines by immigrant status and used Poisson regression models with robust standard errors to estimate the associations of immigrant status and other key equity stratifiers with vaccination. Importance of key determinants, including immigrant status, in predicting both vaccinations were assessed using random forest algorithms.

Results: Immigrant participants reported lower uptake of influenza vaccine in the past 12 months (63.8% [95% CI: 60.9-66.7%] vs. 66.9% [95% CI: 65.5-68.3%]) and pneumococcal vaccine ever (48.7% [95% CI: 45.6-51.8%] vs. 55.8% [95% CI: 54.3-57.3%]). Prevalence of influenza and pneumococcal vaccinations were both lower among immigrant participants compared to non-immigrant participants. Immigrant status was among the 10 most important predictors of pneumococcal vaccination, but among the less important predictors of influenza vaccination.

Conclusions: Overall, we found disparities in influenza and pneumococcal vaccination by immigrant status among older adults in Canada. Further studies on vaccine uptake and decision-making among marginalized communities, including immigrants, are warranted to equitably improve vaccine uptake.

Health Disparities

Quantile Regression Analysis of Socioeconomic and Demographic Determinants of Neighborhood Physical Activity in U.S. 500 Cities Jong Cheol Shin* Jong Cheol Shin

Objective: This study examines how socioeconomic and demographic factors influence the percentage of individuals reporting no leisure physical activity, offering insights across varying levels of inactivity using quantile regression.

Methods: Quantile regression was applied at the 10th, 25th, 50th, 75th, and 90th percentiles of no leisure physical activity. Independent variables included poverty rate, median age, and racial/ethnic majority of census tracts (Asian, Black/African American, Hispanic, and White as reference). The analysis utilized data from CDC PLACES (2014–2021), covering 20,202 U.S. census tracts after eliminating missing values. Model fit was assessed using Pseudo-R^2 and mean absolute error (MAE).

Results: Pseudo-R^2 values increased from 0.274 (10th percentile) to 0.391 (90th percentile), indicating better model fit at higher inactivity levels. Poverty was positively associated with inactivity across quantiles (β=0.384 to 0.540), as was median age (β=0.120 to 0.162). Census tracts with a majority Black/African American or Hispanic population were linked to higher inactivity across all quantiles, with the strongest effects at the 10th percentile (β=6.909 and β=5.667, respectively). Majority Asian tracts showed mixed effects, with significant associations at the 90th percentile (β=1.396).

Conclusion: Disparities in physical inactivity across U.S. census tracts are influenced by poverty and racial/ethnic composition, varying by level of inactivity. Structural and community-level interventions are essential to promote active lifestyles in high-inactivity areas.

Health Disparities

Minority tax in academic epidemiology: its status and recommendations Sarah Bassiouni* Sarah Bassiouni Jada Wiggleton-Little Emily Martin

Background: “Minority tax” is a well-elucidated term within the fields of clinical medicine and academic medicine. However, there has been a paucity of discussion of this concept within public health and epidemiology. Here, we discuss the current state of the research, as well as goals and strategy in incorporating discussions of minority tax within academic epidemiology settings.

Methods: PubMed was searched for “minority tax” in conjunction with “epidemiology”, “epidemiol*”, “public health”, and “population health”.

Results: This resulted in 282 papers with some combination of these specific terms. The vast majority of results were within the context of clinical medicine and academic medicine settings in the U.S.; most of these were through the lens of diversity, equity, and inclusion programs. Two papers outside of academic medicine mentioned the term “minority tax” in their backgrounds: one was within the fields of nutrition and obesity, and the other was in data science.

Discussion: The paucity of literature, peer-reviewed and otherwise, regarding minority tax within both the larger public health field and within epidemiology specifically reflects an opportunity to strengthen our academic training pathways. It is well documented that students and trainees from historically marginalized groups (STHMG) are more likely to take on additional, often uncompensated, roles in their training. Efforts to reduce minority tax among STHMG can include intentional recruitment and retention of STHMG, structured mentorship and advancement programs and transparent resources around funding opportunities.

Conclusions: The results of this search indicate that epidemiology as a field has an opportunity to consider minority tax within an academic setting. This includes not only studying how it presents in our students and trainees, but also incorporating strategies to improve the likelihood that our colleagues can practice epidemiology with their full potential.

Health Services/Policy

The Association Between Free School Meals and Child Mental Health Diagnoses: Evidence from Medical Records Tom Lindman* Tom Lindman Jessica Jones-Smith

Background: The prevalence of ADHD, anxiety, and depression diagnoses among K-12 students in the U.S. has increased over recent decades, exposing challenges faced by children and youth. As a result, supporting mental health is increasingly a priority for public health agencies, schools, and policy makers. Income instability and low socioeconomic status negatively influence mental health, suggesting a role for social policy. Despite child mental health's salience as a public health problem, little research assesses whether U.S. food assistance programs affect child mental health.

Methods: We evaluate whether exposure to free school meals affects the likelihood of ADHD, anxiety, and depression diagnoses among children visiting Federally Qualified Health Centers. Our study leverages the rollout of the Community Eligibility Provision (CEP), a federal policy allowing schools to provide universal free breakfast and lunch.

Our dataset links medical records from the OCHIN Data Warehouse for 2012-2019 with publicly available school data.

Our analysis uses a modern difference-in-differences approach, estimating the association of CEP exposure with mental health diagnoses. Models include child fixed effects and adjust for grade level.

Results: Our sample includes children who visited an OCHIN clinic during consecutive school years and attended a CEP-eligible school (n=201,295).

CEP exposure is associated with a 0.28 percentage point (0.4%) decrease in likelihood of ADHD diagnosis in the first year of exposure (CI: -0.483, -0.082). Estimates for subsequent years are not statistically significant.

CEP exposure is also associated with reductions in depression (-0.30; CI: -0.476, -0.128) and anxiety (-0.24; CI -0.440, -.0039) diagnoses. However, divergent trends for exposed and unexposed groups are present prior to exposure.

Conclusion: Exposure to universal free school meals is associated with a reduction in ADHD diagnoses in a predominantly low-income sample of K-12 students.

Health Services/Policy

Follow-up visits with a physician after discharge from hospital: a retrospective cohort study

Derek Manis* Derek Manis Chantal Backman Colleen Webber Stacey Fisher Wenshan Li Jennifer Watt Peter Tanuseputro Nathan Stall David Kirkwood Andrew Costa

Background: Older adult (65 years and older) residents of assisted living (AL) and community-dwelling home care (HC) recipients have high rates of hospital-based care, yet substantially low rates of primary care and specialist physician visits. The disproportionate use of these services has important implications for single-payer, publicly funded health care systems.

Objective: To examine the 30-day risk of a follow-up visit with a physician after discharge from hospital among residents of AL and HC recipients.

Design, Setting, and Participants: Retrospective cohort study using linked, population-level health system administrative databases and reliable and valid chronic conditions algorithms in Ontario, Canada from July 1, 2018 to June 30, 2023.

Methods: The outcome of interest was an outpatient visit with a primary care or specialist physician within 30 days of hospital discharge. Clinical, community, and health service use variables were obtained. Inverse probability (IP) weighted discrete-time hazards were used to model standardized cumulative incidence curves. From these curves, the 30-day risk of a follow-up visit with a physician was derived.

Results: This study included 3,144 residents of AL (mean [SD] age 88 [6.4] years, 72% female) and 26,046 HC recipients (mean [SD] age 84 [7.4] years, 60% female). The mean of the IP weights was 1.1. The 30-day risk of a follow-up visit was 0.999 and 0.998 among residents of AL and HC recipients, respectively (RD 0.001; RR 1.000).

Conclusions and Implications: These findings demonstrate that older adults receive care from a physician in their community following discharge from hospital, despite narratives suggesting inadequate access. The IP weights mostly balanced the confounders in each population, but underlying differences related to unpaid caregiving and household income, both of which are not available in these health system data, may be important factors to inform future data collection for health system planning.

Health Services/Policy

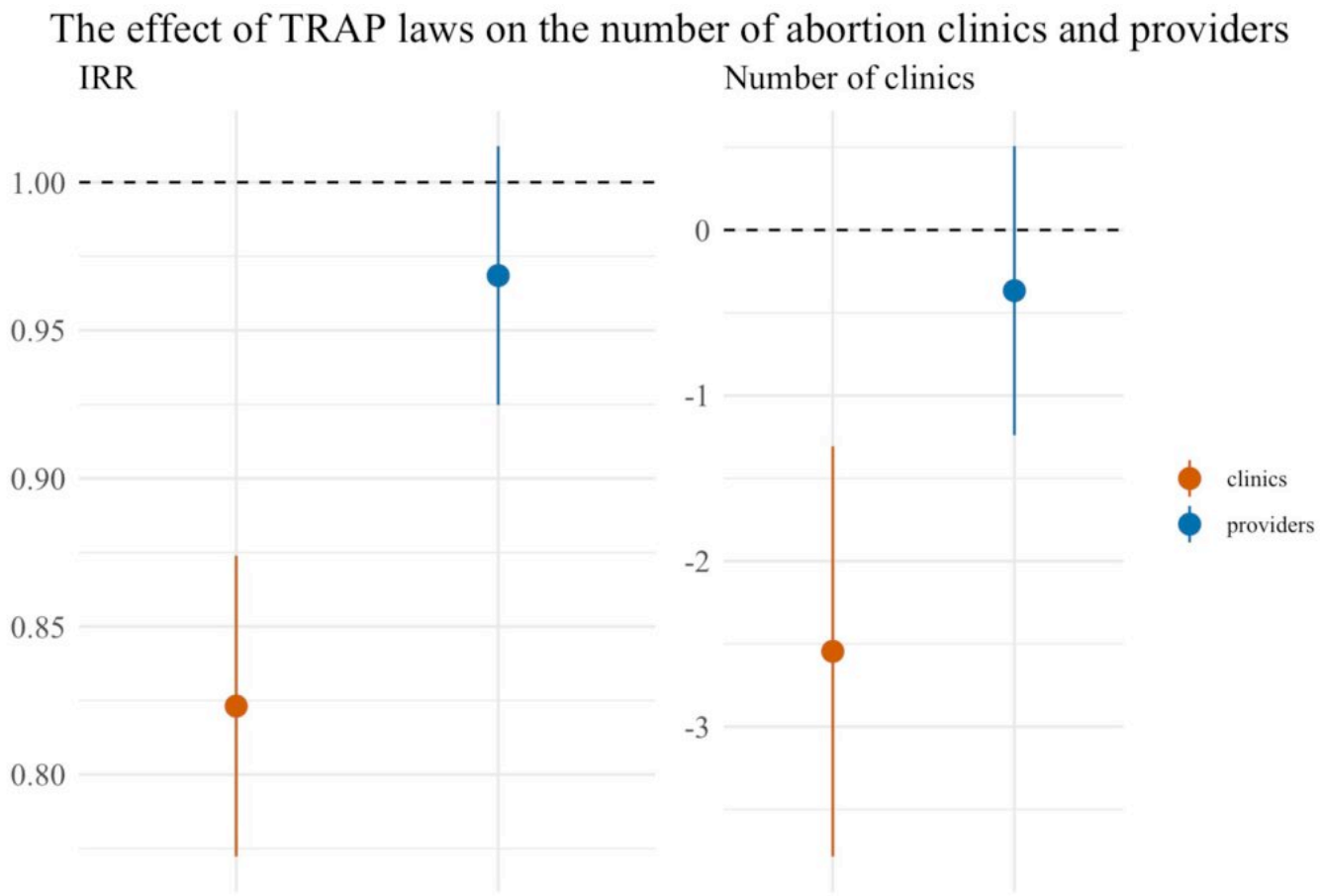
Is TRAP law enforcement associated with an excess change in abortion providers? Kaya Van Roost* Kaya Van Roost Nichole Austin Sam Harper

Background–The number of abortion-providing facilities in the US decreased over the last two decades. Some of this decline is attributable to a reduced need for abortion services, but it is possible that abortion policies that target providers, or TRAP laws, have also played a role in decreasing provider availability. We quantified the relationship between these policies and clinic and provider availability using clinic data from 2008 to 2020.

Data & methods–We merged data we compiled on the timing of TRAP policies with publicly-available data on state-level counts of both abortion and nonspecialized clinics ("clinics") and all abortion providers ("providers") in 2008, 2011, 2014, 2017, and 2020. We estimated changes in the number of clinics and providers post-TRAP enforcement among treated states to the same changes in untreated states using a difference-in-differences method appropriate for staggered treatment designs. To do so, we fit a series of Poisson models saturated with group-time interaction terms and used marginal postestimation to re-express the incidence rate ratios (IRRs) in absolute terms. Standard errors were bootstrapped.

Results–Among treated states, the mean number of clinics and providers was 16.4 and 25.1, respectively, in pre-enforcement years. TRAP enforcement was associated with an excess clinic decline of 18% (IRR: 0.82, 95% CI: 0.77, 0.87) and a smaller decline among providers (IRR: 0.97, 95% CI: 0.92, 1.01). In absolute terms, these findings suggest that TRAP laws resulted in 2.5 fewer clinics (95% CI: -3.8, -1.3) and 0.4 fewer providers (95% CI: -1.2, 0.5), conditional on state and year fixed effects.

Discussion–As abortion restrictions intensify following the Dobbs decision, it is important to understand how abortion policies impact service availability. We found that previous, less restrictive regulation through TRAP laws decreased the number of abortion clinics, where the vast majority of abortions are performed.


The effect of TRAP laws on the number of abortion clinics and providers
IRR
1.00
0.95
0.90
0.85
0.80
Number of clinics
0
-1
-2
-3
clinics
providers

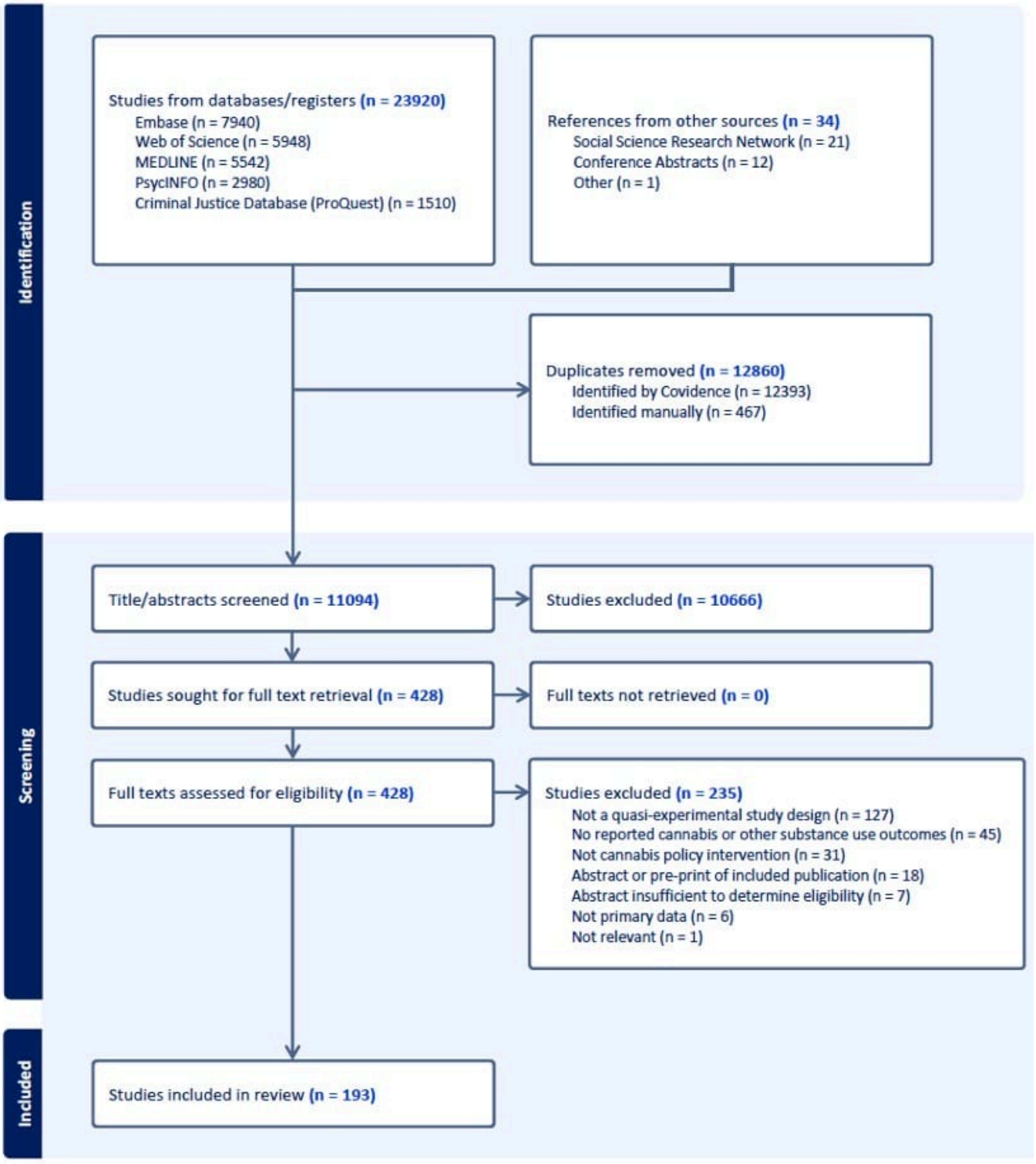
Health Services/Policy

Impact of Global Cannabis Policy Changes on Cannabis and Other Substance Use: A Systematic Review Sarah Windle* Sarah Windle Peter Socha Jasleen Arneja Sam Harper Genevieve Gore Genevieve Gariepy Eva Graham Andrea Benedetti Arijit Nandi

Countries worldwide have liberalized their cannabis policies. Cannabis may be both a complement and a substitute for other substances, but the impacts of cannabis reforms on substance-related harms and benefits remain unclear. We are conducting a systematic review of quasi-experimental studies assessing the impact of cannabis policy changes on cannabis and other substance use (PROSPERO protocol registration: CRD42024547798). In contrast to other observational studies, quasi-experimental designs account for some sources of unmeasured confounding and can estimate the causal effects of policy changes under weaker assumptions.

We screened the title/abstract of 11,094 publications from five databases and grey literature, of which 428 publications were retrieved for full text screening, and 193 met the inclusion criteria (see flow diagram). Many included studies employed a difference-in-differences or interrupted time series approach, although other designs were eligible (e.g., regression discontinuity, instrumental variable). Most studies used data from North America and examined policies liberalizing cannabis use (e.g., medical or recreational legalization, with or without retail sales). Commonly reported outcomes included past-month cannabis, alcohol, or tobacco use, and opioid mortality; other studies examined substance use frequency, initiation, sales, prescribing, dependence, and healthcare utilization.

Next steps include data extraction, risk of bias assessment using ROBINS-I (V2), and synthesis. We anticipate sufficient studies for random effects meta-analysis with inverse variance weighting for the most common treatment-outcome pairs. Other pairs will be synthesized using a descriptive, analytical approach. This systematic review and meta-analysis will summarize the best available evidence concerning the impact of cannabis policies on substance use, to inform policy and public health decision-making worldwide, and to identify gaps in knowledge for future research.


Identification
Studies from databases/registers (n = 23920)
Embase (n = 7940)
Web of Science (n = 5948)
MEDLINE (n = 5542)
PsycINFO (n = 2980)
Criminal Justice Database (ProQuest) (n = 1510)
References from other sources (n = 34)
Social Science Research Network (n = 21)
Conference Abstracts (n = 12)
Other (n = 1)
Duplicates removed (n = 12860)
Identified by Covidence (n = 12393)
Identified manually (n = 467)
Screening
Title/abstracts screened (n = 11094)
Studies excluded (n = 10666)
Studies sought for full text retrieval (n = 428)
Full texts not retrieved (n = 0)
Full texts assessed for eligibility (n = 428)
Studies excluded (n = 235)
Not a quasi-experimental study design (n = 127)
No reported cannabis or other substance use outcomes (n = 45)
Not cannabis policy intervention (n = 31)
Abstract or pre-print of included publication (n = 18)
Abstract insufficient to determine eligibility (n = 7)
Not primary data (n = 6)
Not relevant (n = 1)
Included
Studies included in review (n = 193)

LATEBREAKER

Health Services/Policy

Utilization among New Young Healthplan Members Relative to Primary Care Provider Designation Abigail Eaton* Abigail Eaton Stephanie Prausnitz Nicole Tran

Utilization among New Young HealthPlan Members Relative to Primary Care Provider Designation

Background:

Healthcare utilization patterns have been shown to differ between pediatrics, when parents are responsible, and young adults, who navigate their own health (Lau, Holland). The 18 to 26-year-old population has been shown to more likely to use the emergency department than office-based visits for healthcare (Lau). Holland reported that 18- to 21-year-olds, who did not attend a well-care visit, had 47% greater odds (95% CI: 1.37 – 1.58) of emergency department (ED) visits. A focus on well-care visit attendance has been suggested to reduce ED utilization (Holland). This study aims to understand if young adults newly navigating adult medicine who have a designated PCP early in their membership will have more appropriate usage of the health care system.

Methods:

The study population comprised 19- to 26-year-old, newly enrolled individuals in 2023 at Kaiser Permanente Northern California (KPNC), an integrated healthcare system with more than 4 million members who demographically represent the broader population of Northern California. Excluded were individuals who were not health-plan members for at least one-year post-enrollment, allowing for a three-month gap. Differences in utilization patterns within the first year of membership were examined by whether the new member had a Primary Care Primary (PCP) designated to them within 3 months.

Results:

The study population size was 30,928, with 51 % having a designated PCP within 3 months of becoming a member. Seventeen percent of the study population had an emergency department (ED) visit within the first year of joining (n=5,061). Among those with a designated PCP w/in 3 months, 19% had an ED visit compared with 14% of those w/o PCP visit in the first 3 months. Among the population of ED users, for those with a PCP, 32% of ED visits were for a low acuity event compared with 41% of visits for those without PCP.

Eighteen percent (n=5,609) of the study population had at least one E-visit. An E-visit is defined as an asynchronous structured electronic message between patients and clinicians requiring clinical decision making. Among those w a PCP, 25% had at least one e-visit, compared with 11% of those without. Among those individuals with E-visits the top 50% of topics covered were sexual health, cold/cough/sinus/sore throat/flu, urinary (bladder infection), and birth control.

Conclusions: Although individuals with PCPs may be the members with more complex health care needs (Eaton), the utilization patterns seen here indicate that health care resources may be more appropriately leveraged among those with PCPs designated early on in their membership. Setting a culture and expectations of appropriate utilization of healthcare resources and promoting well-care

visits at this time of transition in a person's life could provide benefits both for an individual's health and for healthcare delivery systems.

Holland JE., Varni SE, Pulcini CD, Simon TD, Harder VS. Assessing the Relationship Between Well-Care Visit and Emergency Department Utlization Among Adolescents and Young Adults. . J Adolesc Health. 2022 Jan;70(1)64-66 DOI: 10.1016/j.jadohealth.2021.08.011

Lau JS, Adams SH, Irwin CE, Jr., Ozer EM. Receipt of preventive health services in young adults. J Adolesc Health. 2013 Jan; 52(1):42-9. doi:10.1016/j.jadohealth.2012.04.017

Eaton A., Prausnitz S., Baskind H., Tran, N. Associations Between Screening Rates and Visits to Primary Care Provider in Young Adults transitioning from Pediatrics to Adult Medicine (under review American Journal of Preventive Medicine FOCUS

LATEBREAKER

HIV / STI

Examining the Intersection of Quality of Life, Viral Suppression, and Race/Ethnicity Among Women with HIV in the Women's Interagency HIV Study (WIHS) Roxana Rezai* Roxana Rezai Sung-Jae Lee Panteha Hayati Rezvan Onyebuchi A. Arah Chunqing Lin Crystal Chapman Lambert Andrew Edmonds Kathleen M. Webber Tracey E. Wilson Janet Brown-Friday Sabina Haberlen Maria L. Alcaide Gina Wingood Heather Freasier Lakshmi Goparaju Matthew J. Mimiaga

Background: HIV viral suppression is critical for the health of people with HIV as well as preventing onward transmission. Higher quality of life (QOL), including mental and physical health and socioeconomic stability, is consistently linked to viral suppression. This analysis assessed the relationship between self-reported QOL and viral suppression among women with HIV (WWH) and differences across racial and ethnic groups.

Methods: Longitudinal data from the Women's Interagency HIV Study (WIHS) over a 5 year period were used to fit generalized mixed effects regression models to assess the relationship between self-reported QOL (scale of 0-10, higher scores=higher QOL) and viral suppression (<200 copies per ml). An interaction term was included to examine a moderating effect by race/ethnicity. Final models adjusted for sociodemographic factors, substance use, and health behaviors.

Results: At the baseline, nearly 20% of the sample (n=1,324) had an unsuppressed viral load and the mean QOL score was 7.6 (SD=1.8). The mean age was 48 years (SD=9.2), and 70% identified as Non-Hispanic/Latinx Black/African American, 16% as Hispanic/Latinx, 11% as non-Hispanic/Latinx white, and 3% were other racial categories. We found a positive association between QOL and viral suppression (aOR: 1.17, 95% CI [1.10, 1.25]). Moreover, the magnitude of this association varied by racial identity, with the largest increase in odds of viral suppression per one-unit QOL increase among non-Hispanic/Latinx whites (aOR: 1.49, 95% CI [1.14, 1.82]) and lowest among Non-Hispanic/Latinx Black/African Americans (aOR: 1.16, 95% CI [1.08, 1.25]). No substantial associations were found among Hispanic/Latinx participants or other racial groups.

Conclusion: These findings highlight a positive association between QOL and viral suppression among WWH and a moderating effect by race. Future research should assess which specific QOL domains are driving this association to inform tailored interventions.

LATEBREAKER

HIV / STI

The Impact of COVID-19 Restriction Policies on Viral Load Suppression for People with HIV: Insights from the NA-ACCORD Yue Zhang* Yue Zhang Brenna Hogan Yawei Cheng Catherine Lesko Milton L. Wainberg Vincent Marconi John Gill Michael A Horberg Sonia Napravnik Michael J Silverberg Ronald Bosch Angela Parcesepe Keri N. Althoff for the North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD)

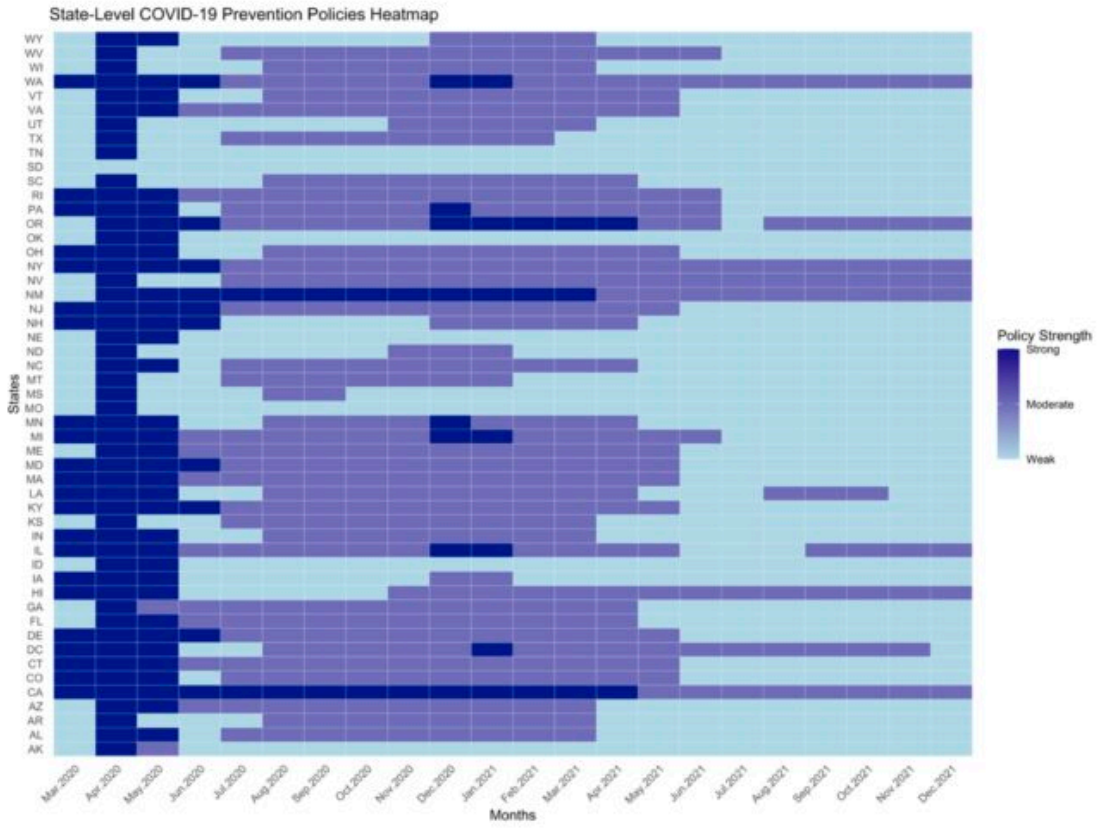
Background: The COVID-19 pandemic affected healthcare access, including among people with HIV (PWH) in care. With antiretroviral therapy (ART), HIV viral load (VL) suppression is maintained, safeguarding the health and reducing transmission. Our objective was to evaluate the association of COVID-19 restriction policies and detectable VL among PWH in care during restrictions.

Methods: The sample was comprised of PWH (≥18 years) from 12 U.S. clinical HIV cohorts contributing to the North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD) who had ≥1 clinical encounter or laboratory result occurring between 09/01/2018–02/29/2020 (pre-pandemic) and between 06/01/2020–12/31/2021 (during the pandemic). State-level COVID-19 prevention policy strength was categorized as strong, moderate, or weak based on closures, and shelter-in-place orders from COVID-19 U.S. State Policies database. A generalized linear mixed model with splined follow-up time estimated adjusted ORs for the association between policy strength and detectable VL (>50 copies/mL), incorporating an interaction between policy strength and calendar month (knot at June 2020). The model accounted for random effects per PWH and adjusted for covariates, including age, sex, race, region, HIV acquisition risk, and baseline CD4 count.

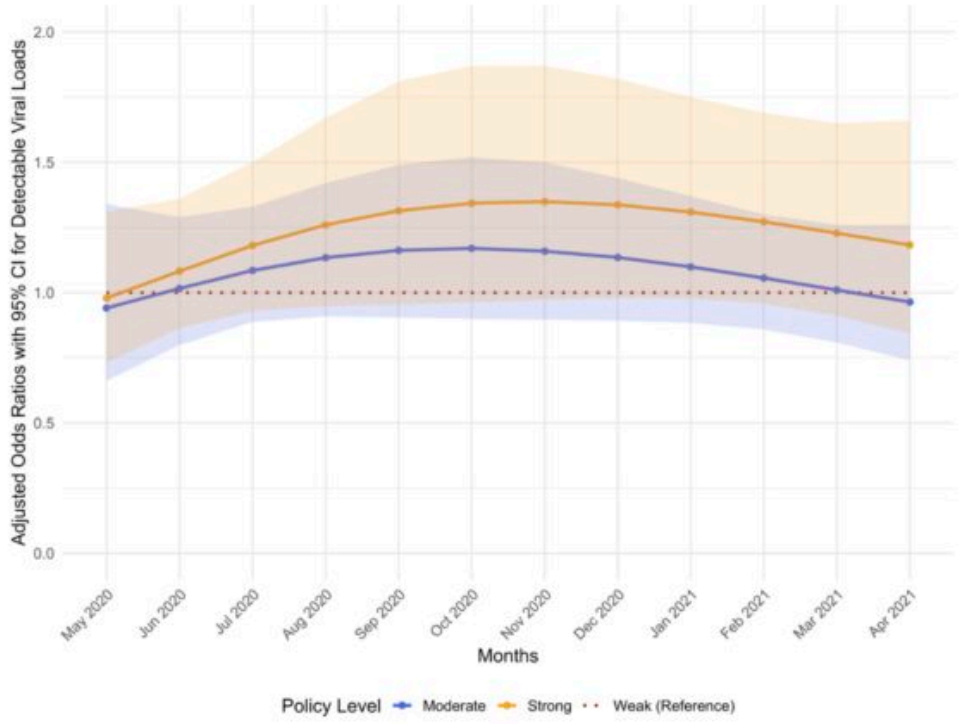
Results: 47,312 PWH (88% male) were included, with a median age of 55 (IQR, 43 – 62) years. Figure (a) shows the monthly distribution of restriction policy strength across states. After adjusting for covariates, neither strong nor moderate (vs. weak) COVID-19 policies were associated with detectable VL for May–June 2020 (aOR = 1.03 [95% CI: 0.80, 1.32] and aOR = 0.98 [95% CI: 0.73, 1.31], respectively) and July 2020–April 2021 (aOR = 1.28 [95% CI: 0.98, 1.66] and aOR = 1.10 [95% CI: 0.90, 1.33], respectively). Both strong and moderate policies were associated with increased odds of detectable VL from June 2020, though the associations remained non-significant throughout follow-up. (Figure (b)).

Conclusions: Our study indicates that both strong and moderate COVID-19 policies were not associated with detectable VL for PWH; but over time, month-specific estimates showed increased odds of detectable VL. These findings inform pandemic preparedness to ensure health services reach those who need them.

(a)


State-Level COVID-19 Prevention Policies Heatmap
States
Months
Policy Strength
Strong
Moderate
Weak

(b)


Adjusted Odds Ratios with 95% CI for Detectable Viral Loads
2.0
1.5
1.0
0.5
0.0
May 2020
Jun 2020
Jul 2020
Aug 2020
Sep 2020
Oct 2020
Nov 2020
Dec 2020
Jan 2021
Feb 2021
Mar 2021
Apr 2021
Months
Policy Level
Moderate
Strong
Weak (Reference)

HIV / STI

The effects of minor consent laws for STI/HIV prevention on STI/HIV testing among adolescents in the United States Alexandra Skinner* Kimberly M. Nelson Alexandra Skinner Shira I. Dunsiger Emily Unger Samantha Haiken Camille LaBranche Michele Ybarra S. Bryn Austin Kristen Underhill

Minor consent laws allow US minors to consent independently to medical care without guardian involvement. Although these state laws are intended to remove barriers to care, research assessing their impact on adolescent health care use is scarce. This study evaluates whether changes in minor consent laws for STI/HIV prevention services are associated with changes in STI/HIV testing among US adolescents.

We linked longitudinal state-level minor consent law data with individual-level National Survey of Family Growth data (2006-2019; 15–20-year-olds: N=13,169). Among 15–17-year-olds (n=6,759), effects of implementing a statewide minor consent law for STI/HIV prevention services on self-reported STI/HIV testing in the past year were modeled using a difference-in-differences approach with event study specification and survey weights to produce nationally representative estimates. Linear regression models included state and year fixed effects and controlled for age, sex, race/ethnicity, sexual minority status, urbanicity, and poverty status. STI testing questions differed depending on participant sex and thus were modeled separately. Conditional effects by age range (15–17-year-olds vs 18–20-year-olds) crossed with sex, sexual minority status, and race/ethnicity were examined.

We found no association between minor consent law implementation and changes in STI testing (females: -0.07, 95% CI: -0.18—0.03; males: 0.001, 95% CI: -0.05—0.05) or HIV testing (-0.02, 95% CI: -0.05—0.01). Effects did not vary by age range, sex, sexual minority status, or race/ethnicity.

Simply enacting minor consent laws for STI/HIV prevention services may be insufficient to increase STI and HIV testing among US adolescents. Research assessing barriers to the implementation of these laws (e.g., youth and provider knowledge of the laws, providers' attitudes about relying on minor consent) is needed to optimize their utility and increase STI/HIV testing among minors.

HIV / STI

Changes in ART Adherence From the Community to the Nursing Home for Adults with HIV

Brianne Olivieri-Mui* Brianne Olivieri-Mui Ellen McCarthy Ira Wilson Mark Brennan-Ing Laura Senier Dae Hyun Kim

Background: Antiretroviral therapy (ART) adherence in nursing homes is lower than adherence in the community for adults with HIV (AWH). ART is necessary for people with HIV to achieve near normal life expectancy and viral suppression. Thus, it is critical to understand changes in ART adherence as people transition from the community to long-term NH residents.

Methods: Descriptive observational study of changes in ART adherence in the transition from the community to long NH stays for AWH in a 5% traditional Medicare 2014-2019 sample. Change in ART adherence was measured as the difference between the proportion of days covered (PDC) by a 3-drug antiretroviral regimen for 90 days before admission and up to 90 days after achieving long stay status. Change was grouped as never had, always had, lost, or gained ART. We describe person- and facility-level factors associated with ART adherence change.

Results: There were 713 long NH stays for 657 AWH across 598 NHs. The mean age of stays for AWH was 61 years (SD 11); 38% were age 65+. Stays of AWH were more often male (n=513, 72%), of Black race (n=393, 55%), for Medicaid dually eligible (n=419, 59%) with frailty (n=517, 73%), and located in the South (n=323, 45%). The average change in adherence from the community to NH long-stay was positive, gaining on average 13.8 days (SD 38) covered by ART. One in four (n=185, 26%) never had ART before or after admission to the NH, 3% (n=23) lost ART in the transition.

Conclusions and relevance: One of four nursing home stays lack ART because most individuals are not on ART at admission and do not initiate it during their stay. This highlights a critical need for prescription continuity and engaging PWH in treatment at the pivotal time of admission to a NH.

HIV / STI

The Impact of the COVID-19 Pandemic on Reported Chlamydia and Gonorrhea Cases Among Youth and Young Adults in Canada Farhan Khandakar* Farhan Khandakar Dr. Sahar Saeed Dr. Nichole Austin

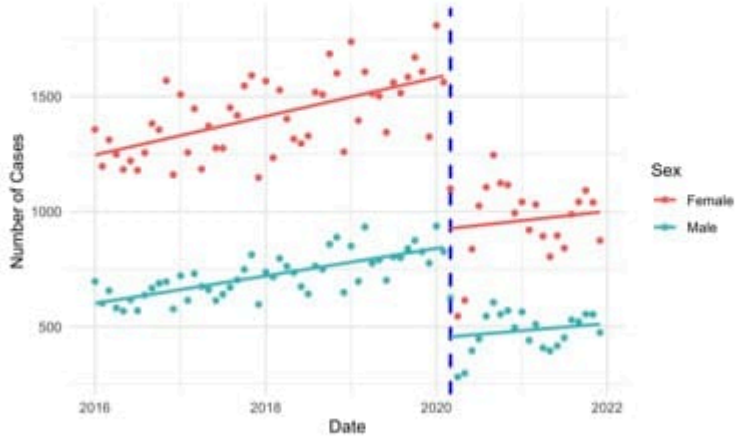
Background: The COVID-19 pandemic caused numerous health service disruptions. We examined the impact of the pandemic on reported chlamydia and gonorrhea cases among young adults in Ontario, Canada.

Methods: Data on laboratory confirmed chlamydia and gonorrhea cases among young adults under 25 years of age were obtained from the integrated Public Health Information System database by Public Health Ontario between 2016–2021. The immediate impact of the pandemic was estimated using an Interrupted Time Series analysis. Linear regression models assessed trends in infections before and after the onset of the pandemic (March 2020) and were stratified by sex.

Results: A total of 138,812 chlamydia cases (92,064 females and 46,748 males) and 16,338 gonorrhea cases (7,575 females and 8,763 males) were reported over the observation period. Pre-pandemic chlamydia and gonorrhea cases were increasing between 2016-2020 (Figure 1). The onset of the pandemic resulted in immediate and statistically significant reductions in reported chlamydia and gonorrhea cases. Chlamydia cases declined by 1,064 cases (95% CI: -1,278, -851) between February to March 2020. Among males there was a decrease of 394 cases (-468, -320), while the reduction among females was by 670.2 cases (-816, -525). Similarly, gonorrhea cases declined, by 109 cases overall (-141, -77); and decreased by 73 cases among males (-93, -53) and 36 case among females (-52, -20). Post-pandemic trends for both infections did not significantly differ from pre-pandemic slopes.

Conclusion: The pandemic significantly disrupted access to sexual health services. The disproportionately larger reduction in reported cases among males underscores the pre-existing gaps in screening strategies for this group, which were further exacerbated by the pandemic. Further studies will investigate if cases have since returned to pre-pandemic levels and if the gap can be leveraged to apply a correction factor to post-pandemic infection rates.

A. **Chlamydia Cases by Sex between 2016-2022 in Ontario, Canada**



B. **Gonorrhea Cases by Sex between 2016-2022 in Ontario, Canada**

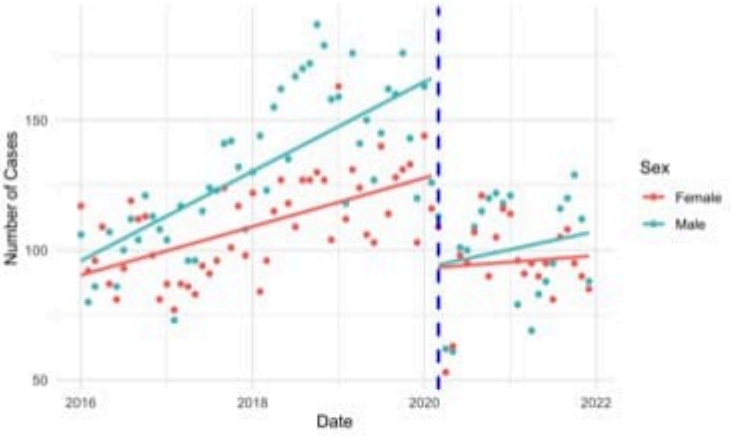


Figure 1: (A) Chlamydia and (B) Gonorrhea Cases Stratified by Sex (Male and Female)

HIV / STI

Housing Instability and Frailty Incidence among People with HIV Engaged in Clinical Care in the United States Carolyn A Fahey* Carolyn Fahey Stephanie A Ruderman Bridget M Whitney Robin M Nance Rob J Fredericksen L Sarah Mixson Sonia Napravnik Allison R Webel Kenneth H Mayer Edward Cachay George Yendewa Amanda Willig Lydia N Drumright Laura Bamford Mike Saag Heidi M Crane Joseph AC Delaney

Background: People with HIV (PWH) in the US disproportionately experience both housing instability and frailty, an aging-related state of functional decline. Emerging research shows that housing instability and frailty are cross-sectionally associated among PWH; however, scant longitudinal research exists on this subject.

Methods: We studied PWH engaged in care at 6 sites across the US within the Centers for AIDS Research Network of Integrated Clinical Systems (CNICS) from 2019-2024. Clinical and self-administered survey data were collected during routine visits. We measured frailty using a previously validated approach based on having at least 3 of 4 components (fatigue, weight loss, immobility, inactivity) vs. less than 3 components. Housing status was based on self-reported living situation in the past month, and dichotomized as Stable vs. Not Stable (“Homeless”, “Unstable”, or “Don’t know”). We estimated the association between time-varying housing status and frailty incidence using Cox proportional hazards models among PWH who were not frail at baseline. We adjusted for site, demographic characteristics, and time-varying HIV viral load, CD4 count, alcohol use, smoking, and drug use.

Results: This analysis included 17,658 observations among 3,115 PWH (84% male, 16% female; 44% White, 38% Black, 13% Hispanic/Latinx, 6% other), with a total time at risk of 6,753 years. The median age at baseline was 49 years (IQR: 37-58). Over the course of the study, 10.6% of PWH (n=329) experienced housing instability and 7.3% (n=228) had incident frailty. In adjusted models, housing instability was associated with 2.2 times greater hazard of frailty (95% CI: 1.5, 3.3) compared to stable housing.

Conclusions: Housing instability was strongly associated with frailty incidence in this large, longitudinal study of diverse PWH. These findings underscore the importance of assessing and addressing housing instability to improve clinical outcomes, including frailty, among PWH.

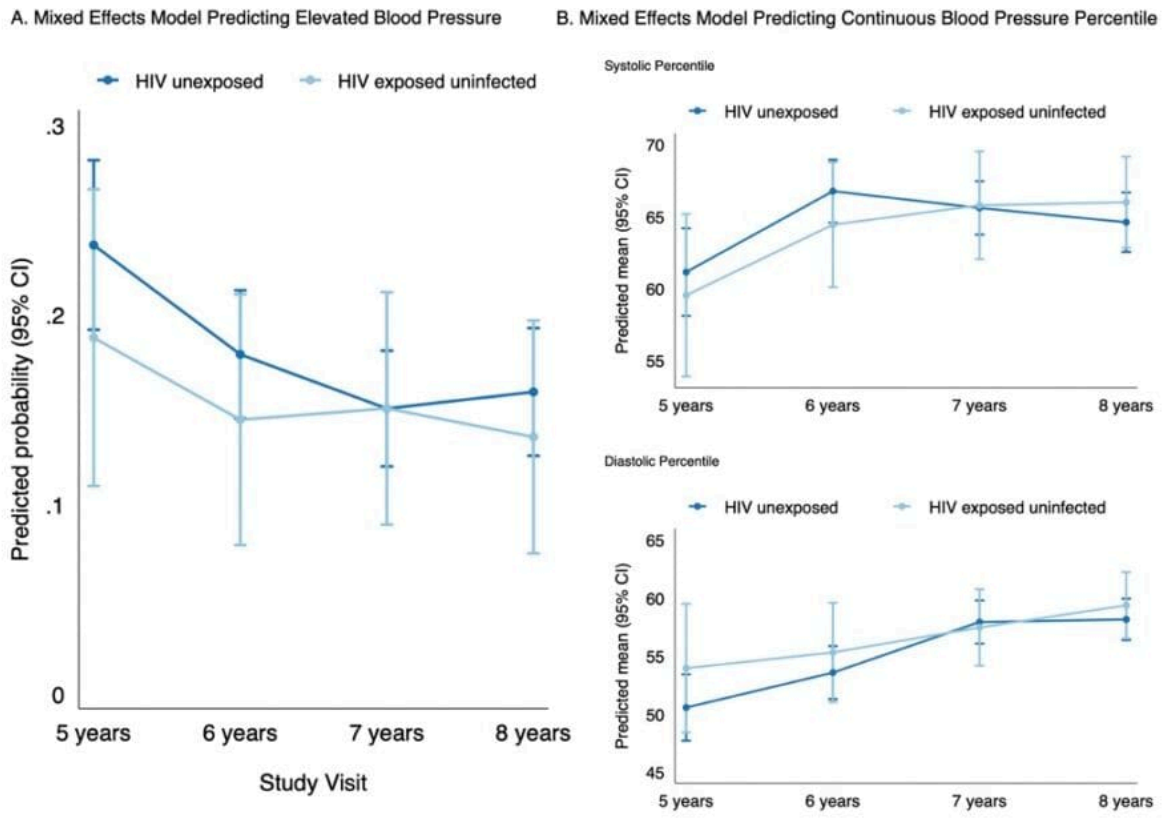
HIV / STI

HIV exposure and cardiometabolic health outcomes among South African children in a birth cohort study: a mixed effects modeling assessment of blood pressure over time

Chelsie Cintron* Chelsie Cintron Maresa Botha Lesley Workman Tiffany Burd Jennifer Pellowski Toby Mansell David Burgner Heather J Zar Angela M. Bengtson

Children exposed but uninfected with HIV (HEU) *in utero* have altered immune function, which may affect cardiometabolic health, including blood pressure (BP). Few data on BP trajectories in HEU and HIV-unexposed (HU) children exist beyond early life (<5 years). To address this gap, we explored the association between HIV-exposure status and BP trajectories in early childhood in a birth cohort of South African children. Maternal participants were enrolled from two communities during pregnancy and their children were followed from birth through 8 years with annual anthropometry and BP (from 5 years). We considered both continuous BP percentiles for child age, sex and height and a binary measure of elevated (≥90th percentile) BP. We used mixed effects models with random intercepts and interaction terms between HIV exposure status and time to assess BP trajectories and the probability of elevated BP over time. Models were adjusted for maternal factors in pregnancy: BMI, alcohol use, psychological distress, smoking, and socioeconomic status and child factors at birth (gestational age, birthweight, being breastfed, age started solid foods), weight at 5-8 years, and physical activity at 7 and 8 years. Among 810 children, (HU= 648; HEU=162) 52% were female, 15% born preterm, 58% exclusively breastfed, median birthweight was 3080g, 5% had an obese bmi zscore from 5 to 8 years, and 88% reported low physical activity. HEU children had a lower probability of elevated BP compared to HU children apart from at age 7 years (Fig 1A).HEU children had marginally lower systolic and higher diastolic BP percentiles at 5, 6, and 8 years and similar levels as HU children at 7 (Fig 1B). Confidence intervals were wide and overlapped across model results (Fig 1 A and B). With similarities in BP by HIV status, our results are largely reassuring. Future studies should investigate BP trajectories into later childhood and factors that mediate or moderate BP trajectories in this population.

Figure 1. Mixed effects model results predicting the probability of having elevated blood pressure (Panel A) and predicted blood pressure percentiles across study visits (Panel B)



HIV / STI

Prevalence of Condomless Sex among Sexually Active Adolescents in the United States: Findings from the 2023 Youth Risk Behavior Survey Precious Patrick Edet* Precious Patrick Edet

Background
Adolescents face varying risks of sexually transmitted infections (STIs) influenced by factors such as early initiation of sex, race, sexual identity, etc., and data on condom use among sexually active U.S. adolescents is limited. This study examined the prevalence of not using a condom during last sexual intercourse across several factors, including having multiple partners in the past three months, race, gender, age group, transgender, and sexual identity.
Methods
The 2023 Youth Risk Behavior Survey (YRBS) data for 5,420 sexually active U.S. adolescents was analyzed. YRBS, administered biennially by the CDC, uses complex sampling for national generalizability. Descriptive statistics and chi-square tests were conducted to provide weighted percentages and p-values, respectively, using SAS v. 9.4.
Results
Condomless sex was more prevalent among those with multiple sexual partners in the past three months than their counterpart (57% vs. 44%; $p<0.001$). Females had a higher prevalence than males (52% vs. 40%; $p<0.001$), while lesbian or gay adolescents reported the highest rates (67%), followed by queer (53%), bisexual (51%), Other (49%), and heterosexual adolescents (42%) ($p=0.003$). Transgender adolescents showed higher prevalence than non-transgender peers (52% vs. 45%), though not statistically significant ($p=0.389$). The prevalence of condomless sex was also highest among Asian and African American adolescents (49%), followed by American Indian (48%), White (46%), Other (43%), and Hispanic adolescents (36%) ($p=0.100$); and highest among 13-year-olds or younger, followed by those aged 17 years or older, and those aged 14–16 years (53% vs. 47% vs. 44%) ($p=0.436$), though findings were not statistically significant.
Conclusion
Findings highlight disparities in condom use among sexually active adolescents. Results underscore the need for tailored sexual health education and interventions to address disparities and promote safer sexual practices among adolescents.

HIV / STI

Acceptability of the common elements treatment approach among women living with in south africa Amy Zheng* Amy Zheng Sithabile Mgnadi-Ncube Laura Murray Pertunia Manganye Kristina Metz Ross Greener Sristhi Sardana Lawrence C Long Donald Thea Matthew P. Fox Jeremy C Kane Sophie Pascoe

Intimate partner violence (IPV) is a barrier to retention in HIV care and achieving viral suppression. We conducted a randomized control trial evaluating the effectiveness of the Common Elements Treatment Approach (CETA), a cognitive-behavioral intervention utilizing lay healthcare workers to improve HIV retention and suppression in Johannesburg, South Africa. Here we describe CETA engagement and acceptability.

This was a single-blind trial among 400 women living with HIV who experienced sexual and/or physical IPV in the last 12-months, initiated antiretroviral therapy and had either an unsuppressed viral load or were at risk for poor adherence in the past year. Women were randomized to receive either 8-12 CETA sessions or weekly safety text messages. Questionnaires on depression, anxiety, trauma, substance use, and IPV were administered at enrollment, 6 and 12-months. Retention and suppression were assessed at 12 and 24-months.

Among the 200 women randomized to CETA, 114 (56.4%) defaulted on treatment in the past year, and 191 (95.5%) were late/missed a visit in the past year. Women reported high levels of depression, anxiety, trauma, and substance use (Table 1). Participants averaged 7.6 (SD: 4.4) sessions over an average of 12 (SD: 7.0) weeks with 115 (57.5%) completing CETA. Of the 10 (5.0%) women who withdrew, 7 did not complete CETA and 1 withdrew prior to starting CETA. The most common reason for withdrawing was having other competing interests such as employment. Of the 15 (7.5%) who were lost to follow-up, 11 did not complete CETA, 3 were lost prior to starting CETA, and 1 was lost during follow-up. Only 23 (11.5%) participants received telehealth CETA; all others had in-person sessions.

Comorbid conditions of anxiety, depression, trauma, and/or substance use was highly prevalent. CETA was largely acceptable given the high number of sessions conducted. As mental health professionals are limited and expensive, CETA could be a potential alternative.

Table 1. Baseline characteristics among 200 women randomized to CETA

	Received CETA
Age, mean (SD)	40.4 (8.3)
Missed a Visit within the Past Year[1]	122 (60.4)
Late to a Visit within the Past Year[1]	69 (34.2)
Defaulted on Treatment within the Past Year[1]	114 (56.4)
Years on ART, mean (SD)	9.0 (5.7)
Viral Load, median (IQR)	30 (20, 107.5)
0 – 50	125 (61.9)
51 - 500	44 (21.8)
501 - 1,000	5 (2.5)
1,001 - 5,000	8 (4.0)
5,001 - 50,000	6 (3.0)
50,001 - 500,000	2 (1.0)
500,001+	2 (1.0)
Missing	10 (5.0)
Have a Current Partner	178 (88.1)
Suicidal Ideation	92 (45.5)
Homicidal Ideation	47 (23.3)
SVAWS Threatened Score, mean (SD) [range][2]	38.9 (13.7) [19-75]
SVAWS Physical Score, mean (SD) [range] [2]	50.9 (19.8) [28-108]
CES-D Score, mean (SD) [range] [3]	30.9 (12.2) [4-54]
HTQ Score, mean (SD) [range] [4]	2.1 (0.5) [1.0-3.2]
Any past three-month substance use[5]	123 (60.9)

[1]Will sum to greater than 200 as people could fulfill multiple categories
[2]Based on the Severity of Violence Against Women Scale
[3]Based on the Center for Epidemiologic Studies Depression Scale
[4]Based on the Harvard Trauma Questionnaire Scale
[5]Based on the Alcohol Smoking and Substance Involvement Screening Test

Infectious Disease

Household Clustering of Malaria, Pneumonia, and Diarrhea Cases: Exploring Co-occurrence Patterns Annika Gunderson* Annika Gunderson Abel Bwambale Emmanuel Baguma Varun Goel Moses Ntaro Edgar M. Mulogo Ross M. Boyce

Introduction: Malaria, pneumonia, and diarrhea are important causes of mortality among children <5 years of age in Uganda. Although low socioeconomic status is a common risk factor, less is known about potential intersecting risk between these diseases at the household level.

Methods: A prospective cohort study was conducted in three villages in rural Western Uganda. Following baseline surveys to assess demographic and household characteristics, and malaria prevention and care seeking, we performed 7 months of clinical surveillance at neighboring health centers. Logistic regression models were fit for malaria, pneumonia, and diarrhea separately including terms for the other two diseases. We then compared characteristics among households with co-occurrences of malaria and pneumonia using Fisher's exact tests.

Results: Among the 324 households included in this analysis, there were 29 cases of malaria and pneumonia occurring within rolling four-week periods. Notably, 26 (90%) of these episodes occurred among 11 households in one village, Kasanzi. We found significant associations with pneumonia cases in households with malaria infections (aOR: 1.30 (95% CI: (1.086, 1.560) and the malaria cases in households with pneumonia infections (aOR: 2.33 (95% CI: 0.969, 5.492). Village was highly significant (p-value: <0.001) and socioeconomic status was marginally significant with co-occurrence of the two diseases (p-value: 0.098) within the high incidence village. Cases of diarrhea did not appear to be associated with cases of either malaria or pneumonia.

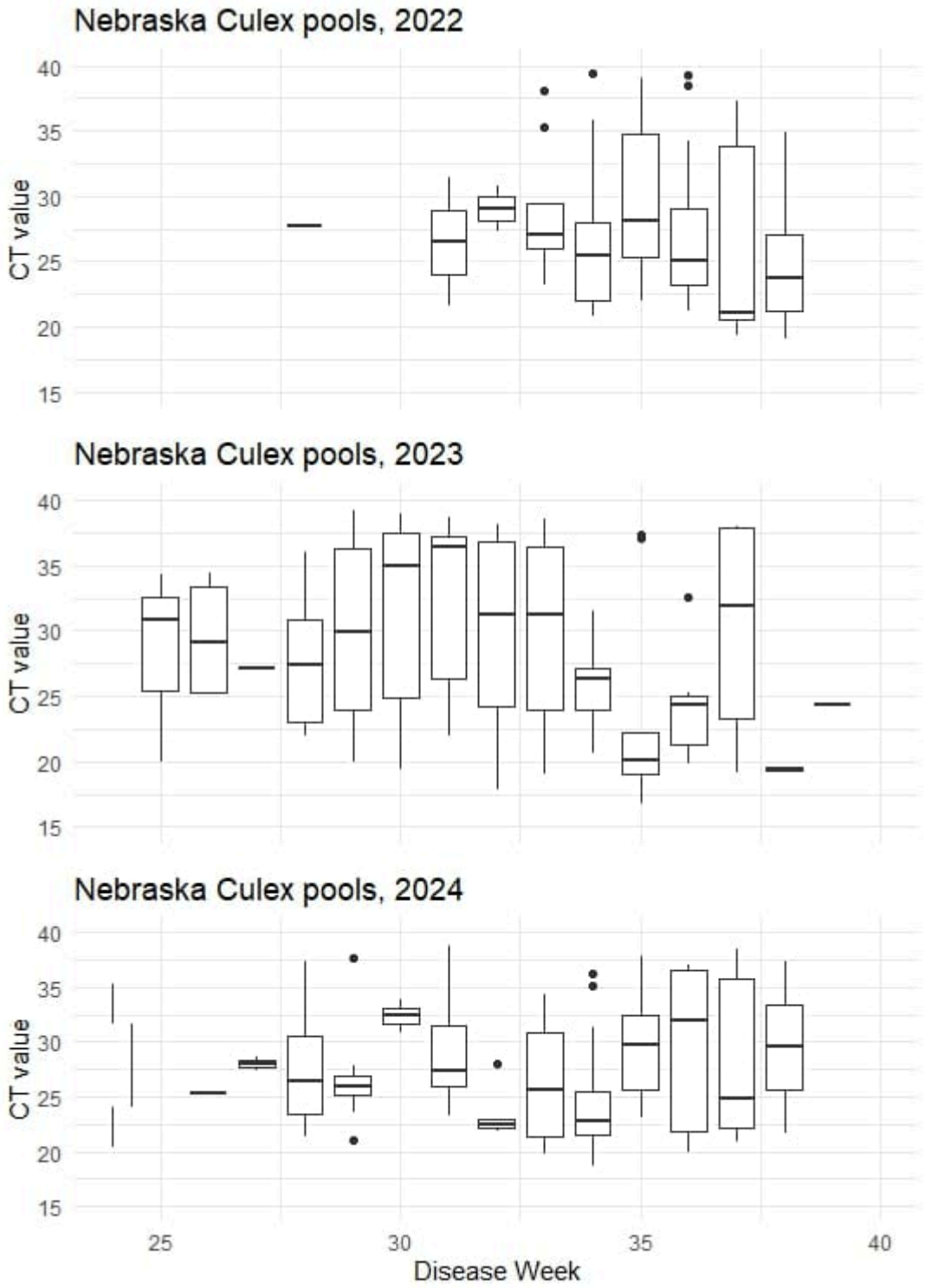
Conclusion: Malaria and pneumonia appear to cluster in specific households and villages. This may be due to shared risk factors or care seeking patterns for respiratory illness that identify asymptomatic parasitemia. Understanding overlap in disease occurrence allows for integrated disease control and treatment measures for households with a double burden of disease.

Infectious Disease

West Nile virus cycle threshold values as supplementary data for human risk estimation: an exploratory investigation Ian Marchinton* Ian Marchinton Joseph Fauver

West Nile virus (WNV) is the most common mosquito-borne infection in the United States, with over a thousand human infections and neuroinvasive cases annually. Given infection risks, the CDC has helped establish robust WNV vector surveillance systems that produce metrics to assess human risk. This entails testing pools of vector species mosquitoes for the presence of WNV RNA to estimate infection rate through maximum likelihood. Cycle threshold (CT) values, produced from every WNV test conducted via reverse transcriptase quantitative polymerase chain reaction (RT-qPCR), are only used categorically for infection estimation despite being a quantitative metric. The current scope of risk analyses can be improved by incorporating these regularly-produced but unused quantitative data into estimations of risk. Our objective is to produce a scalable method for interpreting and utilizing CT values within United States WNV surveillance systems to better define when and where interventions are needed.

We generated a dataset using CT values and trap data from the high-incidence state of Nebraska during the 2022-2024 disease seasons to characterize inter- and intra-weekly variation in CT values across pools. We conducted a preliminary analysis of CT values via time-lagged Pearson correlation, GEE regression, and Poisson regression against state-level human case data to capture a statistical relationship. Based on data from Nebraska over the course of an annual disease season, there is unexplained variation in CT values. We did not detect a direct statistical relationship between CT values and human cases on a state-level, potentially due to heterogeneity by habitat makeup, dominant vector species, and localized effects like climate. We are working to statistically relate CT values to known risk metrics and human cases on a smaller, entomologically-relevant scale, as well as determine environmental factors that influence the variation in CT values we see in the attached figure.


Nebraska Culex pools, 2022
CT value
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Nebraska Culex pools, 2023
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Nebraska Culex pools, 2024
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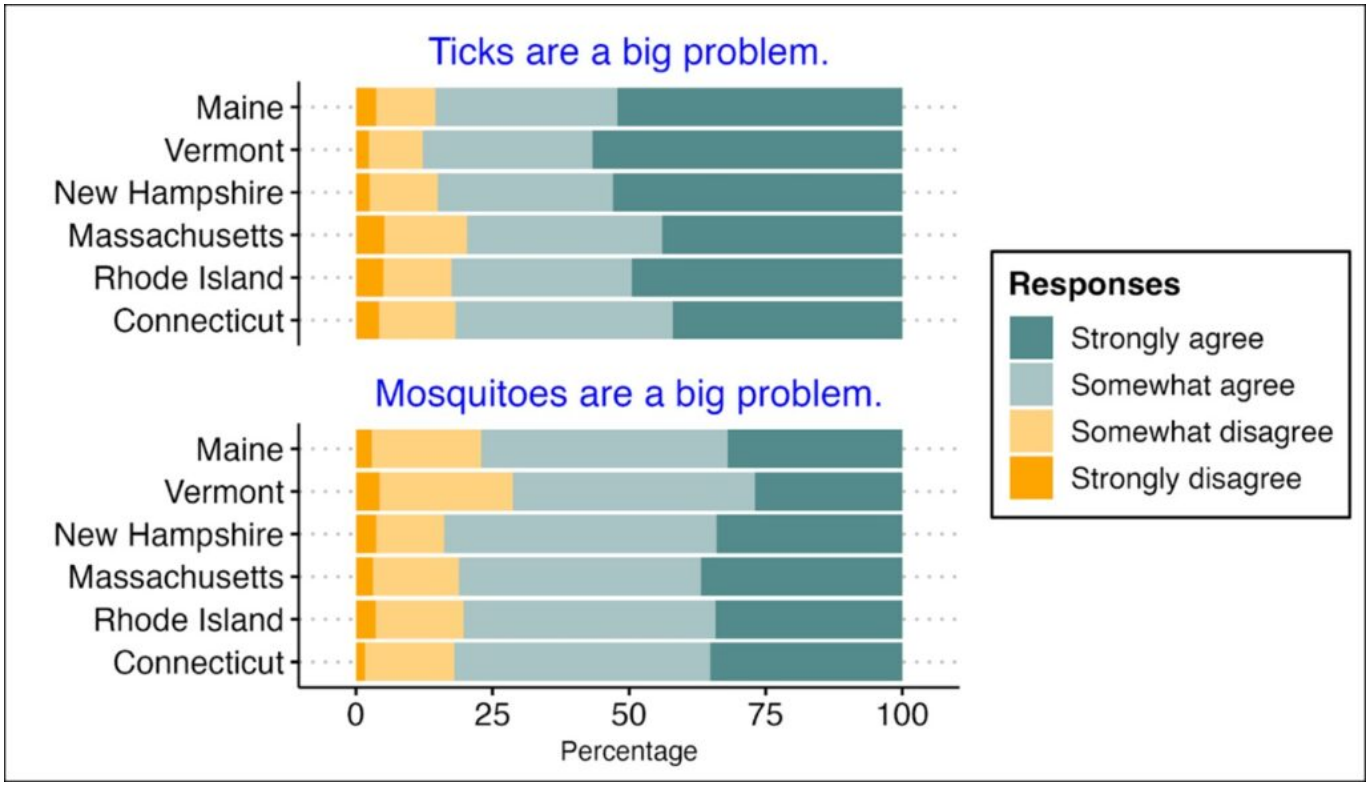
Disease Week

LATEBREAKER

Infectious Disease

Cross-sectional surveys to understand decision-making related to residential vector control across New England Fatma Tufa* Fatma Tufa Johanna Ravenhurst Elissa S. Ballman Neeta P. Connally Nelle Couret Nolan Fernandez Allison M. Gardner Jeff R. Garnas William Landesman Alexis L. White Guang Xu Stephen M. Rich Thomas N. Mather Andrew A. Lover

Tick- and mosquito-borne diseases are a major health issue in New England, where 15% of national Lyme disease cases were reported in 2021. A range of landscape management strategies including pesticide application and deer fencing have been promoted to mitigate peridomestic transmission. However, little is known about the relationship between homeowner concerns about vector-borne diseases and consequent residential vector control practices. As a result, this limits evidence-based health programming. To address this gap, we conducted a coordinated region-wide cross-sectional, internet-based survey. Once released in March, the survey captured 4,957 responses across New England. We found regional variation in the levels of concern about ticks and mosquitoes in residential areas, with Vermont (56%), New Hampshire (52%), and Maine (52%) having higher levels of concern about ticks compared to Connecticut (42%), Massachusetts (44%), and Rhode Island (49%). In addition, the prevalence of resident-initiated vector control interventions varied; participants reported less use of any vector control interventions in Maine (83%) and Vermont (85%), with higher prevalence in New Hampshire (91%), Connecticut (91%), Rhode Island (93%), and Massachusetts (93%). Total number of vector control interventions ranged from 0 – 8 with a median of 2 across all states. Predictors of using more vector control interventions includes primary motivation being protecting health of family versus self (IRR 1.12, 95% CI, 1.07 – 1.17) and any prior diagnosis with a tick-borne disease (IRR 1.07, 95% CI 1.03 – 1.12). Accompanying tick densities will be discussed among homeowners that were enrolled in Phase 2 of the study, where ticks were collected from yards. Findings will guide future interventions to promote evidence-based and socially acceptable residential vector control practices towards reducing peridomestic transmission of vector-borne diseases.


Ticks are a big problem.
Maine
Vermont
New Hampshire
Massachusetts
Rhode Island
Connecticut
Mosquitoes are a big problem.
Maine
Vermont
New Hampshire
Massachusetts
Rhode Island
Connecticut
0
25
50
75
100
Percentage
Responses
Strongly agree
Somewhat agree
Somewhat disagree
Strongly disagree

Infectious Disease

Effectiveness of palivizumab on reducing RSV lower respiratory tract infection in children with Down syndrome Lin Ammar* Lin Ammar Corinne A. Riddell Tan Ding Laura Hopkins Rees L. Lee Tebeb Gebretsadik Sharon C. Enujioke Veronika Pav Angela C. Maxwell-Horn Wendy Funk Tina V. Hartert Pingsheng Wu

Background: We have demonstrated that children with Down syndrome (DS) are at an increased risk of respiratory syncytial virus (RSV) lower respiratory tract infection (LRTI) but are not a currently recommended group to receive palivizumab. The effectiveness of palivizumab in reducing RSV LRTI in children with DS is unknown.

Methods: We conducted a retrospective cohort study of children with DS born and enrolled in the Tennessee Medicaid Program (TennCare, 1998-2019) or the Department of Defense Military Health System (DoD, 2003-2019). Palivizumab administration and RSV LRTI healthcare encounters during children's first two RSV seasons of life were identified using ICD codes. Children's first two RSV seasons were categorized into palivizumab protected time (0-30 days after palivizumab administration) and unprotected time. Children were followed to an RSV LRTI encounter, disenrollment, death, end of RSV season, or end of study (2019), whichever came first. We conducted an extended Cox model, separately for TennCare and DoD, to determine the effect of palivizumab on RSV LRTI and RSV hospitalization unadjusted and adjusting for potential confounders. Sensitivity analyses using the outcomes of any LRTI and any LRTI hospitalization were performed.

Results: Of the 2,796 (TennCare: 1,026, DoD: 1,770) children with DS, 854 (31%) received at least one dose of palivizumab, and 354 (13%) had at least one RSV LRTI event during the first two RSV seasons of life. Palivizumab was associated with a decreased risk of RSV LRTI and RSV hospitalization in both groups, with greater magnitude of effect in the DoD population. Sensitivity analyses showed consistent findings as well (Figure 1).

Conclusion: In this observational study of children with DS, palivizumab receipt was associated with decreased risk of RSV LRTI. Given the high RSV-related morbidity, children with DS may benefit from identification as an at-risk population for whom early life RSV prevention is recommended.

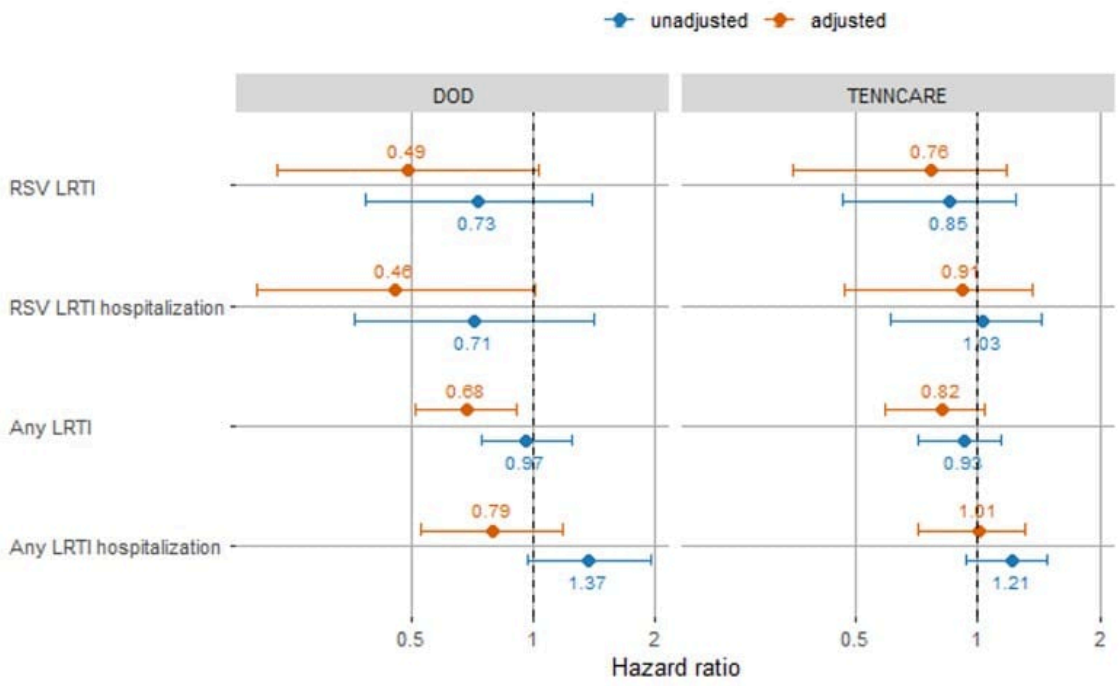


Figure 1. Unadjusted and adjusted hazard ratios for the effect of palivizumab on RSV LRTI, RSV LRTI hospitalization, any LRTI, and any LRTI hospitalization, among children with DS born and enrolled in Tennessee Medicaid Program (1998-2019) and the Department of Defense Military Health System (2003-2019)

Injuries/Violence

Impact of state minimum hourly wage increases on homicide mortality rates in the United States from 2010 to 2020 Kate Vinita Fitch* Kate Vinita Fitch N. Jeanie Santaularia Maryam Tanveer Naoko Fulcher Shabbar I. Ranapurwala

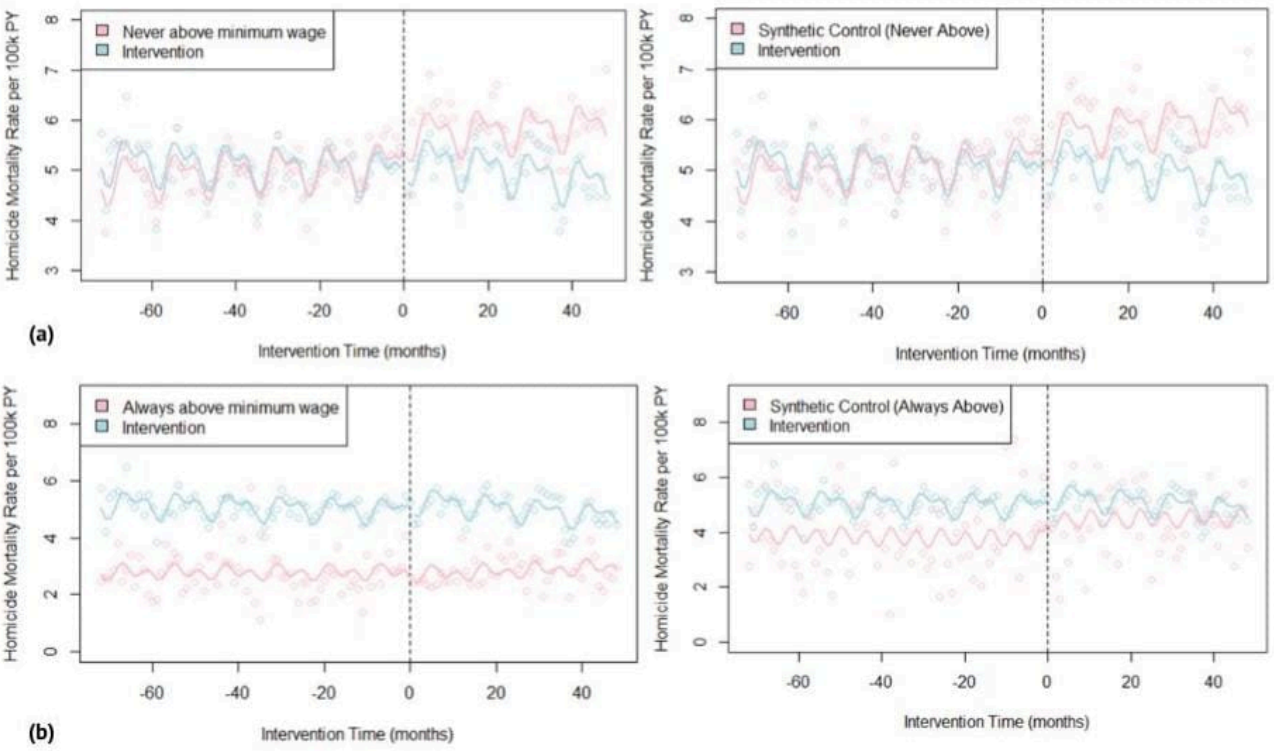
Background: Homicide death is a top cause of premature mortality in the United States and one with extreme race and class inequities. While community-based violence intervention programs can be effective to reduce homicide, it is necessary to address the upstream structural factors that contribute to homicide death including racism, poverty, and class inequality. We evaluated the effectiveness of one upstream approach – increasing state minimum hourly wage – on homicide mortality rates using a decade of data from all 50 US states.

Methods: Using death records from the National Vital Statistics System, we calculated state monthly homicide mortality rates from 2010 to 2020. With controlled interrupted time series and synthetic control interrupted time series analyses using autoregressive integrated moving average models, we compared monthly homicide mortality rates for states implementing a state minimum wage increase.

Results: Implementation of state minimum wage increase of at least $1 above federal minimum was associated with an immediate relative reduction in homicide mortality rates of -0.25 (-0.76, 0.27) deaths per 100,000 PY compared to states never above federal minimum wage and an immediate relative increase of 0.50 (-0.23, 1.23) deaths per 100,000 PY compared to states always above federal minimum wage. Intervention states experienced sustained annual declines of -0.09 (-0.30, 0.12) deaths per 100,000 PY compared to states never above federal minimum and -0.18 (-0.41, 0.05) deaths per 100,000 PY compared to states always above federal minimum over the four years post-intervention. Results using preliminary synthetic controls were similar. Further analyses investigating racialized inequities are forthcoming.

Conclusions: This study suggests that increasing minimum wage is an effective intervention in reducing homicide mortality rates on a state level.

Figures. Homicide mortality rates before and after state minimum wage increases compared to real and synthetic control states with minimum wage (a) never or (b) always above the federal minimum



Injuries/Violence

COVID-19 Onset, Stay-At-Home Orders, and Racialized Inequities in Homicide Mortality Across the US Maryam Tanveer* Maryam Tanveer N. Jeanie Santaularia, PhD MPH Kate Vinita Fitch, BA Naoko Fulcher, MS Shabbar I. Ranapurwala, PhD

Background

We examined the impact of COVID-19 pandemic onset (March 2020) on homicide mortality in the United States and examined effect measure modification by stay-at-home orders (SAHO) and demographics.

Methods

We conducted a single series interrupted time series study using data from the National Vital Statistics System from Jan 1, 2017-Dec 31, 2022, with COVID-19 onset as an interruption. Homicide deaths were identified using ICD 10 codes: X85-Y09, Y87.1. Monthly homicide deaths rates were calculated per 100,000 person-years (PY) to create a monthly time series (72 time points). We used autoregressive integrated moving average (ARIMA) regression, adjusted for seasonality, to model the immediate and sustained trend changes in the homicide mortality due to the pandemic. We stratified models by SAHO (no SAHO, <1 month, >=1 month), race and ethnicity (Hispanic, non-Hispanic (NH) American native, NH black, NH white, NH Asian), sex (male, female), and age (<18, 18-25, 26-35,…, 66-75, >75).

Results

In Jan 2017, the US homicide death rate was 5.9/100,000 PY, and while there were annual seasonal changes, the overall time trend from Jan 2017 to Feb 2020 was stable. However, with COVID-19 onset, there was an increase of 2.0 homicide deaths/100,000 PY (95%CI: 1.5, 2.4) across the US, which persisted until the end of 2022 without additional trend changes, but with seasonal variations. Black, American Native, and Hispanic people experienced the highest rates of being murdered and experienced the largest increases in death rates during the pandemic. Males and age groups 18-55, experienced larger increase in homicide mortality than females and other age groups. COVID-19-related immediate homicide mortality increases occurred in all states regardless of SAHO.

Conclusion

The COVID-19 pandemic had long-lasting impacts on homicide mortality that magnified inequities, especially for black, American native, and Hispanic people, males, and those aged 18-55, but were not impacted by SAHO.

Injuries/Violence

Trends and disparities in pedestrian injuries and fatalities in hit-and-run crashes Liza Lutzker* Liza Lutzker Corinne Riddell Julia Griswold

Hit-and-run (HAR) crashes may yield severe injuries due to delays in emergency medical response. Despite changes in driving after COVID-19's onset, no studies on HAR trends pre- and post-COVID exist, and while some studies examine environmental risks for HAR, none have examined victim race and gender.

California law enforcement agencies submit crash data to the Statewide Integrated Traffic Records System (SWITRS), including environmental data, party characteristics, injury severity, and HAR status. This descriptive study analyzed 2009-22 SWITRS data for single vehicle-pedestrian HAR crash trends and relationships between HAR, injury severity, and both victim and environmental characteristics pre- and post-COVID.

From 2009-22, the percent of HAR crashes increased from 18 to 28%. The percent of HAR crashes that were fatal or serious injury (FSI) crashes increased from 14 to 31%. Both trends increased in the 2010s, with large increases in 2020 and 2021.

Both pre- and post-COVID, Black pedestrians were more likely to be a HAR victim vs non-Black pedestrians; men were more likely to be a HAR victim vs women. Pre-COVID, across race-gender categories, non-Black females had the lowest proportion of HAR (17%) and Black females had the highest (27%). Post-COVID, non-Black females also had the lowest proportion of HAR (23%), but Black males had the highest (36%). The post- vs pre-COVID HAR rate ratio was greatest for Black males (1.37) and lowest for Black females (1.24).

The percent of HAR crashes in dark hours was higher vs non-dark hours (31 vs 18%) and also slightly higher with street lighting present vs absent (31 vs 29%), conditions where drivers can both observe the race/gender of the victim and also flee in darkness. These results provide the basis for further investigation into driver behavior changes relating to the COVID pandemic and race and gender disparities in HAR outcomes.

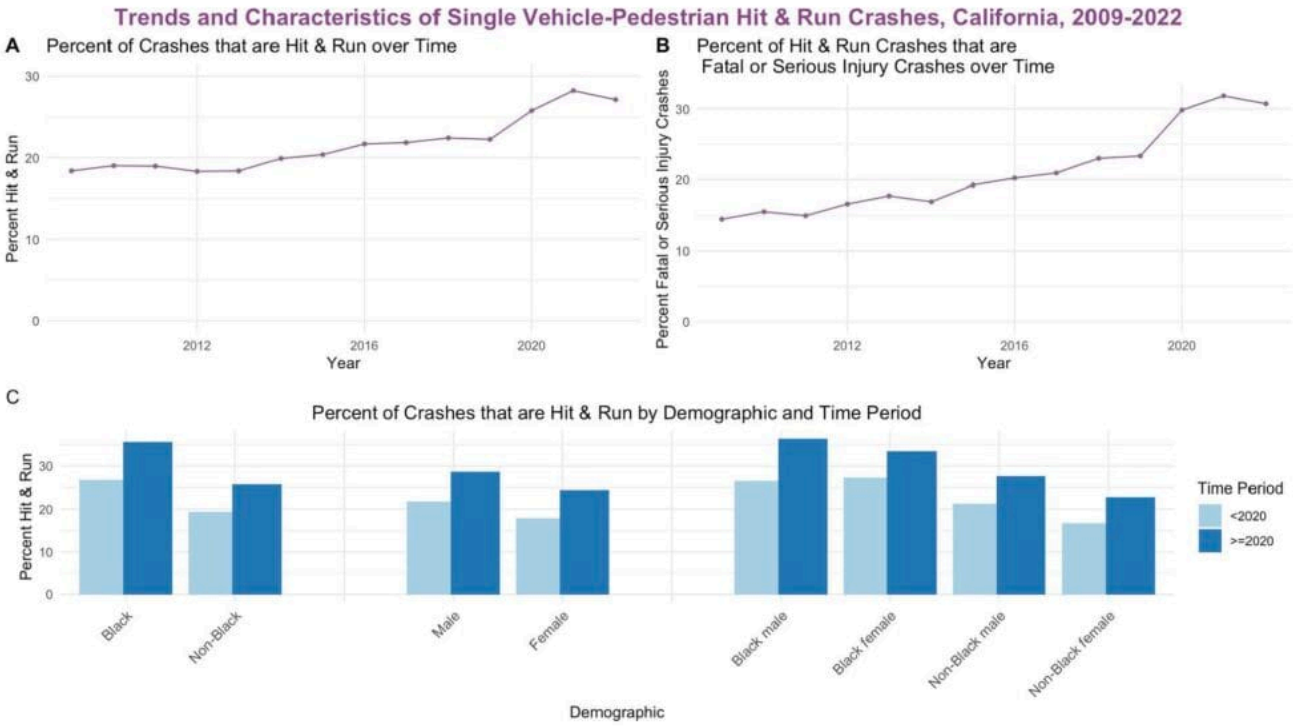


Figure 1: Trends and Characteristics of Single Vehicle-Pedestrian Hit & Run Crashes in California, 2009- 2022; **A:** Percentage of crashes that are hit & run over time; **B:** Percentage of crashes that result in a fatality or serious injury over time; **C:** Percentage of crashes that are hit & run by pedestrian demographic and COVID-related time period

Injuries/Violence

A National Multi-Center Analysis of the Epidemiology of Pediatric Facial Injuries from Fireworks Aidin Gharavi* Aidin Gharavi Chase Lueder Andrew Tom Sergio M. Navarro

Firework injuries remain a significant public health concern, with an estimated 9,700 injuries reported in 2023. This study examines trends in pediatric facial injuries from fireworks over the past decade using the National Electronic Injury Surveillance System (NEISS). Pediatric cases from 2014–2023 were identified using the fireworks consumer code (1313) and filtered for facial injuries (body part code 76). Data was analyzed using chi-square tests to assess significance and logistic regression to evaluate trends. An estimated 4,625 pediatric facial injuries were treated in emergency departments from 2014–2023 (95% CI: 3,884–5,367). Among cases from NEISS-reporting hospitals (n = 177), 68.4% were male and 31.6% were female. Thermal burns (60.5%), lacerations (15.3%), and contusions/abrasions (11.9%) were the most common injuries. Males were more likely to be injured than females (p-value: < 0.001). Overall, 17.5% of injuries required hospitalization or transfer. Older children were significantly more likely to sustain injuries requiring hospitalization (OR: 1.13, 95% CI: 1.04–1.23, p = 0.005). Younger children had higher odds of sparkler-related injuries, although the risk rapidly decreased with age (OR: 0.76, 95% CI: 0.68–0.86, p < 0.001). Our results show fireworks continue to cause significant pediatric facial injuries, with thermal burns being the most common diagnosis. Nearly one in five injuries require hospitalization. To best address the current landscape of facial injuries from fireworks, efforts should focus on minimizing the risk of injury in younger children while ensuring safety protocols are in place to address more significant injuries in older children.

Injuries/Violence

Does school violence impact violence victimisation later in life? Evidence from a cohort study in Luwero, Uganda Amiya Bhatia* Daniel Carter Amiya Bhatia Rebecca Akunzirwe Mathew Amollo Karen Devries

Background. Schools shape children's health as they grow up. There is limited research in low- and middle-income countries of how school contexts shape later life violence outcomes. This study investigates the role of school violence on later violence victimisation among young people in Luwero, Uganda.

Methods. We used three waves of the Contexts of Violence Against Children (CoVAC) cohort study conducted between 2014 and 2022 (n=2312, 67.4% follow up) in primary schools. We constructed three exposure measures of child-reported past year school violence: two at the individual level (any violence and violence relative to peers) and one for lower violence school contexts. Outcomes were physical or sexual violence victimisation in adolescence and adulthood. We fit sex-stratified multilevel logistic regression models with random intercepts for schools to obtain a conditional odds ratio for each exposure. Models were adjusted for age, sex, disability, school attendance, meals in the past 24h, paid work, and violence from caregivers or other adults.

Results. The prevalence of past year individual school violence was 81.6%. The median school-level prevalence of violence was 87.6% (IQR: 74.9%-93.4%). Individual experience of school violence increases risk of physical or sexual violence for young women in adolescence (OR: 1.48, 95% CI: 1.05, 2.07). Being in a less violent school is protective against violence in adolescence for young men (OR: 0.52, 95% CI: 0.26, 1.03). Cross-level interaction terms suggest individual experience of violence increases risk of violence in adolescence even in protective school contexts. Experiencing more violence than peers also increases risk of violence in adolescence for young men (OR: 1.68, 95% CI: 1.25, 2.26) and young women (OR: 1.51, 95% CI: 1.11, 2.06), with similar effects in adulthood.

Conclusion. Prevention of violence across all types of school contexts should be a key part of child health programming to avert later life violence.

Mental Health

Depression screening using the Patient Health Questionnaire (PHQ)-9: discrepancies between the sum score and diagnostic algorithm approach and the role of physical functioning Debbie Huang* Debbie Huang Rasmika Kumar Daniel Hagen Emily Goldmann

Background: The PHQ-9 is a validated instrument commonly used to screen for the presence of depressive symptoms. PHQ-9 scoring methods include a dichotomized sum score (range 0-27) using a cut point of 10 and a two-step diagnostic algorithm approach that reflects diagnostic criteria for major depressive episodes in the Diagnostic and Statistical Manual of Mental Disorders (DSM)-5. Because several PHQ-9 items are somatic in nature, discordance in screening results using these scoring approaches may be related to physical functioning. **Methods**: We used data from the 2021-2023 National Health and Nutrition Examination Survey (NHANES) for adult participants who had a positive screen for depression using the sum score approach (PHQ-9≥10) to compare those who did vs. those who did not also meet criteria for depression using the diagnostic algorithm approach (endorsed at least 5 of 9 PHQ-9 symptoms at least more than half of the days in the past two weeks, with at least one symptom being depressed mood or anhedonia). Logistic regression models examined the association between having a positive screen using the diagnostic algorithm approach and reporting at least one physical functioning limitation (yes/no), controlling for demographic variables. **Results**: Among the 773 participants with PHQ-9≥10 (14% of 5,273 adult NHANES participants), 42% also screened positive using the diagnostic algorithm approach. Adjusting for age, gender, race/ethnicity, education, and marital status, physical functioning impairment was not associated with screening positive for depression using the diagnostic algorithm (adj. OR=1.10; 95% CI: 0.63,1.93). **Conclusion**: Impairment in physical functioning did not explain differences between screening results using the sum score vs. the diagnostic algorithm approach among U.S. adults. Investigators should carefully consider the implications of using either approach. Further research on the comparative utility of PHQ-9 scoring approaches is warranted.

Mental Health

A target trial emulation of retirement and self-rated health and life satisfaction in the UK

Jane Maddock* Jane Maddock Jacques Wels Snehal Pinto Piera Neil Davies Praveetha Patalay

Background: It is unclear whether retirement affects self-rated health or life satisfaction, partly due to challenges in assessing causality. We conducted a target trial emulation to explore this relationship in a population-based study in the UK.

Methods: The UK Household Longitudinal Study is a representative panel study of the UK population where data is collected annually. We used data collected between 2009 and 2019. Figure 1 outlines the criteria for our target trial. Our eligible sample includes those aged 58-68 years self-reporting being employed at recruitment. Self-rated health and life satisfaction were assessed via questionnaire. Higher self-rated health scores indicated poorer health, while higher life satisfaction scores reflected greater satisfaction. Treatment was defined as self-reporting retirement within a year of recruitment or remaining employed for a follow-up period of 2 years. We emulated this trial using sequential trials and intention-to-treat analyses using robust regression models and adjusting for trial cohort and baseline confounders (age, sex, ethnicity, partnership status, education, household income, occupational social class, mental and physical health). In sensitivity analyses, we stratified by occupation type, sex and partnership status.

Results: Out of a total of N=10,997 pooled observations, 14% (N=1,515) retired. We found little evidence that retirement affected self-rated health. However, among those with no partner at baseline, those who retired had slightly worse self-rated health (0.15 (95%CI:0.03, 0.26)). Retirees' life satisfaction increased (0.11 (95%CI:0.06,0.16), different occupational and partnership status strata had similar increases.

Conclusion: In a UK population aged 58-68, retirees had a small improvement in life satisfaction but similar self-rated health to non-retirees up to 2 years post-retirement. We will repeat these analyses using representative data from the US and Germany to test external validity.

Criteria	Target trial	Emulated Trial using UK Household Longitudinal Study
Eligibility	• Aged 58-68 at recruitment • Self-reported in employment at recruitment • SRH and life satisfaction measured at recruitment • Recruited in the UK	Same
Treatment strategies	1. Retired within one year of recruitment 2. Remain employed for the duration of follow-up	1. Self-reported retired within one years of baseline 2. Remain self-reported employed for the duration of follow-up
Randomised assignment	• Participants randomly assigned to retirement within 1 year of recruitment • Participants are not blinded	Randomisation emulated by adjusting for covariates in regression models ensuring exchangeability between treatment arms
Follow-up	Starts at allocation 1 year post recruitment Ends 2 years post-allocation	Same
Outcome	Self-reported self-rated health Self-reported life satisfaction	Same
Causal contrasts of interest	Intention-to-treat	Same
Analysis plan	Regression models and stratified by occupation type, sex, partnership status	Same except adjustments would be made for baseline covariates and due to lack of power, we will create sequential trials

Mental Health

Mental illness after bereavement before and during the COVID-19 pandemic in Sweden: a matched cohort study Shiyu Li* Shiyu Li Mary M Barker Huiqi Li Krisztina László Fen Yang Mikael Rostila Sandra Rogne Maria Feycthing Unnur A Valdimarsdóttir Fredrik Nyberg Fang Fang

Background

Compelling evidence suggests that bereavement is associated with an increased risk of mental illness. The COVID-19 pandemic led to an increase in the number of bereavements, which in combination with the applied social restrictions may have amplified bereavement's mental health impact. We aimed to compare the risk of mental illness in relation to bereavement experienced before and during the pandemic in Sweden.

Methods

We conducted two nationwide cohort studies using Swedish national register data, including 2,828,747 individuals (282,875 bereaved [lost a parent, sibling, child or spouse]) before the pandemic (2018-2019) and 3,055,310 individuals (305,532 bereaved) during the pandemic (2020-2021), respectively. Mental illness was defined as the first occurrence of a psychiatric diagnosis, prescription of psychiatric medication, or suicidal behavior. Multivariable Cox regression models were used to estimate HRs with 95% CIs.

Findings

Bereaved individuals had a higher risk of mental illness compared to non-bereaved both before (HR 1.51, 95%CI 1.49-1.54) and during the pandemic (HR 1.54, 95%CI 1.51-1.56). The risk was highest shortly after bereavement, and was greater among females, the elderly, and individuals with lower socioeconomic status (SES) in both periods. The risk of mental illness was similar between bereavement due to COVID-19 (HR 1.59, 95%CI 1.49-1.70) and natural causes (HR 1.48, 95%CI 1.46-1.51) compared to non-bereavement.

Interpretation

Bereavement was associated with an increased risk of mental illness both before and during the pandemic. Female, the elderly and individuals with lower SES experienced a higher risk. Bereavement due to COVID-19 was not associated with a higher risk of mental illness than due to natural causes. The pandemic did not magnify the mental health impact by bereavement in Sweden. Given the varying mitigating strategies, further studies are needed to investigate if these findings are generalizable to other societal contexts.

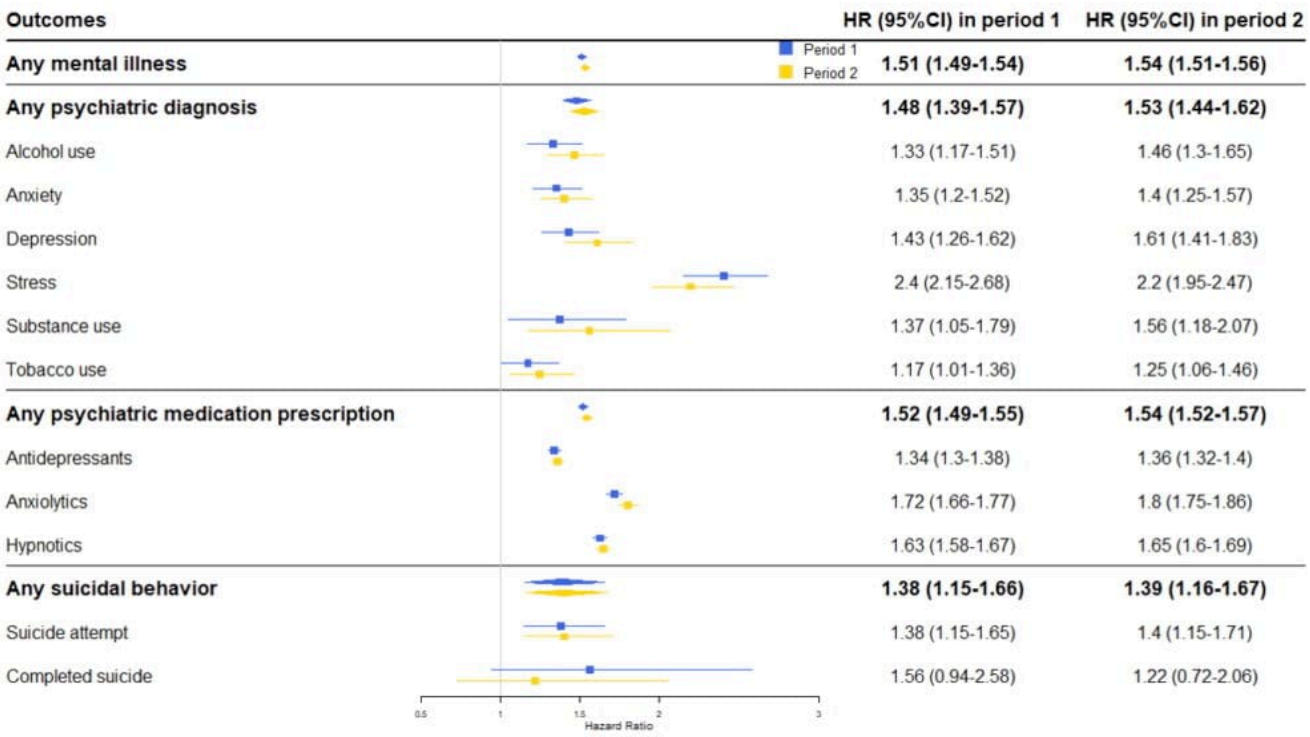


Figure 4. Risk of mental illness in relation to bereavement during study period 1 (before pandemic, Jan.1, 2018 – Dec.31, 2019) and study period 2 (during pandemic, Jan.1, 2020 – Dec.31, 2021).

HRs and 95%CIs are presented on a logarithmic scale and adjusted for education and household income. 'Any mental illness' was defined as the first occurrence of any psychiatric diagnosis, psychiatric prescription, or suicidal behavior. HR, hazard ratio; CI, confidence interval.

Mental Health

The role of alcohol in sexual orientation-related disparities in youth suicidal thoughts and behavior Sarah McKetta* Sarah McKetta Ran Barzilay

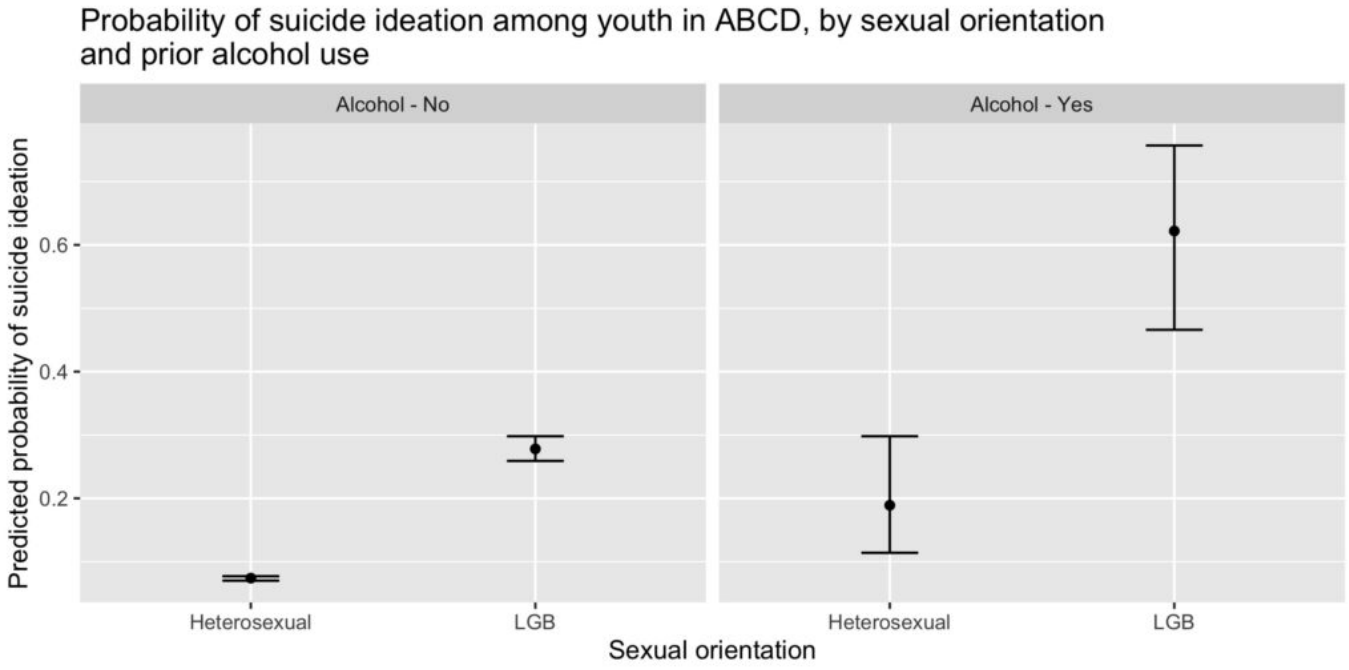
Background: Youth who identify as lesbian, gay, or bisexual (LGB) experience markedly higher rates of suicidal ideation (SI) than their heterosexual peers. They additionally report higher alcohol use, which is itself a critical contributor to suicide. Despite extensive evidence linking both LGB identity and alcohol use to suicide risk, no research to date has explored the contributing role of alcohol consumption in LGB youth SI.

Methods: The purpose of this study was to evaluate the role of alcohol consumption in LGB youth SI disparities using the Adolescent Brain Cognitive Development (ABCD) Study, a national cohort of US youth followed annually since 2016 (eligible N=11,669 unique respondents with N=38,578 observations). Using general estimating equations, we examined interactions in disparities in SI by LGB identity and alcohol consumption, i.e., whether they had ever consumed a full drink of alcohol, adjusting for age.

Results: In bivariate models, the age-adjusted odds ratio (AOR) for SI was 4.91 (95% CI 1.42-5.46) for LGB youth compared to heterosexual youth. The AOR for alcohol use (vs. none) was 4.42 (95% CI 2.93-6.66). Interaction models showed that alcohol use increased the risk of SI for LGB youth: in the absence of alcohol use, the AOR was 4.84; in the presence of alcohol use, the AOR was 7.06. The relative excess risk due to interaction was 14.11 (95% CI 0.58-27.23), demonstrating supra-additivity, and the proportion of SI attributable to interaction was 0.67 (95% CI 0.45-0.91).

Conclusions: Disparities in SI among LGB youth are dramatically increased in the presence of alcohol use. These results underscore the public health urgency of addressing youth alcohol use for suicide prevention efforts.

The CI on this AOR was extremely blown out, so we'll want to decide how we show this information. I've chosen to report AOR w/o CI in text and show predicted probabilities in figure, but for the paper we'll need a better strategy


Probability of suicide ideation among youth in ABCD, by sexual orientation and prior alcohol use
Alcohol - No
Alcohol - Yes
Predicted probability of suicide ideation
0.6
0.4
0.2
Heterosexual
LGB
Heterosexual
LGB
Sexual orientation

Mental Health

Risk factors for mental disorders in pregnant women: A comparison between the Jundiaí and Araraquara cohorts in Brazil Audêncio Victor* Audêncio Victor Perla Pizzi Argentato Liania A. Luzia Rinaldo Artes Patricia Helen Rondó

Introduction: Mental disorders during pregnancy are a significant public health problem due to the substantial physiological and psychological changes that occur during this period. This study aims to investigate the risk factors for mental disorders in pregnant women by comparing data from two distinct cohorts in Jundiaí and Araraquara, Brazil.

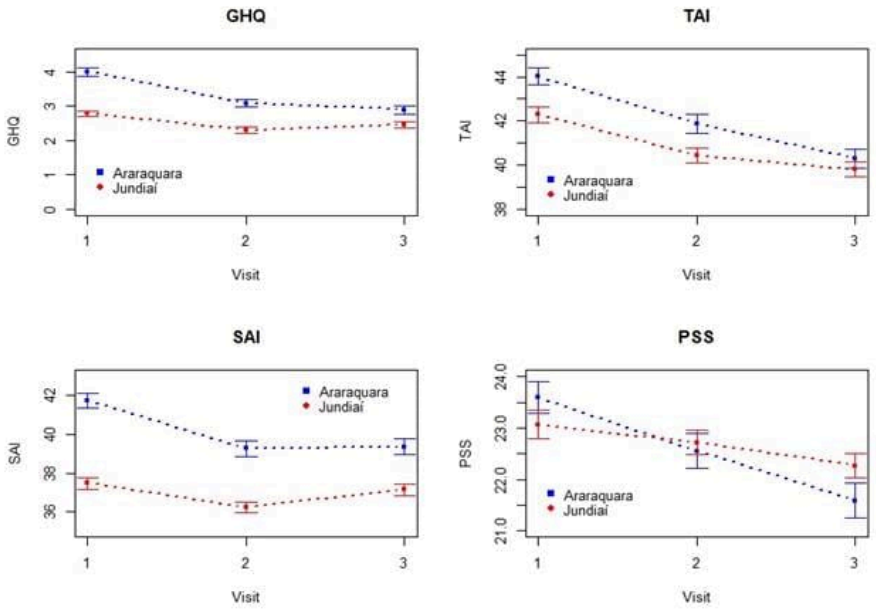
Methods: This is a prospective cohort study that included pregnant women from two Brazilian cohorts. The Jundiaí cohort (1997-2000) included 865 pregnant women, while the Araraquara cohort (2017-2023) included 755 pregnant women. Socioeconomic, demographic, obstetric history, and mental health data were collected and analyzed. Mental health was assessed using standardized questionnaires, including the General Health Questionnaire (GHQ), the State-Trait Anxiety Inventory (STAI), and the Perceived Stress Scale (PSS). Statistical analysis included bivariate tests and univariate and multivariate random-effects models for panel data.

Results: The results indicated higher levels of anxiety, depression, and perceived stress in the Araraquara cohort compared to the Jundiaí cohort study. Socioeconomic factors such as being single, separated or widowed, lower per capita income, lower educational levels, higher household density, and morbidity during pregnancy such as urinary infection, pyelonephritis, gestational hypertension, tuberculosis, cervicitis, and vaginitis were the risk fators identified.

Conclusions: The findings of this study highlight the need for targeted interventions for pregnant women in vulnerable situations, including socioeconomic support, improvements in living conditions, and access to adequate health care. Additionally, it is essential to integrate mental health services into prenatal care to monitor and treat health complications that may affect the mental health of pregnant women.

Keywords: Mental disorders, pregnancy, depression, risk factors, public health.

Profiles (mean and standard deviation) of the scales GHQ, SAI, TAI, and PSS over three visits in the Jundiai and (1997-2000) and Araraquara (2017-2020) cohorts.



Mental Health

Prevalence and risk factors of anxiety/depression by county classification among US adults

Maryam Elhabashy* Maryam Elhabashy David Adzrago Faustine Williams

Introduction. Current research pays limited attention to the prevalence of anxiety/depression and its risk factors in urban, suburban, and rural areas, especially since the COVID-19 pandemic. A deeper understanding of anxiety/depression by county classification can aid in effective resource allocation and access. This research aims to estimate the prevalence of anxiety/depression among US adults and assess the potential associated factors based on county classification. **Methods.** Data from the 2019 and 2022 National Health Interview Surveys (NHISs) were analyzed using weighted Chi-square test and logistic regression analyses. The sample of US adults (N=43,608) was classified as living in urban (n= 21,199), suburban (n=14,463), or rural counties (n=7,946). **Results.** Prevalences of anxiety/depression were slightly higher in rural (10.68%) compared to urban (9.14%) and suburban (10.22%) counties. Being female, obese, and a former/current cigarette smoker were significantly associated with anxiety/depression across all county classifications. Older age was negatively associated with anxiety/depression in urban counties. Being Black was associated with lower odds of anxiety/depression in urban and suburban counties only, and being an immigrant was associated with lower odds urban counties only. Unemployment and living below the poverty threshold were associated with higher odds of anxiety/depression across all county classifications, with stronger associations in rural and urban counties, respectively. Being uninsured was significantly associated with lower odds of anxiety/depression in rural counties, but higher odds in urban and suburban counties, though these associations were not significant. **Conclusion.** The findings reveal some variations in anxiety/depression prevalence, with higher prevalence in rural counties, and multiple risk factors differing by county classification. Efforts in anxiety/depression prevention and intervention should be tailored accordingly.

Mental Health

Using large biobanks for psychiatric genomic research: investigating selection and generalizability through sample composition Catherine Gimbrone* Catherine Gimbrone Katherine Keyes Louisa Smith Philip Greenland Jordan W. Smoller Maria Argos

Introduction:

Large biobanks offer unprecedented data for psychiatric genomic research, but concerns exist about sample representativeness and generalizability. This study examined depression prevalence, correlates, and polygenic risk score (PRS) associations by U.S. state in the NIH All of Us Study data to assess potential impacts of non-representative sampling.

Methods:

Depression prevalence and correlates were analyzed in two All of Us Study subsamples: those with self-reported personal medical history (PMH) data (n=162,718) and those with electronic health record (EHR) data (n=270,902). Associations between PRS and lifetime depression were examined by race/ethnicity and U.S. state of residence in genomic subsamples.

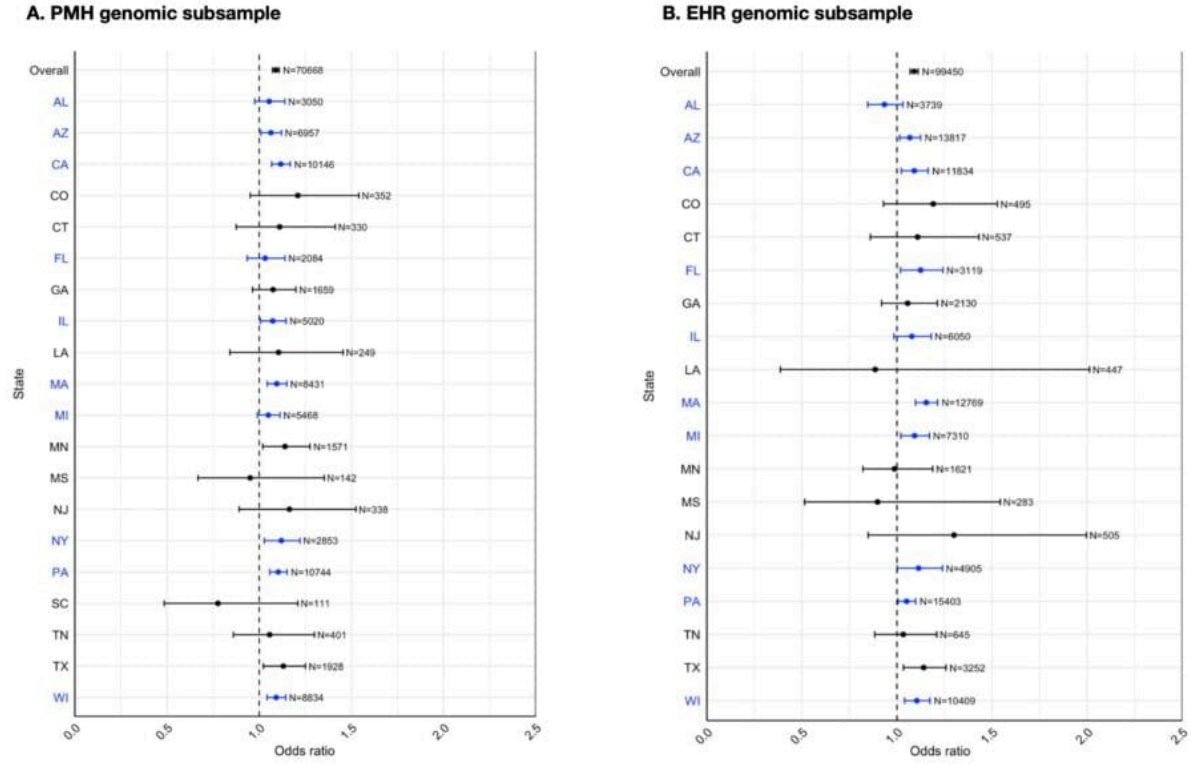
Results:

Depression prevalence varied across states in both PMH (16.62-33.24%) and EHR (0.21-41.83%) data. Younger age and lower educational attainment were associated with lifetime depression based on self-reported medical history (PMH); whereas, older age and higher educational attainment were associated with lifetime depression diagnosis (EHR). Among non-Hispanic whites, the depression PRS was associated with lifetime depression based on PMH (OR=1.09, 95% C.I. 1.07-1.11) and EHR (OR=1.09, 1.07-1.11). Results were generally consistent for other self-reported racial/ethnic groups. Associations between PRS and lifetime depression were largely consistent and varied minimally (ORs: 0.78 – 1.30) by state of residence in both datasets.

Discussion:

There is substantial variation in lifetime depression prevalence across states in All of Us, likely reflecting recruitment differences, EHR data completeness, and true geographic variation, yet PRS associations remained relatively stable. As studies with data like All of Us expand, accounting for sample composition and measurement approaches will be crucial for generating actionable findings.

Figure 1. Forest plot of logistic regression estimates of PRS on lifetime depression among White participants overall and stratified by state of residence



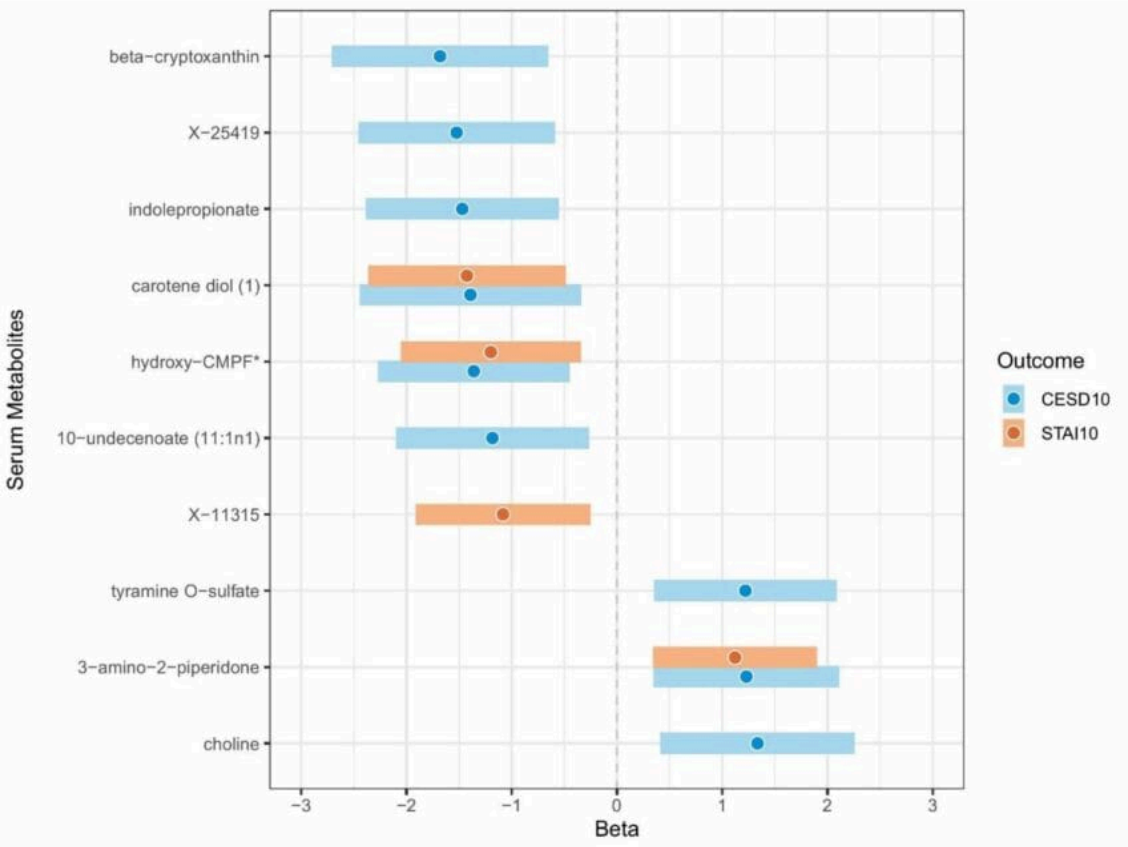
Notes: States and corresponding estimates in blue denote locations of All of Us enrollment centers. Stratified regressions adjusted for the first three principal components to account for ancestry. Small sample sizes in some states precluded subgroup analyses and estimates should be interpreted with caution.

Mental Health

Serum Metabolites Associated with Depression and Anxiety in Hispanic Community Health Study/Study of Latinos Xinye Qiu* Xinye Qiu Yu Zhang Qibin Qi Bing Yu Jan Bressler Carmen Isasi Linda Gallo Tamar Sofer

Establishment of relevant molecular profiles may aid in early identification of at-risk individuals for targeted intervention. We aim to identify serum metabolomic signatures for depression and anxiety in the Hispanic Community Health Study/Study of Latinos (HCHS/SOL). We performed metabolome-wide association analyses for depression and anxiety symptoms measured by Center for Epidemiologic Studies Depression Scale-10 (CES-D-10) and Spielberger State Trait Anxiety Inventory -10 items (STAI-10) among 4,002 Hispanic/Latino adults who participated at baseline clinic visit and had metabolomics assayed in 2017 (batch 1). False-discovery-rate (FDR) correction was applied to address multiple testing. Replication was conducted using metabolites with FDR $p<0.05$ in the discovery stage in a separate set of 2,178 individuals from baseline, and had metabolomic assayed in 2021 (batch 2). Depression and anxiety symptoms were modeled as continuous outcomes in a survey-based generalized linear regression for each metabolite, separately. Participants were 42.6% males with an average age of 45.9 yrs and an average BMI of 29.8 kg/m2. We identified 35 metabolites (9 replicated in batch 2) associated with depression symptoms, and 10 (4 replicated) with anxiety symptoms adjusting for age, sex, study center and Hispanic/Latino background. Carotene diol and hydroxy-CMPF were associated with lower depression and anxiety symptoms. In addition, we found that 3-amino-2-piperdone was linked to higher symptoms (depression $p=0.03$; anxiety $p=0.02$). Tyramine O-sulfate and choline were also linked to higher depression symptoms (both $p=0.03$). Other metabolites uniquely linked to lower depression symptoms were beta-cryptoxanthin ($p=0.02$), unknown X-25419 ($p=0.02$), indolepropionate ($p=0.02$), and 10-undecenoate (11:1n1) ($p=0.04$). Details are shown in the attached Figure. After further accounting for income, education, smoking, alcohol, exercise and diet, carotene diol remained associated with lower depression symptoms ($p=0.02$). Associated biological pathways include antioxidation, furan/long chain omega-3 fatty acids metabolism, lipids metabolism, and microbial metabolic pathways. In summary, we identified several serum metabolites associated with psychological symptoms in Hispanic/Latino adults.

Figure. Batch 2 Replicated Metabolites Associated with Depression and Anxiety Symptom Scores in HCHS/SOL at Baseline. CESD10 represents the Center for Epidemiologic Studies Depression Scale-10 items. STAI10 represents the Spielberger State Trait Anxiety Inventory -10 items. Scores were treated as continuous outcomes. Beta coefficient (beta) indicates the change of depression or anxiety score per 1 standard deviation (SD) increase in associated serum metabolites level after adjusting for age, sex, study center and Hispanic/Latino origins. The color bar covers the 95% confidence interval while the middle point is the point estimate of beta.



Mental Health

Association between Gestational Diabetes Mellitus and Child Mental Disorders: Population-based Target Trial Emulation in Taiwan Chin-Kuo Chang* Chin-Kuo Chang Pei-Chun Chen

Background Gestational diabetes mellitus (GDM) prevalence has been increasing globally, and maternal hyperglycemia is known as a risk factor for adverse birth outcomes, but limited to offspring's mental health in later life.

Methods The National Health Insurance Database (NHID) is a data source of the universal health insurance system in Taiwan, with a high population coverage. We constructed a population-based birth cohort by linking mothers' health records to their offspring to evaluate the effect of GDM during pregnancy on child mental disorders detected in follow-up defined by ICD-9 and ICD-10 codes, focusing on externalizing disorders and neurodevelopmental disorders. Kaplan-Meier curves and Cox proportional hazard models were applied to estimate the hazard ratio of GDM for their offspring's mental disorders. To enhance comparability between exposure groups, a series of statistical attempts were carried out in models, including full confounding adjustment, propensity score, and inverse probability of treatment weighting, to emulate a hypothetical randomized trial.

Results From 2005 to 2017, NHID recorded more than 2.44 million pregnancies as the basis of assembling a population-based birth cohort by a linkage to the mothers' offspring, excluding the ones who were not the first single birth of a mother, whose mothers had a diagnosis of either type of diabetes before pregnancy or on antidiabetics, and stillbirths. A total of eligible 1,399,039 children were followed up for up to 13 years for analyses, with a mean age of 30.06 (SD=4.94) years old for mothers, and 91,351 of them were diagnosed with GDM during pregnancy. Significantly elevated risks were identified for a wide range of child mental disorders, especially for attachment disorder (adj.HR=1.25; 95% CI: 1.04, 1.51), followed by Asperger's syndrome (adj.HR=1.22; 95% CI: 1.09, 1.36). Similar outcomes were found in sensitivity analyses showing robustness.

Conclusion GDM during pregnancy is significantly associated with increased risks of various mental disorders in offspring, particularly attachment disorder and Asperger's syndrome, with confounding fully considered.

Mental Health

Unpacking the Impact of Social Determinants of Health on Adolescent Mental Health: Pathways to Equity and Intervention Damilola Sherifat* damilola Sherifat Shaba

Abstract:

Background: Mental health outcomes are profoundly shaped by social determinants of health (SDOH), including economic status, education, neighborhood environment, and access to healthcare. Disparities in these determinants disproportionately affect racial and ethnic minorities, low-income populations, and marginalized communities, exacerbating mental health conditions such as depression, anxiety, and substance use disorders. Adolescents are particularly vulnerable to these inequities, as early-life experiences significantly influence long-term mental health trajectories. This research synthesizes findings from peer-reviewed studies and national health reports to explore how inequities in SDOH contribute to adolescent mental health burdens and to identify intervention strategies that promote health equity.

Aims:

- To assess the relationship between key social determinants and adolescent mental health outcomes across diverse populations.
- To identify systemic barriers contributing to mental health disparities among adolescents.
- To propose policy and community-based interventions that address SDOH as a means of improving adolescent mental health equity.

Methods: A comprehensive literature review was conducted, drawing from national health databases and peer-reviewed articles published between 2010 and 2024. Databases such as PubMed, Google Scholar, and PsychINFO were utilized to collect relevant studies.

Quantitative Component: National health surveys (e.g., Youth Risk Behavior Surveillance System – YRBSS, National Survey on Drug Use and Health – NSDUH) were analyzed to evaluate adolescent mental health indicators across different socioeconomic and racial groups. Multivariate regression models in existing studies were reviewed to assess correlations between income, education, housing stability, and mental health outcomes such as depression, anxiety, and suicidal ideation.

Qualitative Component: Secondary analysis of qualitative research from existing literature provided insights into adolescents' lived experiences regarding mental health and social determinants.

Results:

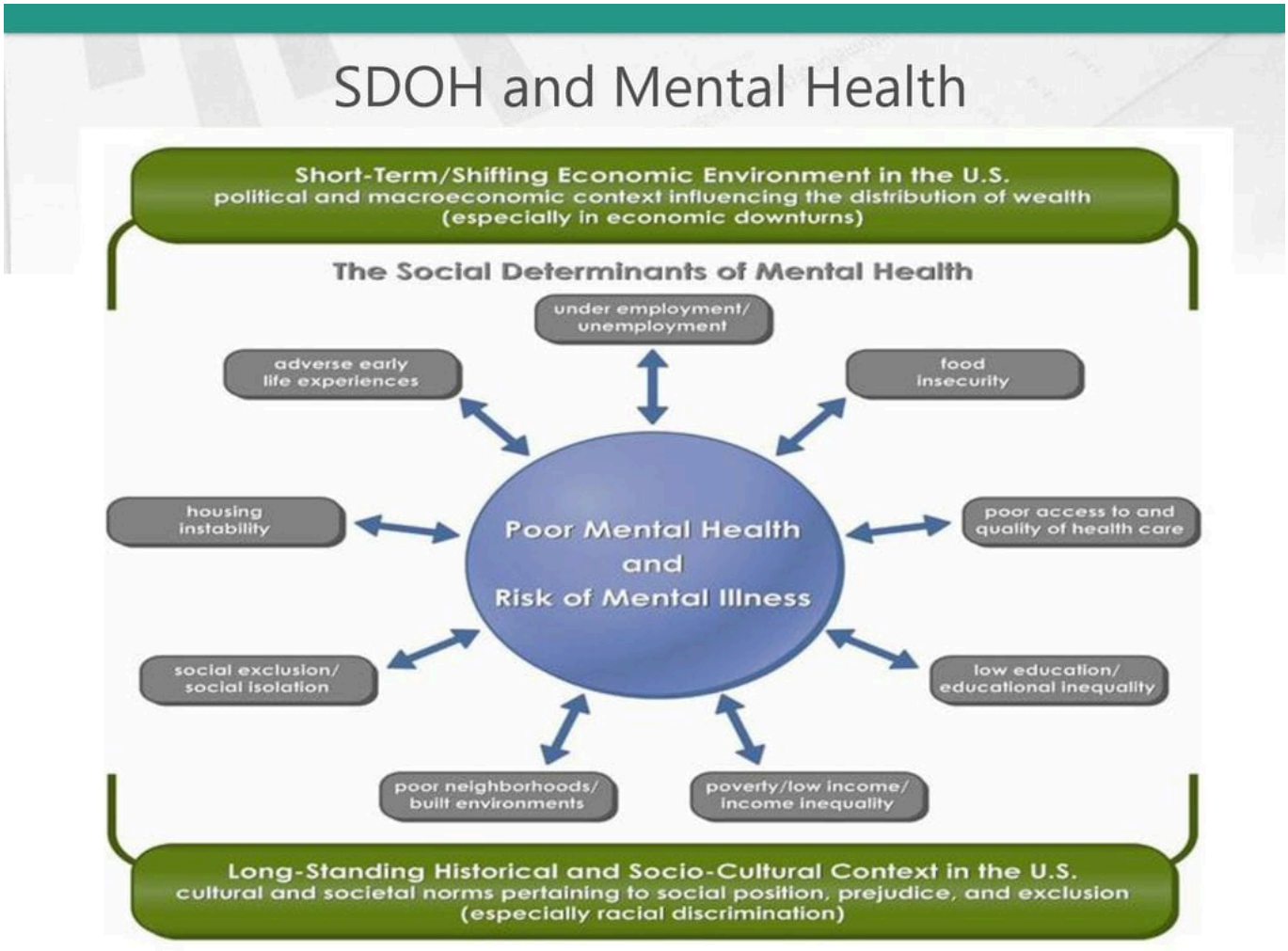
Quantitative analysis from reviewed studies revealed a strong correlation between low socioeconomic status and increased prevalence of depression, anxiety, and suicidal ideation among adolescents ($p < 0.01$). Adolescents in communities with limited healthcare access reported 2.1 times higher rates of untreated mental health conditions compared to those in communities with better access. Studies highlighted that academic pressure, social media influence, and adverse childhood experiences significantly contribute to mental health challenges. Neighborhoods with greater access to green spaces, recreational facilities, and community youth programs demonstrated lower rates of psychological distress among adolescents.

Learning Objectives:

- Understand the multifaceted role of SDOH in shaping adolescent mental health outcomes.
- Recognize systemic barriers contributing to mental health inequities in adolescent populations.
- Develop evidence-based strategies to integrate SDOH into adolescent mental health policies and interventions.
- Advocate for cross-sector collaborations to address adolescent mental health through a public health lens.

Conclusion: Addressing adolescent mental health disparities requires a holistic approach that extends beyond traditional healthcare models. By prioritizing social determinants as part of adolescent mental health frameworks, policymakers and public health professionals can foster environments that promote psychological well-being, reduce inequities, and drive sustainable community health improvements. This research emphasizes the urgency of embedding social determinant considerations into national and local adolescent mental health strategies.

Keywords: Social Determinants of Health, Adolescent Mental Health Disparities, Equity, Public Health, Community Interventions, Health Policy



Mental Health

Newborns' congenital malformations and parents' depression diagnosis: a matched cohort study in Japan Yuta Taniguchi* Yuta Taniguchi Masao Iwagami Yoko Hamasaki Takehiro Sugiyama Rie Masuda Takahiro Kido Mitsuki Ikeda Taeko Watanabe Nanako Tamiya

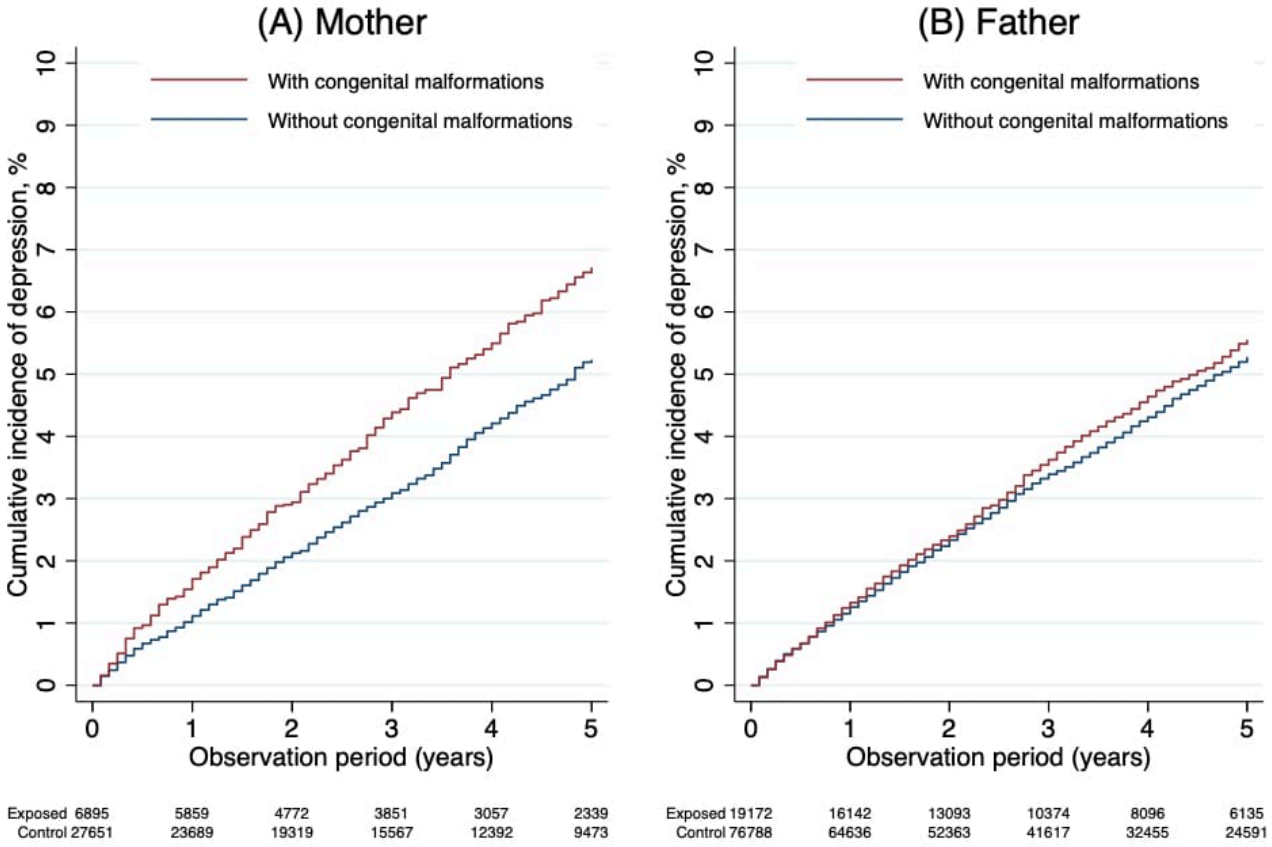
Objective: We aimed to examine the association between newborns' congenital malformations and parents' depression.

Methods: This retrospective cohort study used the JMDC Claims Database, a medical claims database from Japanese health insurance associations for company employees and their dependent families, containing about 17 million individuals. We identified 7,010 mothers and 19,521 fathers of newborns with congenital malformations born between January 2007 and March 2023 (exposed group) and matched them 1:4 with controls (28,040 mothers and 78,084 fathers) whose children did not have congenital malformations. We excluded parents with a history of depression before pregnancy. Congenital malformations were defined by the ICD-10 codes of Q00–Q99 (congenital malformations, deformations and chromosomal abnormalities) in the month of birth or the next month. Matching was based on parental age (±1 year) and the sex and birth year of the child. We examined the association between congenital malformations in newborns and the onset of depression diagnosis among the parents by plotting cumulative incidence curves.

Results: Of 35,050 mothers and 97,605 fathers, the median (IQR) age was 33 (30–36) for mothers and 33 (29–37) for fathers. The median follow-up was 41 (18–72) months for mothers and 39 (17–69) months for fathers, and the depression occurred in 1,714 mothers (4.9%) and 4,684 fathers (4.8%). The cumulative incidence curves (**Figure**) showed a higher cumulative incidence for mothers in the exposed group than in the control (1.7%, 2.9%, 4.4%, 5.5%, and 6.7% for the exposed and 1.1%, 2.1%, 3.1%, 4.2%, and 5.2% for controls at 12, 24, 36, 48, and 60 follow-up months), while it was similar for fathers (1.3%, 2.4%, 3.6%, 4.6%, and 5.6% for the exposed and 1.3%, 2.3%, 3.4%, 4.3%, and 5.3% for controls).

Conclusions: Our findings underscore the importance of support for the parents of newborns with congenital malformations, particularly mothers.

Figure. Cumulative incidence curves for parents' depression



Mental Health

Longitudinal Analysis of the Impact of Cardiovascular Health on Subsequent Depressive Symptoms, Anxiety, and Post-Traumatic Stress Disorder Jeong Hyun Ahn* Jeong Hyun Ahn Sun Jae Jung Dongkyu Lee Ji Su Yang

Background: There is limited longitudinal research examining the association between cardiovascular health, as measured by Life's Essential 8 metrics from the American Heart Association, and mental health outcomes such as anxiety symptoms, depressive symptoms, and post-traumatic stress disorder (PTSD) symptoms.

Methods: This study utilized follow-up data from individuals enrolled in a community-based cohort study in Korea. A total of 2,869 individuals who participated in at least one of the five surveys were included. The CVH was measured at baseline visits in 2013-2018, and divided into health behaviors (diet, physical activity, nicotine exposure, and sleep health) and health factors (body mass index, blood lipids, blood glucose, and blood pressure). CVH is categorized into "low (0–<50, poor CVH)", "moderate (50–<80, intermediate CVH)", and "high (80–100, ideal CVH)". We measured three mental health outcomes: anxiety symptoms, depressive symptoms, and PTSD symptoms at each follow-up. This study evaluated the odds ratio (OR) and 95% confidence intervals (CI) using the generalized estimating equation model, adjusting for sex, age, cohort enrollment year, income, education, marital status, and current drinking status.

Results: Compared to participants with high CVH at baseline, likelihoods for subsequent anxiety symptoms (OR=1.67, 95% CI=1.17–2.38), depressive symptoms (OR=1.91; 95% CI=1.30–2.82), and PTSD symptoms (OR=2.24, 95% CI=1.31–3.85) increased among participants with low CVH. Low health behaviors were associated with increased anxiety symptoms (OR=1.54, 95% CI=1.17–2.02) and depressive symptoms (OR=1.71, 95% CI=1.28–2.28) compared to high health behaviors.

Conclusion: In this prospective study, low CVH at baseline was associated with overall poor mental health including increased anxiety, depressive, and PTSD symptoms. Early management of ideal CVH and healthy behaviors may act as essential intervention for preventing mental health.

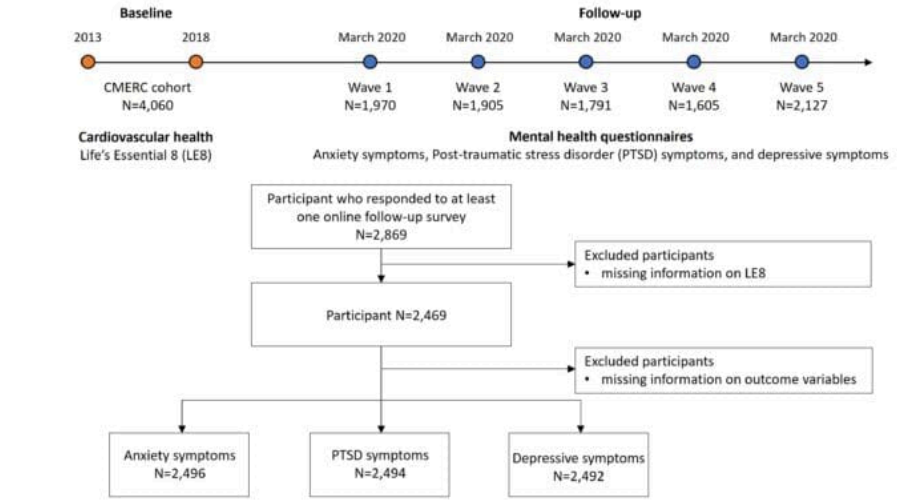


Figure 1. Study participants in Cardiovascular and Metabolic Diseases Etiology Research Center (CMERC) cohort

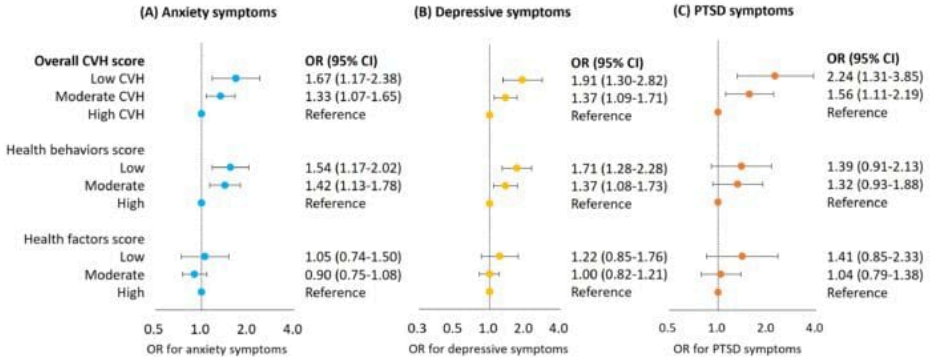
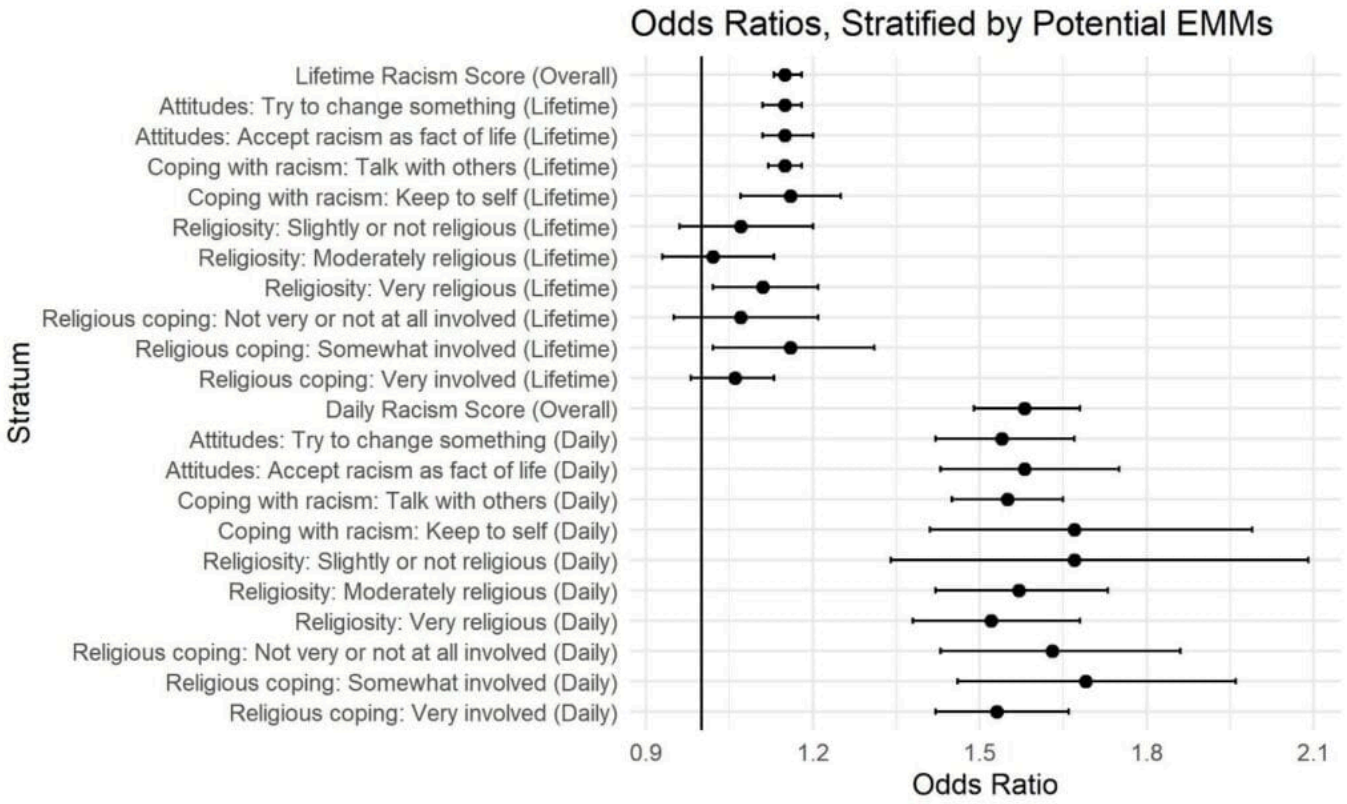


Figure 2. Longitudinal association between cardiovascular health and (A) anxiety symptoms, (B) depressive symptoms, and (C) PTSD symptoms. Adjusted for cohort enrollment year, sex, age, education, income, marital status, and alcohol consumption.
Abbreviation: CVH=Cardiovascular health; PTSD=Post-Traumatic Stress Disorder;

Mental Health

Perceived racism and depression in a cohort of middle-aged US Black women: the role of potential modifiers Virginia Cafferky* Yvette Cozier Virginia Cafferky Jeanine Nasser Jaimie Gradus

Exposure to racism is linked to poor mental health outcomes, but the role of hypothesized social and interpersonal modifiers (e.g., religious coping) among Black women remain poorly understood. The Black Women's Health Study (BWHS) is a prospective cohort of US Black women followed biennially beginning in 1995 when they were 21-69 years of age. Our analytic sample consisted of 20,333 women with no history of depression, who completed both the 2009 and 2019 BWHS follow-up questionnaires. Exposure to racism (assessed in 2009) was defined as how often participants experienced various types of daily discrimination (e.g., people act as if you are dishonest), as well as specific kinds of institutional racism (e.g., healthcare settings). Depression (assessed in 2019) was defined as scoring ≥ 16 on the Center for Epidemiologic Studies Depression (CES-D) scale or reporting diagnosed depression with medication use. Logistic regression models adjusted for age, education, and socioeconomic status. Stratified analyses assessed effect measure modification by self-reported coping strategies. High levels of daily and lifetime racism were associated with increased odds of depression: OR=1.6; 95% CI 1.5, 1.7 and OR=1.2; 95% CI 1.1, 1.2, respectively. Coping strategies provided little EMM. The effect of daily racism was slightly stronger among those keeping experiences to themselves (OR=1.7; 95% CI 1.4, 2.0) than those who cope by talking to others (OR=1.6; 95% CI 1.5, 1.7). High levels of religious coping weakly buffered the effect of daily racism (OR=1.5; 95% CI 1.4, 1.7) compared to moderate (OR=1.7; 95% CI 1.5, 2.0) and low levels (OR=1.6; 95% CI 1.4, -1.9). Our findings suggest that frequent exposure to racism is associated with increased odds of depression, with little EMM by hypothesized buffers. Future work is needed to better understand the impact of discrimination, and the role of social and interpersonal factors, on Black women's mental health.



LATEBREAKER

Mental Health

Barriers to outpatient mental health services experienced by adult Medicaid recipients: A scoping review Navdep Kaur* Navdep Kaur Katherine M. Keyes Charles C. Branas Ramin Mojtabai Mark Olfson

Introduction

Medicaid recipients commonly face challenges in accessing outpatient mental health services. This scoping review will categorize existing evidence for barriers to outpatient mental health services experienced by adult Medicaid recipients and identify knowledge gaps that warrant further investigation.

Methods

We will consider peer-reviewed studies published after most of the provisions of the Affordable Care Act became effective on January 1st, 2014. We will identify studies through PubMed, Scopus, and Embase. Two independent reviewers will 1) screen titles and abstracts and then 2) examine the full text of selected studies against the inclusion criteria. Unresolvable issues will then be decided by an independent third reviewer. The full search strategy is available at Open Science Framework (https://osf.io/3mt5b). We will use the Barriers to Healthcare Access Framework (Figure 1)1–5 to map all identified barriers and assess remaining gaps in the literature.

Preliminary Results

A MEDLINE (Ovid) search using our search strategy (undertaken on February 19th, 2025) yielded 1219 studies. In screening the first 100 articles, we identified several studies that examined the following policy-related structural barriers: state-level adoption of Medicaid expansion through the Affordable Care Act,6,7 mental health service coverage,8 provider network adequacy standards,9 and reimbursement policies.12,13 We also identified studies that examined structural barriers related to insurance type10,11 and spatial accessibility.14 Additionally, we identified several studies that investigated provider-level barriers related to logistics: appointment availability for psychiatrists15 and telemental health service access.16,17

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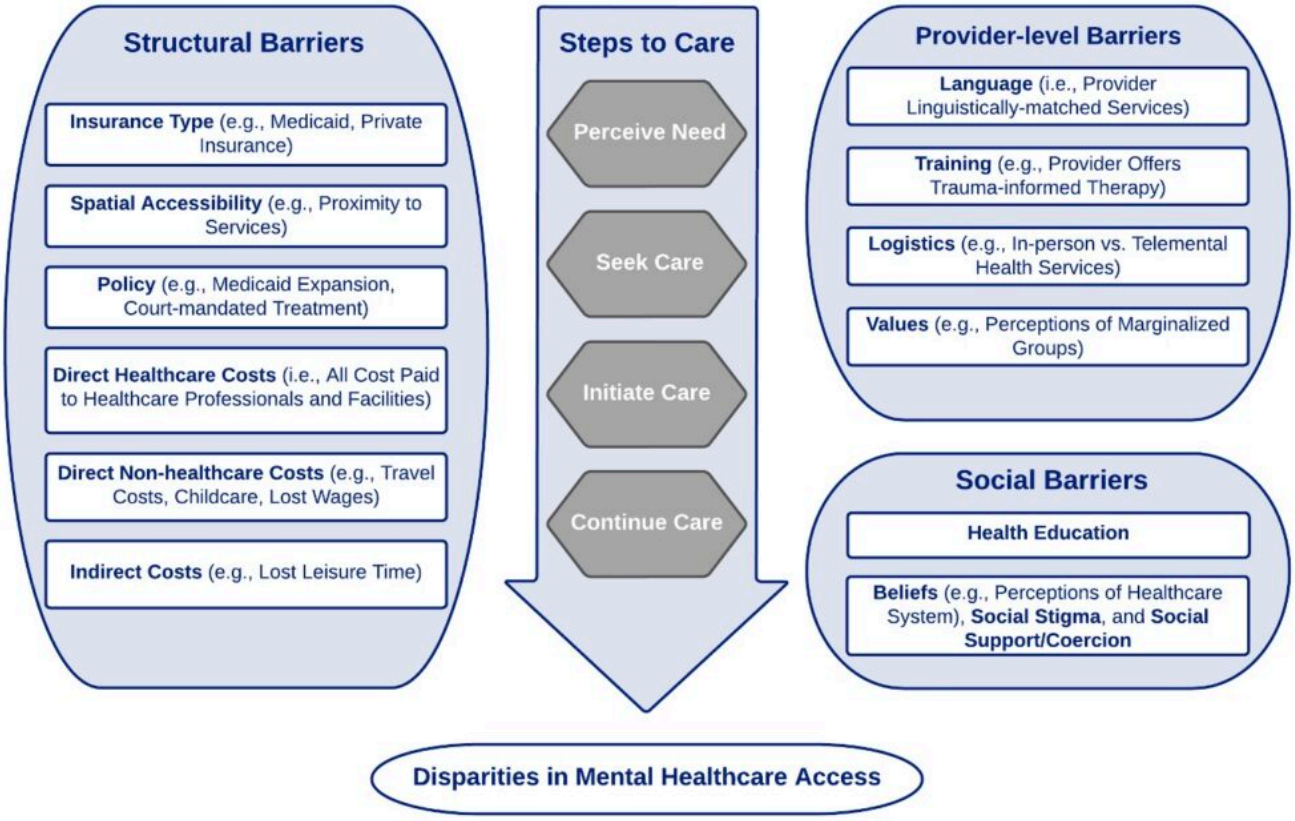


Figure 1. Framework for Barriers to Healthcare Access

LATEBREAKER

Mental Health

Maternal Depression and Offspring Inflammation: Association with hsCRP Levels across Age and Sex Ji Su Yang* Ji Su Yang

Background

Previous research has suggested a link between maternal depression and offspring inflammation, but most studies have focused on prenatal or early postpartum maternal depression and its effects during infancy or childhood. Limited evidence exists on how maternal depression beyond early caregiving years influences inflammation in offspring, particularly across different age groups and between sexes. This study examines the association between maternal depression severity and offspring hsCRP levels in a nationally representative sample while considering offspring age, sex, and paternal depression.

Methods

This cross-sectional study used data from the Korea National Health and Nutrition Examination Survey (KNHANES) 2016, 2018, and 2022. A total of 3,907 offspring aged 10 years or older nested within 2,792 mothers were included. Maternal depression severity was assessed using the Patient Health Questionnaire-9 (PHQ-9), and offspring hsCRP levels were measured via blood tests. Linear mixed models with random intercepts were used to account for family clustering, adjusting for sociodemographic factors and health behaviors.

Results

Severe maternal depression was significantly associated with elevated hsCRP levels in offspring (β: 0.84, 95% CI: 0.15 to 1.54). The association was strongest in adolescents and young adults but was not observed in older offspring. Sex-stratified analyses showed significance in female offspring but not in males. No significant association was found between paternal depression and offspring hsCRP levels.

Conclusion

These findings suggest that maternal mental health may influence offspring inflammation, particularly in younger and female offspring. Addressing maternal depression and optimizing home environments may help reduce inflammation-related health risks in offspring.

LATEBREAKER

Mental Health

The association of objectively and subjectively measured modifiable lifestyle factors with internalizing problems: The role of genetic confounding and shared method variance bias

Yingzhe Zhang* Yingzhe Zhang Henning Tiemeier Karmel Choi Leonard Frach Jean-Baptiste Pingault Elise Robinson Tian Ge

Background: Sleep duration and physical activity have been associated with internalizing problems. However, genetic confounding and measurement error may introduce bias. We assessed genetic confounding in the associations of modifiable lifestyle with internalizing problems using device-based and questionnaire assessments to estimate shared genetic risk across different assessments in adolescents.

Methods: In this preregistered study in the Adolescents Brain Cognitive Development cohort, we included European adolescents with both self-reported and device-based sleep duration (N=2283) and moderate/vigorous physical activity (MVPA, days/week, N=2772). We used the Brief Problem Monitor to assess self-reported internalizing problem scores. Genetic sensitivity analyses were conducted to assess genetic confounding by combining polygenic scores and molecular-based heritability of internalizing problems.

Results: Longer sleep duration was associated with lower internalizing problems using both self-reported (-0.15-SD, SE=0.02-SD) and objective (-0.10-SD, SE=0.02-SD) assessments. More frequent MVPA was associated with lower internalizing problems using both self-reported (-0.09-SD, SE=0.02-SD) and device-based (-0.06-SD, SE=0.02-SD) assessments. Substantial genetic confounding (81%) was found between self-reported sleep duration and internalizing problems, predominantly among boys. No clear evidence of genetic confounding was found in the associations of device-based sleep duration or either measures of MVPA with internalizing problems.

Conclusion: The observed negative relationship between reported child sleep duration and internalizing problems may be partly due to genetic confounding, particularly among boys. This genetic influence likely captured reporting measurement error of shared method variance. The impact of adolescent sleep duration on internalizing problems may be overestimated by self-reports, especially among boys, whereas associations of physical activity were not genetically confounded.

Mental Health

Unmet Need for Depression Treatment Before and After the Affordable Care Act Daniel Hagen* Daniel Hagen Emily Goldmann Rebecca M. Schwartz Jacqueline Moline

Background:

The 2010 Affordable Care Act (ACA) expanded access to depression screening and care. However, its effect on unmet need for depression treatment remains understudied.

Methods:

Data from the National Health and Nutrition Examination Survey (NHANES) from 2005 to 2020 were used to examine changes in unmet need for depression treatment (no current use of antidepressants or receipt of past-year psychotherapy despite current depressive symptoms [Patient Health Questionnaire (PHQ)-9 score ≥ 10]). Modified Poisson regression models were used to estimate the association between time period (post-ACA, 2013-2020 vs. pre-ACA, 2005-2010) and unmet need for depression treatment, both overall and stratified by socio-demographic and health care-related variables. Unadjusted models and models adjusted for socio-demographic characteristics and physical comorbidity yielded prevalence ratios (PRs) and 95% CIs.

Results:

Unmet need for depression treatment decreased from 56% in 2005-10 to 47% in 2013-20. After adjusting for covariates, this corresponded to a 14% reduction in unmet need post- vs. pre-ACA (PR=0.86; 95% CI: 0.79,0.95). In stratified models, the decline was statistically significant among men, Hispanic respondents, those 18-34 and 65+ years old, and participants with a Bachelor’s degree or more (at $p<0.05$). Only those reporting Medicare vs. another type of insurance coverage experienced a significant decrease in unmet need for depression treatment (PR=0.77; 95% CI: 0.60,0.99). A similar decrease in unmet need was observed regardless of having a regular point of care or not, but only detected among those who had used health care services in the prior year (PR=0.80; 95% CI: 0.70,0.92) vs. those who had not (PR=1.13; 95% CI: 0.92,1.37).

Conclusion:

Unmet need for depression treatment decreased after ACA implementation but remains common. Reductions in barriers to primary care visits and universal screening policies may further decrease unmet need for depression treatment.

Mental Health

Change in hospitalization rates for mental health and substance use disorders from before to after the start of the COVID-19 pandemic among Illinois youth, overall and by sex Caitlin Meyer* Caitlin Meyer Julia Howland SJ Doi Abigail Holicky Kristin Rankin

Background: The COVID-19 pandemic exacerbated mental health and substance use (MHSU) disorders among youth, who may be hospitalized if their MHSU needs are not met by outpatient services. This study examined changes in hospitalization rates for MHSU disorders among Illinois youth from before (2018-2019) to after (2021-2022) the start of the COVID-19 pandemic, overall and by sex.

Methods: This study used Illinois hospital discharge data for youth aged 3-17 to examine rates of inpatient MHSU hospitalizations (n=21,992 annually) per 10,000 population, before and after the start of the pandemic. Primary diagnosis codes were used to identify hospitalizations for MHSU disorders and categorize them into disorder subtypes. Rate ratios (RR) and 95% CIs for change over time were estimated using Poisson regression with an interaction term for sex.

Results: MHSU hospitalization rates for Illinois youth decreased significantly from before (96.2 per 10,000) to after (89.5 per 10,000) the start of the pandemic. This masks divergent trends by sex; females' rates increased (RR=1.05, 95% CI: 1.03-1.07), while males' rates decreased (RR=0.76, 95% CI: 0.75-0.78; interaction p-value<0.0001). By 2021-2022, females had double the rate of MHSU hospitalizations as males (95% CI: 1.97-2.05). Overall, about three-quarters of youth MHSU hospitalizations were for mood disorders. Despite an overall decrease in MHSU hospitalization rates over time for males, they saw a similar increase as females in hospitalization rates for suicide attempts (overall RR=1.80, 95% CI: 1.58-2.05) and non-suicidal self-injury (RR=1.80, 95% CI: 1.72-1.88).

Conclusion: Nearly 22,000 hospitalizations for MHSU disorders occur each year among Illinois youth, with females bearing the largest burden. Enhanced access to and coordination of outpatient mental health services may reduce these hospitalizations, particularly for suicide attempts and non-suicidal self-injury, which have increased in recent years for both sexes.

Mental Health

Smartphone use, sleep dissatisfaction, and mental health in Korean adolescents Yujin Kim*
Yujin Kim Hannah Oh

Background: Studies have shown that problematic smartphone use is associated with poor sleep quality and mental health among adolescents. However, little is known about whether the moderate use of smartphone without addiction is also associated with poor mental health and whether the association is independent of sleep quality.

Objective: Using nationally representative survey data, this study examined the association of duration of smartphone use with sleep dissatisfaction and poor mental health (depressive symptoms, general anxiety disorder (GAD), and suicidal thoughts/attempts).

Methods: We conducted a cross-sectional analysis of 51,718 adolescents who participated in the Korea Youth Risk Behavior Web-based Survey 2023. Participants reported their average duration of smartphone use, sleep dissatisfaction, and symptoms of poor mental health. Multivariable logistic regression was used to estimate odds ratios (ORs) and 95% confidence intervals (CIs) for the associations between smartphone use duration and poor mental health, adjusting for potential confounders.

Results: Among participants without problematic smartphone use, prolonged smartphone use (≥ 420 vs. <180 min/d) was positively associated with sleep dissatisfaction (OR: 1.22; 95% CI: 1.14, 1.30), GAD (OR: 1.27; 95% CI: 1.15, 1.41), presence of depressive symptoms (OR: 1.42; 95% CI: 1.32, 1.52), and experience of suicidal thoughts/attempts (OR: 1.36; 95% CI: 1.26, 1.48). The positive associations were attenuated but remained statistically significant after additional adjustment for sleep dissatisfaction. When stratified by sex, the magnitudes of positive associations were higher among girls (vs. boys; all p-interaction<0.01).

Conclusions: Our findings suggest that prolonged smartphone use is associated with sleep dissatisfaction and poor mental health among Korean adolescents without problematic smartphone use.

Mental Health

Optimism and Preventive Healthcare Use Hayami Koga* Hayami Koga Koichiro Shiba Tyler J VanderWeele Laura Kubzansky

Objective: Identifying factors that promote preventive healthcare use is important for aging societies. Optimism has been linked to healthier behaviors and better physical health. However, less is known about the association between optimism and preventive healthcare use. We evaluated if optimism is associated with increased use of flu shots, cholesterol tests, mammograms, Pap smears, and prostate exams.

Methods: Participants were adults over age 50 from the Health and Retirement Study. Optimism was assessed using the Life Orientation Test Revised in 2006/2008, 2010/2012, 2014/2016, and 2018/2020. Preventive healthcare use was assessed in 2008, 2012, 2016, and 2020. We examined the association between optimism at baseline and subsequent service use using Generalized Estimating Equations. We also assessed the extent to which optimism measured over time is associated with preventive service use in 2020 using Marginal structural models (MSM).

Results: The final analytic sample included 13,805 adults (mean [] age, 69 [10] years). After adjusting for sociodemographic factors, health conditions, and pre-baseline healthcare use, a 1-SD increase in optimism was associated with higher odds of receiving subsequent cholesterol tests (OR=1.06; 95%CI,106-.14), mammograms (OR=1.05; 95%CI, 1.02-1.09), and prostate exams (OR=1.11; 95%CI, 1.06-1.16). For Pap smears, associations were observed only when adjusting for sociodemographic factors. MSM analyses showed that consistently high versus low optimism levels over time was associated with higher odds of receiving cholesterol tests (OR=1.49; 95%CI, 1.17-1.90) and prostate exams (OR=1.59; 95%CI, 1.15-2.19).

Conclusion: Higher levels of optimism at baseline and over time were associated with increased subsequent use of preventive healthcare for some but not all services. Optimism may be a promising target of intervention to increase the uptake of preventive healthcare.

Mental Health

Gut microbiome variations associated with depressive symptomatology in a cohort of Boston-area Puerto Rican older adults Deepika Dinesh* Deepika Dinesh Xochitl Morgan Sherman Bigornia Mahdi Garelnabi Kelsey M. Mangano Sabrina Noel Curtis Huttenhower Katherine L. Tucker Natalia Palacios

Background
Evidence suggests that gut microbiome variations and dysbiosis may be associated with depression. However, there is a lack of research on the microbiome, especially the virome, associated with depression, particularly in Hispanics/Latinos, who have unique lifestyle characteristics impacting gut and mental health. Here, we examined gut bacterial and viral variations associated with depressive symptomatology in the Boston Puerto Rican Health Study (BPRHS).
Methods
The BPRHS is a prospective cohort of Boston-area Puerto Rican adults. Our study comprised of 321 participants with fecal metagenomic sequencing and depressive symptomatology measured by the Center for Epidemiological Studies Depression (CESD) scale. Taxonomic profiling of bacterial and viral taxa was performed using MetaPhlAN and BAQLaVa 1.0., respectively. We examined cross-sectional associations between overall composition, measured by alpha (Shannon) and beta (Bray-Curtis) diversity, and CESD scores. We identified bacterial and viral taxa associated with CESD scores in feature-wise analyses using multivariate linear regression models (MaAsLin2).
Results
Among 321 participants (mean age 68.7y, 76% female), CESD score was not associated with alpha ($P=0.66$) or beta diversity ($P=0.37$). In feature-wise analyses, adjusted for age, sex and BMI, an enrichment of Klebsiella pneumoniae ($\beta=0.74$, $P<0.01$, FDR $P=0.15$), Clostridim AT4 ($\beta=0.74$, $P<0.01$, FDR $P=0.15$), Anaerotruncus colihominis ($\beta=0.57$, $P= 0.01$, FDR $P=0.22$), and Faecalibacterium phage Brigitvirus ($\beta=0.41$, $P<0.01$, FDR $P=0.02$), was associated with high CESD scores (increasing severity).
Conclusions
The observed enrichment of K. pneumoniae, associated with immune dysfunction, and Brigitvirus, reportedly enriched in patients undergoing antibiotic therapy, suggests that gut microbiome variations may be associated with depressive symptomatology. Future work will test interactions of gut bacteriome, virome and functional pathways related to depression.

Mental Health

Effect of antidepressant treatment on suicidal behavior among women with postpartum depression: a target trial emulation Jing Zhou* Jing Zhou Donghao Lu

Background: Postpartum depression (PPD) affects one fifth of new mothers worldwide and as illustrated in our recent work, confers 7.2-fold higher risk of suicide attempt and suicide death within the first year after diagnosis. It is however unknown whether the first-line pharmaceutical treatment (antidepressants) can mitigate such risk among women with PPD.

Methods: We conducted an emulated target trial of 26,232 women diagnosed with PPD during 2007-2022 in Sweden using national and regional healthcare registers. Initiation of antidepressants within 28 days after diagnosis was ascertained from the Prescribed Drug Register, with one-year follow-up for any suicide attempt and suicide death recorded in registers. Multivariable Cox regression was employed to estimate the efficacy of antidepressants on suicidal behavior risk. Inverse probability weighting was applied to account for baseline confounding in the intention-to-treat analysis, as well as for treatment non-adherence and time-varying confounding in the per-protocol analysis.

Results: At a mean age of 31.6 (SD 5.3) years, antidepressants was dispensed for 11,186 (42%) women with PPD. During the follow-up, 426 events (10.17 per 1000 person-years) of suicidal behavior were observed in the initiators while 422 events (7.54) in the non-initiators. In the ITT analysis, initiation of antidepressants was associated with 25% increased risk of suicidal behavior (HR 1.25, 95% CI 1.14-1.38). Future analysis will focus on different types of antidepressants, subtypes of suicidal behavior, and implement per-protocol analysis.

Conclusions: While no randomized clinical trial is available or justifiable, the present target trial provide preliminary evidence that antidepressants alone may not be effective enough to mitigate the suicidal risk among patients with PPD. While antidepressants remain widely prescribed for this group, it is important to develop patient-centered treatment plans and implementable suicidal screening and prevention strategies.

Mental Health

Associations Between Economic Hardships and Mental Health Outcomes in Idaho Deborah Taye* Deborah Taye Kailey Belcher J'Neka Claxton Guixiang Zhao Machell Town

Introduction

Economic stability is a key social determinant of health that influences mental health. Idaho's Division of Public Health has prioritized mental health, making it important to examine the associations between economic stability and mental health outcomes among adults.

Methods

We analyzed data from Idaho's 2022-2023 Behavioral Risk Factor Surveillance System, which included core questions and an optional module for social determinants and health equity, totaling to 12,528 adult participants, aged ≥ 18 years. Weighted prevalences of economic hardship variables (e.g., lost or reduced hours of employment, housing insecurity, experiencing threat to shut off utility services, receiving food stamps or SNAP, and food insecurity) and mental health related variables (e.g., mental stress and frequent mental distress) were estimated by demographic characteristics. Using log-linear regression analyses with robust variance estimator, the adjusted prevalence ratios were used to assess the associations between economic hardships and mental health related variables, adjusting for demographic characteristics.

Results

Prevalence estimates of economic hardship variables ranged from 5.8% (experiencing threat to shut off utility services) to 11.1% (food insecurity) and were generally higher among younger adults and those with less than a high school education. Prevalence estimates of mental stress and frequent mental distress were 14.6% and 14.2% respectively, highest among adults aged 18-34 years, women, those with less than a high school education, those with a household income <$25,000, and unmarried individuals. After adjusting for demographics, individuals reporting economic hardships had 2.1 to 4.0 times higher prevalence of mental stress and 1.7 to 2.6 times higher prevalence of frequent mental distress compared to those without hardships.

Conclusion

Addressing and providing support to those experiencing economic hardships may help improve mental well-being in Idaho.

Methods/Statistics

Extending Intersectional Methods to Population Health Research Victoria Fisher* Victoria Fisher Kiana Ramos Nicole Alkhouri Nadia N. Abuelezam

Background: Intersectionality theory has been used to describe the interconnectedness of identities within social, institutional, and structural systems of power. Recently introduced methods aim to produce better intersectional analyses (beyond multiple interactive terms), including multilevel analysis of individual heterogeneity and discriminatory accuracy (MAIHDA). MAIHDA relies on categorical strata as both fixed and random effects but has been met with concerns of collinearity and issues with interpretation. We propose an extension of MAIHDA to population-level infectious disease data, which allows for the use of continuous fixed effects to address potential collinearity.

Methods: Concerns about MAIHDA come from the reduction in random effects variance after the strata are added to the model as fixed effects. We propose using continuous measures as fixed effects that correspond to the categorical strata. This allows for greater within-group variation and the possible application to population-level research. We apply our proposed methods to U.S. county-level COVID-19 mortality data (CDC Wonder) via three multilevel models: random effects only, with continuous fixed effects, and with the strata as fixed effects (3044 counties were included in our analysis).

Results: The results from our three models suggest that using continuous count fixed effects provided the best fit. Continuous fixed effects reduced variance accounted for by the strata from 19% (null model) to 14%, while categorical fixed effects reduced the variance accounted for to 1.2%, suggesting that the use of categorical fixed effects may be sufficient for modeling the data on their own, but would not capture the interactive effects integral to intersectional analyses.

Conclusions: We illustrate the use of a novel application of MAIHDA methods in a population-level analysis, where strata were created from continuous variables. This method may be beneficial when individual-level data is not accessible.

Methods/Statistics

Optimal sampling strategies for observational epidemiologic studies using big data

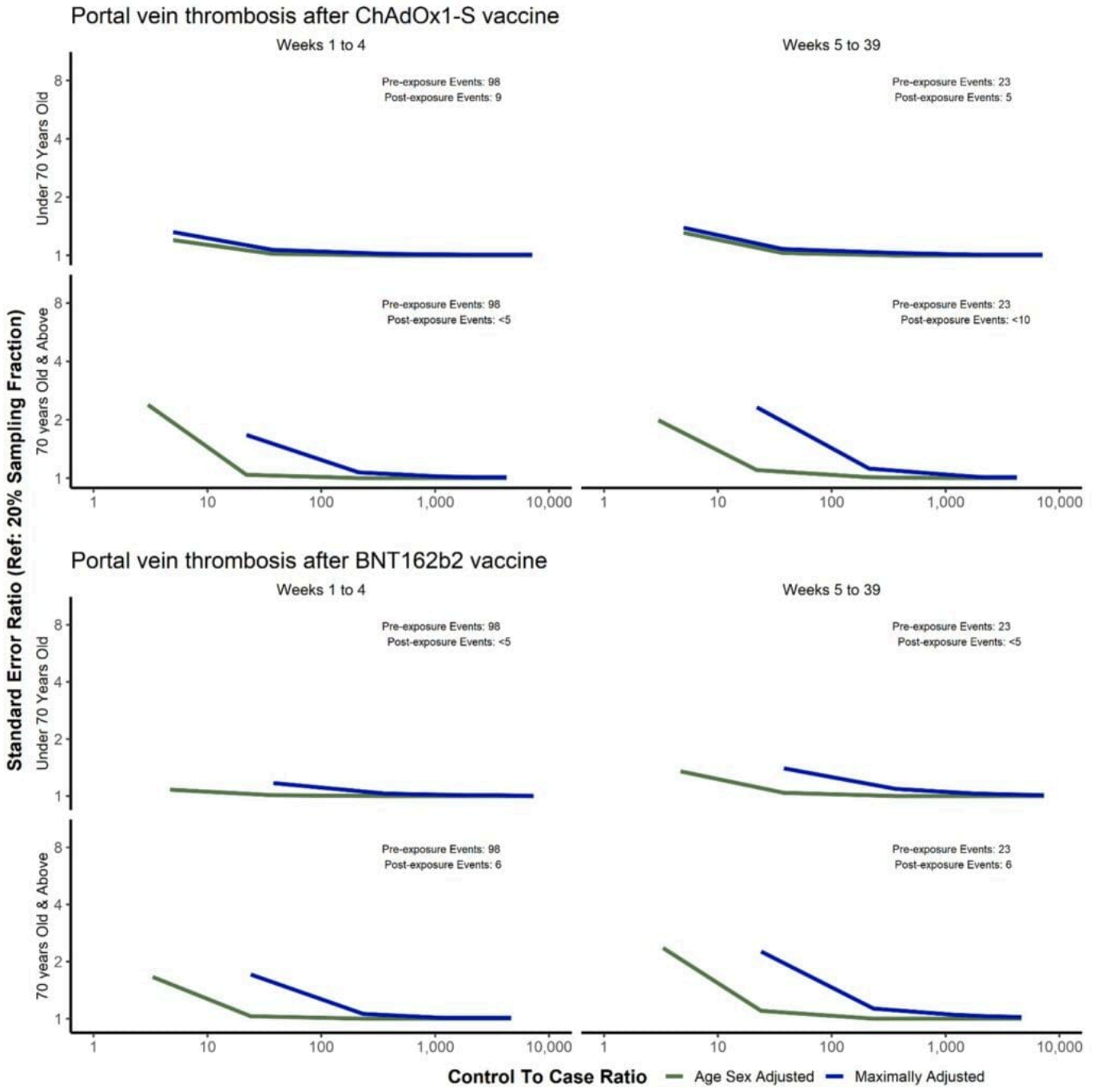
Jonathan Sterne* Jonathan Sterne Arun Karthikeyan Suseeladevi Venexia Walker Samantha Hiu Yan Ip Rochelle Knight William Whiteley Angela Wood

Background: Observational epidemiologic studies based on population-scale linked electronic health records are increasingly reported, but statistical analyses may entail substantial computational costs, or be unfeasible. Simple random sampling reduces computation time but loses precision. Subsampling based on exposure or outcome status, with analyses adjusted using inverse probability weighting, may maintain precision.

Methods: We examined the impact of different sampling fractions on precision of estimated hazard ratios (HRs) from Cox models, based on a published study (https://doi.org/10.1371/journal.pmed.1003926) using linked data on 46 million adults of associations of COVID-19 vaccination with incidence of pulmonary embolism (common outcome) and portal vein thrombosis (rare outcome). We created 50 different datasets including all people with and randomly sampled subsets of people without the outcome, for each of sampling fractions 0.001%, 0.01%, 0.1%, 1%, 2%, 5%, and 10%, and five datasets using sampling fractions 20% and 50%.

Results: Geometric mean HRs and 95% CIs were identical for sampling fractions of 10% or more. Consistent with standard case-control study theory, for the common outcome there was little or no loss of precision when there were at least 10 times as many people with versus without the outcome in the sampled dataset. However, for the rare outcome ratios of much greater than 10 were required to avoid loss of precision in multivariable models controlling for substantial numbers of confounding variables. For rare exposures, precision can be optimized by randomly sampling unexposed people without the outcome event.

Conclusions: Subsampling people based on the outcome and/or exposure, with analyses weighted to account for this, can maintain precision while reducing computation times. Such approaches to improve computational efficiency will be required as very large population scale datasets become increasingly available for epidemiologic research.


Portal vein thrombosis after ChAdOx1-S vaccine
Weeks 1 to 4
Weeks 5 to 39
Pre-exposure Events: 98
Post-exposure Events: 9
Pre-exposure Events: 23
Post-exposure Events: 5
Pre-exposure Events: 98
Post-exposure Events: <5
Pre-exposure Events: 23
Post-exposure Events: <10
Portal vein thrombosis after BNT162b2 vaccine
Pre-exposure Events: 98
Post-exposure Events: <5
Pre-exposure Events: 23
Post-exposure Events: <5
Pre-exposure Events: 98
Post-exposure Events: 6
Pre-exposure Events: 23
Post-exposure Events: 6
Under 70 Years Old
70 years Old & Above
Standard Error Ratio (Ref: 20% Sampling Fraction)
1
2
4
8
1
10
100
1,000
10,000
Control To Case Ratio
Age Sex Adjusted
Maximally Adjusted

Methods/Statistics

Evaluating methods for imputing race and ethnicity in electronic health record data Sarah Conderino* Sarah Conderino Jasmin Divers John A. Dodson Lorna E. Thorpe Mark G. Weiner Samrachana Adhikari

Background: Race/ethnicity is often missing on a substantial proportion of patients due to challenges with data collection. Gold standard imputation approaches rely on identifiable information, including names and addresses, that are not readily available in many research databases. Using electronic health record data from NYU Langone Health and the INSIGHT Clinical Research Network, we compared methods to assess whether anonymized variables are sufficient for the imputation of race/ethnicity.

Methods: We first conducted simulation analyses under different missing data mechanisms to compare the performance of Bayesian Improved Surname Geocoding (BISG), single imputation with neighborhood majority, random forest imputation, and multiple imputation with chained equations (MICE). Performance was measured compared to self-reported race/ethnicity using sensitivity, positive predictive value, and overall accuracy, and agreement was measured with Cohen's kappa (κ). We then applied these methods to impute race/ethnicity in two EHR-based data sources and compared chronic disease burden by race/ethnicity across imputation approaches.

Results: Under simulation analyses, non-anonymized BISG imputation provided the most accurate classification of race/ethnicity, ranging from 66% to 73% across missing data mechanisms. Anonymized imputation methods were more sensitive to the missing data mechanism, with agreement dropping when race/ethnicity was missing not at random (MNAR) (κMICE=0.25, κsingle= 0.25, κrandom forest=0.33). When these methods were applied to the NYU and INSIGHT cohorts, racial/ethnic distributions and chronic disease burden were consistent across all imputation methods.

Conclusions: BISG imputation may provide a more accurate racial/ethnic classification than single or multiple imputation using anonymized covariates, particularly if the missing data mechanism is MNAR. Descriptive studies of disease burden may not be sensitive to methods for imputing missing data.

Methods/Statistics

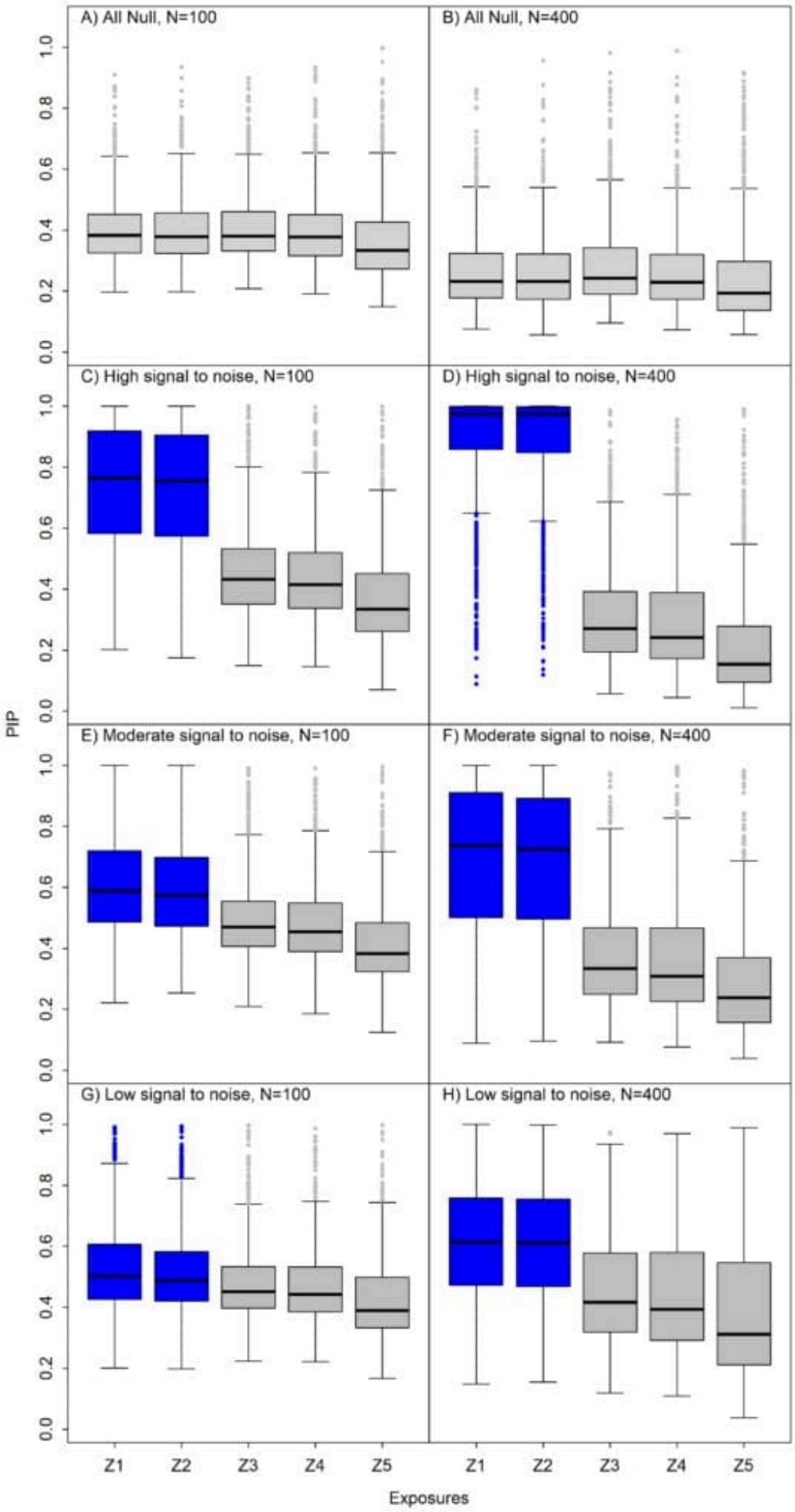
Performance of Bayesian Kernel Machine Regression (BKMR): A Simulation Study Stacey Alexeeff* Stacey Alexeeff Juanran Feng Jennifer F Bobb

Background: Bayesian Kernel Machine Regression (BKMR) is a widely used statistical methodology that flexibly models complex exposure mixtures. This study expands on the simulation study in the original BKMR paper by varying the signal-to-noise ratio, evaluating larger sample sizes, and running more simulations per scenario to evaluate performance.

Methods: We conducted a simulation study to assess the performance of BKMR with 1,000 simulations per scenario. We evaluated four signal-to-noise ratios (high, moderate, low, and null) under two sample sizes (n=100 and n=400) with a mixture exposure response function that included two main effects and an interaction. We summarized the distributions of the posterior inclusion probabilities (PIPs) using boxplots and by comparing the rank ordering. We computed the bias, model standard error, empirical standard error, and coverage of the Bayesian 95% credible intervals.

Results: We found that the PIPs of truly associated exposures can vary widely, and their magnitudes depend on the signal-to-noise ratio and the sample size (Figure). For high signal-to-noise and higher sample size of n=400, truly associated exposures generally had higher PIPs than null exposures, with higher PIP rank ordering in 92% of simulations. For low signal-to-noise and lower sample size of n=100, truly associated exposures often did not have higher PIPs than null exposures, with higher PIP rank ordering in only 27% of simulations. Across scenarios, bias was low (-0.3 to 0.4), and the model standard error reflected the empirical standard error, leading to good coverage of the Bayesian 95% credible intervals (89% to 99%).

Conclusion: BKMR had low bias and credible intervals had good coverage. However, PIPs showed high variability, where null exposures may have higher PIPs than truly associated exposures, particularly in low signal-to-noise scenarios. BKMR is a reliable method, but caution is needed when interpreting PIPs.


A) All Null, N=100
B) All Null, N=400
C) High signal to noise, N=100
D) High signal to noise, N=400
E) Moderate signal to noise, N=100
F) Moderate signal to noise, N=400
G) Low signal to noise, N=100
H) Low signal to noise, N=400
PIP
0.0
0.2
0.4
0.6
0.8
1.0
Z1
Z2
Z3
Z4
Z5
Exposures

Methods/Statistics

Sociodemographic, health-related, and clinical characteristics and their associations with mortality among All of Us participants compared with the United States general population

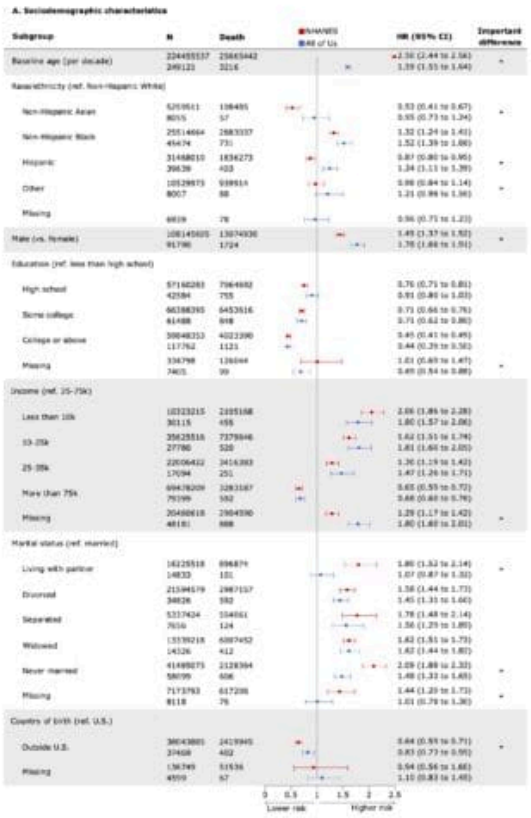
Jingxuan Wang* Jingxuan Wang Erin L. Ferguson Peter Buto Ruijia Chen Anna Pederson Minhyuk Choi Deborah Blacker M. Maria Glymour

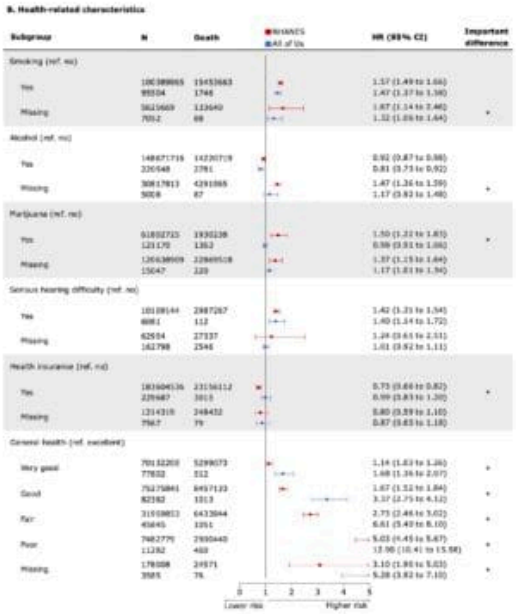
Background: The large and diverse All of Us Research Program offers tremendous opportunities for health research. However, results may not be generalizable to the US population due to the program's targeted recruitment efforts.

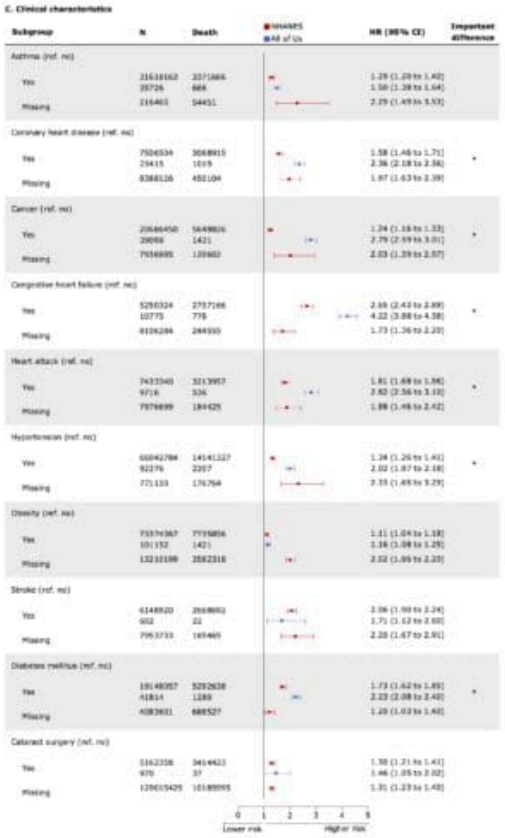
Methods: We compared All of Us participants to those from the nationally representative continuous 1999-2018 National Health and Nutrition Examination Survey (NHANES) with respect to: overall mortality rates; the distribution of sociodemographic, health-related, and clinical characteristics; the association of each characteristic with mortality (estimated using Cox proportional-hazards models); and population attributable fraction (PAF) for mortality for each characteristic.

Results: All of Us participants were older, less likely to be Non-Hispanic White, had more years of education, and had a higher prevalence of major chronic conditions than NHANES. Mortality rates were generally lower for All of Us participants, especially at older ages. For example, the mortality rates for participants aged 50-60 were 4.4 per 1,000 person-years in All of Us, compared to 5.5 in NHANES. For those aged 60-70, the rates were 6.1 in All of Us and 11.7 in NHANES; mortality of participants aged 80 and above was 17.5 in All of Us and 93.0 in NHANES. The direction of associations in All of Us and NHANES matched for almost all comparisons, but differed in magnitude for some conditions, primarily clinical diagnoses. For example, in All of Us, mortality among participants with a prevalent cancer diagnosis was 2.79 (95% CI: 2.59 to 3.01) times higher than among participants without cancer; in NHANES the hazard ratio was only 1.24 (95% CI: 1.16 to 1.33). PAFs were generally higher in All of Us.

Conclusions: Predictors of mortality in All of Us do not consistently generalize to the US population. Analytical approaches are needed to address non-representativeness and mitigate potential biases associated with the selection into the All of Us cohort.


A. Sociodemographic characteristics
Subgroup
N
Death
NHANES
All of Us
HR (95% CI)
Important difference
Baseline age (per decade)
Race/ethnicity (ref. Non-Hispanic White)
Non-Hispanic Asian
Non-Hispanic Black
Hispanic
Other
Missing
Male (vs. female)
Education (ref. less than high school)
High school
Some college
College or above
Missing
Income (ref. 25–75k)
Less than 10k
10–25k
25–35k
More than 75k
Missing
Marital status (ref. married)
Living with partner
Divorced
Separated
Widowed
Never married
Missing
Country of birth (ref. U.S.)
Outside U.S.
Missing
0
0.5
1
1.5
2
2.5
Lower risk
Higher risk


B. Health-related characteristics
Subgroup
N
Death
NHANES
All of Us
HR (95% CI)
Important difference
Smoking (ref. no)
Yes
Missing
Alcohol (ref. no)
Yes
Missing
Marijuana (ref. no)
Yes
Missing
Serious hearing difficulty (ref. no)
Yes
Missing
Health insurance (ref. no)
Yes
Missing
General health (ref. excellent)
Very good
Good
Fair
Poor
Missing
0
1
2
3
4
5
Lower risk
Higher risk


C. Clinical characteristics
Subgroup
N
Death
NHANES
All of Us
HR (95% CI)
Important difference
Asthma (ref. no)
Yes
Missing
Coronary heart disease (ref. no)
Yes
Missing
Cancer (ref. no)
Yes
Missing
Congestive heart failure (ref. no)
Yes
Missing
Heart attack (ref. no)
Yes
Missing
Hypertension (ref. no)
Yes
Missing
Obesity (ref. no)
Yes
Missing
Stroke (ref. no)
Yes
Missing
Diabetes mellitus (ref. no)
Yes
Missing
Cataract surgery (ref. no)
Yes
Missing
0
1
2
3
4
5
Lower risk
Higher risk

Methods/Statistics

What goes wrong in prediction models if you ignore mortality? Stephanie Armbruster*
Stephanie Armbruster Sebastien Haneuse Harrison Reeder Daniel Kramer

Prediction is a central pillar to epidemiology; it supports informed healthcare decisions on a patient and population level and is essential to research in the design and analysis stage. In many settings of epidemiological interest, the force of mortality is strong. Mortality – as a competing risk – prevents health-related outcomes from happening. It partly determines a prediction; it truncates and implies non-existence of outcomes post-death. Yet, standard prediction models, such as regression-based methods, frequently ignore mortality and models imply a 'pretend reality' in which patients are considered immortal. Ignoring mortality may result in bias. If used in clinical practice, it can compromise patient-specific health-care decision making, mislead risk stratification in targeted trial design or misinform the implementation of public health interventions. The agnosticism to mortality also misaligns with a patient's reality; health-related decisions naturally involve a complex trade-off between survival and quality-of-life.

We will illustrate what goes wrong in prediction when ignoring mortality by presenting real-world scenarios in which bias arises based on data from the PIPER-ICD study. Sudden Death (SD) is the primary cause of death in the US. Patients at increased risk of suffering a SD are primarily treated with an implantable cardioverter defibrillator (ICD). ICD-related predictions among older patients are biased if they do not account for higher risk of all-cause mortality at the end-of-life. In this vein, PIPER-ICD observed geriatric conditions, frailty metrics, and quality-of-life endpoints among patients over the age of 65 with ICD devices to analyze the end-of-life experience with an ICD.

Methods/Statistics

Issues in measurement and causal modelling of complex social exposures: examining typologies of violence in young people in Luwero Uganda Daniel J Carter* Daniel Carter Amiya Bhatia Jenny Parkes Dipak Naker Karen Devries

Background. Like many exposures in social epidemiology, operationalising measures of interpersonal violence is complex. Experiences of different acts of violence from different perpetrators co-occur across an individual's life course, particularly in high-prevalence settings. Using measures such as binary or sum scores may result in a wide array of experiences being classified as the same exposure to violence, biasing estimates of the consequences of violence as the exposure is not well-defined.

Methods. We draw on three waves of data from the Context of Violence in Adolescence Cohort (CoVAC), a prospective cohort study of 3431 young people in Luwero, Uganda, to examine how approaches like latent class analysis (LCA) could offer more consistent measurement for violence exposure. We fit LCAs at each wave to estimate underlying typologies of violence in early adolescence, late adolescence, and early adulthood. We investigated solutions ranging from two to nine classes and compared fit statistics and qualitative class cohesion to select the optimal number of classes.

Results. Three-class, six-class and five-class solutions were returned in early adolescence, late adolescence, and early adulthood respectively. Lowest violence classes were characterised by experiencing no or common acts of violence, often in school. Highest violence classes were characterised by violence across many places and perpetrators, including at work, and from caregivers and partners, and including acts of severe violence and sexual violence. Middle classes reflected both common acts of violence and violence experienced in a specific domain. Movement between classes was fluid across the lifecourse.

Conclusion. Measurement accounting for co-occurence demonstrates distinct patternings of violence. Such operationalisation of complex exposures may reduce misclassification and help mitigate consistency assumption violations, not just in violence research, but across the field of social epidemiology.

Methods/Statistics

Tree-based scan statistics to evaluate drug safety in pediatric populations: sulfamethoxazole/trimethoprim as a positive test case Kelly Fung* Kelly Fung Loreen Straub Timothy Savage Massimiliano Russo Helen Mogun Thomas Deramus Georg Hahn Shirley V. Wang Krista F. Huybrechts

Clinicians treating pediatric patients rely on evidence generated in adults. However, the safety profile of medications may differ for children. Tree-based scan statistic (TBSS) approaches can be used to identify safety issues by screening thousands of potential adverse outcomes while controlling type 1 error, but their performance in pediatric populations has not been evaluated.

Th study objective was to assess whether TBSS can identify rare, serious adverse effects and describe the pattern of unsuspected alerts using the known association of sulfonamides and Stevens-Johnson Syndrome (SJS) as a test case.

Using Medicaid (2008-2018) and MarketScan (2008-2021) databases, we compared children who initiated sulfamethoxazole/trimethoprim (SMX-TMP) to those initiating cephalexin and clindamycin, respectively. The outcome tree was based on hierarchical groupings of diagnostic codes in the International Classification of Disease system. Incident outcomes were identified in the 30 days after treatment initiation, using a 90-day washout. We adjusted for confounders using propensity score overlap weights. A p-value threshold of 0.05 was used to define statistical alerts for potential safety signals.

There were 2,939,183 children exposed to SMX-TMP, 3,908,066 to cephalexin, and 755,945 to clindamycin. Comparing SMX-TMP to cephalexin, 278 statistical alerts were detected out of 8,517 outcomes screened. Among these, 11 alerts were considered clinically plausible adverse events; the remainder being related to infections or chronic illnesses. Compared to clindamycin, 144 alerts were identified, 10 of which were clinically plausible. Increased risks for SJS were identified in both comparisons.

TBSS detected the known risk of SJS, a rare but serious condition associated with SMX-TMP, without raising many additional clinically plausible alerts, supporting the feasibility of the approach. Follow-up of these plausible alerts and further evaluation of the TBSS approach will be important.

Table: Clinically Plausible Statistical Alerts Comparing Sulfamethoxazole/Trimethoprim (SMX-TMP) to Cephalexin and Clindamycin with Propensity Score Overlap Weights

SMX-TMP vs. Cephalexin				
Outcome	Events in Exposed	Events in Referent Group	Relative Risk	P-Value
Poisoning by sulfonamides	177	<11	62.43	0.001
Poisoning by other and unspecified anti-infectives	22	<11	10.25	0.017
Drug dermatitis	4,975	1,908	3.89	0.001
Other drug allergy	3,822	1,291	3.79	0.001
Poisoning by other specified antibiotics	55	16	3.75	0.005
Drug induced neutropenia	119	43	3.75	0.001
Steven-Johnsons Syndrome	194	69	3.71	0.001
Unspecified adverse effect of other drug, medicinal and biological substance	2,032	1,157	2.87	0.001
Poisoning by other medications and drugs	9,938	4,929	2.69	0.001
Poisoning	13,180	8,738	1.99	0.001
Injury and poisoning	42,605	56,122	1.04	0.001
SMX-TMP vs. Clindamycin				
Outcome	Events in Exposed	Events in Referent Group	Relative Risk	P-Value
Poisoning by sulfonamides	177	<11	35.79	0.001
Steven-Johnsons Syndrome	194	24	2.57	0.012
Drug induced neutropenia	119	28	2.32	0.023
Other drug allergy	3,822	523	1.69	0.001
Drug dermatitis	4,975	890	1.58	0.001
Poisoning by other medications and drugs	9,938	1,856	1.46	0.001
Unspecified adverse effect of other drug, medicinal and biological substance	2,677	503	1.39	0.001
Unspecified adverse effect of unspecified drug, medicinal and biological substance	2,032	536	1.38	0.001
Poisoning	13,180	2,676	1.32	0.001
Injury and poisoning	42,604	11,486	1.06	0.009

Methods/Statistics

Random error units, a novel method to express random error in epidemiological studies

Imre Janszky* Imre Janszky Johan Håkon Bjørngaard Pål Romundstad Lars Vatten Nicola Orsini

The most frequently used methods for handling random error are largely misunderstood or misused by biomedical researchers. We propose a simple approach to quantify the amount of random error which does not require solid background in statistics for its proper interpretation. Expressing random error with the number of random error units (REU) does not require solid background in statistics for a proper interpretation and cannot be misused for making oversimplistic interpretations relying on statistical significance.

Methods/Statistics

Obtaining a Probability Sample of a Pregnancy Cohort of Births Michael Elliott* Michael Elliott Jean Kerver Alexa Drew Kaitlyn Watson Breanna Kornatowski Gwendolyn Norman Glenn Copeland Eva Leissou Terri Ridenour Shonda Kruger-Ndiaye Tengfei Ma Douglas Ruden Charles Barone Daniel Keating Robert Sokol Christine Johnson Nigel

The Michigan Archive for Research on Child Health (MARCH) study produced a probability sample of Michigan births between 2017 and 2023, with data collection beginning at first prenatal visit and continuing up to age 4. Birth certificate data were used to create a sampling frame of hospitals and associated obstetric clinics, from which a probability-proportional-size sample of 10 hospitals was drawn. Approximately 100 pregnancies were then recruited in clinics serving each sampled hospital, yielding an approximately equal probability sample of 1,021 births. This sample was supplemented with 109 births from a certainty selection of a Flint, MI hospital, for a total sample of 1,130. The resulting response rate was extremely high, with 100% of sampled hospitals and 65% of sampled clinics participating. Comparing the resulting sample with all 2017-2023 Michigan births showed close correspondence with respect to birth outcomes (birthweight, gestational age, Apgar scores, gestational diabetes) and mothers' demographics (age, race, education, marital status), with underrepresentation of Hispanic ethnicity and overrepresentation of reported smoking. Given the recent failures of two major prospective birth cohorts (the US National Childrens' Study and the UK Life Study), our work shows a way forward for obtaining probability samples for pre- and post-natal studies of births

Methods/Statistics

Much ado about nothing? Do we need harmonized census tract data to study longitudinal associations between neighborhood conditions and the health of individuals? Tongtan Chantarat* Tongtan Chantarat David C. Van Riper Jenny L. Wagner Michelle J. Ko

Epidemiologists use population data from the Decennial Census to describe various neighborhood conditions and their associations with health. The Census Bureau redraws census tract boundaries before each Decennial Census to reflect neighborhood and population changes, making it challenging to characterize neighborhood conditions consistently across time. To account for the potential "noise" introduced by measuring conditions using changing neighborhood boundaries, epidemiologists can use data from different censuses harmonized onto a single set of census tract boundaries. However, boundary harmonization is a resource-intensive, time-consuming process. We used a case study of exposure to residential segregation in mid-life and later-life cognitive decline to examine differences in model estimates using census year-specific vs. harmonized boundaries. Using survey data from Black participants in the Health and Retirement Study who lived in urban areas at least once between 1990-2010, we characterized exposure to county-level residential segregation by calculating indices of dissimilarity and isolation in two ways, using: (1) population estimates based on the 1990, 2000, and 2010 boundaries, and (2) estimates based on 2010-harmonized boundaries from the National Historical Geographic Information System, the Longitudinal Tract Database, and the Neighborhood Change Database. Using linear mixed-effects regressions, we found no significant differences in the model estimates when using census year-specific vs. harmonized data. Boundary harmonization may not be needed to accurately capture the relationship between life-course exposure to neighborhood conditions and health outcomes in later life, opening up opportunities for epidemiologists to characterize the exposure from much earlier in life.

Methods/Statistics

Cognitive data harmonization across two racially diverse cohorts in the United States

Michelle Flesaker* Michelle Flesaker A. Zarina Kraal Justina F. Avila-Rieger M. Maria Glymour Emily M. Briceño Jennifer J. Manly Lindsay C. Kobayashi Marcia Pescador Jimenez

Introduction: Few cohorts have sufficient racial diversity to identify drivers of racial disparities in Alzheimer's Disease and related dementias (ADRD). Pooling individual participant data from different samples can effectively increase sample size and diversity. We harmonized cognitive function data from two US samples, the Reasons for Geographic and Racial Differences in Stroke (REGARDS) and the Health and Retirement Study (HRS) for these purposes.

Methods: Data were from dementia-free participants in the 2010 HRS (n = 19,887) and 2009-2013 REGARDS waves (n = 19,690). We evaluated comparability of cognitive test items between cohorts. We used confirmatory factor analysis (CFA) models to derive harmonized factor scores for general and domain-specific (memory, orientation, language) cognitive function, leveraging common cognitive test items across cohorts to link scales, while retaining those unique to each study. We assessed construct validity of the resultant factor scores by regressing them on variables known to be associated with cognitive function (age, sex/gender, and education).

Results: The combined sample (n = 39,577) had a mean age of 67.4 (SD = 10.3) years. 28% were Black/African American and 68% were White. We identified 4 cognitive items shared by the cohorts and 12 unique items. CFA models demonstrated adequate fit based on predetermined criteria. Younger age (β = -0.36, 95% CI [-0.37, -0.35]), female sex/gender (β = 0.29, 95% CI [0.27, 0.31]), and higher education (β = 0.63, 95% CI [0.61, 0.66] for some college, reference = less than high school) were associated with higher general (results shown) and domain-specific cognitive scores, supporting construct validity.

Discussion: We harmonized cognitive tests across two population-based studies of aging in the US to increase sample size for the examination of racial differences. This work provides a foundation for researchers to improve inferences on drivers of ADRD racial disparities.

Methods/Statistics

Transporting a Causal Effect of Treatment Assignment from a Trial to an External Target Population When Trial Participation Impacts Adherence Rachael Ross* Rachael Ross Amy J. Pitts Elizabeth A Stuart Kara E. Rudolph

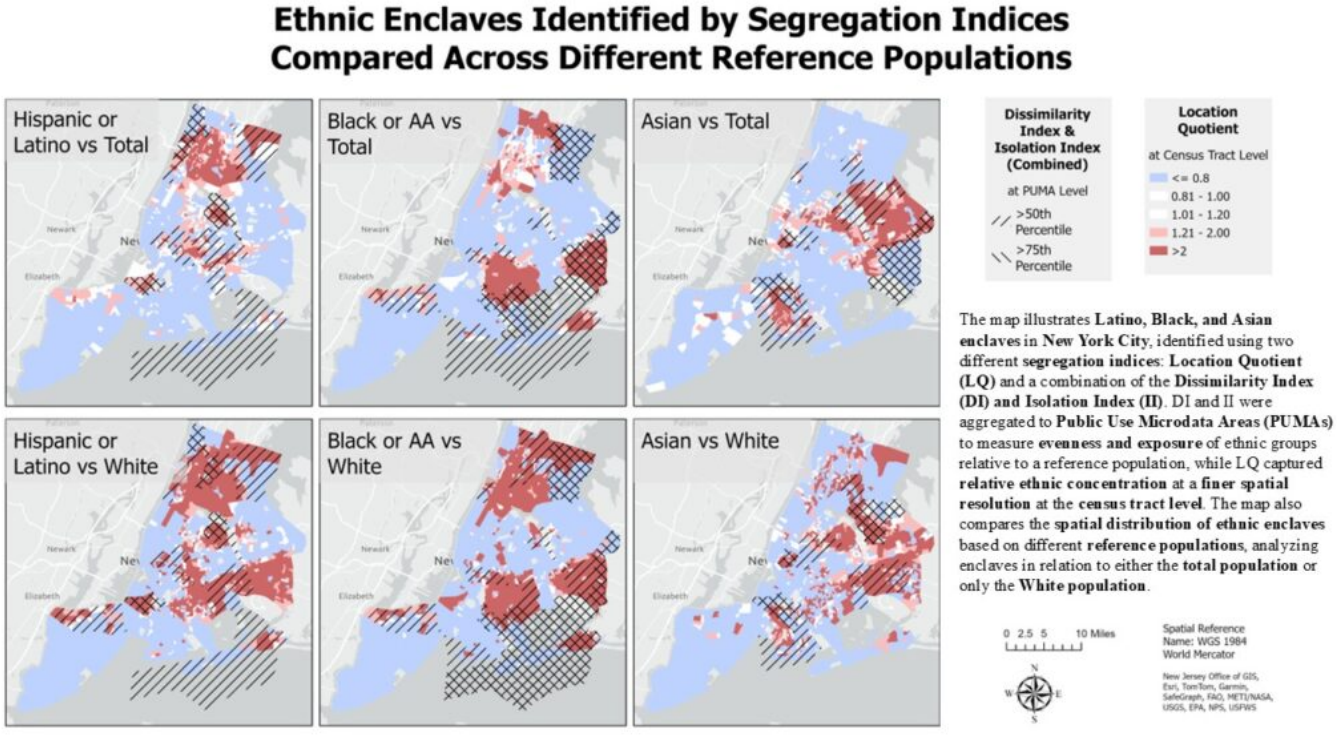
Transportability methods can extend inferences from trial samples to real-world populations (external targets); however, complications arise when trial activities such as incentives and follow-up visits impact treatment adherence. Here we consider the setting where the trial includes data on covariates, treatment assignment, adherence, and outcome; the target includes data on covariates only. When trial participation impacts adherence, we can identify the joint effect of treatment assignment and scaling up trial activities that impact adherence (e.g., incentives) in the real-world treatment setting, but scaling up such trial activities is not often realistic. We propose an alternative estimand taken from mediation analysis (an interventional mediation effect): the effect of treatment assignment when the adherence distribution is set to the distribution of adherence in the target. Since adherence in the target is unknown, we define a parameter, delta, as the target:trial adherence ratio, which allows us to leverage the trial adherence data. Delta is unknown, but we can use expert knowledge to set bounds or a reasonable distribution. In the analysis, the estimand is repeatedly estimated using random draws from the proposed delta distribution similar to quantitative bias analyses. We provide a g-computation estimator and an augmented inverse probability weighted estimator and discuss variance estimation. We illustrate our approach in a case study to transport the comparative effect of extended-release naltrexone and sublingual buprenorphine for the treatment of opioid use disorder on relapse from a trial to a real-world Medicaid population. Adherence to treatment in the trial was much higher than previously reported in real-world treatment settings and in other trials. We use the proposed approach to transport the effect under more realistic adherence.

LATEBREAKER

Methods/Statistics

Comparing Segregation Indices for Ethnic Enclave Identification in NYC: Methodological Insights for Health Research Emily M. D'Agostino* Yuntian Bi Emily M. D'Agostino Cody Neshteruk Sophie Ravanbakht Karen Florez

Ethnic enclaves, characterized by high concentrations of specific ethnic groups, have been extensively studied for their role in shaping health outcomes. However, methods for defining enclaves vary widely, leading to distinct conclusions about enclave effects on health. While many studies rely solely on demographic composition to identify enclaves, segregation indices offer a more nuanced approach by capturing spatial, social, and behavioral dimensions of clustering. **New York City (NYC)**, with its rich immigrant history and patterns of ethnic residential distribution, is an ideal setting to examine how different segregation indices define ethnic enclaves. This study compares the **Diversity Index (DI), Isolation Index (II), and Location Quotient (LQ)** in identifying **Latino, Black, and Asian enclaves**. Using 2015 American Community Survey (ACS) data at the census tract level, DI and II were aggregated to Public Use Microdata Areas (PUMAs) to assess evenness and exposure of ethnic groups relative to a reference population, while LQ captured relative ethnic concentration at a finer tract-level spatial resolution. The study finds that DI and II, when combined using percentile-based thresholds, provide a more appropriate definition of enclaves compared to using them separately. The study further determined that reference group selection affects enclave identification, revealing significant differences in spatial distribution and enclave magnitude when computing indices relative to the total population versus White population. These variations led to distinct distribution patterns with potential to support future analyses that relate ethnic enclaves to health outcomes. Findings highlight the critical role of methodological approaches in defining ethnic enclaves and underscore the value of multi-index approaches to provide a more nuanced framework for **understanding neighborhood effects in health research**.



LATEBREAKER

Methods/Statistics

Distributionally Equivalent Urns for the Truncation by Death Problem Jaffer Zaidi* Jaffer Zaidi

The analysis of causal effects when the outcome of interest is possibly truncated by death has a long history in
statistics and causal inference. The survivor average causal effect is commonly identified with more assumptions
than those guaranteed by the design of a randomized clinical trial. This paper demonstrates that individual
level causal effects in the ‘always survivor’ principal stratum can be identified and quantified with no stronger
identification assumptions than randomization even in the presence of informative censoring. Distributionally
equivalent sufficient cause urns are defined and developed on exhaustive and sufficient condition regions to quantify individual and population level ’always survivor’ causal effects
under truncation by death, censoring and interference. Such urn models also enable sensitivity and multiverse
analysis at the individual and population level, as well as enable comparison of different identification strategies.
We illustrate the practical utility of our methods using randomized clinical trials in perinatal surgery and oncology. Our comprehensive methodology is the first and, as of yet, only proposed procedure that enables
quantifying individual level causal effects in the presence of truncation by death and censoring using only the
assumptions that are guaranteed by design of the clinical trial.

Molecular

Transgenerational impact of obesity-associated genotypes on early life proteomics Jian Huang* Jian Huang Jinyi Che Michelle Z.L. Kee Dennis Wang

Parental non-transmitted alleles yield an indirect transgenerational impact. Early-life proteomics elucidates the mechanisms underlying developmental processes including obesity. Considering the gene-environment interplay, we investigated the influence of parental non-transmitted obesity-associated genotype on early-life proteomics in the Growing Up in Singapore Towards healthy Outcomes (GUSTO) cohort.

Haplotypes were estimated by accounting for trio information using SHAPEIT v2. Parental non-transmitted alleles for 706 trios were inferred from a local long-range (+/- 500kb) haplotype. Parental non-transmitted and child polygenic risk scores (PRS) were constructed using a trans-ancestry method (PRS-CSx) incorporating both European and East Asian GWAS of body mass index. Plasma neurology-related and inflammation proteins were measured at ~8 years (N=528). We used multiple linear regression, accounting for multiple comparisons of 2 parental PRS, 182 proteins and 3 child sex groups (boys, girls, and both).

Paternal non-transmitted PRS was inversely associated with MSR1 and SIGLEC1 in boys (MSR1: beta=-0.45, 95% CI [-0.60,-0.32], p=1.5*10-9; SIGLEC1: -0.38, [-0.52, -0.24], 4.6*10-7). Both proteins are relevant to immune response. These associations were sustained after adjusting for child PRS for obesity. No associations were observed for maternal non-transmitted PRS.

Our findings suggest paternal non-transmitted obesity-associated genotype influences offspring’s early-life proteomics, indicating the role of paternal factors in children’s development.

Neurology

Tinnitus Risk Factors in Young Adults in the United States: National Longitudinal Study of Adolescent to Adult Health (Add Health) Howard J. Hoffman* Howard J. Hoffman Chuan-Ming Li Christa L. Themann Bryan K. Ward Gregory A. Flamme

Objectives: Estimate tinnitus prevalence and risk factors in adults aged 24-42.

Methods: Add Health, a nationally representative, longitudinal cohort study, recruited students aged 12-19 from Grades 7-12 in 1994-1995. Participants in Wave 4 (2008; age 24-32, n=15,701) and Wave 5 (2016-2018; age 32-42, n=14,738) were asked: “In the past 12 months have you been bothered by ringing, roaring, or buzzing in your ears or head (tinnitus) that lasts 5 minutes or more?” Additional questions asked about hearing and balance, other health issues, work, and social/lifestyle factors. We used multivariable logistic regression to estimate odds ratios (OR) and 95% confidence intervals (CI).

Results: Tinnitus prevalence in Wave 4 was 6.7% (7.3% males; 6.1% females) and in Wave 5 was 11.1% (13.0% males; 8.9% females). Tinnitus prevalence was 30% higher for non-Hispanic whites. Persistent tinnitus (Waves 4 and 5) was reported by 0.8%; 10.3% had new onset tinnitus in Wave 5. Tinnitus was strongly associated with hearing loss. In Wave 5 multivariable models, risks included: male (OR=1.9; 95% CI: 1.5-2.7); head trauma (OR=1.5; CI: 1.2-1.9); headaches (OR=1.8; CI: 1.5-2.2); anxiety (OR=1.3; CI: 1.0-1.6); balance/dizziness problems (OR=2.7; CI: 2.2-3.3); and “moderate or worse trouble” hearing (OR=16.2; CI: 10.9-24.1). Persistent tinnitus in Waves 4 and 5 was associated with age (OR=1.15; CI: 1.02-1.3); head trauma (OR=1.3; CI: 1.1-3.6); headaches (OR=2.3; CI: 1.3-3.9); balance problems (OR=3.3; CI: 1.8-5.9); and “moderate or worse trouble” hearing (OR=13.3; CI: 3.5-49.9).

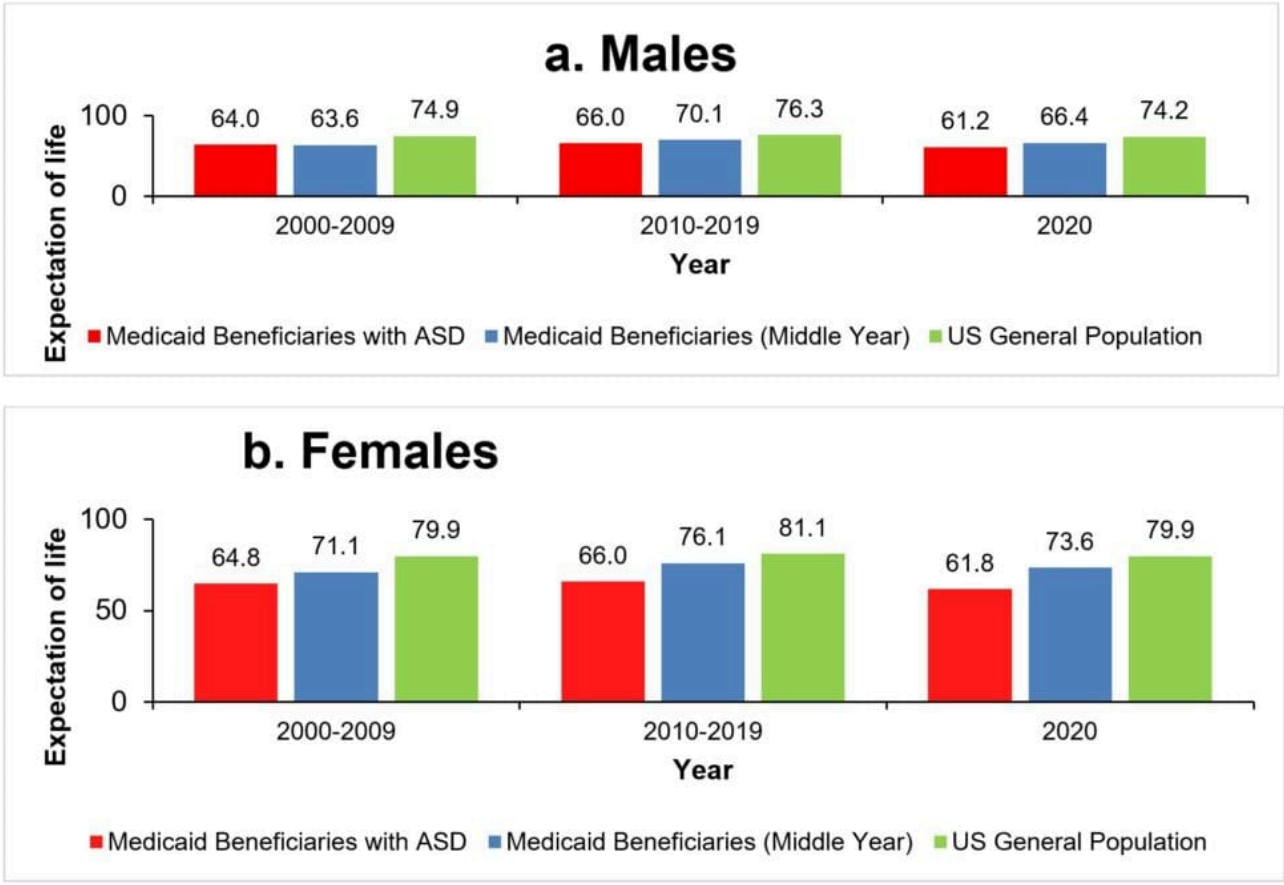
Conclusions: Tinnitus is a common impairment; risk factors include lower income and education, occupation, head trauma, headaches, and hearing and balance trouble. Most tinnitus reported in Wave 4 (age 24-32) appeared to resolve. At Wave 5, 93% of reported tinnitus was from new onset cases in the 8-10 years since Wave 4. Tinnitus status should be assessed for age-related changes in future Add Health waves.

Neurology

Sex-Specific Life Expectancies for People with Autism Spectrum Disorder Enrolled in Medicaid, United States, 2000-2020 Guohua Li* Guohua Li Zhixin Yang Ashley Blanchard Carolyn DiGuiseppi Caleb Ing

People with autism spectrum disorder (ASD) are known to be at heightened risk of death from injury and some diseases. But epidemiologic research on life expectancy and lifespan issues in ASD is scant. The objective of this study was to estimate sex-specific life expectancies for Medicaid beneficiaries with ASD. Medicaid is the largest public health insurance program in the US. Research-identifiable files from Medicaid [i.e., Medicaid Analytic eXtract (MAX) data files and T-MSIS Analytic Files] and the enhanced MAX mortality data (i.e., mortality data through linkage of Medicaid beneficiaries to the National Death Index) from 2000 to 2020 were analyzed to determine age-specific death rates for beneficiaries with ASD. The standard life table method was used to calculate life expectancies at birth by sex, which were compared with life expectancies for all Medicaid beneficiaries and the US general population as reported by the Centers for Disease Control and Prevention. During the 21-year study period, there were a total of 18,263 deaths among Medicaid beneficiaries with ASD; of them, 13,286 were male and 5,877 were female. Life expectancies at birth for Medicaid beneficiaries with ASD were 64.6 years for males and 65.0 years for females. Compared to the Medicaid population and the general population, male Medicaid beneficiaries with ASD had a 1.9-year deficit and an 11.6-year deficit in life expectancy, respectively, whereas female Medicaid beneficiaries with ASD had an 8.2-year deficit and a 16.0-year deficit in life expectancy, respectively. This study indicates that people with ASD have substantially shorter life expectancies than the general population. The gap in life expectancy between people with ASD and the general population is greater for women than for men.

Figure 1. Sex-Specific Life Expectancies at Birth for Medicaid Beneficiaries with Autism Spectrum Disorder, All Medicaid Beneficiaries, and the General Population, United States, 2000-2020



Nutrition/Obesity

Tracking of serum 25-hydroxyvitamin D levels over 11 years in the Norwegian HUNT study

Xiao-Mei Mai* Xiao-Mei Mai Marit Næss Kristin S Sætermo Anne Jorunn Vikdal Yi-Qian Sun

Introduction: Serum 25-hydroxyvitamin D (25(OH)D), a marker of vitamin D status derived from sunlight exposure and diet, may influence various health conditions. This study investigates the tracking of serum 25(OH)D levels over 11 years in a general adult population in Norway and evaluates factors that may affect future serum 25(OH)D levels.

Research Design and Methods: Tracking of serum 25(OH)D levels was conducted among 3511 adults who participated in both the HUNT2 (1995–1997) and HUNT3 (2006–2008) surveys, with an 11-year interval. Serum 25(OH)D levels from HUNT2 and HUNT3 were measured using a chemiluminescent assay and calibrated for batch effect and seasonal variation. Correlation coefficient between the two measurements was calculated, as well as intra-individual variability using the intraclass correlation coefficient (ICC) and coefficient of variation (CV). Multivariable linear regression models were used to estimate the relations between various factors in HUNT2 and 25(OH)D levels in HUNT3.

Results: Findings showed a correlation coefficient of 0.50 (95% CI: 0.47 to 0.52), an ICC of 0.64 (95% CI: 0.56 to 0.70), and a CV of 18% between the two measurements. An average 43% (range: 20.4% to 54.9%) of participants remained in the same vitamin D category (<30.0, 30.0–49.9, 50.0–74.9, and ≥75.0 nmol/L) across both surveys. Male sex, vitamin D-decreasing polygenic score, higher body mass index, and current smoking were associated with lower 25(OH)D levels, while higher education, moderate alcohol intake, and vitamin D supplementation were associated with higher levels.

Conclusions: This study found moderate reliability of serum 25(OH)D levels over an 11-year follow-up period, suggesting that a single measurement may not suffice for long-term vitamin D status assessment. Repeated measurements are desirable for accurate evaluation of vitamin D’s role in chronic disease risk.

Nutrition/Obesity

Associations of in utero overnutrition and early life emotional health with child body size and composition: The Healthy Start Study Madeline Farron* Madeline Farron Greta Wilkening Wei Perng Dana M. Dabelea

Background: Childhood obesity is a public health challenge affected by multiple factors. We explored in utero overnutrition, child anxiety and depression, and possible joint effects of these exposures on child body size and composition at ages 4-8 years using data from Healthy Start, a pre-birth cohort in Colorado. We aimed to assess independent and synergistic effects of these in utero and early childhood exposures on adiposity outcomes.

Methods: In utero overnutrition was defined as maternal gestational diabetes and/or pre-pregnancy body mass index (BMI)≥25 kg/m2. Child anxiety and depression were each assessed by parent-reported Child Behavior Checklist DSM-oriented T-scores (<60/≥60) at age 4-8 years. Outcomes included child BMI z-scores, fat mass (kg), % fat mass, and fat free mass (kg) measured by whole body air displacement plethysmography. We used multivariable linear regression in base models adjusted for child age and sex, and fully adjusted models additionally adjusted for maternal age, education, parity, and household income among N=524 mother-child pairs. Interaction terms between overnutrition and anxiety, and overnutrition and depression were used to assess joint effects in base models.

Results: In base models, in utero overnutrition exposure was associated with higher child BMI z-score (β=0.57, 95% CI=0.38,0.77), fat mass (β=0.77, 95% CI=0.46,1.08), % fat mass (β=2.47, 95% CI=1.34,3.60), and fat free mass (β=0.53, 95% CI=0.16,0.90). Fully adjusted models yielded similar results. Child anxiety and depression were not associated with any outcome, and there were no significant interactions with overnutrition on any of the outcomes.

Discussion: In utero overnutrition exposure, but not child emotional health, was associated with larger body size and adiposity in early childhood specifically. Future studies that explore the role of multi-level environmental factors in increasing or protecting against adiposity throughout the life course are warranted.

Nutrition/Obesity

Are BMI-for-Age percentile curves a valid measure of obesity in older adults? Chris Kim* Christopher Kim Claire Cook Hailey Banack

Chris Kim, MPH, Claire Cook, MPH, Hailey Banack, PhD

Background: A body mass index (BMI) cutpoint of 30 kg/m2 is widely used to define obesity in clinical settings and epidemiologic research. However, its use is associated with poor validity, especially in postmenopausal women. The objective of the present work is to determine the validity of BMI-for-age percentile curves as a measure of obesity in older adults aged 45-86 years compared to an objective measure of obesity status, total body fat percent (BF%) measured by dual energy x-ray absorptiometry (DXA) scan.

Methods: Data from the Canadian Longitudinal Study on Aging (CLSA) baseline study visit were used. BMI was calculated from measured height and weight BF % was measured from whole-body DXA scan. Sensitivity (Se), specificity (Sp), positive predictive value (PPV), and negative predictive value (NPV) and their 95% confidence intervals were estimated for 1) BMI percentile vs. total BF % and 2) BMI category vs. total BF% using sampling weights. Empirical optimal BMI and BMI percentiles cutpoints were also computed for obesity defined based on BF% using Youden's Index. Obesity was defined as BMI greater than the 85th percentile; BMI category >30 kg/m2; or using cutpoints of 35%, 38%, and 40% for BF%.

Results: Table 1 describes Se, Sp, PPV and NPV comparing a BMI cutpoint of 30 kg/m2 and BMI ≥85th percentile to a gold standard measure of DXA-defined BF% in 28,764 CLSA participants. Using a 40% BF cutpoint to define true obesity status, Se, Sp, PPV, and NPV for BMI ≥ 30 kg/m2 were 0.60 (0.59, 0.61), 0.77 (0.76, 0.77), 0.48 (0.47, 0.49), and 0.84 (0.84, 0.85). For BMI ≥ 85th percentile, Se, Sp, PPV, and NPV results were 0.35 (0.34, 0.36), 0.92 (0.92, 0.93), 0.63 (0.61, 0.64) and 0.80 (0.79, 0.80) at 40% BF%. Empirical optimal BMI cutpoints were 33.24, 34.71, and 35.91 for 35%, 38%, and 40% BF%, respectively. Empirical optimal BMI percentile cutpoints were 81, 88, and 91 for 35%, 38%, and 40% BF%, respectively.

Conclusions: Defining obesity using BMI-for-age percentile values (≥85th percentile) resulted in greater specificity and positive predictive value than the standard measure of obesity cutpoint of 30 kg/m2. However, this comes at a cost of reduced specificity. BMI-for-age percentiles are a valid measure of obesity status among older adults that accounts for age-related change.

Table 1. Sensitivity, specificity, positive predictive value, and negative predictive value of BMI ≥ 30 kg/m^2 and BMI $\geq 85^{th}$ percentile at 35%, 38%, and 40% body fat percent (N = 29,961)

	35% Body Fat	**38%** Body Fat	**40%** Body Fat
BMI ≥ 30 kg/m^2			
Sensitivity (95%CI)	0.47 (0.46, 0.48)	0.53 (0.52, 0.54)	0.60 (0.59, 0.61)
Specificity (95% CI)	0.79 (0.78, 0.79)	0.77 (0.77, 0.88)	0.77 (0.76, 0.77)
Positive predictive value (95% CI)	0.65 (0.64, 0.66)	0.55 (0.54, 0.56)	0.48 (0.47, 0.49)
Negative predictive value (95% CI)	0.64 (0.63, 0.65)	0.76 (0.75, 0.77)	0.84 (0.84, 0.85)
Empirical optimal cut point	33.24	34.71	35.91
BMI ≥ 85th percentile			
Sensitivity (95%CI)	0.26 (0.26, 0.27)	0.30 (0.29, 0.31)	0.35 (0.34, 0.36)
Specificity (95% CI)	0.95 (0.94, 0.95)	0.93 (0.93, 0.93)	0.92 (0.92, 0.93)
Positive predictive value (95% CI)	0.81 (0.79, 0.82)	0.69 (0.68, 0.70)	0.63 (0.61, 0.64)
Negative predictive value (95% CI)	0.60 (0.60, 0.61)	0.72 (0.71, 0.72)	0.80 (0.79, 0.80)
Empirical optimal cut point	81	88	91

Nutrition/Obesity

Postpartum bean consumption and maternal weight outcomes Xiaozhong Wen* Xiaozhong Wen Jeremy Nguyen Fatima Makama Chhime Lama Adobea Addo Jasmine Thai Zhenglin Yuan Todd C. Rideout

Objectives: We assessed the associations between postpartum bean consumption and maternal weight outcomes from a U.S. national cohort.

Methods: We analyzed data from 1,363 U.S. mothers from the Infant Feeding Practices Study II. Mothers were followed throughout their pregnancy and up to 6 years postpartum. At the 3-month follow-up survey, frequency and amount of bean consumption were approximated using a food frequency questionnaire. Mothers reported heights and weights before pregnancy, at 3, 6, 9, 12 months, and 6 years postpartum.

Results: Compared to non-consumers, mothers who consumed dried beans 1+ time per week had a lower risk of overweight/obesity at 3 months (OR=0.46, 95% CI: [0.24-0.88]) and 9 months postpartum (0.45 [0.22-0.92]). For every 1-cup/week increment of dried bean consumption, mothers had a lower risk of overweight/obesity at 3 months postpartum (0.68 [0.47-0.99]). Mothers who consumed chili 2-3 times per month or more had a higher risk of obesity at 12 months postpartum than mothers who consumed chili 1 time per month (2.18 [1.00-4.74]). Every 1-cup/week increment of chili consumption was associated with a higher risk of obesity at 6 months (1.52 [1.01-2.29]) and 9 months postpartum (1.51 [1.04-2.21]). However, mothers who consumed chili 2-3 times per month or more had a lower risk of obesity at 6 years postpartum than non-consumers (0.50 [0.25-0.99]).

Conclusions: High consumption of dried beans postpartum may be linked with a lower risk of overweight or obesity. Consumption of chili postpartum showed mixed results.

Nutrition/Obesity

Grip strength: are some adiposity phenotypes more detrimental than others? A mendelian randomisation study Amy Taylor* Amy Taylor John Vincent Dylan Williams Rachel Cooper Snehal Pinto Pereira

Background
Improved understanding of associations between location and type of adiposity with grip strength may help identify specific underlying mechanisms and inform interventions for maintaining muscle strength.

Methods
In up to 340,258 UK Biobank participants (aged 38-73 years) of European ancestry, we investigated cross-sectional observational associations between regional adiposity (visceral, abdominal subcutaneous and gluteofemoral adipose tissue [VAT, ASAT and GFAT respectively] and anterior thigh muscle fat infiltration [ATMFI]), body fat (BF) percentage, and grip strength. We also performed Mendelian Randomisation (MR) to estimate effects of total (BF) and regional (VAT, ASAT, GFAT, ATMFI) adiposity, along with 'metabolically favourable' (MetFA) and 'metabolically unfavourable' adiposity (MetUFA), on grip strength.

Results

Higher BF percentage, MetFA and ATMFI were consistently associated with lower grip strength across observational and MR analyses. In MR analysis, an SD increase in BF was associated with a -0.12SD decrease in grip strength (95%CI:-0.16,-0.08), a one SD increase in MetFA was associated with a -0.30SD decrease in grip, (95% CI:-0.44,-0.16) and a one SD increase in ATMFI was associated with a -0.05SD decrease in grip (95% CI:-0.09,-0.01). Higher VAT was associated with lower grip in observational but not in MR analyses. Associations for higher ASAT were inconsistent: observational analyses suggested weaker grip; MR analyses indicated stronger grip (particularly in females). Higher GFAT was associated with stronger grip in observational analyses only and there was no strong evidence in MR for associations with MetUFA.

Conclusions
This study confirms the importance of muscle fat infiltration in determining muscle strength. Future interventions to improve muscle function might benefit from focusing on preventing and reducing fat infiltration in muscles. 'Metabolically favourable' adiposity may have detrimental consequences for muscle strength.

Nutrition/Obesity

The Association Between Visceral Obesity and Mild Cognitive Impairment Sujeong Han*
Sujeong Han Jun-Young Lee Sung-il Cho Dae Jong Oh Dae Hyun Yoon

Objective

The aim of this study was to determine whether visceral obesity is a risk factor for Non-Amnestic Mild Cognitive Impairment and Amnestic Mild Cognitive Impairment.

Methods

The data from the Seoul National University Hospital Healthcare System, Gangnam Center, from 2005-2020. The number of study subjects was 569 who underwent regular cognitive function test. Cox's proportional hazard analysis was conducted to compare survival rates between visceral obesity and people without visceral obesity.

Results

The Kaplan-Meier survival curves for Non-Amnestic MCI(na-MCI) risk differed significantly between the obesity groups. The risk was significantly higher in the visceral obesity group than in the non-visceral obesity group (Log-rank p=0.014). After 2 years, the cumulative incidence of Non-Amnestic Mild Cognitive Impairment increases by at least 50%, and after 5 years it exceeds 60%. The adjusted Hazard ratio (HR) for Non-Amnestic Mild Cognitive Impairment in the subjects with visceral obesity was HR=1.43, 95% CI=1.10-1.86.

Conclusion

Our findings suggest that visceral obesity is associated with a higher risk of Non-Amnestic Mild Cognitive Impairment. It is important to consider whether visceral obesity after a Mild Cognitive Impairment diagnosis increases the risk of future dementia. Early detection of Mild Cognitive Impairment in obese individuals is important to prevent future cognitive decline.

Keywords Visceral obesity; Mild Cognitive Impairment; Older adults; Longitudinal; Survival analysis; Cox's proportional hazard analysis

LATEBREAKER

Nutrition/Obesity

Healthy and plant-based dietary and nutrient patterns are associated with lower odds of chronic kidney disease Yohannes Adama Melaku* Yohannes Adama Melaku Zumin Shi Danny Eckert Robert Adams

Background: Chronic kidney disease (CKD) is a growing public health concern, with dietary patterns playing a significant role in its prevention and progression. This study examines the association between various dietary indices and CKD in the North West Adelaide Health Study (NWAHS, Australia), with a focus on plant-based, animal-sourced, and mixed dietary patterns.

Methods: A total of 1,925 participants were included in this cross-sectional analysis. Dietary patterns were assessed using the Plant-Based Diet Index (PDI), Healthy Plant-Based Diet Index (hPDI), Unhealthy Plant-Based Diet Index (uPDI), and nutrient-based dietary patterns, including animal-sourced, plant-sourced, and mixed-source nutrient patterns. CKD was defined based on glomerular filtration rate (eGFR) values. Multivariable logistic regression models adjusted for energy intake, demographic, lifestyle, and health-related confounders were used to estimate the odds ratios (ORs) and 95% confidence intervals (CIs) for CKD across quintiles of dietary pattern adherence.

Results: Higher adherence to an hPDI was associated with a significantly lower risk of CKD (Q5 vs. Q1: OR=0.51, 95% CI: 0.26–0.99). Similarly, adherence to a plant-sourced nutrient pattern was inversely associated with CKD risk (Q5 vs. Q1: OR=0.36, 95% CI: 0.17–0.79). In contrast, adherence to an uPDI or an animal-sourced nutrient pattern did not show associations with CKD risk. A mixed-source nutrient pattern showed a positive association with CKD (Q5 vs. Q1: OR=1.82, 95% CI: 0.88–3.76).

Conclusion: Our findings suggest that adherence to a healthy plant-based diet and a plant-sourced nutrient pattern may be protective against CKD, whereas unhealthy plant-based and animal-sourced nutrient patterns do not show clear associations. These findings highlight the potential role of dietary modification in CKD prevention and highlight the importance of promoting plant-based nutrient sources.

LATEBREAKER

Nutrition/Obesity

Weight loss interventions and changes in lean mass: how much muscle do you actually lose? Aubrey K. Roberts* Aubrey Roberts Daniel J. Panyard Brady Hislop Catherine P. Ward Michael Snyder Francois Haddad Christopher Gardner

Background. Weight loss interventions can improve metabolic health. An emerging concern is that weight loss also leads to loss of muscle mass. Few studies accurately quantify changes in muscle mass, assess its clinical significance, or connect changes to molecular correlates.

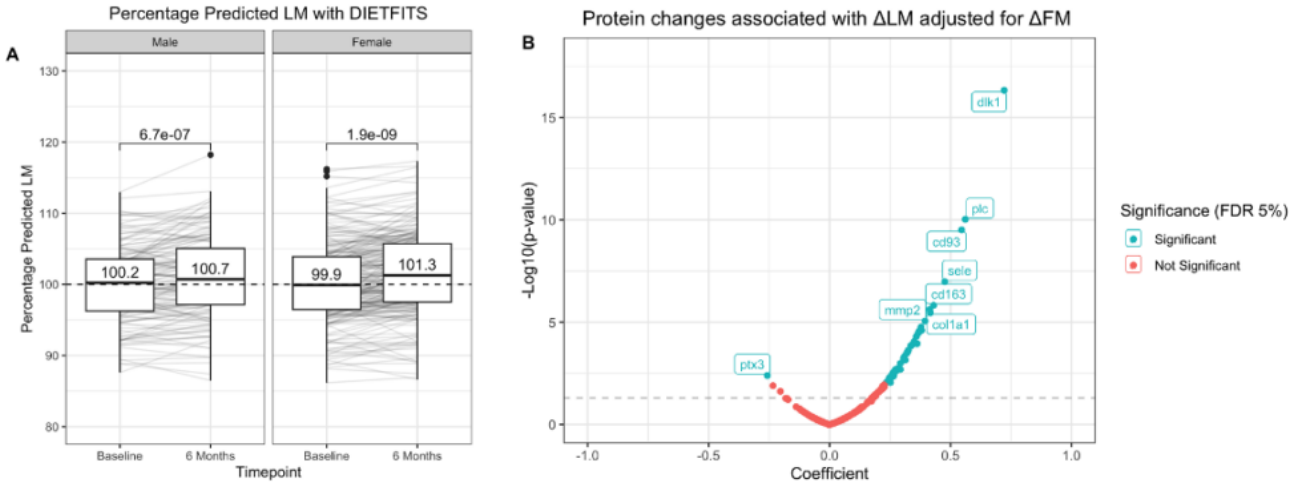
Objective. To assess changes in lean mass (LM) after 6 months of weight loss, while using a novel adjustment for fat-free adipose tissue (FFAT) content. We also contextualize LM relative to demographics (Percentage Predicted LM) and matched changes in the plasma proteome.

Methods. As part of the Diet Intervention Examining The Factors Interacting with Treatment Success (DIETFITS) study, we analyzed LM from dual-energy X-ray absorptiometry (DXA), FFAT-adjusted LM, and Percentage Predicted LM (observed/predicted LM) at baseline vs. 6 months, for total body and appendicular regions. We developed and tested new metrics for LM based on recent studies of FFAT. 242 plasma proteins were examined as predictors of change in LM, adjusted for change in fat mass (FM).

Results. 374 participants (age: 39.4 ± 6.7 years, BMI: 32.3 ±3.2 kg/m2) were evaluated at baseline vs. 6 months. Total mass changed by -5.9 kg (95% CI: -6.51, -5.29 kg) in females and -7.18 kg (95% CI: -8.2, -6.16 kg) in males. Change in Appendicular LM, a surrogate for skeletal muscle mass, was modest: -0.80 kg (95% CI: -0.92, 0.69 kg) in females and -1.02 kg (95% CI: -1.22, 0.83 kg) in males. After FFAT adjustment, losses in LM were attenuated. Percentage Predicted LM increased at 6 months. Change in 48 proteins including protein delta homolog 1 (DLK1)–an inhibitor of adipogenesis–predicted change in LM (5% FDR).

Conclusion. Changes in LM and Appendicular LM were modest after 6 months of diet-based weight loss. Percentage Predicted LM increased at 6 months, indicating participants had more LM than expected given their demographics. Several proteins, including DLK1, provide novel mechanistic insight on LM changes during weight loss.

Figure 1. Assessing lean mass (LM) and associated proteomic changes after weight loss: a) Percentage Predicted Lean Mass (LM) increases at 6 months, indicating participants had more LM than expected given their demographics; **b)** Protein changes (n=48) including protein delta homolog 1 (DLK1)–a known inhibitor of adipogenesis–were significantly associated with change in LM (5% FDR).



Occupational

Work-related psychological health: Latent profiles and mediating effects of well-being among Chinese priests Yu-Ting Chin* Yu-Ting Chin Wen-Cheng Li I-Ling Ling Chien-Hung Lee

Background: The new-style work situation model promotes a multidimensional perspective on work-related psychological health and emphasizes the discussion of the etiology of personality traits and types of well-being in relation to mental health issues in the workplace. In this study, we developed a latent typology of working status profiles for Chinese priests and assessed the potential mediating effects of well-being types on the associations between personality orientations and working status profiles. **Methods**: In 2023, a survey was conducted with 703 priests in Taiwan. Chinese versions of the clergy psychological type scale, well-being scale, and work-related psychological health scale were used to measure study variables. Latent profile analysis was conducted to explore working status profiles, while generalized structural equation modeling was used to assess structural associations, adjusting for covariates. **Results**: The identified working status profiles, which demonstrated a good model fit, were as follows: Profile 1 (hiES-lwFB, 57.2%): high engagement/stability and low fatigue/burnout; Profile 2 (moES-miFB, 28.2%): moderate engagement/stability and mild fatigue/burnout; Profile 3 (lwES-hiFB, 6.8%): low engagement/stability and high fatigue/burnout; and Profile 4 (mhES-hiFB, 7.8%): moderate-to-high engagement/stability and high fatigue/burnout. Using the hiES-lwFB group as a reference, subjective, psychological, and spiritual well-being mediated 16.5%, 11.7%, and 13.2% of the relationship between outgoing propensity and the lwES-hiFB group, respectively. Additionally, priests with high rational propensity scores had a lower likelihood of being in the mhES-hiFB group. **Conclusion**: This study identified four mental status profiles in the workplace for Chinese priests. The data demonstrated the mediated effects of three types of well-being on the association between outgoing propensity and the low engagement/stability and high fatigue/burnout working profile.

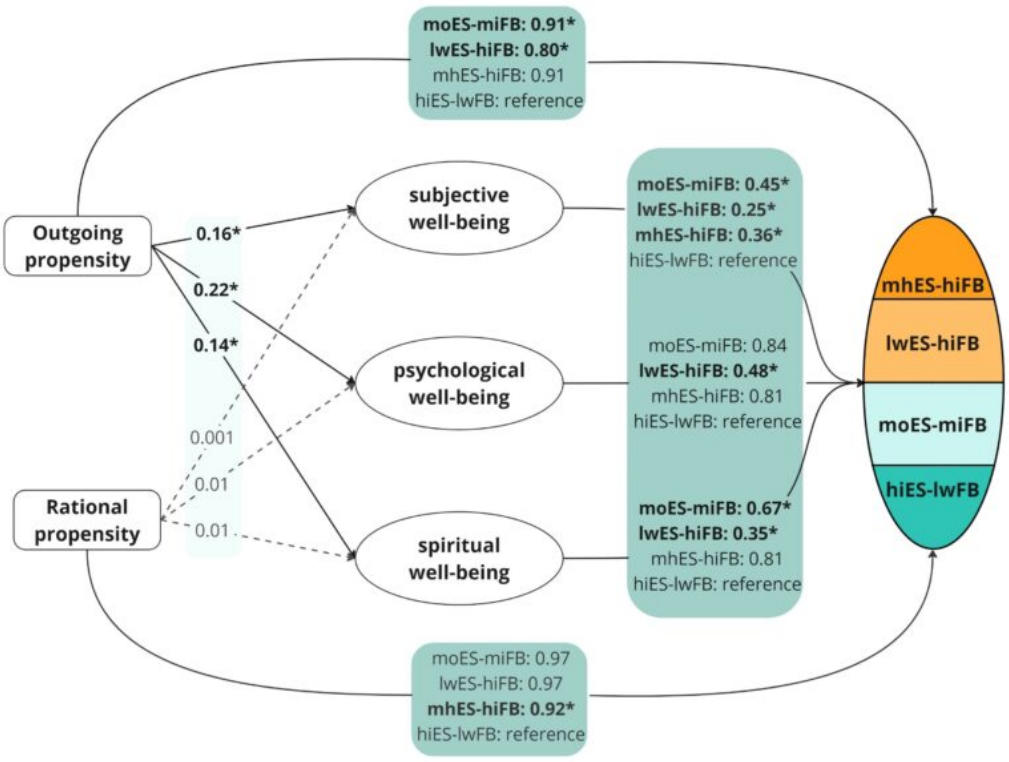


Figure. Covariates-adjusted structural relationships among personality orientation, well-being, and working status profile.
Note: Personality orientation included outgoing propensity and rational propensity; well-being encompassed subjective, psychological, and spiritual well-being; working status profile contained high engagement and stability and low fatigue and burnout (hiES-lwFB), moderate engagement and stability and mild fatigue and burnout (moES-miFB), low engagement and stability and high fatigue and burnout (lwES-hiFB), and moderate-to-high engagement and stability and high fatigue and burnout (mhES-hiFB). All path coefficients were adjusted for sex, age, marital status, and service year.
* denoted P < 0.05 for the path coefficients. The hiES-lwFB working profile served as the reference group.

Occupational

Covid-19 burden and vaccination coverage trends in the Mexican Social Security Institute workforce: A nationwide cohort study using linked administrative data Edgar Ortiz Brizuela*
Edgar Ortiz Brizuela

Background: The Covid-19 pandemic placed immense demands on global healthcare systems, disproportionately affecting healthcare workers (HCWs). In Mexico, where resources were limited compared to OECD averages, the pandemic's impact was severe, particularly for the workforce of the Mexican Institute of Social Security (IMSS), the largest healthcare institution in the country. This study aims to describe the pandemic's effects on IMSS personnel by estimating the incidence of SARS-CoV-2 infection, progression to hospitalization and death, and trends in Covid-19 vaccination coverage from February 28, 2020, to May 9, 2023.

Methods: We will employ an open and closed cohort designs, leveraging linked administrative datasets. The closed cohort will provide cumulative incidence estimates, computed using pooled logistic regression with inverse probability of censoring weighting to address potential bias. The open cohort will allow for the dynamic nature of the IMSS workforce, estimating incidence rates using Poisson regression. Analysis will be presented overall and stratified by geographic location, work unit type, and job category. The study population includes over 450,000 IMSS employees, spanning healthcare and non-healthcare roles. SARS-CoV-2 infections, hospitalizations, and deaths will be identified through epidemiologic surveillance, hospital discharge records, and death certificates. Vaccination data were sourced from institutional and national registries.

Conclusion: This comprehensive analysis will highlight the pandemic's burden on the IMSS workforce. The findings inform future preparedness strategies, guiding resource allocation, infection prevention, and support for healthcare workers in similar settings.

Occupational

Geographic trends in the gender composition of US physicians from 2014-2024 Jag Lally*
Jag Lally Amanda Bunting David M. Kline Amanda Bunting

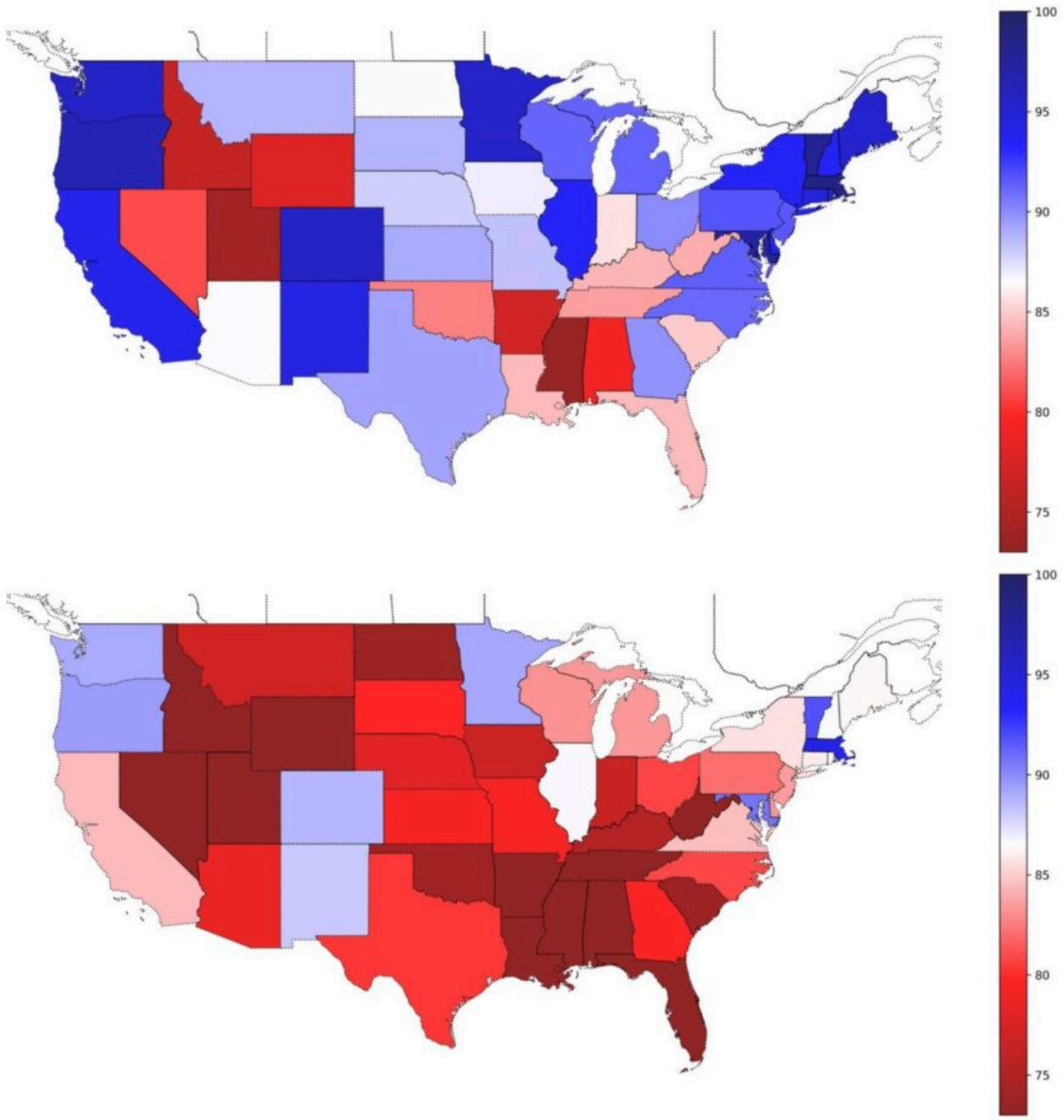
Background: The gender composition of the physician workforce in the United States is constantly evolving. We aimed to determine how female physician representation has changed from 2014-2024 with attention to geographic and rural trends.

Methods: Data were obtained from Centers for Medicare and Medicaid Services (CMS) Doctors and Clinicians national downloadable file (2014-2024). All physician providers with valid National Provider Identifiers (NPIs), zip code, and gender data were included. The Gender Diversity Index (GDI), a metric that relates to the likelihood that two randomly selected providers in a country would be of different genders, was utilized (0 is a population of only one gender, 100 is full gender parity). The state of provider practice was utilised and rurality was defined using Rural-Urban Continuum Codes (RUCC) with codes 1-3 as urban and 4-9 as rural.

Results: Female physician representation across the US rose from 28.9% (2014) to 35.1% (2024), corresponding to a GDI increase from 82.2 (2014) to 91.1 (2024). The average GDI increase per state was 9.0 with a SD of 2.1, from a mean of 79.9 (2014) to a mean of 88.9 (2024). The state with the highest GDI in 2024 was Massachusssets and the state with the lowest GDI in 2024 was Mississippi. The GDI for providers in urban areas increased from 83.4 (2014) to 91.7 (2024), while the GDI for providers in rural areas increased from only 70.2 (2014) to 78.5 (2024).

Conclusions: Although there have been broad increases in female representation in many regions throughout the US, some regions remain disparate and enduring rural-urban gaps underscore the complexity of achieving gender parity. Targeted interventions such as rural recruitment incentives, enhanced loan-forgiveness programs, and mentorship opportunities could assist in fostering a more equitable physician workforce.

Figure: Choropleth Graph of State-Level Gender Diversity Index of female physicians in 2024 (top) and 2014 (bottom), centered with 2024 mean GDI:



Perinatal & Pediatric

Specific patterns of placental injury differentiate preeclampsia from other hypertensive disorders of pregnancy Marni Jacobs* Marni Jacobs Mariko Horii

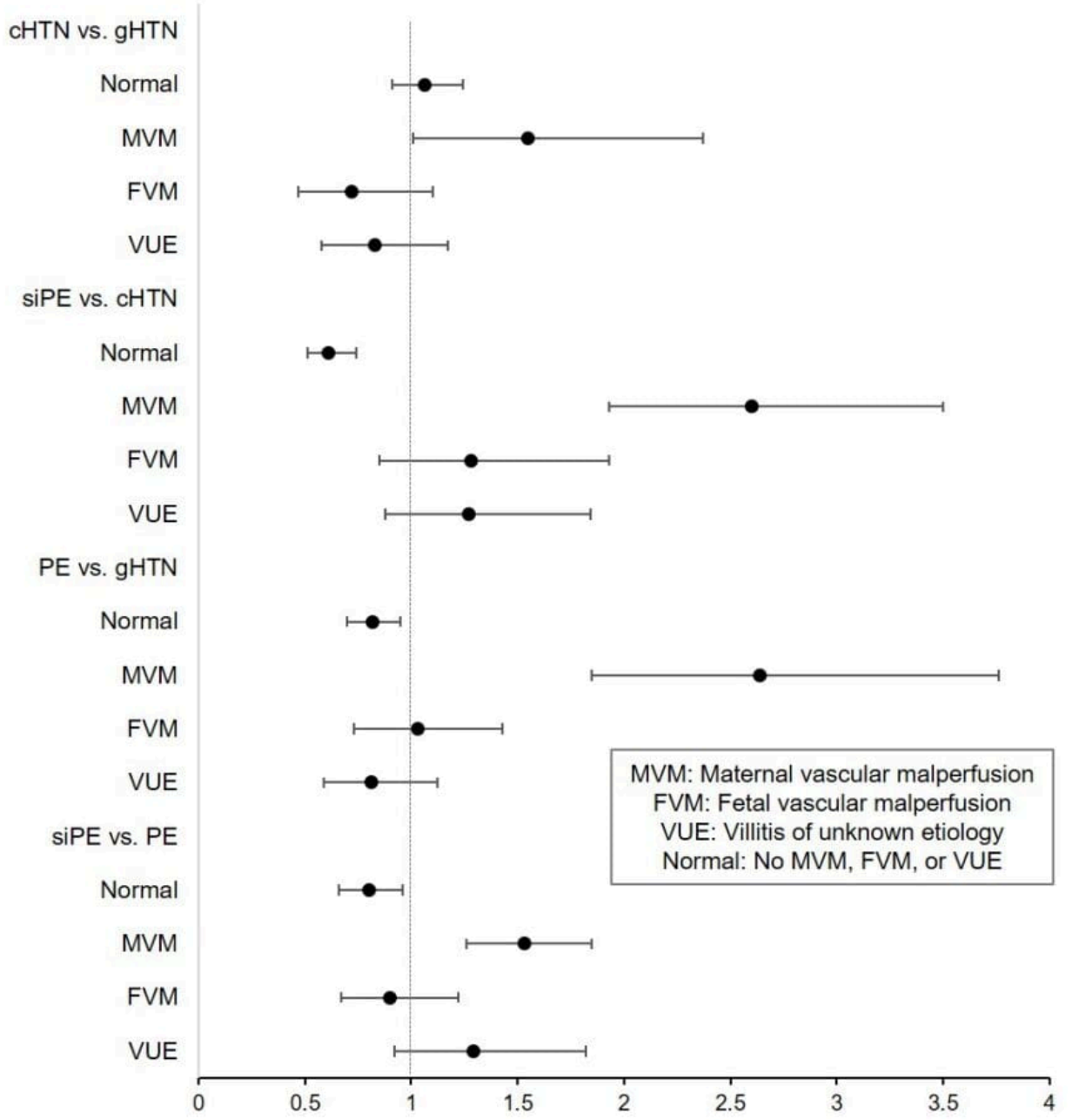
Introduction: Hypertensive disorders of pregnancy (HDP) include both gestational hypertension (gHTN) and preeclampsia (PE), a severe pregnancy disorder thought to arise from abnormalities in placentation. PE may arise de novo in women normotensive prior to pregnancy, or on top of underlying pre-pregnancy chronic hypertension (superimposed PE, siPE). Although often characterized as a spectrum of disease severity, whether placental pathology differs between HDP subtypes, which may suggest differences in underlying disease etiology, is unclear. Here, we evaluate placental pathological lesions associated with HDP subtypes in a well characterized cohort.

Methods: We identified 266 chronic hypertension (cHTN), 259 gHTN, 281 siPE, and 497 primary PE cases with available placental pathology from our Obstetric Registry. Clinical diagnosis was based on current ACOG criteria, and all placentas had gross and histologic examination performed by two perinatal pathologists. Placental lesions were compared between groups using chi-square and prevalence ratios adjusted (aPR) for relevant clinical characteristics using log-binomial regression.

Results: Overall, few differences in placental pathology were noted between cHTN and gHTN groups, which were more likely to have normal pathology (cHTN: 58%, gHTN: 54%, PE: 36%, siPE: 44%). Maternal vascular malperfusion (MVM) was more common in both PE subtypes adjusting for maternal age, BMI, nulliparity, and diabetes (cHTN vs. gTHN: aPR 1.6, 95% CI 1.0-2.4; siPE vs. cHTN: aPR 2.6, 1.9-3.5; PE vs. gHTN: aPR 2.6, 1.9-3.8, siPE vs. PE: aPR 1.5, 1.3-1.8).

Conclusion: MVM was significantly elevated in PE compared to HTN, suggesting that MVM specifically differentiates pregnancies that progress to PE. MVM is thought to initiate in early gestation, indicating the cascade to PE is likely differentiated from HTN early in pregnancy. Future work, including molecular and cellular analysis, is needed to identify specific disease pathways.

Figure. Comparison of specific placental lesions by hypertensive disorders of pregnancy diagnosis: adjusted* prevalence ratios and 95% CIs



* Adjusted for maternal age, BMI, nulliparity, and diabetes; VUE additionally adjusted for GA.

Perinatal & Pediatric

Breast Milk Interacts with the Infant Gut Microbiome to Impact the Fecal Metabolome and Child Blood Pressure Tiange Liu* Tiange Liu Charisse Petersen Stuart Turvey Ni Zhao Noel T. Mueller

Importance: Breast milk and gut microbes may have mutually dependent associations with blood pressure (BP), as components like human milk oligosaccharides (HMOs) rely on microbial conversion to BP-lowing metabolites (e.g., acetic acid). However, human studies on the joint effects of breastfeeding and gut microbes on childhood BP, an early-life risk factor for cardiovascular disease, remain limited.

Objective: To investigate if breastfeeding and the infant gut microbiome, particularly Bifidobacterium infantis—an efficient degrader of HMOs—interact to influence fecal metabolites and childhood BP.

Design: Prospective, population-based cohort study using data from the Canadian Healthy Infant Longitudinal Development (CHILD) study (2009-2012).

Exposures: Gut microbiome (measured by whole genome shotgun metagenomic sequencing), fecal metabolome, and breastfeeding status at 3 months and 1 year.

Outcome: Systolic blood pressure (SBP) at 3 and 5 years.

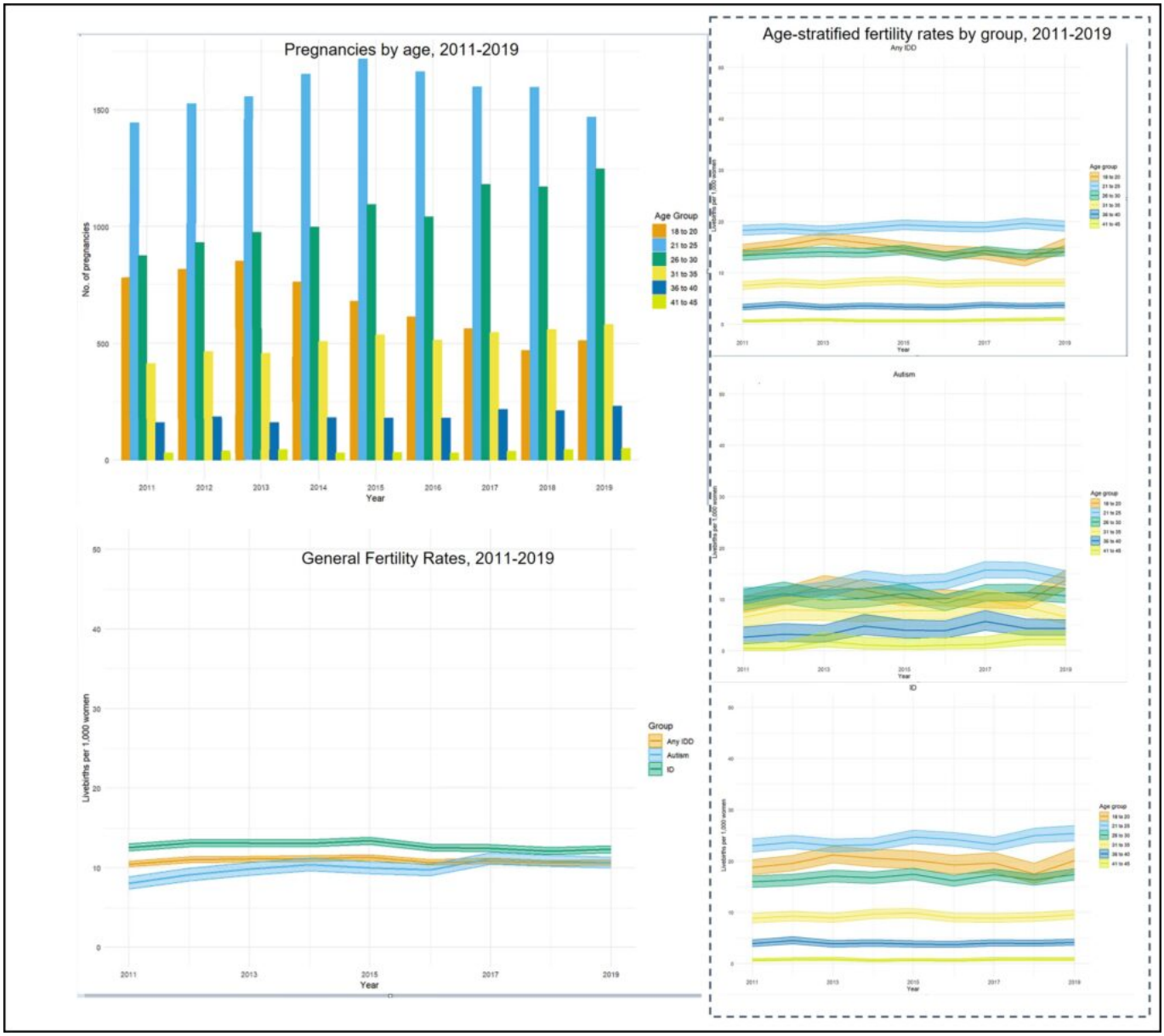
Results: Among 1,324 children (46.1% girls, 74.2% vaginally delivered, 74.0% white mothers), breastfeeding and B. infantis at 3 months interacted to influence gut microbial composition, fecal microbial metabolites, and SBP. Breastfeeding at 3 months, either exclusive or mixed with formula, was associated with lower SBP from 3 to 5 years in infants with B. infantis, but not in those without. Acetic acid increased with breastfeeding only in infants with B. infantis. These interactions were not observed at 1 year. Other gut microbes (e.g., Eggerthella lenta, Veillonella dispar) and fecal metabolites (e.g., creatinine, succinic acid) were also differentially associated with SBP depending on breastfeeding and B. infantis presence.

Conclusions: Early-life nutrition-microbe interactions, specifically between breastfeeding and B. infantis, shape the gut microbiome, metabolome and influence BP. Interventions such as co-supplementation of B. infantis with breast milk may help to lower childhood BP.

Perinatal & Pediatric

Fertility rates in women with intellectual and developmental disabilities enrolled in Medicaid or Medicare, 2011-2019 Josue Antonio Estrada* Josue Antonio Estrada Nina Cesare Kathryn Barger Megan B. Cole Samantha E. Parker Sowmya Rao Martha Werler Eric Rubenstein

Women with intellectual and developmental disability (IDD) have historically been sterilized and institutionalized to prevent them from exercising their reproductive rights. As sterilization laws have been repealed and protections against institutionalization enacted, stigma in childbearing persists but may be changing over time. Our objective was to describe fertility rates among women aged 18-45 with IDD who were enrolled in Medicaid, Medicare or both, using 9 years (2011-2019) of national claims data. Medicaid and Medicare cover many low-income and disabled adults, including most adults with intellectual disability in the US. IDD was identified using claims with International Classification of Disease (ICD) 9 or 10 codes for intellectual disability or autism spectrum disorder (ASD). Using data on livebirths and total number of women with IDD, wee calculated general fertility rate (GFR), age-specific fertility rate (ASFR), and total fertility rate and corresponding 95% confidence intervals for each year. From 2011-2019, there were 36,407 livebirths from 25,027 women with IDD, of which 51.0% were White, non-Hispanic,29.8% Black, non-Hispanic, and 14.7% Hispanic. GFR, expressed as number of livebirths per 1,000 women with IDD, was relatively constant across years, with a rate of 10.5 (95% CI: 10.1, 10.8) in 2011 and 10.7 (95% CI: 10.3,11.0) in 2019. For women with autism and those with an intellectual disability (ID), the highest ASFR occurred at 21 to 25 years. Total fertility rates, defined as the average number of children of women born from age 18 to 45,were slightly higher for those with ID (ranging from 0.32 to 0.34 across years) than women with autism (ranging from 0.17 to 0.24 across years). In general, fertility rates in women with IDD were lower than documented rates in peers without IDD and there was little change from 2011-2019. Future work will evaluate differences in fertility rates between Black and white and Hispanic and non-Hispanic women with IDD.


Pregnancies by age, 2011-2019
No. of pregnancies
Year
Age Group
18 to 20
21 to 25
26 to 30
31 to 35
36 to 40
41 to 45
General Fertility Rates, 2011-2019
Livebirths per 1,000 women
Year
Group
Any IDD
Autism
ID
Age-stratified fertility rates by group, 2011-2019
Any IDD
Autism
ID
Age group

Perinatal & Pediatric

The Special Supplemental Nutrition Program for Women, Infants, and Children and Cerebral Palsy Risk Among Hispanic Mothers and Children in California Yunyue Shi* Yunyue Shi Haoran Zhuo Giselle Bellia Zeyan Liew

Cerebral Palsy (CP) is the most common childhood physical disability in the United States, affecting 2 to 3 per 1,000 children. While the Special Supplemental Nutrition Program for Women, Infants, and Children (WIC) has been associated with improved birth outcomes, the potential impact of WIC on CP risk is unclear, particularly among Hispanic groups. To estimate the effect of maternal use of WIC on offspring CP risk, we conducted a California statewide cohort study by analyzing birth records from 2007 to 2015 and CP diagnostic records from the Department of Developmental Services. Our analysis included 1,455,242 Hispanic mothers and their singleton births covered by Medi-Cal (California's Medicaid program) who were eligible for enrollment in WIC. We performed logistic regression analysis to estimate the OR and 95% CI for CP associated with prenatal WIC use, adjusting for confounding factors. We used causal mediation analyses to examine the mediating roles of preterm birth and low birth weight. Overall, 91.2% of Hispanic mothers covered by Medi-Cal used WIC during pregnancy. WIC users were more likely to be younger, foreign-born, overweight or obese, have three or more children, and have lower education compared with non-users. Overall, a 20% lower odds of CP (OR=0.80, 95% CI: 0.68–0.93) was observed among the offspring of Hispanic mothers covered by Medi-Cal who used WIC compared with non-users. The estimated protective effect of WIC on CP was stronger among Hispanic mothers covered by Medi-Cal who had less than a high school education (OR=0.63, 95% CI: 0.50–0.80). Approximately 10–19% of the total association was estimated to be mediated through preterm birth or low birth weight. Our findings suggest that prenatal WIC use was associated with reduced CP risk in the offspring of Hispanic mothers with lower socioeconomic status. Maximizing WIC enrollment is recommended to benefit this vulnerable population for CP risk.

Perinatal & Pediatric

Sub-phenotyping of gestational diabetes with machine learning in a large cohort study in China Song-Ying Shen* Song-Ying Shen Cheng-Rui Wang Francesca Crowe Jin-Hua Lu Dong-mei Wei Wan-Qing Xiao Xiao-yan Xia Li-Fang Zhang Yi-xin Guo Jian-Rong He Hui-Min Xia Krishnarajah Nirantharakumar Xiu Qiu

OBJECTIVE

To develop a new classification scheme for gestational diabetes (GDM) in GDM women in the Born in Guangzhou Cohort Study, China.

RESEARCH DESIGN AND METHODS

Using the Density-Based Spatial Clustering of Applications with Noise method, clusters of GDM were identified based on high-dimensional epidemiological and medical data. Prevalence ratios (PRs) of adverse perinatal outcomes for each cluster were estimated using Poisson regression. Algorithms were developed using classification and regression trees (CART) to assign women to the subtypes.

RESULTS

We identified six replicable and distinct clusters in 5689 GDM women. Women in cluster 2 (48.8%) were mainly primiparous, youngest, and with few adverse conditions. Women in cluster 1 (39.9%) were multiparous, older, and had a higher rate of large-for-gestational-age and cesarean section (CS). Women in cluster 3 (5.4%) had higher proportions of preterm delivery and neonatal complications and had significantly higher PRs of maternal, placental, and neonatal complications when compared to cluster 2. Cluster 4 (4.3%) was enriched by placental dysfunction/malformation and perinatal asphyxia. Cluster 5 (0.6%) was dominated by fetal macrosomia and CS. Cluster 6 (0.4%) was characterized by maternal congenital uterus malformation, CS, and early fetal deaths. Trajectories of biological processes using biomarkers like bile acid throughout pregnancy differed and matched the enriched outcomes. CART algorithms assigned 91.6% of women accurately using early-to-mid pregnancy variables, improving to 95.9% with additional variables collected at birth.

CONCLUSIONS

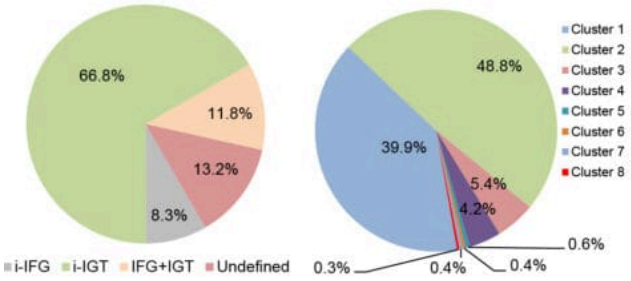
The clustering and new classification system could serve as a basis to develop subtype-specific therapeutic strategies and aid in exploring the underlying disease mechanisms.

Figure legends

Fig Clustering of GDM patients and patient distribution according to the method of classification (n=5698). Distribution of GDM subtypes based on (a) glucose measurements from OGTT and (b) clustering. (c) The plot of the GDM clustering cohort using principal component analysis. (d) Distribution of 8 clusters of patients according to main individual maternal, placental conditions, fetal, or newborn conditions.

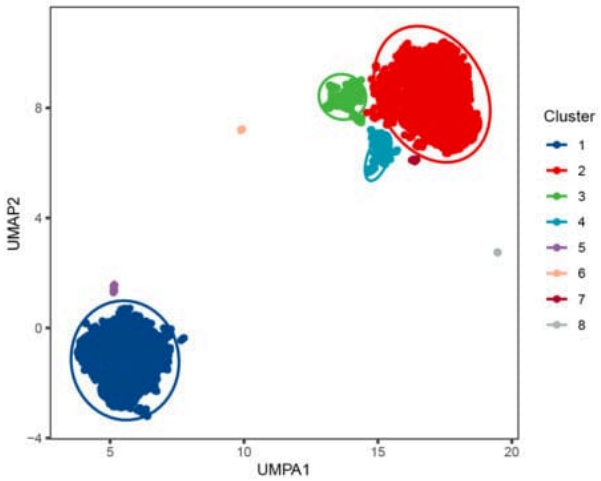
i-IFG: isolated impaired fasting glucose if fasting glucose≥5.1mmol/l and both 1-hour glucose<10.0 mmol/l and 2-hour glucose<8.5 mmol/l; i-IGT: isolated impaired post-load glucose tolerance if 1h glucose≥10.0 mmol/l and /or 2-hour glucose ≥ 8·5 mmol/l and fasting glucose□5·1mmol/L; IFG+IGT: combined IFG and IGT if 1-hour glucose≥10·0 mmol/l and/or 2-hour glucose ≥ 8·5 mmol/l and

fasting glucose≥5·1 mmol/l; UMAP: Uniform Manifold Approximation and Projection; LAG, large for gestational age; CS, cesarean section; GDM, gestational diabetes; SGA, small for gestational age; CHD, congenital heart disease. *Composite neonatal complication was defined as the presence of any of the following: birth trauma, respiratory distress, syndrome of infant of GDM mother, neonatal hypoglycemia, neonatal jaundice, perinatal hematological disorder, transitory neonatal disorders of calcium and magnesium metabolism, pneumonia, other neonatal infections, respiratory disease or cardiovascular disorders originating in the perinatal period, and intracranial nontraumatic hemorrhage of the fetus and newborn/Haemorrhagic disease of the fetus and newborn.



(a)

(b)



(c)

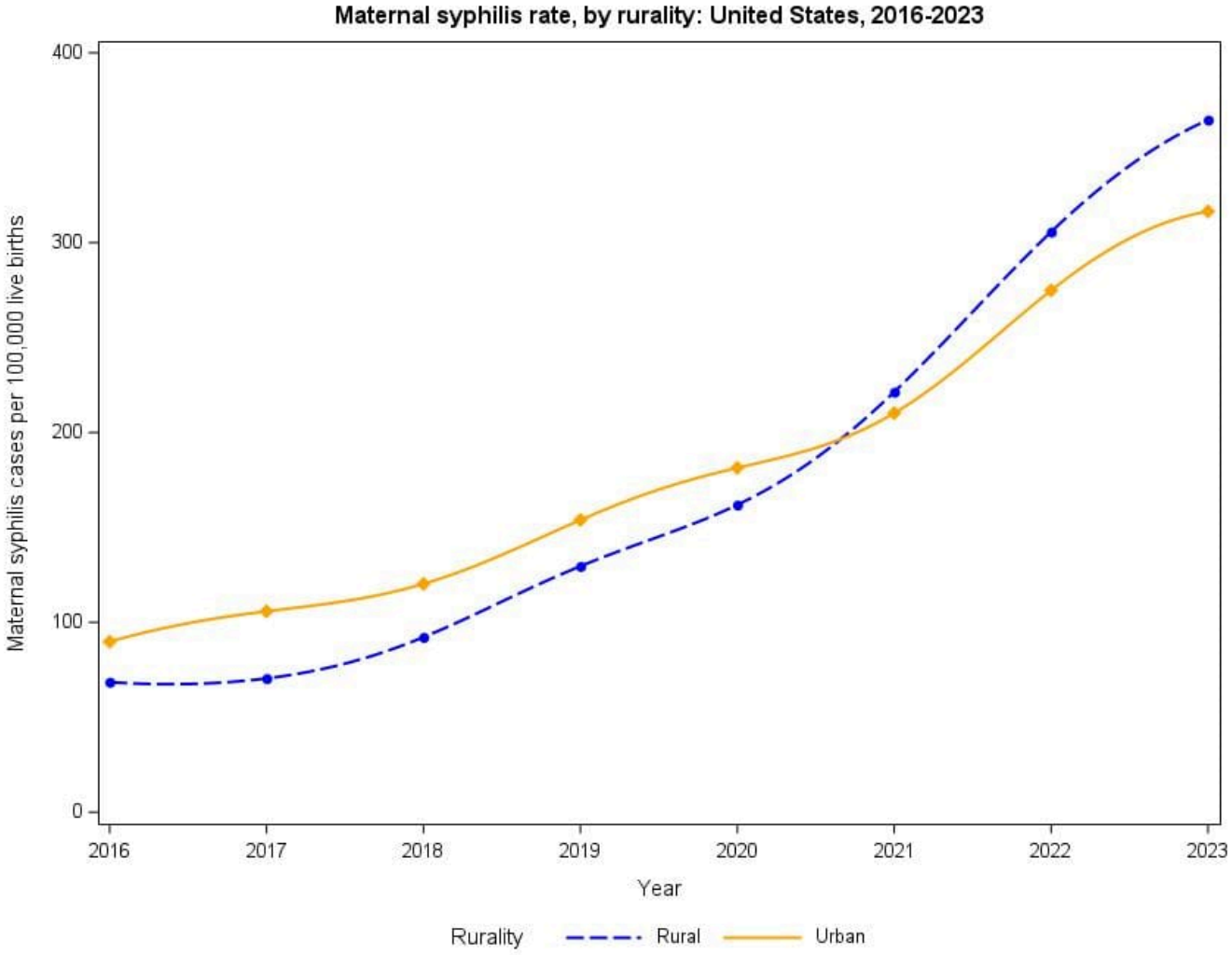
Cluster	Namely	No. (%)	Main Condition (%)	Most Frequent Associated Conditions (%)
1	Multiparous and advanced age subtype (MAA)	2273 (39.9)	LGA (10.6) and CS (45.6)	Multiparous (99.9), advanced age women (mean ± SD, 34.1 ± 3.9 years), overweight/obesity (23.6), histroy of GDM (19.0) and deliverying macrosomia baby(8.4), ,histroy of CS (43.0), and infections of genitourinary tract in pregnancy (13.8)
2	Primiparous and healthy subtype (PH)	2780 (48.8)	None	Primiparous (99.96), lowest mean age (mean ± SD, 30.0 ± 3.5 years)
3	Co-morbidity subtype (CM)	305 (5.4)	Gestational hypertension (3.1)/ pre-eclampsia/Eclampsia (8.6), liver disorder (11.5), preterm birth (38.5), SGA (14.8) and composite neonatal complications* (93.8)	Primiparous (81.8)
4	Placental disorder subtype (PD)	242 (4.3)	Placental dysfunction or malformation (54.7) and perinatal asphyxia (71.3)	Primiparous (99.96) and term birth (98.8)
5	Fetal overgrowth subtype (FOG)	32 (0.6)	Maternal care for disproportion due to unusually large fetus (100) and cesarean section (79.4)	overweight/obesity (48.5), histroy of deliverying macrosomia baby (11.0)
6	Early fetal death subtype (EFD)	24 (0.4)	Maternal congenital malformation of uterus (75.0),cesarean section (82.4), and early fetal deaths (29.2)	SGA (17.7) and fetal abnormality and damage excluding central nervous system malformation and CHD (8.0)
7	-	25 (0.4)	Fetal abnormality and damage excluding central nervous system malformation and CHD (92.6%)	SGA(30.4), Gestational hypertension (11.1)
8	-	17 (0.3)	Central nervous system malformation and CHD (91.3%)	Pre-exsiting (4.4)/Gestational hypertension(8.7)

(d)

Perinatal & Pediatric

Rural-Urban Differences and Racial Disparities in Maternal Syphilis in the United States, 2023 Clara Busse* Clara Busse Danielle Gartner Katy Backes Kozhimannil

Cases of syphilis during pregnancy (hereafter, “maternal syphilis”) have risen dramatically in the United States. National trends in maternal syphilis have not been disaggregated by rurality, despite the availability of this information and its importance for directing resources for prevention and treatment. Using 2016-2023 United States natality data for live births available from Center for Disease Control and Prevention’s Wide-ranging ONline Data for Epidemiologic Research, we compared maternal syphilis rates among rural and urban residents, stratifying by race, age, timing of prenatal care, and state. We observed that maternal syphilis rates in urban areas tripled from 2016 to 2023 (90 vs. 317 cases per 100,000 live births) while rates quintupled in rural areas over the same years (69 vs. 365 cases per 100,000 live births) (Figure 1). Since 2021, rural rates have exceeded urban rates, and the rural/urban gap has widened over time. Maternal syphilis rates were extraordinarily high among American Indian or Alaska Native (AIAN) birthing people: in 2023, the rate among rural AIAN birthing people was 1.6 times the rate among urban AIAN birthing people (2,089 vs. 1,272 cases per 100,000 live births), and 8.8 times the rate among rural White birthing people (2,089 vs. 239 cases per 100,000 live births). From 2020-2023, birthing people ages 35-39 years had rates of maternal syphilis that exceed those of their urban peers. Rates by trimester of prenatal care initiation were similar in rural and urban areas, with the highest rates in the no prenatal care group. Of the 34 states that reported maternal syphilis for both rural and urban areas in 2023, 14 had higher rates in rural areas compared with urban areas (13 states had suppressed case counts, 3 states and the District of Columbia do not have rural areas). These findings are essential for identifying rural populations most in need of resources and health care to prevent and treat maternal and congenital syphilis.


Maternal syphilis rate, by rurality: United States, 2016-2023
Maternal syphilis cases per 100,000 live births
400
300
200
100
0
2016
2017
2018
2019
2020
2021
2022
2023
Year
Rurality
Rural
Urban

Perinatal & Pediatric

Comparing COVID-19 vaccine confidence, recommendations, and practices among healthcare providers caring for pregnant persons, Fall DocStyles Survey, United States, 2021–2023 Grayson Waits* Grayson Waits Rebecca Hall Jessica Meeker Cristin McArdle Ayeesha Sayyad Romeo Galang Sascha Ellington Regina Simeone Carrie Shapiro-Mendoza

Vaccination during pregnancy can provide important protections for pregnant women and their infants; however, maternal COVID-19 vaccination in the U.S. remains low. Pregnant women are more likely to be vaccinated if their provider recommends it.

We used DocStyles, a web-based panel survey of US physicians, to compare three attitudes and behaviors from 2021–2023: confidence in counseling pregnant patients on COVID-19 vaccination (2022–2023), recommending the COVID-19 vaccine to pregnant patients (2022–2023), and offering the COVID-19 vaccine to pregnant patients (2021–2023). Adjusted prevalence ratios (aPRs) and 95% confidence intervals (CIs) estimated associations between year and these three outcomes; aPRs were adjusted for provider age, gender, and number of years practicing.

Of the 3,198 respondents (78% primary care physicians [PCPs] and 22% obstetrician-gynecologists [OB-GYNs]), neither provider type experienced a significant change in confidence in counseling pregnant patients about the COVID-19 vaccine from 2022 to 2023. However, PCPs and OB-GYNs recommended COVID-19 vaccination to their pregnant patients less often in 2023 than in 2022 (aPR: 0.95 [CI: 0.91, 0.99] and aPR: 0.95 [CI: 0.90, 1.00]). In both years, a higher proportion of OB-GYNs reported confidence in counseling and recommending the vaccine compared to PCPs. Overall, PCPs and OB-GYNs confident in counseling pregnant patients on COVID-19 vaccination were more likely to recommend the vaccine than those who were not confident, regardless of year (aPR: 2.0 [1.72, 2.32] and aPR: 2.6 [1.35, 5.25]). PCPs offered the COVID-19 vaccine less often in 2023 than in 2021 (aPR: 0.84 [0.76, 0.92]). PCPs whose practice offered the vaccine were more likely to recommend it than those who did not offer (aPR: 1.33 [1.27, 1.40]).

It is important to understand patterns in physician attitudes and practices regarding maternal COVID-19 vaccination to inform focused messaging and resources to physicians in the US.

Perinatal & Pediatric

Infant Clinical Signs Associated with Mortality and Bacteremia in Young Infants Aged 0-59 Days: A Systematic Review and Meta-analysis Sophie Driker* Sophie Driker Alastair Fung Suci Ardini Widyaningsih Naomi Schmeck Yumin Kim Jana Adnan Anum S. Hussaini Sitarah Mathias Tessa Kehoe Yasir Shafiq Carrie G. Wade Anne CC Lee

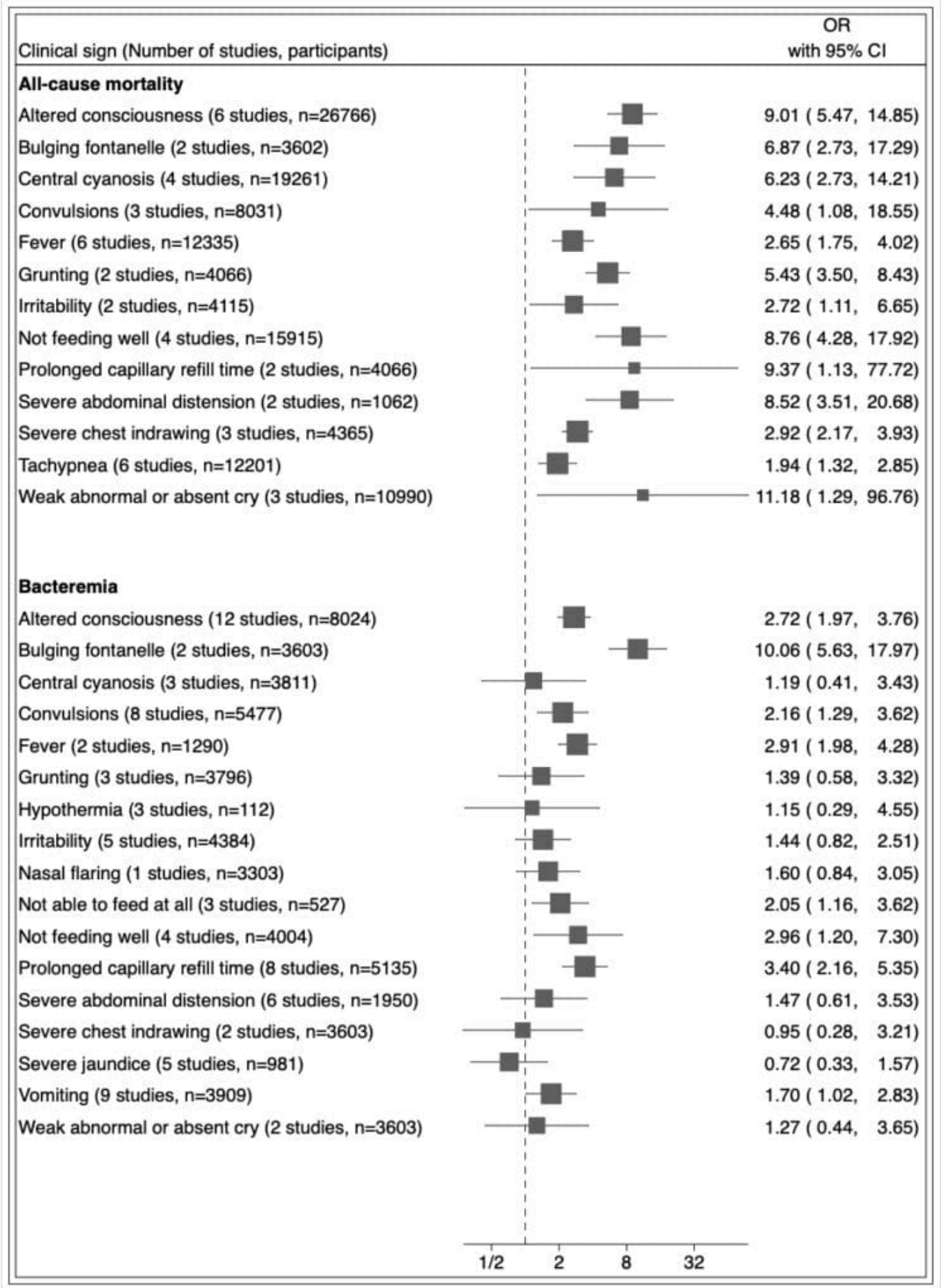
Background: Certain clinical signs are early indicators of infection and may be associated with mortality or bacteremia in young infants. Understanding these associations is important to optimize clinical algorithms to identify the highest-risk infants.

Aim: To systematically review evidence on the association of various individual infant clinical signs with mortality or bacteremia among young infants aged 0-59 days.

Methods: We searched Medline, Embase, CINAHL, Global Index Medicus, and Cochrane CENTRAL Register in September 2024 for studies evaluating the association of individual signs with all-cause mortality or bacteremia. We used Cochrane methods for study screening, data extraction, and performed quality assessment using QUADAS, QUAPAS, and Newcastle-Ottawa Scales. We reviewed clinical signs in the current WHO integrated management of childhood illness (IMCI) algorithm for management of sick young infants, plus 7 additional signs.

Results: Of 6701 studies identified, 37 were included. Of 21 clinical signs reviewed, 13 signs were significantly associated with mortality and 8 with bacteremia. The 5 clinical signs with the highest risk of mortality were weak or absent cry, prolonged capillary refill, altered consciousness (defined as “no movement when stimulated, movement only when stimulated, drowsy, unconscious, or lethargic”), not feeding well, and severe abdominal distension. The top 5 clinical signs associated with bacteremia were bulging fontanelle, prolonged capillary refill, not feeding well, fever, and altered consciousness.

Conclusion: Several infant clinical signs included in the current WHO IMCI algorithm are significantly associated with mortality and bacteremia. Bulging fontanelle and prolonged capillary refill were significantly associated with mortality and bacteremia in this review and are not included in the current IMCI algorithm. Future analyses will additionally assess the prevalence and predictive accuracy of individual infant clinical signs.


Clinical sign (Number of studies, participants)
OR with 95% CI
All-cause mortality
Altered consciousness (6 studies, n=26766) 9.01 (5.47, 14.85)
Bulging fontanelle (2 studies, n=3602) 6.87 (2.73, 17.29)
Central cyanosis (4 studies, n=19261) 6.23 (2.73, 14.21)
Convulsions (3 studies, n=8031) 4.48 (1.08, 18.55)
Fever (6 studies, n=12335) 2.65 (1.75, 4.02)
Grunting (2 studies, n=4066) 5.43 (3.50, 8.43)
Irritability (2 studies, n=4115) 2.72 (1.11, 6.65)
Not feeding well (4 studies, n=15915) 8.76 (4.28, 17.92)
Prolonged capillary refill time (2 studies, n=4066) 9.37 (1.13, 77.72)
Severe abdominal distension (2 studies, n=1062) 8.52 (3.51, 20.68)
Severe chest indrawing (3 studies, n=4365) 2.92 (2.17, 3.93)
Tachypnea (6 studies, n=12201) 1.94 (1.32, 2.85)
Weak abnormal or absent cry (3 studies, n=10990) 11.18 (1.29, 96.76)
Bacteremia
Altered consciousness (12 studies, n=8024) 2.72 (1.97, 3.76)
Bulging fontanelle (2 studies, n=3603) 10.06 (5.63, 17.97)
Central cyanosis (3 studies, n=3811) 1.19 (0.41, 3.43)
Convulsions (8 studies, n=5477) 2.16 (1.29, 3.62)
Fever (2 studies, n=1290) 2.91 (1.98, 4.28)
Grunting (3 studies, n=3796) 1.39 (0.58, 3.32)
Hypothermia (3 studies, n=112) 1.15 (0.29, 4.55)
Irritability (5 studies, n=4384) 1.44 (0.82, 2.51)
Nasal flaring (1 studies, n=3303) 1.60 (0.84, 3.05)
Not able to feed at all (3 studies, n=527) 2.05 (1.16, 3.62)
Not feeding well (4 studies, n=4004) 2.96 (1.20, 7.30)
Prolonged capillary refill time (8 studies, n=5135) 3.40 (2.16, 5.35)
Severe abdominal distension (6 studies, n=1950) 1.47 (0.61, 3.53)
Severe chest indrawing (2 studies, n=3603) 0.95 (0.28, 3.21)
Severe jaundice (5 studies, n=981) 0.72 (0.33, 1.57)
Vomiting (9 studies, n=3909) 1.70 (1.02, 2.83)
Weak abnormal or absent cry (2 studies, n=3603) 1.27 (0.44, 3.65)
1/2
2
8
32

Perinatal & Pediatric

Planetary Health Diet During Pregnancy and Major Pregnancy Complications: Findings From a Multisite, Diverse United States Cohort Shan-Xuan Lim* Shan-Xuan Lim Elizabeth A DeVilbiss Priscilla K Clayton Neil J Perkins Jessica L Gleason Katherine L Grantz Cuilin Zhang Jagteshwar Grewal

Emerging data from non-pregnant populations revealed Planetary Health Diet (PHD)'s role in promoting cardiometabolic health. However, such data during pregnancy is lacking. As such, we aimed to (1) characterize PHD scores in a racially/ethnically diverse cohort of US women, and (2) examine associations between PHD scores and major pregnancy complications.

A FFQ assessed 1st trimester diet, and ASA24 at up to 4 visits assessed 2nd and 3rd-trimester diets of women enrolled in the NICHD Fetal Growth Studies–Singletons (N=1980). Presence of major pregnancy complications was abstracted from medical records. To increase generalizability of findings, the analytical sample was weighted according to the race/ethnic distribution of low-risk US births in 2011. Overall and stratified PHD scores by race/ethnicity, pre-pregnancy BMI and vegetarian status were calculated. Adjusted odds ratios (95% CI) of major pregnancy complications were estimated using logistic regression.

Weighted mean (SD) PHD scores were 95.7 (10.7) during 1st trimester (8-13 weeks) and were lower but remained consistent throughout pregnancy [Mean (SD) of 16-22, 24-29, 30-33, and 34-37 weeks: 87.5 (12.8), 87.5 (13.3), 87.0 (12.5) and 86.9 (12.5)]. Mean PHD scores did not vary significantly by race/ethnicity, pre-pregnancy BMI or vegetarian status. Compared with women in the lowest tertile of the PHD (≤ 91.4), those in the highest tertile (≥ 100.4) had increased odds of gestational anemia [OR (95% CI): 1.09 (0.59, 2.02)] and reduced odds of hypertensive disorders of pregnancy [Mild: 0.38 (0.07, 2.04), Severe: 0.41 (0.09, 1.91)], gestational diabetes mellitus [0.51 (0.16, 1.64)] and preterm birth [0.46 (0.14, 1.46)], although associations were not statistically significant.

Higher PHD adherence was not significantly associated with major pregnancy complications among low-risk singleton pregnancies. Future studies of larger sample sizes are warranted to examine the health implications of PHD during pregnancy.

Perinatal & Pediatric

Birth outcomes among infants born to Middle Eastern and North African immigrant women in California: a retrospective cohort 2007-2020 Laila Hamzai* Laila Hamzai Rebecca J Baer Gretchen Bandoli

Background: Although inequities in infant health outcomes by race and ethnicity have been documented, very little research is available about the Middle Eastern and North African (MENA) population in the United States (US). It is challenging to identify MENA people in datasets as they are often collapsed into the 'non-Hispanic White' category, which stems from their lack of representation within the US Census system. The objective of this study was to disaggregate infants born to MENA individuals from the non-Hispanic White group to determine how their birth outcomes may differ.

Methods: Using a retrospective birth cohort in California with linked health records for mother-child pairs for one year before and after delivery between 2007-2020, we identified infants born to MENA birthing individuals by using country of birth data. The study sample was limited to infants of MENA-born and US-born (non-MENA) non-Hispanic White individuals. Age adjusted log-linear regression models were used to assess perinatal outcomes among the MENA group compared to the non-MENA group.

Findings: Of >6.9 million births, 66,194 were to MENA individuals and 1,371,184 were to non-MENA individuals. Infants from the MENA group had increased risk for being small for gestational age (aRR 1.5, 95%CI 1.4, 1.5) and reduced risk for preterm birth (aRR 0.8, 95%CI 0.8, 0.9), NICU admission (aRR 0.8, 95%CI 0.8, 0.8), and infant death (aRR 0.7, 95%CI 0.6, 0.8) compared to the non-MENA group. Within the MENA group, infants of those who preferred English were less likely to have a hospital readmission (aRR 0.9, 95%CI 0.8, 0.9) and emergency room visit (aRR 0.8, 95% CI 0.7, 0.8) within one year of birth compared to those who reported another preferred language.

Conclusions: The outcomes of infants born to MENA individuals differ from the White group with which they have historically been collapsed, which supports and highlights the need for the upcoming addition of a MENA category to the 2030 Census.

Table 2. Risk ratios for birth outcomes among infants born to Middle East North Africa-born (MENA) individuals in comparison to non-MENA US-born individuals who identified as non-Hispanic White in California (2007-2020)

Outcome	N (%) MENA	N (%) non-MENA	RR	95% CI	Adjusted RR[a]	95% CI
Preterm birth	3,299 (5.0%)	81,528 (5.9%)	0.8	(0.8, 0.9)	0.8	(0.8, 0.9)
Small for gestational age	6,295 (9.5%)	89,874 (6.6%)	1.5	(1.4, 1.5)	1.5	(1.4, 1.5)
NICU admission	2,918 (4.4%)	75,428 (5.5%)	0.8	(0.8, 0.8)	0.8	(0.8, 0.8)
Hospital readmission within 1 year of birth	5,867 (8.9%)	130,112 (9.5%)	0.9	(0.9, 1.0)	0.9	(0.9, 1.0)
Emergency room visit within 1 year of birth	15,571 (24%)	330,030 (24%)	1.0	(1.0, 1.0)	1.0	(1.0, 1.0)
Infant death	165 (0.2%)	4,767 (0.3%)	0.7	(0.6, 0.8)	0.7	(0.6, 0.8)

RR, risk ratio; 95% CI, 95% confidence intervals; a, adjusted for maternal age ≤34, >34 years; NICU, neonatal intensive care unit.

LATEBREAKER

Perinatal & Pediatric

Unearthing Hidden Burdens: Socioeconomic Determinants of Childhood Anemia in West Africa Colette Davis* Anam Khan Colette Davis

Introduction:
Childhood anemia remains a critical public health issue in Sub-Saharan Africa, impairing cognitive and physical development. This study examines the prevalence and determinants of anemia among children aged 6-59 months in Mali, Burkina Faso, and Nigeria.

Methods:
Using 2021 Demographic and Health Survey (DHS) data, a cross-sectional analysis was performed on 16,001 children. Anemia severity was categorized as severe, moderate, or mild based on hemoglobin levels. Multinomial logistic regression assessed associations with residence, wealth index, maternal education, and age.

Results:
Anemia prevalence was high across all three countries. In Burkina Faso, children from the poorest households had significantly higher odds of severe anemia (Odds ratio (OR) = 7.18, 95% Confidence interval (CI): 1.86-27.64). In Mali, rural children were more likely to experience moderate anemia (OR = 1.72, 95% CI: 1.34-2.20). In Nigeria, male children had higher odds of severe (OR = 1.31, 95% CI: 1.03-1.66) and moderate anemia (OR = 1.22, 95% CI: 1.10-1.36) compared to females.

Discussion:
The findings highlight significant disparities in anemia prevalence based on socioeconomic and demographic factors. Rural residence, lower household wealth, and lower maternal education levels were consistently associated with higher anemia severity. These results emphasize the need for targeted interventions focusing on the most vulnerable populations.

Conclusion:
Addressing childhood anemia in these regions requires strategies that reduce socio-economic disparities, improve nutrition, and enhance healthcare access. This study provides evidence-based insights for public health policies aimed at reducing anemia prevalence in Sub-Saharan Africa.

LATEBREAKER

Perinatal & Pediatric

Experiences of Housing Insecurity among Black Mothers: Prevalence of Housing Insecurity Using Survey Tools at Delivery Jaime Slaughter-Acey* Dawn Misra Jaime Slaughter-Acey Sarah Haight

Background: Experiencing homelessness during pregnancy has been associated with adverse perinatal outcomes. However, most studies documenting perinatal housing insecurity use hospital diagnosis codes or pre-pregnancy estimates and none have investigated this question post-2020. Up-to-date research considering housing insecurity during the entire pregnancy period using self-reported measures is needed.

Objective: To describe the prevalence and nature of housing insecurity during pregnancy in a sample of Black postpartum mothers.

Methods: Data were from 400 self-identified Black women aged 18-45 years in the Life-course Influences on Fetal Environments 2 (LIFE-2) study who delivered at one of two private hospitals in metro Detroit MI. Participants completed questionnaires during postpartum hospitalization that included items assessing housing insecurity.

Results: Approximately 20.7% of women reported housing insecurity during pregnancy (not always having a safe, stable place to sleep and store possessions). During pregnancy, 9.1% reported usually or always worrying about being forced to move from their primary residence and of those who rented, 8.8% experienced eviction. 7.1% spent 1 night of their pregnancy sleeping in a covered area not meant for human habitation (e.g., vehicle, RV or camper, encampment or tent, abandoned building) and among these mothers, 60% slept there more than half the time. 3.4% spent 1 night of their pregnancy sleeping in an outdoor area (e.g., a sidewalk or alley, bus or train stop, campground or woods, park, beach or riverbed, or under a bridge or overpass) and among these mothers, 40% slept there more than half the time.

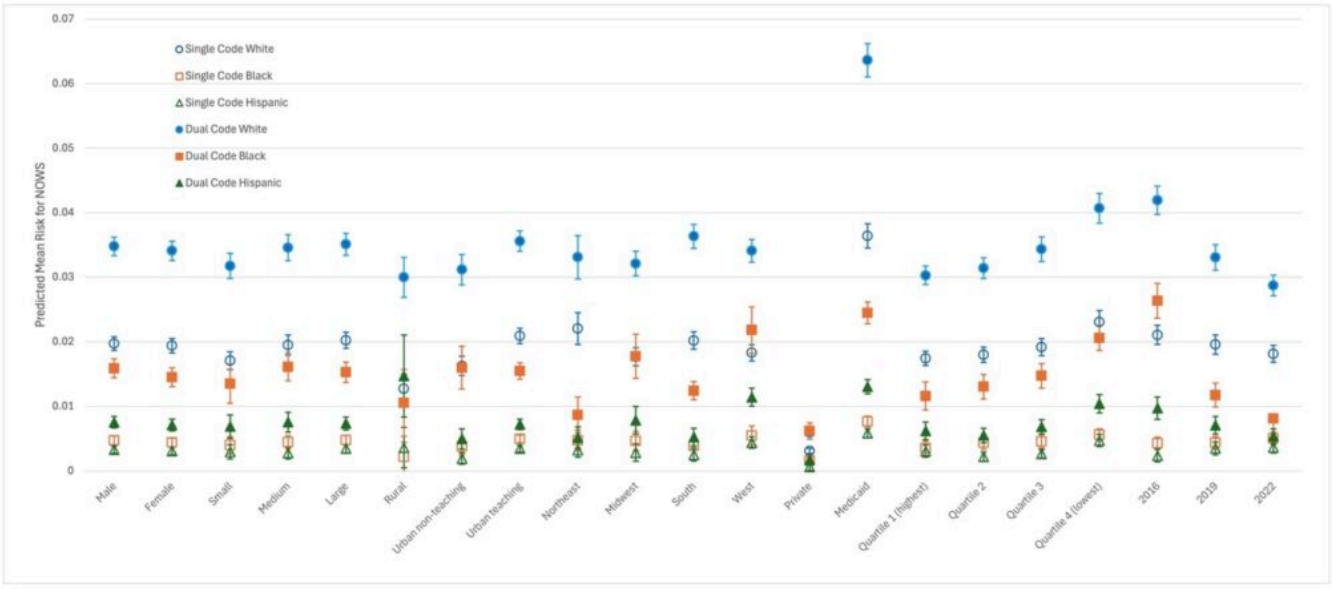
Conclusion: Housing insecurity during pregnancy is not rare. Approximately one in five women reported not always having a safe, stable place to sleep and store possessions, to varying degrees of severity. Future analysis will explore characteristics of women experiencing housing insecurity and adverse perinatal outcomes.

Perinatal & Pediatric

Race/ethnicity disparities in U.S. prevalence of neonatal opioid withdrawal syndrome in neonates ≥35 weeks GA using dual ICD-10CM exposure and withdrawal codes Hannah Neuman* Hannah Neuman Keith A. Dookeran James Groh Marina Feffer Janine Y. Khan

Neonatal opioid withdrawal syndrome (NOWS), a subset of neonatal abstinence syndrome (NAS), is an opioid-specific withdrawal syndrome in neonates that occurs after in-utero exposure to opioids. While previous studies have looked at NOWS prevalence based on the single ICD-10CM code for withdrawal (P96.1), a recent CDC study suggests that use of ICD-10CM codes for exposure (P04.49) along with withdrawal diagnosis (P96.1) may be more sensitive for identifying NOWS, with dual exposure/withdrawal codes capturing newborns exhibiting NOWS symptoms, identified by the exposure code, who have not received a withdrawal diagnosis. Using cross-sectional data from 2016, 2019, and 2022 cycles of the U.S. all-payer Kid's Inpatient Database (KID), part of the Healthcare Cost & Utilization Project (HCUP), weighted NOWS prevalence per 1,000 live births was estimated for neonates ≥35 weeks gestational age from in-hospital births, excluding iatrogenic cases, using both single and dual codes. Multivariable generalized linear regression models with predictive margins were used to estimate RDs and 95% CIs for select sociodemographic factors —sex, payer-type, ecologic income level, and hospital size, location/teaching status, and region— stratified by race/ethnicity (R/E) (Figure 1). Using dual codes, overall NOWS prevalence decreased from 2016 (25.55) to 2022 (14.30). While the prevalence of NOWS for White (25.15) and Hispanic (10.27) neonates doubled when using dual codes compared to single, with White neonates having the highest across all factors, prevalence tripled for Black neonates (19.67). Prevalence was highest for Medicaid (35.93), rural locations (33.22), and the lowest income quartile (29.43), and these factors had the greatest increase in prevalence when using dual codes. Future research using this dual code approach may be beneficial to prevent missing NOWS cases, reducing the potential for underrepresenting U.S. NOWS prevalence and suboptimal management of affected infants.

Figure 1. Stratified estimates (predictive margins) for select factors related to R/E disparities



Perinatal & Pediatric

The Association of Maternal Intellectual and Developmental Disabilities with Infant Death in California Catherine Psaras* Catherine Psaras Gretchen Bandoli Rita Ryu

Background. Intellectual and developmental disabilities (IDD) involve cognitive and adaptive deficits that begin before age 18–22. While fertility rates among individuals with IDD are rising alongside recognition of their reproductive rights, they still face significant health disparities during pregnancy. This study aimed to examine the relationship between maternal IDD subtypes and infant death. **Methods.** This population-based study analyzed linked data from California (2007–2021), including birth, infant death, discharge, emergency department, and ambulatory surgery center records. We compared singleton births to women with preexisting IDD (autism [ASD], cerebral palsy [CP], intellectual disability [ID], chromosomal abnormalities, and other IDD) to those without IDD, using ICD codes to identify disabilities. We limited IDD subtype-specific analyses to ID and chromosomal abnormalities due to the low number of deaths in other IDD subtypes. The primary outcome was infant death within the first year of life, identified via infant death certificates. Relative risks from modified Poisson regressions and hazard ratios from Cox proportional hazards models were adjusted for maternal age at birth and the competing risk of death where appropriate. **Results.** The data included 6,430,534 singleton infants born from 2007–2021. Of these, 4,713 were born to women with IDD (non-mutually exclusive subtypes: ASD: 458; CP: 1019; ID: 1817; chromosomal abnormalities: 1571; other IDD: 600). Infants of mothers with any IDD had significantly elevated hazards of death due to all causes (all COD HR: 9.38 [7.79, 11.30]). When analyzed by IDD subtype, there was heterogeneity (all COD HR [95% CI]: ID: 7.25 [4.78, 11.02]; chromosomal abnormalities: 17.03 [13.40, 21.65]). **Discussion.** Infants of women with IDD face significantly higher risks of infant death. Given the increasing fertility rates in this population, further research is essential to develop strategies to prevent infant mortality.

Perinatal & Pediatric

Mediation of the racial disparity in Neonatal Hypoxic Ischemic Encephalopathy (HIE) by socioeconomic position (SEP) in the HCUP KID Database Hailey Jaschob* Hailey Jaschob Keith A. Dookeran James Groh Janine Y. Khan

HIE may be more common among Black compared to White newborns in the U.S. We hypothesize that this disparity is mediated by SEP factors. Cross-sectional HCUP KID data from 2016, 2019, and 2022 was used to examine weighted prevalence of HIE and Therapeutic Hypothermia (TH) among neonates 35 weeks gestational age. We estimated Black/White HIE and TH risk differences (RDs and 95% CIs) reported as cases per 1000, using multivariable generalized linear models adjusting for year, sex, hospital size and region. We also estimated average controlled direct associations (ACDA) to evaluate the adjusted prevalence difference for HIE by race and performed a series of ACDA controlling for SEP factors [payer (Medicaid/Private), and income (ecologic quartiles)] using the Baron and Kenny method for mediation analysis. Overall weighted record counts were White, 510,745, and Black, 154,984. Compared to Whites, Blacks were more likely to be on Medicaid (36% vs 73%) and have lowest ecologic income quartile (20% vs 47%). Overall weighted HIE prevalence was 4.06 and increased with each cycle (2016=3.17; 2019=4.01; 2022=4.95). Overall weighted TH prevalence was 1.00 and increased with each cycle (2016=0.70, 2019=1.04, 2022=1.25). Crude models showed a significant increase in HIE among Blacks compared to White (1.31; 0.82, 1.80). Crude models for TH revealed a significant reduction in application among Blacks compared to Whites with HIE (-0.05; -0.09, -0.12). In fully adjusted models, compared with Whites, Blacks had a significant 1.11 (0.61, 1.62) increase in HIE. The racial disparity in HIE reduced by 39% to a value of 0.68 (0.09, 1.27) after additionally adjusting for SEP factors, and payer type accounted for most of the mediated effect (87%). Our findings suggest that observed racial differences in HIE prevalence are, at least partially, mediated by differences in SEP, which are likely upstream factors that affect prenatal health. Application of TH in newborns with HIE differs by race.

Perinatal & Pediatric

Cognitive and behavioral scores at age 7 in relation to maternal mid-pregnancy plasma nutrient mixtures in a Singaporean family follow-up cohort Jordana Leader* Jordana Leader Damaskini Valvi Chai-Yang Chen Yap Seng Chong Kok Hian Tan Sharon Ng James Chun Yip Chan Johan G. Eriksson Mary Foong-Fong Chong Shiao-Yng Chan Jonathan Huang Youssef Oulhote

Background: Maternal nutrition during pregnancy has been shown to impact offspring's health, especially neurodevelopment. While there is substantial research on individual nutrients such as folate, iron and vitamin D, little is known about the impact of mixtures of essential nutrients including both vitamins and minerals. This study explored the associations between mixtures of maternal essential minerals and vitamin concentrations and child behavior and cognition at age 7.

Methods: Data from 332 mother-child pairs in the Growing up in Singapore Towards healthy Outcomes birth cohort with both plasma nutrient and all neurodevelopmental outcome data were used. Mothers provided overnight fasting blood samples between 26 and 28 weeks of gestation. Plasma samples were analyzed for 10 essential minerals and 12 B and D vitamers. Child cognition and behavior functions at 7 years were assessed using the Wechsler Abbreviated Scale of Intelligence 2nd Edition (WASI-II) [n=331] and the Behavior Rating Inventory of Executive Function 2nd Edition (BRIEF-2) [n=332], respectively. Single nutrients were analyzed in association with BRIEF-2 and WASI-II index and composite scale T-scores using covariate-adjusted multivariable regressions. Grouped weighted quantile sum regression (gWQS) was used to investigate the associations of the nutrient mixture with child behavior and cognitive scores.

Results: A one unit increase in maternal sodium concentrations was associated with higher block design (β=1.54, 95% CI: 0.56, 2.53) and perceptual reasoning T-scores (β=1.49, 95% CI: 0.02, 2.95) as measured by the WASI-II. Additionally, a one unit increase in maternal concentrations of magnesium were associated with higher block design T-scores (β=1.10, 95% CI: 0.11, 2.09). When examining the mixture of the 22 nutrients, a one quartile increase of the nutrient mixture index composed of sodium, magnesium, vitamin B2-flavin, vitamin B2-neopterin, vitamin B3-nicotinamide, and vitamin D was associated with higher block design T-scores (β= 2.17, 95% CI: 0.03, 4.31). We found no associations with the BRIEF-2 T-scores.

Conclusions: In this study, we found that a mixture of maternal gestational minerals and vitamins, was associated with a greater ability in children to analyze and understand abstract visual items.

Perinatal & Pediatric

Obesity and Physical Activity in Children with Early Vision Problems: A Secondary Analysis of Data from the Growing-Up in Ireland Study Carolyn Drews-Botsch* Carolyn Drews-Botsch Siofra Harrington

Background: An association between obesity and vision problems such as amblyopia or myopia has been observed in cross-sectional analyses. However, longitudinal studies are needed in order to understand the direction of the association.

Methods: We used deidentified data from the Growing Up in Ireland (GUI) infant cohort. We limited analyses to the 6621 children who were followed at either age 3 or age 5, who had anthropometry measures at age 9 and whose parents did not report that the child had a chronic illness or disability. was measured at each time point. WHO standards were used to classify the child's Body Mass Index (BMI) as either overweight (BMI > 85th percentile) or obese (BMI >95th percentile). At age 9, children used a time use diary to report the number of minutes spent in physical exercise and in sedentary activities on a single day. Mean differences in BMI and activity times were assessed using t-tests and multiple linear regression. Differences in the incidence of becoming obese or overweight between ages 5 and 9 were assessed using multiple logistic regression after excluding children who were obese or overweight at age 5.

Results: The primary caregiver of 752 (11.4%) children reported that their child had a sight problem requiring correction at either age 3 or 5. Average BMI increased more between ages 5 and 9 in children with early vision problems than children without such problems (adjusted mean difference 0.23, 95% CI 0.01,0.45), but time spent in either physical exercise or sedentary activities at age 9 did not differ between the two groups. Among children who were not overweight at age 5, the odds of becoming overweight by age 9 was 40% higher (OR 1.39, 95% CI 1.04, 1.85) among children reported to have early vision problems than those without.

Conclusions: Children who have vision problems early in their lives are at greater risk of gaining weight and becoming overweight suggesting that vision problems precede weight gain in childhood.

Perinatal & Pediatric

Comparative effectiveness and safety of labetalol and nifedipine for the treatment of chronic hypertension during pregnancy Stephanie A. Leonard* Stephanie Leonard Sara Siadat Krista F. Huybrechts Elliott K. Main Mark A. Hlatky Brian T. Bateman

Clinical guidelines for treatment of chronic hypertension in pregnancy recommend labetalol and nifedipine as first-line agents. We used a target trial framework to evaluate the comparative effectiveness and safety of labetalol (an alpha/beta blocker) versus nifedipine (a calcium-channel blocker) in treatment of chronic hypertension in pregnancy. Study data for individuals with live- and stillbirths were sourced from the U.S. MerativeTM Marketscan® Database of commercial insurance claims for 2007 to 2022. The primary effectiveness outcome was a composite of preeclampsia with severe features or eclampsia, medically indicated preterm birth, placental abruption, or stillbirth. The primary safety outcome was infant born small-for-gestational age. We used log-binomial regression models to estimate associations between the treatment and outcomes, using stabilized inverse probability of treatment weights to adjust for confounding by year, gestational age at treatment initiation, maternal age, region, comorbidities, and other medications. The study included 6,784 pregnant individuals with chronic hypertension who initiated labetalol or nifedipine treatment during the first 20 weeks of pregnancy. Of these, 5,553 (82%) used labetalol and 1,231 (18%) used nifedipine. The composite effectiveness outcome occurred in 42% of births exposed to labetalol and 43% of births exposed to nifedipine. The safety outcome occurred in 13% of births exposed to labetalol and 12% of births exposed to nifedipine. Comparing nifedipine with labetalol, the adjusted risk ratio (RR) was 1.03 (95% confidence interval (CI): 0.96, 1.11) for the composite effectiveness outcome and 0.98 (95% CI: 0.82, 1.16) for the safety outcome. These results, using a cohort nested in nationwide healthcare utilization data, suggest that labetalol and nifedipine have comparable effectiveness and safety when used for the treatment of chronic hypertension during pregnancy.

Perinatal & Pediatric

Quantifying the Benefits of Preventive Periodontal Care in Pregnancy Using Advanced Causal Inference Methods Ishan Suthar* Ishan Suthar Dr. Anwar Merchant Rokonuzzaman SM

Periodontal disease during pregnancy poses significant risks due to hormonal changes that exacerbate inflammation, potentially leading to adverse outcomes like preterm birth and low birth weight. Few studies have assessed the causal effects of preventive periodontal treatment on perinatal outcomes. Standard methods for analysis of randomized control studies may give biased estimates of exposure effects in the presence of time-varying confounding. G-estimation helps address this limitation.

Data were obtained from Obstetrics and Periodontal Therapy, a longitudinal randomized controlled trial with 823 pregnant women aged 18–44 recruited from urban and suburban clinics. They were randomly assigned to receive non-surgical periodontal treatment. The test group received scaling and root planning treatment before 20 weeks gestation, at 21-24 weeks gestation, and at 29-32 weeks gestation. Periodontal markers including bleeding on probing (BOP), pocket depth (PD ≥ 4 mm and PD ≥ 5 mm), and calcium deposits were evaluated across all visits. G-estimation and inverse probability censor weights were applied to adjust for covariates, time-varying confounders and loss-to-follow-up bias.

Results revealed substantial improvements in periodontal health among treated participants; BOP decreased by 19.05% (95% CI: -19.10 to -19.00, $p < 0.0001$), PD ≥ 4 mm by 9.56% (95% CI: -9.60 to -9.53, $p < 0.0001$), PD ≥ 5 mm by 4.15% (95% CI: -4.17 to -4.12, $p < 0.0001$), and calcium deposits by 8.80% (95% CI: -8.85 to -8.74, $p < 0.0001$). These reductions highlight the treatment's efficacy in mitigating periodontal disease progression during pregnancy.

This study’s innovative use of g-estimation strengthens the evidence base for causal relationships, providing precise insights into treatment efficacy. Clinically, the findings advocate for integrating preventive periodontal care into prenatal programs, emphasizing its potential to improve both maternal oral health and perinatal outcomes.

Perinatal & Pediatric

Adolescent Cardiovascular Risk Trajectories and Later Life Maternal Morbidity Annabelle Ng* Annabelle Ng Natalie Boychuk Teresa Janevic Katharine McCarthy

Nearly one-third of U.S. pregnancy-related deaths are attributable to poor cardiovascular health (CVH). Less is known about how CVH risk progresses from adolescence to young adulthood to influence pregnancy health in later life. We estimated the relative risk of gestational diabetes (GDM) and hypertensive disorders of pregnancy (HDP) among individuals in midlife by their cardiovascular risk in adolescence and young adulthood. Data were drawn from the National Longitudinal Study of Adolescent and Adult Health, where waves I-II corresponded to ages 11-19 years (adolescence), wave III ages 18-26 (young adulthood), and wave V ages 33-43. The final sample was 1,095 birthing individuals who completed all follow-up assessments and did not have pre-pregnancy diabetes. CVH risk was assessed using an adapted Life's Essential 8 scale, categorized into low, medium and high risk. Ever experiencing a pregnancy complication was self-reported in wave V. Risk of GDM and HDP was estimated using log binomial regression adjusting for maternal and sociodemographic characteristics. We found that those with high vs. low CVH risk in adolescence had 2.4 times (95% CI: 1.4, 4.2) the risk of future GDM. No association was observed among those with moderate vs. low CVH risk (adjusted risk ratio (aRR) 1.2, 95% CI: 0.70, 2.0). We found a small increased risk of HDP among those with high (aRR 1.2, 95% CI: 0.8, 1.7) or moderate adolescent CVH risk (aRR 1.2, 95% CI: 0.9, 1.6) vs. low risk but confidence intervals were inclusive of the null. The highest incidence of GDM was observed among those who maintained high risk status between adolescence and young adulthood (34.9%), relative to those who stayed low (8.3%) or moderate risk (12.1%) over time, or who were high risk and reduced their risk to low (16.7%) or moderate (17.8%). Findings support the potential of prevention efforts targeting CVH risk trajectories in adolescence to offset maternal morbidity later in the lifecourse.

Pharmacoepidemiology

Study design and comparator choices in evaluating the risk of suicidal ideation and suicidality with semaglutide: A real-world study Qoua Her* Qoua Her Tiansheng Wang Til Sturmer John Buse Virginia Pate Michele Jonsson-Funk Michael Webster-Clark

Semaglutide, a GLP-1 analog, is prescribed for both type 2 diabetes and weight loss. After reports of suicidal ideation (SI) prompted regulatory review, a real-world study estimated a HR of 0.27 for SI comparing new users of semaglutide to prevalent users of weight loss ingredient (WLI) drugs (bupropion, naltrexone, orlistat, phentermine, or topiramate). Robust pharmacoepidemiologic designs with active comparators are warranted.

We conducted two different real-world studies in the Merative MarketScan™ Databases. We identified overweight or obese patients who initiated semaglutide, WLI drugs, or active comparators (combination bupropion/naltrexone, orlistat, phentermine, or combination phentermine/topiramate) and followed them for SI and suicidality (SI, suicide attempt, or intentional self-harm). We compared semaglutide to WLI drugs (Study 1) and active comparators (Study 2) using two distinct study designs: New user vs. Prevalent-user (NUPU) and New user (NU) to evaluate the influence of study design and comparator choice. WLI and active comparators patients were weighted to resemble semaglutide initiators to reduce confounding. We estimated risk ratios (RR) for SI and suicidality within the 183 days of drug initiation using Kaplan-Meier methods with 95% confidence intervals from 1,000 bootstrap replicates.

In Study 1, semaglutide was associated with a reduced SI risk (RR 0.49 [0.32–0.73]) versus WLI drugs (NUPU), but this association was attenuated with the NU design (SI: RR 0.74 [0.39–1.13]). In Study 2, semaglutide was associated with a higher SI risk (NUPU: RR 1.87 [1.00–4.22]; NU: RR 1.36 [0.62–6.14]) compared to active comparators. These results were similar when examining suicidality.

Semaglutide was not associated with increased SI or suicidality when using an appropriate study design and compared to active comparators. Careful consideration of study design and appropriate comparator choice are essential in drug safety studies.

Outcome	Semaglutide	Comparator	Risk Difference (95% CI)	Risk Ratio (95% CI)
New user vs. Prevalent user studies				
Study 1: Semaglutide vs. Weight loss ingredient drugs				
Suicidal ideation	0.09% (48.0)	0.20% (101.7)	-0.11% (-0.18%, -0.05%)	0.49 (0.32, 0.74)
Suicidality	0.10% (50.0)	0.25% (124.3)	-0.15% (-0.23%, -0.08%)	0.42 (0.27, 0.62)
Study 2: Semaglutide vs. Active comparator drugs				
Suicidal ideation	0.10% (51.0)	0.05% (27.2)	0.04% (-0.01%, 0.09%)	1.87 (0.92, 4.31)
Suicidality	0.10% (53.0)	0.06% (30.1)	0.04% (-0.01%, 0.08%)	1.74 (0.90, 3.73)
New user studies				
Study 1: Semaglutide vs. Weight loss ingredient drugs				
Suicidal ideation	0.08% (13.0)	0.11% (17.8)	-0.03% (-0.07%, 0.01%)	0.74 (0.39, 1.13)
Suicidality	0.08% (14.0)	0.13% (21.1)	-0.04% (-0.09%, 0.00%)	0.66 (0.36, 1.00)
Study 2: Semaglutide vs. Active comparator drugs				
Suicidal ideation	0.08% (13.0)	0.05% (8.9)	0.02% (-0.02%, 0.07%)	1.36 (0.62, 6.14)
Suicidality	0.08% (14.0)	0.07% (11.0)	0.02% (-0.03%, 0.07%)	1.18 (0.57, 3.63)

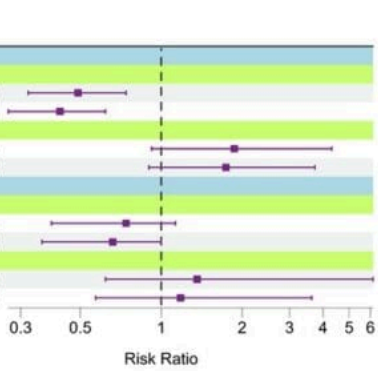


Figure 1: We assessed the risk of SI and suicidality (SI, suicide attempt, or intentional self-harm) of semaglutide compared to weight loss ingredient drugs (Study 1) and active comparators (Study 2) with two different study designs: New-user vs. Prevalent-user (NuPu) and New-user (Nu) and evaluated the influence of the study design and comparator choice.

Pharmacoepidemiology

Feasibility of applying pharmacoepidemiologic drug-drug interaction screening methods to a population of nursing home residents: an application to clopidogrel Adam M. D'Amico*
Adam M D'Amico Charles E. Leonard Daniel A. Harris Yu-Chia Hsu Lori A. Daiello Douglas P. Kiel Andrew R. Zullo

Background: The self-controlled case series (SCCS) design has been used to screen potential drug-drug interactions (DDI) and inform etiologic research among community-dwelling older adults. The nature and extent of DDI among nursing home (NH) residents remains underexplored despite high rates of polypharmacy, frailty, and adverse events in this population.
Objective: To assess the feasibility of using SCCS-based screening methods to identify potential DDIs among NH residents.
Methods: We used Minimum Data Set and Medicare data from 2013 to 2020 to identify NH residents ≥65.5 years old who were enrolled in Medicare fee-for-service and received the object drug clopidogrel. New use of clopidogrel was identified using a 6-month washout. Among residents hospitalized for a major bleed, SCCS studies were conducted to test all common (30+ users) precipitant drugs for potential DDIs with clopidogrel. Rate ratios (RR) and 95% CIs for major bleed were calculated for periods of concomitant use versus clopidogrel use alone. We used semi-Bayes adjustment to reduce false positives from multiple estimation. An expert panel reviewed results for biological plausibility.
Results: We identified 987 major bleed events. Of 40 precipitant drugs analyzed, five (12.5%) had RR and 95% CI >1: amoxicillin-clavulanate [2.18 (1.19, 3.98)], sertraline [2.09 (1.14, 3.80)], potassium [2.02 (1.28, 3.21)], cephalexin [1.96 (1.11, 3.48)], and tramadol [1.90 (1.13, 3.19)]. Sertraline was the only signal considered biologically plausible.
Conclusion: Despite using a common object drug associated with adverse events and eight years of Medicare claims, this analysis yielded few DDI signals to inform future studies. Given the size of the NH population and rarity of many outcomes, SCCS-based screening methods face significant challenges when applied in the NH setting. Pairing SCCS findings with robust clinical review is important when triaging potential DDIs for subsequent etiologic work.

Pharmacoepidemiology

Statin Use and Dementia: A comparison of findings from different causal questions in UK Biobank Neal Jawadekar* Neal Jawadekar Adina Zeki Al Hazzouri

Prior studies conducted on the relationship between statins and dementia have been largely mixed. While randomized trials have failed to find a meaningful effect of statins on dementia risk, multiple longitudinal studies suggest statins may help protect against dementia. Amidst these findings, competing risk of death (i.e., loss-to-follow-up or censoring due to death) remains a pervasive problem across longitudinal dementia research which may bias results when left unaddressed. In this paper, we utilize the UK Biobank cohort to estimate the effects of statin initiation on dementia. We estimate the controlled direct effect (i.e., the direct effect of statins on dementia which does not go through death) as well as the total effect (capturing both the direct and indirect effects). We performed this analysis on a cohort of individuals aged 55+ by the end of UKB enrollment period in 2010, without a history of dementia, and no statin use in the 6 months prior to baseline. We estimated a controlled direct effect (absolute risk difference) of statin initiation (vs. no statin initiation) on 10-year dementia risk of +0.58% (+0.13% , +1.04%), and a total effect +0.39% (+0.23%, +0.55%). Even after accounting for the competing risk of death, our findings suggest that statin initiators have an increased risk of dementia.

Table 1. Total Effect and Controlled Direct Effect of Statins on the Risk of Dementia, as well as the Total Effect on the Risk of Mortality, at 10 years of Followup

Method: Weighted Kaplan Meier Survival Estimator

Causal Effect	**Risk** in statin users	**Risk** in non-users	**Causal Risk Difference** (95% CI)	**Causal Risk Ratio** (95% CI)
Total Effect* on Dementia	**1.35%** (1.20% , 1.51%)	**0.96%** (0.95%, 0.98%)	**+0.39%** (+0.23%, +0.55%)	**1.40** (1.24, 1.57)
Controlled Direct* Effect on Dementia	**2.19%** (1.74% , 2.68%)	**1.62%** (1.56% , 1.65%)	**+0.58** (+0.13% , +1.04%)	**1.36** (1.08 , 1.65)

*Covariates include: age at baseline, sex, college education, smoking status at baseline, **time-varying blood pressure medication,** physical activity level, **incident cardiovascular disease, incident diabetes, incident stroke,** LDL cholesterol at baseline, and total triglycerides at baseline

Pharmacoepidemiology

Opioid and other analgesic use in older adults initiating a biologic disease-modifying therapy for treatment of autoimmune diseases Meghan Cupp* Meghan Cupp Andrew R Zullo Nina Joyce Francesca Beaudoin Arman Oganisian

Background

Autoimmune diseases cause significant pain, particularly in older adults, who experience high rates of opioid use amid unclear pain management guidelines. Biologic disease-modifying therapies (bDMTs) are expected to alleviate pain and reduce analgesic use, but this remains empirically unverified. This study assesses changes in opioid and other analgesic use in older adults initiating a bDMT for autoimmune disease.

Methods

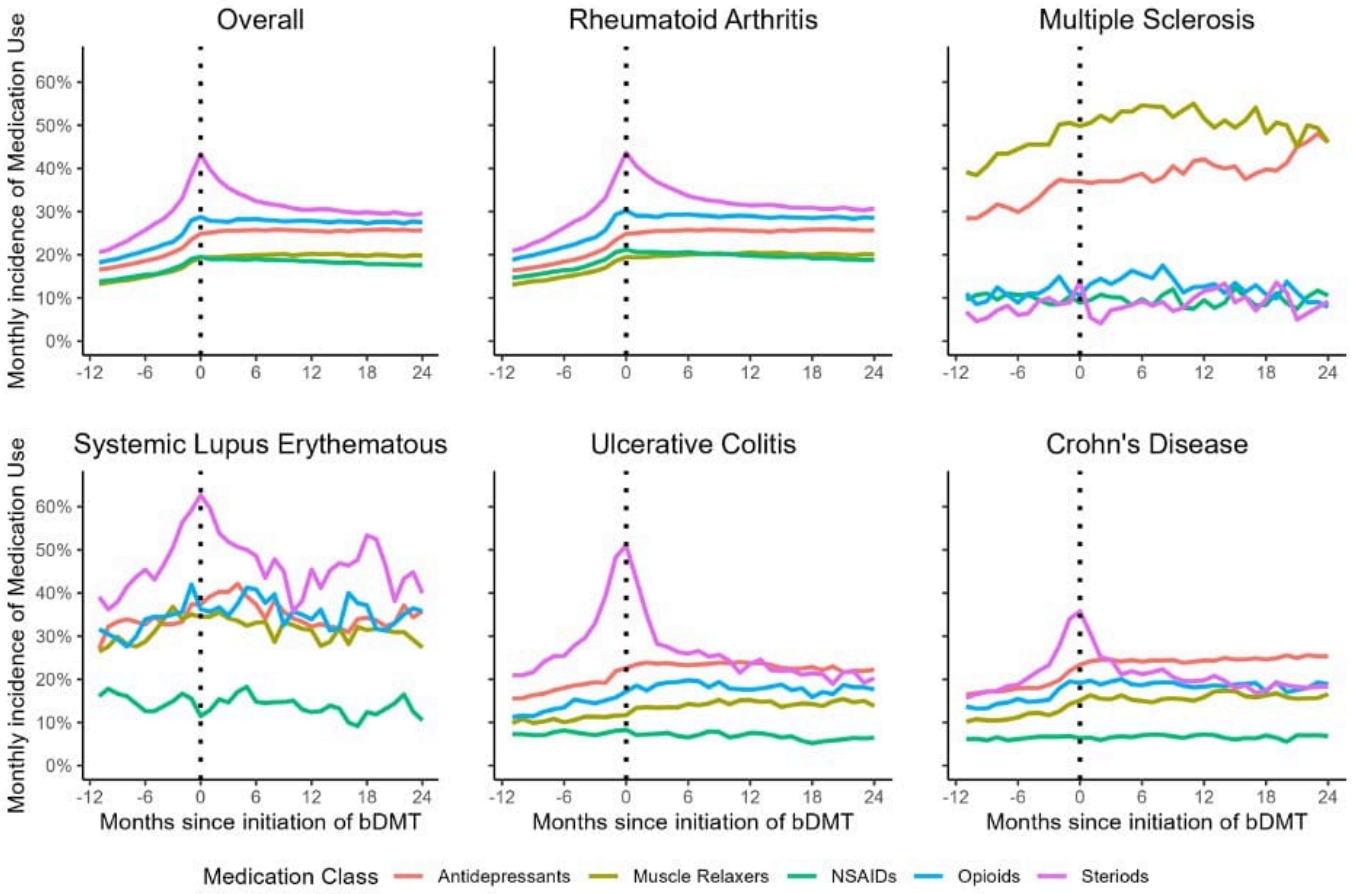
This retrospective, longitudinal descriptive study included community dwelling US Medicare beneficiaries aged >65 years who initiated a bDMT for treatment of rheumatoid arthritis, multiple sclerosis, systemic lupus erythematosus (SLE), ulcerative colitis or Crohn’s disease in 2008-2019. We estimated analgesic use incidence in the 12 months pre- and 24 months post-initiation of a bDMT. Risk of analgesic use in the first and second years post-initiation versus pre-initiation were analyzed using a generalized estimating equation model. Subgroup analyses were conducted by sex, condition, and bDMT initiation prior to 2015.

Results

Among 1,061,463 eligible individuals, 22,671 initiated a bDMT during the study period. Opioids were the most used analgesic, surpassed only by corticosteroid use which was considered as an indicator of symptom severity. The incidence of opioid and other analgesic use increased steadily in the 12 months prior to initiation and remained high throughout the subsequent 24 months of follow-up (see Figure). Opioid use rose post-initiation in the overall cohort (RRyear1 1.04 [95%CL 1.03, 1.06]; RRyear2 1.05 [95%CL 1.03, 1.07]) and only SLE patients had a decrease (RRyear1 0.86 [95%CL 0.76, 0.98]; RRyear2 0.83 [95%CL 0.67, 1.04]).

Conclusion

In all conditions but SLE, opioid and other analgesic use increased after initiation of a bDMT, underscoring the need for careful consideration of pain management strategies in this population. Future research should assess the dynamic between pain, bDMT use, and pain management strategies.


Overall
Rheumatoid Arthritis
Multiple Sclerosis
Systemic Lupus Erythematous
Ulcerative Colitis
Crohn's Disease
Monthly incidence of Medication Use
60%
50%
40%
30%
20%
10%
0%
-12
-6
0
6
12
18
24
Months since initiation of bDMT
Medication Class
Antidepressants
Muscle Relaxers
NSAIDs
Opioids
Steriods

Pharmacoepidemiology

Safety signal identification in the Sentinel System: Consistent findings for medical products over various study designs Ashley I. Michnick* Ashley I. Michnick Leah B. Herity Geetha S. Iyer Suraj Rajasimhan Jummai Apata Jillian Burk Derek Campbell José J. Hernández-Muñoz Michelle Hines Nathan Kim Joy Kolonoski Nora McElroy Sampada Nandyala Amelia Thyen Megan Wiley Judith C. Maro Monica A. Muñoz

Introduction. The U.S. FDA performs medical product (MP) safety signal identification (SI) in its Sentinel System using tree-based scan statistics that detect unexpected health outcomes of interest (HOIs) after MP initiation. HOIs occurring more frequently ($p<0.05$) are considered alerts, which are investigated and classified as a clinically meaningful safety signal or not.

Methods. In the Sentinel Distributed Database, we performed SI for new users of risankizumab-rzaa and guselkumab using propensity score-matched active comparator (PSMAC) and self-controlled risk interval (SCRI) study designs where each agent served both as exposure and comparator. Tree-based methods scanned across inpatient and emergency department diagnosis codes. The SCRI was inherently adjusted, and the PSMAC design used 1:1 high-dimensional PSM. We assessed whether HOIs occurred more frequently in the risk vs. control period (SCRI) or group (PSMAC) and evaluated whether clusters of HOIs occurred more frequently in variable risk windows after treatment compared to all other periods in the same window.

Results. The SCRI had approximately 30,000 new users of each drug, and the PSMAC had 14,819 matched new users. For both MPs, no HOIs occurred more frequently in the risk vs. control period (SCRI) or group (PSMAC). No clusters of HOIs occurred more frequently in variable risk windows after guselkumab treatment, but we identified an increase ($p<0.05$) in cholelithiasis without cholecystitis on days 9-11 after risankizumab-rzaa initiation compared to all other days in the six months after. Further investigation of line-level healthcare claims suggested this was likely incidental, therefore it wasn't considered a safety signal.

Conclusions. This study demonstrates the feasibility of using two study designs with varying strengths to perform signal identification among large numbers of MP users. Tree-based scan statistics are valuable complementary methods to augment MP safety surveillance.

Disclosures. This project was supported by Task Order 75F40123F19009 under Master Agreement 75F40119D10037 from the US Food and Drug Administration (FDA). The contents are those of the authors and do not necessarily represent the official views of, nor an endorsement, by FDA/HHS, or the U.S. Government.

Pharmacoepidemiology

Semaglutide versus liraglutide and incidence of diabetes and cardiovascular disease: an analysis of real-world data Ethan Cannon* Ethan Cannon Wendy Wang Faye Norby Rob Walker Pamela Lutsey

Introduction: Semaglutide (2.4 mg) and liraglutide (3.0 mg) are glucagon-like peptide-1 receptor agonists (GLP-1 RAs) initially indicated for treating obesity, though clinical trials have also shown CVD risk reduction and improved glycemic control. While semaglutide is superior for weight loss, no trials have compared these drugs head-to-head for CVD risk, nor assessed incident diabetes as a primary endpoint.

Methods: Using the MarketScan insurance claims database from 2020-22, we matched diabetes-free patients prescribed semaglutide with up to 2 controls prescribed liraglutide by age, sex, enrollment date and prescription date. We used Cox regression to compare semaglutide versus liraglutide use and incident 1) diabetes, 2) hard CVD (myocardial infarction, stroke and heart failure), and 3) a composite of hard CVD plus unstable angina and coronary revascularization. Models adjusted for age, sex and a propensity score determined by comorbidities and use of other medications.

Results: 15,017 semaglutide users and 21,431 matched liraglutide users initiated treatment during 2021 or 2022 (mean age 45; 83% female). Follow-up concluded at the end of 2022 or insurance disenrollment. Over a mean of 0.7 years, there were 631 diabetes, 30 hard CVD, and 64 composite CVD events. Comparing semaglutide with liraglutide, the HR (95% CI) was 0.60 (0.35-1.02) for the composite CVD outcome and 0.57 (0.26-1.25) for hard CVD. The proportional hazards assumption was violated in the analysis of diabetes (p=.01); semaglutide was associated with higher risk in the first six months of follow-up (2.07 [1.70-2.53]) and lower risk thereafter (0.70 [0.54-0.92]).

Conclusions: In this real-world study of GLP-1 RAs, results directionally favored semaglutide for CVD outcomes. For diabetes, the change in directionality may be supported by the SUSTAIN 10 and PIONEER 4 trials, where liraglutide initially had a greater effect on glycemic control but semaglutide was superior at completion of the study.

Pharmacoepidemiology

Associations between COVID-19 vaccination during pregnancy and postpartum and human milk feeding initiation and continuation Elisabeth Brandstetter Figueroa* Elisabeth Brandstetter Figueroa Gabriela Vasquez-Benitez Kirsten Ehresman Elisabeth M Seburg Malini B DeSilva Yihe G Daida Kimberly K Vesco Abbey Sidebottom Heather S Lipkind Elyse O Kharbanda Kristin Palmsten

We assessed the association of COVID-19 vaccination during pregnancy and postpartum with human milk feeding initiation and duration.

Using EHR data from 3 geographically diverse healthcare systems, we included persons with a live birth (Jan ‘21-Oct ‘22), infant linkage, and milk feeding documentation (breast milk, formula or other milk, both). COVID-19 vaccination was determined from EHRs and state vaccine registries. Two analyses were performed based on timing of COVID-19 vaccination: pregnancy (≥20 weeks gestation vs no vaccination during pregnancy; N=10,757) and postpartum (≤6 months after delivery vs none; N=17,160). We estimated the adjusted prevalence ratio (aPR) for prenatal COVID-19 vaccination with human milk feeding initiation and continuation (at 2 and 6 months) using Poisson regression. We estimated the aHR for postpartum COVID-19 vaccination and human milk feeding discontinuation using a time-dependent Cox model. We used multiple imputation by chained equations for missing covariates, stabilized inverse probability of attrition weights to account for differences in those missing outcomes, and stabilized inverse probability of treatment weights to account for confounding by demographic, clinical, and socioeconomic characteristics, healthcare utilization, and calendar time.

In the pregnancy analysis, 36% received a COVID-19 vaccine. Among the unexposed, 95% initiated human milk feeding. Initiation did not differ by COVID-19 vaccination during pregnancy [aPR: 1.01 (1.00-1.02)]. Human milk feeding at 2 months [aPR: 1.02 (0.97-1.07)] and 6 months [aPR: 1.06 (0.98-1.15)] postpartum did not differ by prenatal COVID-19 vaccination. In the postpartum analysis, 26% received a COVID-19 vaccine. The human milk feeding discontinuation rate was 6/1,000 person-days in the unexposed. Discontinuation did not differ by postpartum vaccination [aHR: 1.03 (0.95-1.11)].

COVID-19 vaccination in pregnancy and postpartum were not associated with infant milk feeding practices.

Pharmacoepidemiology

High Prevalence and Variable Duration of Potentially Clinically Relevant Drug-Drug Interactions Among U.S. Nursing Home Residents Laura A. Reich* Laura Reich Adam M. D'Amico Sarah D. Berry Lori A. Daiello Andrew R. Zullo

Background: Nursing home (NH) residents are at increased risk of drug-drug interactions (DDIs) due to multimorbidity and polypharmacy. Despite guidelines discouraging providers from concurrently prescribing medications that lead to DDIs, the extent of exposure to potentially clinically relevant DDIs among U.S. NH residents is largely unknown.

Objective: To determine the prevalence of potential DDIs among NH residents and the proportion of residents' time exposed to these DDIs.

Methods: This observational study included Medicare fee-for-service beneficiaries aged ≥66 years living in NHs with observable prescription drug data in Medicare Part D claims between 2018 and 2020. We calculated the proportion of residents exposed to 91 potential DDIs identified from three expert consensus publications, as well as the proportion of time residents were exposed to each DDI. DDI exposure was defined as at least one day of concurrent use between orally administered medications.

Results: Among 485,251 NH residents, 61.6% were exposed to at least one potential DDI during 272,967 person-years of follow-up. Residents spent a combined 43.9% of their total NH time exposed to at least one DDI. Across the 91 potential DDIs, the median proportion of residents exposed to a DDI was 0.1% (IQR 0.01-2.0%), and residents were exposed to a DDI for a median of 0.04% of their time in the NH (IQR 0.003-1.0%). The most common DDI, "concomitant use of ≥3 centrally acting drugs," was observed in 27.1% of residents, with 14.5% of residents' total NH time spent exposed to the DDI.

Conclusion: Nearly two-thirds of NH residents were concurrently exposed to medications linked to potential DDIs, although the prevalence and exposure time associated with individual DDIs varied considerably. Because DDIs can be harmful even during brief exposure, future research should examine the role of DDI exposure duration on adverse drug events for the most prevalent potential DDIs among U.S. NH residents.

Association between steps per day and mortality in people with and without metabolic syndrome: NHANES 2005-2006 Pardis Parvizi* Pardis Parvizi Shivangi Bajpai Lingsong Kong Amanda Paluch

Background: Metabolic syndrome (MetS) is a constellation of conditions including elevated waist circumference, high blood pressure, elevated fasting glucose, high triglycerides, and low high-density lipoprotein (HDL) cholesterol. Individuals with three or more of these criteria are classified as having MetS, which increases the risk of cardiovascular disease and mortality. Physical activity, including daily step counts, may help mitigate these risks. **Purpose:** To examine the association between daily steps and all-cause mortality among adults aged 40 years and older with and without MetS using data from the 2005–2006 National Health and Nutrition Examination Survey (NHANES). **Methods:** Participants (n=1,041 without MetS; n=1,356 with MetS) aged ≥40 years with valid accelerometer-based physical activity data (≥1 valid day with ≥10 hours of wear time) were included. MetS was classified by meeting at least three of five risk factors using examination, questionnaire, and laboratory data. Daily steps were categorized as <4,000 (reference), 4,000–7,999, 8,000–11,999, and ≥12,000 steps. Mortality status was followed through 2019. Survey-weighted Cox proportional hazards models estimated hazard ratios (HR) for mortality across step ranges, adjusting for age, sex, race, BMI, smoking, and comorbidities. **Results:** Over 12.0±3.7 years of follow-up, 255 deaths occurred in the non-MetS group and 459 in the MetS group. There was a non-linear dose-response relationship, in which higher daily step ranges were associated with less mortality risk in both groups, until plateauing at 8,000 to 12, 000 daily steps. Adults with or without MetS who walked at least 8,000 daily steps had a 60-70% less risk of mortality, compared to adults taking <4,000 daily steps (Table 1). **Conclusion:** Higher daily steps are associated with lower mortality risk in both adults with and without MetS. These findings highlight the importance of physical activity for longevity across all risk groups.

Table 1: Association Between Daily Steps and All-Cause Mortality in Adults With and Without Metabolic Syndrome (MetS) using NHANES 2005–2006

	MetS Group			Non-MetS Group		
Step Ranges per day	n	Deaths / person-years	HR [95% CI]	n	Deaths / person-years	HR [95% CI]
<4,000 (Ref)	237	177/1944	1	101	79/782	1
4,000–7,999	501	186/5904	0.58 [0.48 – 0.69]	296	105/3442	0.64 [0.44 – 0.91]
8,000–11,999	421	73/5480	0.41 [0.29 – 0.59]	377	45/4989	0.28 [0.17 – 0.46]
≥12,000	197	23/2642	0.30 [0.12 – 0.72]	267	26/3588	0.28 [0.14 – 0.55]

Model adjusted for age, sex, race, BMI, smoking, CVD, and cancer.

Policing/Incarceration

Exploring Body Mass Index Changes in Federal Adults in Custody Enid Velez-Valle* Enid Velez-Valle Mitchel Holliday Ellen Smith

The obesity epidemic affects both communities and correctional institutions alike. While previous studies have highlighted disparities in obesity rates based on age, sex, race and ethnicity within correctional settings, there is a limited information on fluctuations in Body Mass Index (BMI) during long-term incarceration. This retrospective analysis included Adults in Custody (AICs) from federal institutions across the United States who began incarceration at any point between January 1, 2018, and December 31, 2021, and who had at least two recorded measures of height and weight within two years of incarceration. BMI was calculated using weight and height and categorized as Underweight (BMI < 18.5), Healthy Weight (BMI 18.5-24.9), Overweight (BMI 25-29.9), Obese Class 1 (BMI 30-34.9), Obese Class 2 (BMI 35-39.9), or Obese Class 3 (BMI 40+). Changes in BMI score from the last to the first measurement were tracked and categorized as a change if they constituted a change in BMI category (No Change, Category Increased, Category Decreased). Information on age, sex, race, ethnicity and education attainment was also collected to identify fluctuations by demographics among the incarcerated population. All analyses were conducted using SAS Enterprise Guide version 8.3. A total of 37,261 AICs were identified and followed for two years. On average, there was no change in BMI score during this period. However, when stratified by category, notable changes emerged. AICs initially in the Underweight category gained weight (81.9%) and those AICs initially in Obese categories lost weight (23.1-34.3%). Significant differences by demographics were observed by race (chi-square ($\chi 2$)=0.017), ethnicity ($\chi 2$=0.049), age group ($\chi 2$=0.013) and education attainment ($\chi 2$=0.003). These findings suggest the need of targeted public health efforts including age, cultural background and educational attainment to support individuals at both ends of the BMI spectrum and reach desired weight outcomes.

LATEBREAKER

Policing/Incarceration

Associations between parent/caregiver incarceration and adolescent health, leveraging universal ACEs screening in Kaiser Permanente Northern California, an integrated health system Joshua Nugent* Joshua Nugent Ilya Moskalenko Wendy Dyer Kevin Su Stacy Sterling Stacey Alexeeff Kelly Young-Wolff

Background: Parent/caregiver incarceration (P/CI) may have detrimental health impacts on adolescents. However, a limitation of prior research is the difficulty of controlling confounding from risk factors such as other adverse childhood experiences (ACEs). To examine the associations between P/CI and adolescent health outcomes, we leveraged unique data collected during routine clinical practice in Kaiser Permanente Northern California on ACEs, including an indicator for P/CI.

Methods: 167,844 adolescents with ACEs screening between 3/1/2021 and 6/30/2024 were included. The exposure was P/CI. Medical and behavioral health outcomes were based on universal self-report data from the Teen Well-Check Questionnaire (TWCQ), along with diagnosis codes and other measures from the electronic health record. Analyses were adjusted for socioeconomic and demographic variables for both the patient and their caregiver, as well as patient responses to the other (non-P/CI) ACE questions. Associations with outcomes were estimated using targeted maximum likelihood estimation with Super Learner, targeting both the average treatment effect (ATE) and average treatment effect in the treated (ATT). P-values were multiplicity-corrected using the Benjamini-Hochberg method.

Results: Risk differences (RDs) are shown in the Figure for unadjusted, ATT, and ATE analyses. The largest significant detrimental associations were observed for P/CI with sexual health measures (e.g. STIs, past-year sex without a condom) and all self-reported substance use measures (e.g. cannabis, alcohol). Physical health, mental health and social/behavioral outcomes showed smaller, varying positive and negative associations depending on the estimand (ATT or ATE).

Conclusion: P/CI is a risk factor for adolescent substance use and sexual behaviors, even after adjusting for other ACEs and measured confounders. Differences between the ATT and ATE estimates demonstrate i) the importance of estimand choice in drawing conclusions and ii) the possibly different risk profiles of those most likely to be exposed. Screening for specific ACEs may provide more relevant risk information than a count of total ACEs and health systems should consider assessment and intervention for specific ACEs risk factors.

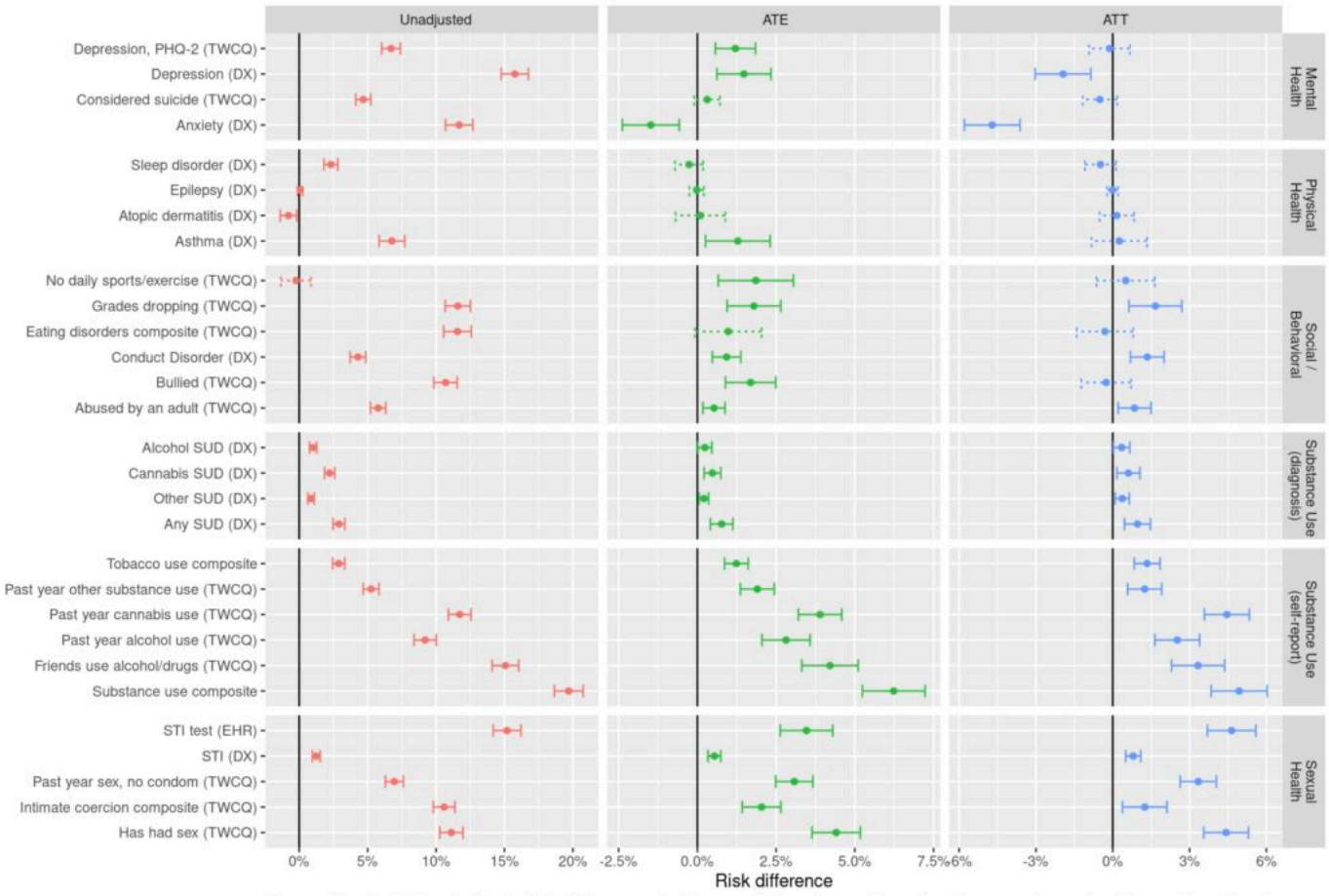


Figure. Unadjusted and adjusted risk differences for the association of parent/caregiver incarceration and adolescent health outcomes. For associations that were not significant after p-value adjustment for multiple testing, the error bars are shown with dotted lines.
Abbreviations: ATE: Average treatment effect; ATT: Average treatment effect among the treated; SUD: Substance use disorder; DX: Diagnosis; TWCQ: Teen well-check questionnaire.

Practice of research

Sounds like a plan: pre-specified analysis plans in epidemiologic research Amanda Irish* Amanda Irish Aayush Khadka Jillian Hebert Whitney Wells Jade Benjamin-Chung Anusha Vable

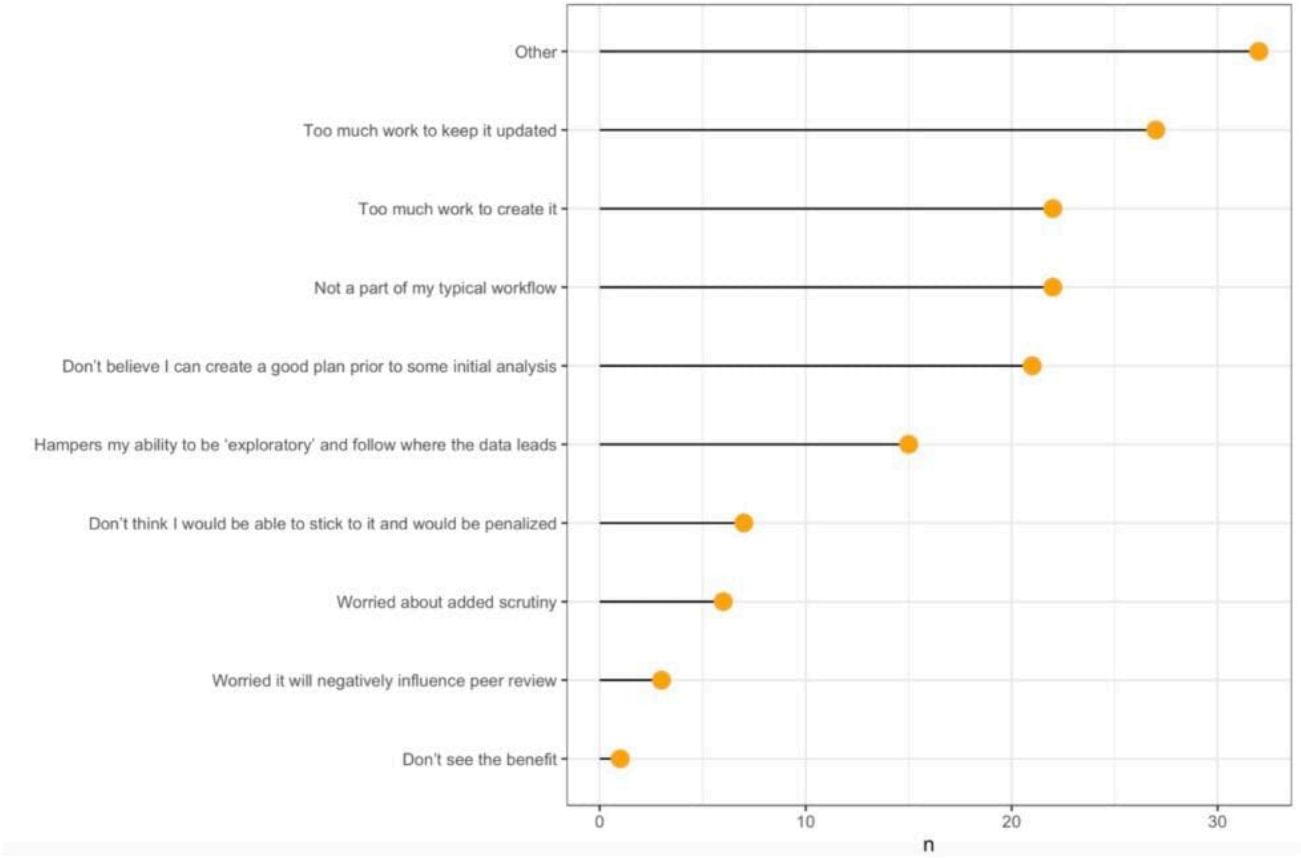
Introduction. Pre-analysis plans (specified prior to beginning analysis) are a valuable component of the research lifecycle, helping to increase reproducibility and transparency and avoid pitfalls such as hypothesizing after results are known, data dredging, and cherry-picking. The use of pre-analysis plans has become standard practice in clinical trials, but has not yet been widely adopted in observational epidemiology.

Methods. We polled a convenience sample (N = 79) of people engaged in epidemiologic research asking whether, how, and why (or why don't) they use pre-analysis plans. We also performed a scoping review to assess the extent to which completing a pre-analysis plan is reported in original research papers in the epidemiologic literature. We searched the full text of research articles in the American Journal of Epidemiology (AJE) published between Jan 2014 to Dec 2023 for terms relating to pre-analysis plans (e.g., "analysis plan", "pre-spec*"). We further restricted to articles that specified using an analysis plan prior to conducting analyses.

Results. Among the 79 respondents to our poll, 32 (40.5%) were faculty, 27 (34.2%) were students or post-docs, and 18 (22.8%) were staff. Most (88.6%) had used a pre-analysis plan at some point; of these, 25.7% reported using a pre-analysis plan for all papers. A minority (29.1%) had seen a pre-analysis plan mentioned when reviewing manuscripts. In our AJE scoping review, of the 2555 research articles published during this period, we found 8 that included their pre-analysis plan either in the main text or linked to the plan, and an additional 7 articles that mentioned using a pre-specified analysis plan but did not include (or link to) the plan itself. Of these 15 articles, 11 were observational studies.

Conclusion. Our poll suggests there is considerable interest in and informal use of pre-analysis plans; however, this has not yet translated into widespread or standardized use in observational epidemiology.

Figure. Responses to the question "What prevents you from using a pre-analysis plan at all or more often?"



N = 79 respondents; note that this question allowed respondents to select all applicable answers. Respondents were also allowed to write in their own responses, which are aggregated into the "other" category in this graph.

Rare Disease

Analysis of U.S. real world data reveals underreporting of Ehlers-Danlos Syndromes (EDS) prevalence and differences in diagnosis between men and women. Chloe Basch* Chloe Basch Janna Manjelievskaia Jennifer Cheng Natalia Coenen Megan Allen

EDS is a collection of connective tissue disorders with symptoms including hypermobility, extreme fatigue, easy bruising, and dizziness. Diagnosis is difficult and prevalence rates of EDS vary at 0.01-0.02%, but are widely believed to be underreported. We hypothesize that EDS is more common than reported in the literature. Our results, using real world data, suggest prevalence is double that of published estimates. We also find that a higher proportion of diagnosed EDS patients are women, yet men are diagnosed earlier. We used data from the Veradigm Network Electronic Health Record database linked to claims to capture EDS patients in 2010-2023. Results were presented by EDS subtype (hypermobile, classical, vascular, other/unspecified, multiple). A total of 107,862 EDS patients were included, representing 0.04% of the database. The most common subtype was other/unspecified (87%), then hypermobile (11%), classical (1%), vascular (<1%), and multiple subtypes (<1%). Mean age was 35 and most were female (83%) and white (72%). Hypermobile EDS patients were younger (mean age 32) and had the highest proportion of females (89%), while vascular EDS had the highest proportion of males (28%) and were older (mean age 40). Further, we report on the most common diagnoses shared by EDS patients. Gender discrepancies in diagnosis are evident, with data showing overall EDS is found in 1 in 5,818 men vs 1 in 1,473 women, yet diagnosis is delayed in women. Time from first clinical symptom to EDS diagnosis was longer for women vs men (mean yrs 4.2 vs. 3.7, p<.0001) and age at diagnosis was older (mean 35.5 vs. 32.2, p<.0001). Most patients with EDS are categorized as other/unspecified, suggesting a lack of knowledge about EDS and lack of available diagnostic tools. In summary, demographic differences by EDS subtype exist and impact the patient journey. Increased awareness about EDS, which affects women in higher numbers and is difficult to definitively diagnose, is needed.

Reproductive

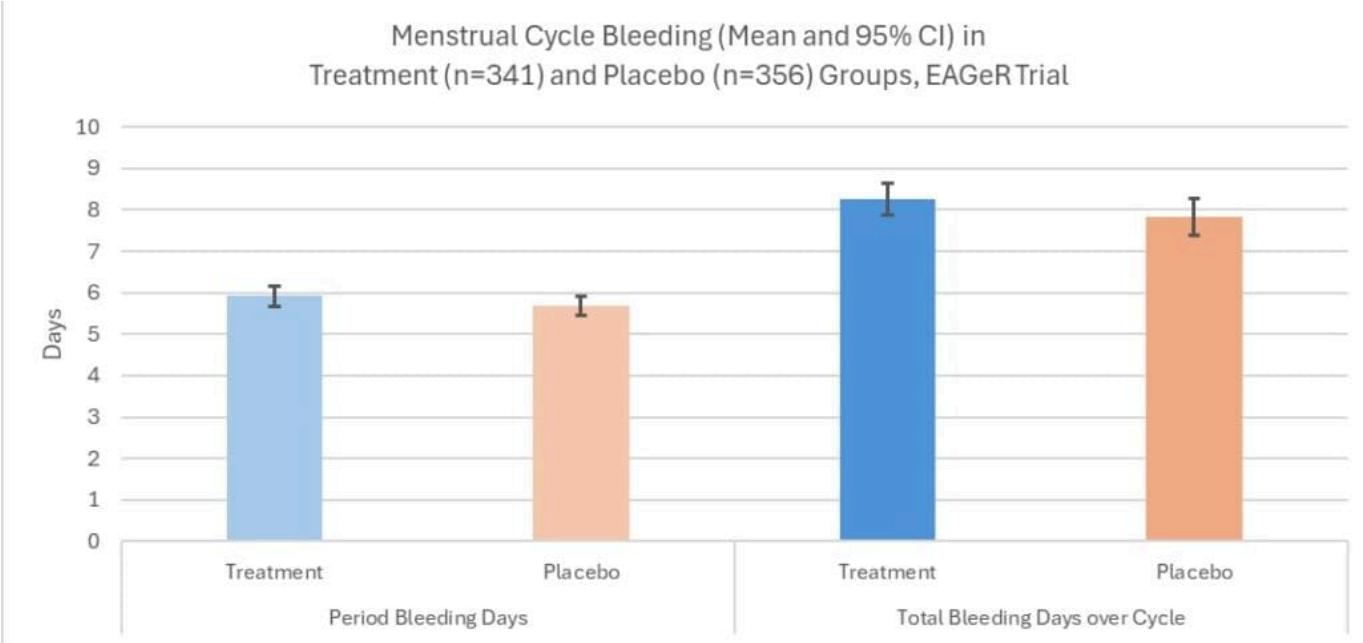
The effect of daily low dose aspirin use on bleeding patterns. Ibironke A. Ajayi* Ibironke Ajayi Maegan E. Boutot Brian W. Whitcomb

Background: The menstrual cycle has been described as a "vital sign" of women's reproductive health and wellbeing. Abnormal bleeding patterns may indicate reproductive abnormalities or other conditions. Low dose aspirin(LDA) is widely used for disease prevention but increases risk of bleeding. There is limited data evaluating the impact of aspirin on menstrual bleeding and its role as a "vital sign" to provide an evidence-basis for clinical recommendations.

Methods: The Effects of Aspirin in Gestation and Reproduction (EAGeR) trial randomly assigned women aged 18-40 years with history of one or two pregnancy losses to LDA treatment (daily 81mg/day aspirin plus daily 400-mcg folic acid) or placebo (daily 400-mcg folic acid). Daily LDA(81mg). For this analysis, two outcomes were compared by treatment assignment: period bleed days (number of menses bleeding days of any intensity allowing no more than 1 bleed free day to define a consecutive bleeding segment) and total menstrual cycle days of bleeding (including bleeding of any intensity and at any time within the menstrual cycle) from the 2nd cycle (defined as the longest string of bleeding of any intensity between days 20 and 50) of follow up, used for completeness of data recorded by participants in daily diaries.

Results: LDA was associated with minor, non-significant higher period bleed days (p= 0.23). Average total bleeding days among the LDA groups (8.2days, 95%CI= 7.9,8.6) were non significantly higher than that in the placebo group (7.8days, 95%CI= 7.4,8.3).

Conclusion: The results do not indicate a significant effect of daily LDA on menstrual cycle bleeding that would compromise the use of bleeding patterns as a "biomarker". Due to the modest sample size, limited participant diversity (95% of total participants were white), and the overall healthy study population, further research is necessary to confirm these findings and assess their generalizability across broader populations.



Reproductive

Examining the Association Between Endometriosis and Cardiovascular Disease: The Role of Race and Age at Diagnosis of Endometriosis Chidinma Oli* Chidinma Oli Shaira Kee Robert Cook

Background: Endometriosis, a chronic gynecological condition, has been associated to an increased risk of cardiovascular disease (CVD). However, little is known about whether this relationship varies by race or how age at diagnosis influences CVD risk. This study aimed to examine if the association between endometriosis and CVD differs across racial groups and whether the age at endometriosis is associated with CVD risk.

Methods: We analyzed data from the National Health and Nutrition Examination Survey (NHANES) 1999–2006 from women aged 20-54 years who reported an endometriosis diagnosis and self-reported history of CVD (congestive heart failure, coronary heart disease, angina, heart attack, or stroke). Age at endometriosis diagnosis was grouped into 13–29 and 30+ years. Race was categorized as Non-Hispanic White and Black. Multivariable logistic regression with stratified analysis was conducted to assess if the association between endometriosis and CVD varies by race, and whether age at endometriosis is associated with CVD risk, adjusting for age, smoking and education.

Results: Among 3,719 women, 320 (10.3%) reported a diagnosis of endometriosis, with a CVD prevalence of 130 (3.3%). Women with endometriosis had a higher prevalence of CVD (6.7%) compared to those without endometriosis (2.9%, $p < 0.0003$). Stratified by race, Black women with endometriosis (aOR = 4.5; 95% CI: 2.0–9.9) and White women with endometriosis (aOR = 2.0; 95% CI: 1.0 –3.9) had higher odds of CVD compared to those without. The mean age at endometriosis diagnosis was 29.1 years (IQR: 22.3, 33.9). Women diagnosed at age 30+ had higher odds of CVD compared to those without endometriosis (aOR = 2.7; 95% CI: 1.4–5.2), while no significant difference was observed for those diagnosed at 13–29 (aOR = 1.8; 95% CI: 0.8–4.1).

Conclusion: These findings emphasize the need to consider race and age at endometriosis diagnosis in assessing CVD risk and highlight the importance of targeted intervention

Reproductive

Concurrent pregnancy and GLP-1 use is on the rise, but interest in outcomes remain sparse

Erin N. Hulland* Erin Hulland Marie-Laure Charpignon Thomas Berkane Maimuna S. Majumder

Glucagon-like peptide-1 receptor agonists (GLP1s) like Ozempic and Wegovy have become household terms nearly overnight, with a recent meteoric rise in internet search popularity in the United States. However, with this rise in interest, there has also been a surge in “off-label” use, described as the acquisition of drugs through means other than via a provider’s prescription or alternate use than that approved by the FDA (e.g. Ozempic for weight loss). This off-label use is often accompanied by a lack of oversight by physicians, sometimes resulting in incorrect dosing, unmonitored sequelae, or other unforeseen effects. One such effect is unintentional pregnancy, as there is increasing evidence of improved fertility among a cohort of GLP-1 users previously facing infertility. Animal trials of Ozempic and Wegovy observed increased rates of miscarriage, fetal anomalies, and fetal demise with GLP1 use during pregnancy; current guidance thus recommends waiting two months after discontinuing GLP1s to get pregnant. Given the recency of the approval of GLP1 use for weight loss, data on such use during pregnancy are sparse, resulting in a dearth of information about pregnancy outcomes; formal cohort studies are ongoing.

Our analysis of Google Search Trends data for GLP1-related terms revealed markedly lower search interest in pregnancy-related GLP1 compared to other common GLP1-related queries for each Ozempic and Wegovy (Fig. 1A & 1B). Importantly, though interest in pregnancy-related GLP1 queries has exhibited noticeable growth since late 2019 (Fig. 1C), it has failed to meet the exponential rate exhibited by interest in Ozempic or Wegovy alone (Fig. 1D). The relative paucity of searches for concurrent pregnancy and GLP1 use echoes the scarcity of studies in this research area. Future research will expand to include other name-brand GLP1 drugs like ‘Mounjaro’ or generics like ‘semaglutide’ and other outcome indicators like ‘birth defects’, ‘miscarriage’, or ‘stillbirth’.

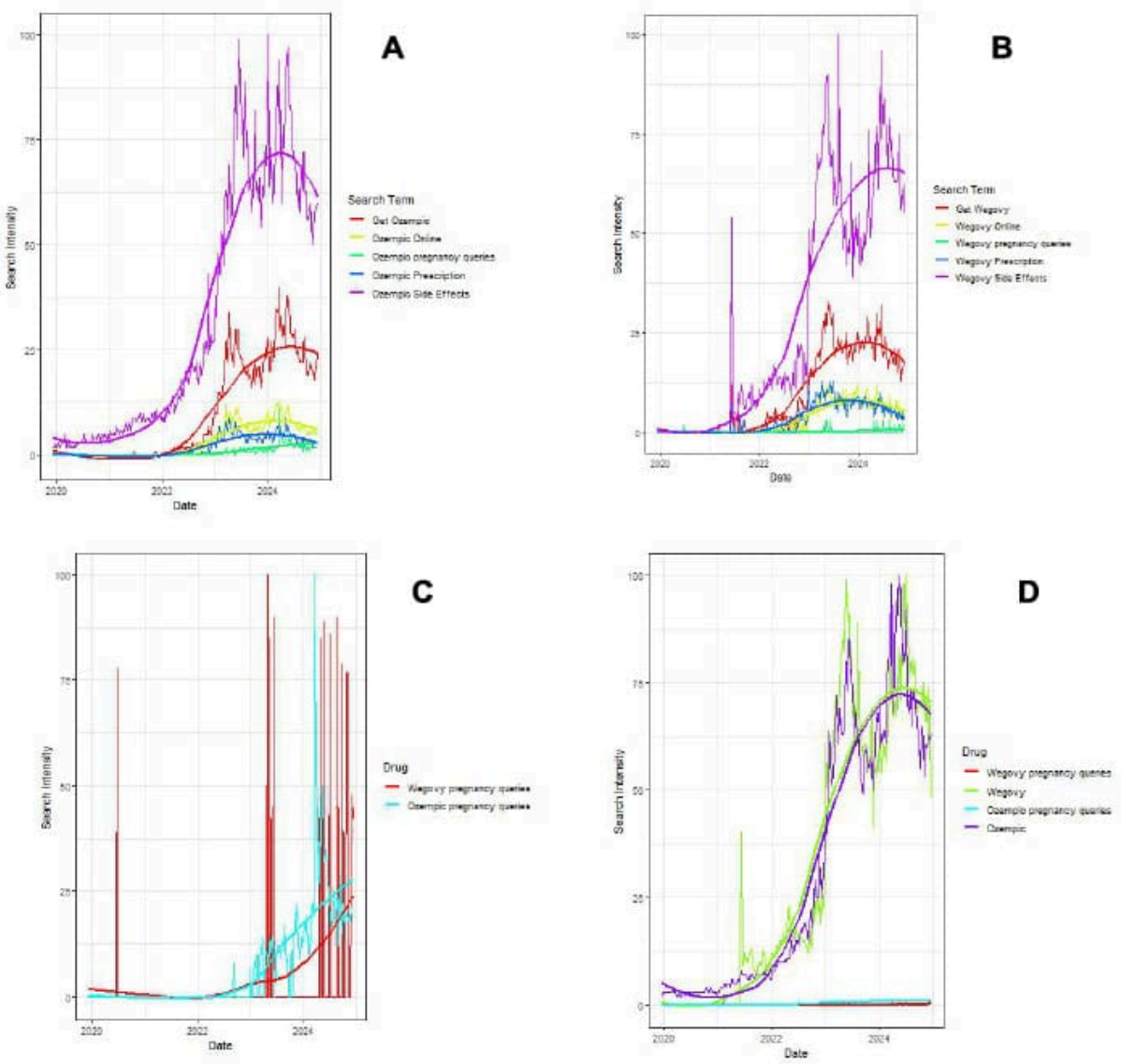


Figure 1: Weekly search interest from Google Search Trends (GST) on key GLP1-related queries between December 12, 2019 and December 11, 2024. Panel A) shows the relative search volume for the queries "Get Ozempic", "Ozempic Online", "Ozempic Prescription" and "Ozempic Side Effects," as well as a combination of search terms related to Ozempic use and pregnancy: "Ozempic pregnant", "Ozempic pregnancy", "Ozempic while pregnant" and "Pregnant on Ozempic". Panel B) shows the results for the same queries, simply replacing "Ozempic" for "Wegovy". Panel C) shows the search interest for the aforementioned pregnancy queries for Ozempic versus Wegovy over time, each queried individually. Last, Panel D) shows the search interest for "Ozempic" overall and Ozempic pregnancy queries taken together, and "Wegovy" overall and Wegovy pregnancy queries taken together. All figures incorporate the raw time series from GST as well as a Loess fit curve showing the trend over time.

Reproductive

The impact of prenatal nutrition interventions including balanced energy protein supplementation on maternal metabolomic profiles in rural Amhara, Ethiopia Unmesha Roy Paladhi* Unmesha Roy Paladhi Nebiyou Fasil Sophie Driker Firehiwot Workneh Kalkidan Yibeltal Alemayehu Worku Yemane Berhane Anne CC Lee

Background
Prenatal nutritional supplementation with balanced energy protein and micronutrients may prevent adverse birth outcomes yet the impacts of such interventions on the maternal metabolome during pregnancy is understudied.

Methods
In a cluster randomized clinical effectiveness trial in Amhara, Ethiopia, we randomized 12 health centers to provide an Enhanced Nutrition Package (ENP: iodized salt, iron folic acid, and for women with mid-upper arm circumference <23cm, a micronutrient fortified balanced-energy protein [BEP]) or routine nutrition care (iron folic acid only). We enrolled pregnant women at <24 weeks gestation and collected maternal whole blood at enrollment and a 3rd-trimester follow-up visit via volumetric absorptive microsampling. We conducted untargeted metabolomics analysis via rapid liquid chromatography-mass spectroscopy. Using logistic regression models, we identified the maternal metabolites that differed between women on ENP vs. non-ENP in trimester 3, post-intervention. Non-singleton births were excluded from these analyses.

Results
From 284 pregnant women, we collected 448 samples (63 in trimester 1, 212 in trimester 2, 173 in trimester 3) and conducted complete case analysis on the post-intervention trimester 3 samples. From the total 38,668 metabolites found in the women, 504 were identified and matched to known metabolites in trimester 3 of which 1 – n-acetylglutamine – was significantly negatively associated with the nutrition package group (FDR<0.1) compared to routine care. Among the subset of women taking BEP, 19 metabolites were identified; they were more likely to have higher levels of acetylaspartic acid and lower levels of 22:6 cholesterol ester compared to those not taking BEP.

Conclusions
Women receiving the nutrition intervention package had lower levels of n-acetylglutamine, which has a role in removing ammonia from the body. Women consuming BEP had higher acetylaspartic acid, which is linked to fetal neuronal development.

Funding Sources: Bill & Melinda Gates Foundation

Reproductive

Evaluating Measurement Error in the Relationship Between Uterine Fibroids and Atherosclerotic Cardiovascular Disease Julia DiTosto* Julia DiTosto Sunni Mumford Jennifer Lewey Jarcy Zee Anuja Dokras Kyle Busse Snigdha Alur-Gupta Stefanie Hinkle Enrique Schisterman Ellen Caniglia

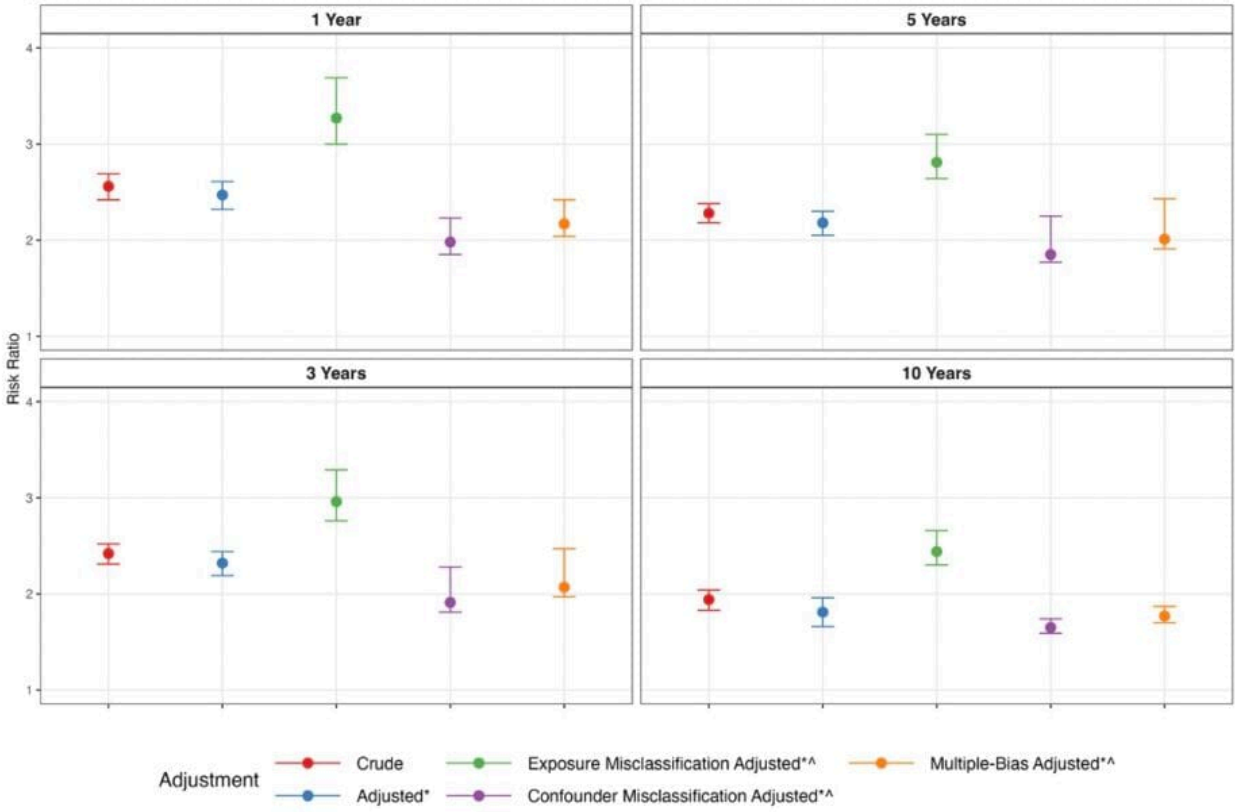
Preliminary claims data suggest that uterine fibroids, a common gynecologic condition, increase the risk of atherosclerotic cardiovascular disease (ASCVD). However, risk estimates may be affected by misclassification.

Females aged 18-50 with uterine fibroids (N=450,177), age-matched to 5 females with gynecologic claims in the same month, were identified in Optum Clinformatics DataMart (2000-2022). Pooled logistic regression models estimated Crude and Adjusted 1, 3, 5, and 10-year RR and 95% CI for fibroids on ASCVD, weighted for baseline confounding, incident fibroid diagnoses in controls, and Optum disenrollment. Probabilistic bias analyses with 1,000,000 simulations addressed measurement error using validation study parameters for misclassification of exposure (fibroids) and a confounder (obesity), assuming non-differential misclassification. Sensitivity and specificity were modeled using beta distributions. Multiple bias modeling sequentially adjusted for biases in reverse order of occurrence and accounted for random error. The distribution median was reported as the point estimate, with the 2.5th and 97.5th percentiles defining 95% simulation intervals (SI). Final estimates were obtained by dividing bias-adjusted RRs by the RR from measured confounding (calculated by dividing the Adjusted by the Crude RR).

The Adjusted RRs before probabilistic bias analyses ranged from 2.46 (1-year) to 1.81 (10-years). Adjusting for exposure misclassification shifted results away from the null (1-year RR: 3.27, 95% SI 3.00, 3.69), while obesity misclassification shifted results toward the null (1-year RR: 1.98, 95% SI 1.85, 2.23). The multiple bias-adjusted RR attenuated the Adjusted RR (1-year RR: 2.17, 95% CI 2.04, 2.42). Analysis results were consistent across timeframes for the 3, 5, and 10-year RRs.

Probabilistic bias analyses for measurement error attenuated results but confirmed the robust relationship between uterine fibroids and ASCVD.

Figure.



*Adjusted models were weighted for exposure to fibroids by race and ethnicity, age (linear + quadratic terms) at entry and baseline values for smoking, obesity, diabetes or medication use, hypertension or medication use, hyperlipidemia or statin use, parity, history of hypertensive disorder of pregnancy, history of gestational diabetes mellitus, polycystic ovary syndrome, infertility or medication use, oral contraceptive use, depression or medication use, anxiety or medication use, cancer, and recent annual physical exam. Time-varying weights were used to adjust for disenrollment and fibroid diagnosis in control group using the same baseline variables and monthly updates of these variables.

^Probabilistic bias analyses using 1,000,000 simulations were conducted for misclassification of the exposure and obesity. We assumed beta distributions for exposure misclassification ($sensitivity \sim beta(\alpha = 56.2, \beta = 27.1)$, with a mean of 67.5%; $specificity \sim beta(\alpha = 1217.9, \beta = 42.9)$, with a mean of 96.6%). We assumed beta distributions for confounder misclassification ($sensitivity \sim beta(\alpha = 36.4794, \beta = 54.719)$, with a mean of 40.0%; $specificity \sim beta(\alpha = 239.5, \beta = 1.69)$, with a mean of 99.3%). 95% CI are presented for the Crude and Adjusted estimates. 2.5th percentile and 97.5th percentile estimates are presented from the simulations.

LATEBREAKER

Reproductive

Mapping traditional birth attendance in sub-Saharan Africa between 2012 and 2023; analysis of data from demographic and health surveys. Daniel G. Belay* Daniel Gashaneh Belay Gizachew A. Tessema Jennifer Dunne Kefyalew Addis Alene Tefera Taddele Theodros Getachew Richard Norman

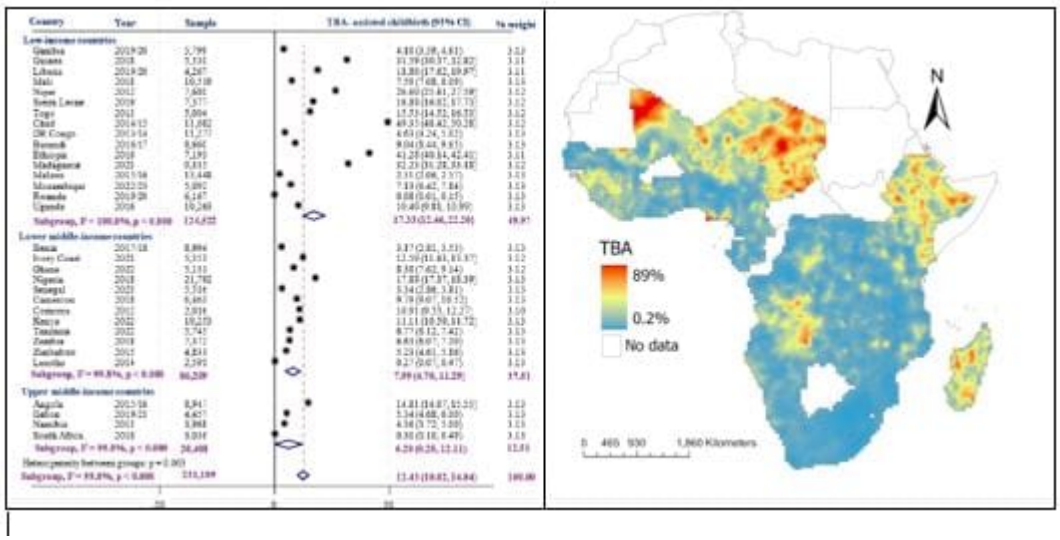
Abstract

Background: Traditional birth attendance (TBA) remains common in Sub-Saharan Africa (SSA), impacting maternal and neonatal mortality rates. This study aimed at producing high-resolution geospatial estimates and identifying predictors of TBA-assisted childbirth in SSA.

Methods: We used the latest Demographic and Health Survey (DHS) data (2012-2023) from 32 SSA countries. Our sample included 231,189 reproductive-aged women who had given live birth to a child within the past five years. A multilevel binary logistic regression model was employed to identify the predictors of TBA-assisted childbirth, accounting for individual, household, and community-level factors. Geospatial analysis identified geographic hotspot areas where TBA is most prevalent.

Result: The proportion of TBA-assisted childbirth among reproductive-aged women in SSA was 12.43% (95% CI: 10.02%, 14.84%), ranging from 0.3% (South Africa) to 49.4 % (Chad). Hotspot clusters of TBA-assisted childbirth were found in Chad, Ethiopia, Madagascar, Guinea, and Niger. TBA-assisted childbirth was associated with women with community low women literacy (AOR=2.82; 95% CI; 2.57, 3.09), low household wealth status (AOR=1.42; 95% CI; 1.34, 1.49), and residing in rural areas (AOR=2.95; 95% CI; 2.68, 3.24) or had major problems with distance from the health facilities (AOR=1.22; 95% CI; 1.17, 1.26).

Conclusion: Significant geographic variation in TBA-assisted childbirth among women in SSA indicates the need for targeted health interventions to improve access to skill delivery services and empower women through financial and literacy initiatives.



LATEBREAKER

Reproductive

Estimation of relative risk of pre-pregnancy BMI on gestational diabetes: preliminary findings from a burden of proof study Sunny Lin* Sunny Lin Ke, Pan Maegan, Dirac

Introduction: Gestational Diabetes Mellitus (GDM) is a condition of hyperglycemia that occurs during pregnancy and increases health risks for pregnant persons and their children during pregnancy and at delivery. The relationship between body mass index (BMI) and the risk of GDM has been widely studied, but few examined the full spectrum of BMI values. The current body of research reflects the prioritization of higher-risk populations but lacks a comprehensive view that summarizes findings across heterogeneous populations.

Method: We conducted a systematic review of studies on pre-pregnancy anthropometric measures and nine pregnancy-related complications, including GDM. We utilized a Bayesian, regularized, trimmed meta-regression approach to test and adjust for study design bias, quantify between-study heterogeneity, and evaluate other potential biases. Employing the burden of proof framework, we summarized the available data to produce estimations of excess risk levels.

Results: We included 29 studies in our preliminary model, which tested the influence of non-representative study sampling, varying case definitions, the adjustment of socioeconomic status and gestational weight gain. Using a BMI of 23 as a midpoint, our model concluded an increased risk of GDM among people with higher pre-pregnancy BMI and a slightly lowered risk among those with lower BMI. The relative risk of GDM for people with a BMI of 18.5, 25, and 30 are 0.76 (0.70, 0.84), 1.40 (1.25, 1.54), and 2.50 (1.83, 3.30).

Conclusion: Our current model supports a dose-response relationship between pre-pregnancy BMI and GDM, even after quantitatively accounting for heterogeneity across studies extracted to date. We anticipate strengthening this evidence further as we incorporate all studies from the completed systematic review. With the escalating global pandemic of obesity, prevention of high BMI would need to be strengthened along with the implementation of strategic screening and control of GDM to ensure safer pregnancies.

LATEBREAKER

Respiratory

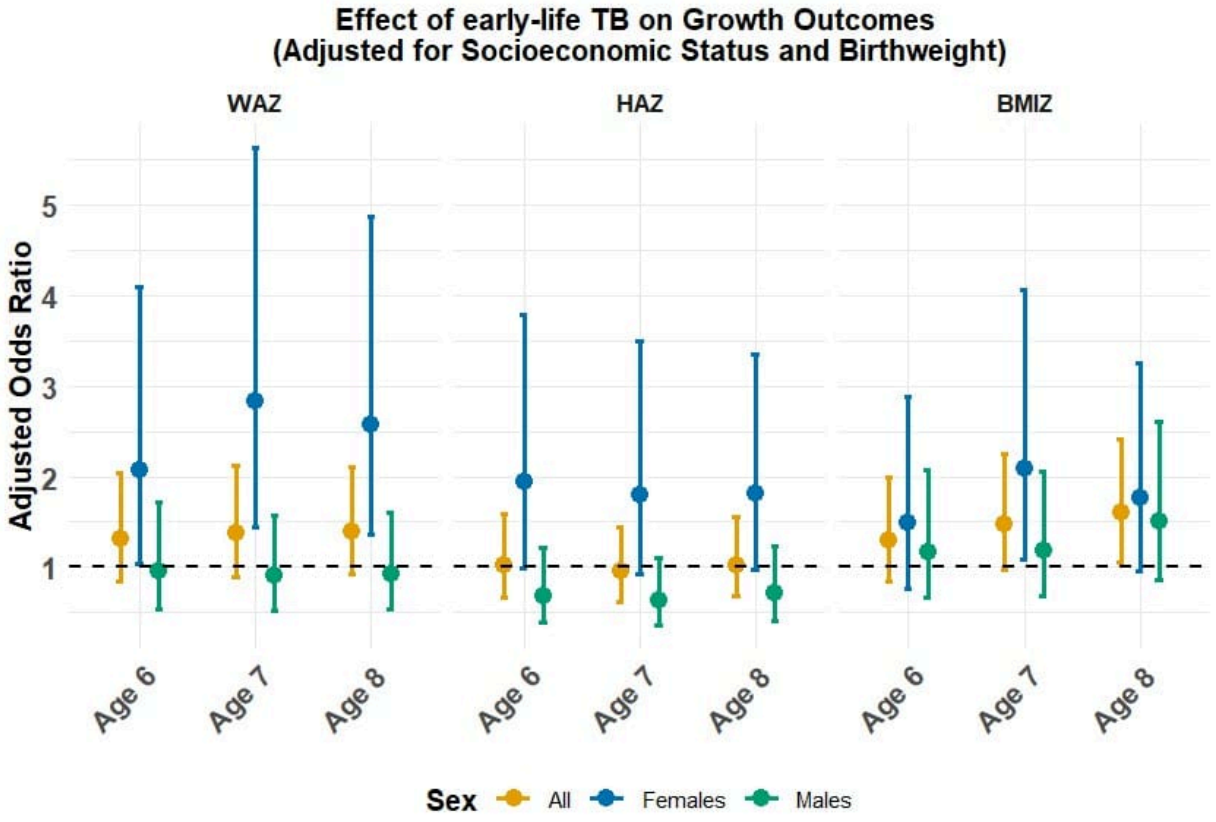
Long-term impact of early childhood tuberculosis on growth Alick Sixpence* Alick Sixpence Mark Nicol Liz Goddard Francesca Little Noëlle Van Biljon Maresa Botha Lesley Workman Heather Zar Leonardo Martinez

Pediatric tuberculosis (TB) remains a global health concern, with 1.3 million cases and 191,000 deaths reported in 2023 among children and adolescents. While TB may have lasting health effects, most studies focus on adults and respiratory outcomes. The impact of early-life TB on long-term child growth remains understudied.

We followed children from the Drakenstein Child Health Study, a South African birth cohort outside Cape Town. Pregnant women were enrolled and followed through childbirth, with their children monitored throughout childhood. TB cases and anthropometric measurements (weight, height) were tracked at multiple time points from infancy to age 8. Z-scores for weight-for-age (WAZ), height-for-age (HAZ), and body mass index (BMIZ) were calculated using WHO growth standards. Growth outcomes at ages 6, 7, and 8 were assessed using proportional odds regression to estimate odds of being in the lowest quartile by TB history.

TB incidence was 1,198 cases per 100,000 person-years over 7,347 child-years. Children with TB history had higher odds of being in the lowest WAZ quartile (ORs: 1.32; 0.85–2.04 at 6 years, 1.38; 0.90–2.12 at 7, 1.39; 0.92–2.10 at 8) and BMIZ quartile (ORs: 1.29; 0.84–1.99 at 6, 1.48; 0.97–2.26 at 7, 1.60; 1.06–2.41 at 8). No effect was seen on HAZ (ORs: 1.03; 0.67–1.59 at 6, 0.95; 0.62–1.45 at 7, 1.03; 0.69–1.55 at 8). Effects varied by sex, with females showing higher odds of being in the lowest WAZ quartile at 6 (OR, 2.07; 1.04–4.10), 7 (OR, 2.84; 1.44–5.63), and 8 (OR, 2.58; 1.36–4.87), whereas effects in males were not observed. A similar pattern was seen for HAZ, with increased risk in females at 6 (OR, 1.94; 0.99–3.79), 7 (OR, 1.80; 0.93–3.49), and 8 (OR, 1.81; 0.97–3.36), while males had lower odds. For BMIZ, the strongest effect was at age 7 in females (OR, 2.09; 1.08–4.07).

Early-life TB led to long-term growth impairment, particularly in females. Preventing TB in early childhood may yield substantial long-term health benefits.


Effect of early-life TB on Growth Outcomes
(Adjusted for Socioeconomic Status and Birthweight)
WAZ
HAZ
BMIZ
Adjusted Odds Ratio
1
2
3
4
5
Age 6
Age 7
Age 8
Sex
All
Females
Males

Respiratory

Impact of the 2020 ‘Gigafire’ on in-hospital mortality among respiratory failure patients in the western United States: an interrupted time-series analysis Katie Feng* Kathleen Lynch Katie Feng Mari Armstrong-Hough

Background: In 2020, the western United States experienced the most extreme wildfire season on record and produced California’s first ‘gigafire’, buring over one million acres and dispersing smoke plumes across the region. Temporal trends suggest hospital admissions coincide with peak wildfire smoke exposure, yet mortality among those with pre-existing respiratory failure remains poorly understood.

Methods: We analyzed acute respiratory distress syndrome (ARDS) and respiratory failure hospitalizations (RF) between January 1, 2017- December 30, 2020 using Premier Hospital Alliance data, and used a high-resolution wildland fire smoke dataset to estimate daily county-level PM2.5 concentrations. We applied an interrupted time-series design, defining the event as September 2020 (the gigafire’s peak smoke intensity; PM2.5 >300 µg/m^3). Mixed-effects logistic regression estimated odds ratios of daily in-hospital mortality during smoke exposure and non-exposure periods, adjusting for seasonal trends (i.e., influenza, COVID-19), patient characteristics (i.e., age, race/ethnicity, gender, BMI, length of hospitalization), and insurance status.

Results: 162 hospitals were exposed to excessive wildfire smoke during the study period; those with ARDS (n=7,588) had a mortality rate (MR) of 47.3%, followed by acute RF (n=483,037; MR 13.9%) and chronic RF (n=7,884; MR 2.6%). During the gigafire smoke event, 1,666 patients (8.9%) died before discharge. In the final adjusted model, the odds of in-hospital mortality increased by 31.6% during the gigafire smoke event (OR 1.32, 95% CI 1.24–1.42) and by 13.2% after the event (OR 1.13, 95% CI 1.12–1.14).

Conclusion: The 2020 Gigafire smoke event was associated with increased in-hospital mortality among respiratory failure patients after adjusting for seasonal trends and patient characteristics, suggesting that exposure to wildfire smoke pollutants may exacerbate acute respiratory distress.

Respiratory

CFTR modulator therapy improves 8-year survival for individuals with cystic fibrosis

Katherine E. Kurgansky* Katherine Kurgansky Joseph M. Collaco Derek K. Ng Catherine Lesko

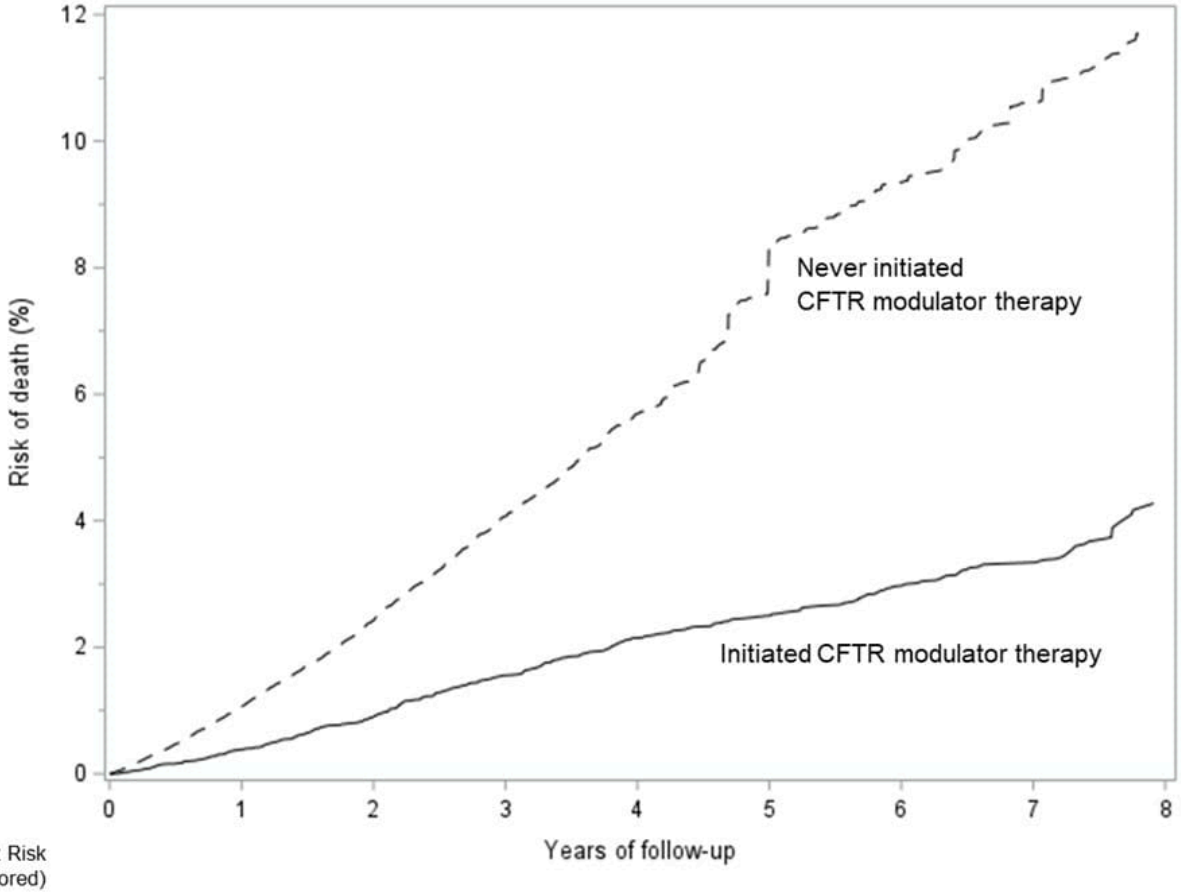
Background: To date clinical trials of cystic fibrosis transmembrane regulator (CFTR) modulator therapies have focused on pulmonary, nutritional, and quality of life outcomes that can be captured within relatively short follow-up periods. The effectiveness of CFTR modulators on survival has not yet been fully described.

Methods: We conducted a retrospective cohort study using data from the United States Cystic Fibrosis Foundation Patient Registry between 2012 and 2022. We included individuals who were eligible to receive an initial prescription for any CFTR modulator therapy (based on age and genotype of 2020 regulatory approvals and no prior use). At every clinic or telehealth visit we assessed eligibility and classified treatment status based on registry records. We included individuals in the analysis multiple times if eligibility was met at multiple visits. We followed individuals from each eligible visit until death (outcome), lung transplantation, loss to follow-up, or administrative censoring. We censored untreated observations if they later initiated a CFTR modulator**.** We estimated 8-year risk curves for each treatment group using Kaplan-Meier and hazard ratios from Cox regression models. We used inverse probability of treatment weighting to balance baseline covariates between treatment groups and inverse probability of censoring weights to account for non-random censoring.

Results: We included 25,103 individuals who attended 178,835 clinic or telehealth visits and were eligible to receive a prescription for CFTR modulator therapy; 18,056 initiated therapy. The 8-year risk of death for initiating a CFTR modulator compared to not initiating was -7.2% (95% CI: -9.6,-4.9) (full risk curves presented in Figure). The overall hazard for death over 8 years was 66% lower after CFTR modulator initiation (HR=0.34; 95% CI:0.28,0.41).

Conclusions: Over an 8-year period, CFTR modulator therapy initiation reduces the risk of death among people living with cystic fibrosis.

Figure. Inverse probability weighted cumulative risk functions based on the Kaplan-Meier estimator for death (from a single imputation) for individuals in the US Cystic Fibrosis Patient Registry who did and did not initiate CFTR modulator therapy between January 2012 and December 2020 with follow-up through 2022



Number at Risk (censored)									
Initiated	18,506 (0)	18,320 (268)	17,995 (430)	13,876 (4,223)	10,518 (3,427)	7,990 (2,562)	5,641 (2,380)	3,620 (2,041)	899 (2,738)
Never Initiated	160,329 (0)	110,213 (51,368)	74,334 (36,787)	47,040 (27,892)	29,357 (17,990)	17,536 (11,980)	9,782 (7,843)	5,451 (4,382)	3,496 (1,974)

Science Communication & Media

Finding Meaning Behind the Numbers: The Importance of Risk Communication in Epidemiology Hannah Mazzotta* Hannah Mazzotta Tony Cappello Alex Liz Best

Historically, scientific communication of epidemiological findings to the general population in a public health context have often been misunderstood and/or blighted by inaccurate information or interpretation. Compliance with public health recommendations and trust in epidemiologists is highly dependent on the scientific community's ability to effectively communicate complex scientific information on exposure and disease risk in a candid and consistent manner. Mistrust and resistance to public health recommendations can often be seen in response to controversial and emerging topics that have been misconstrued in the media, such as the relationship between vaccines and autism, misinformation related to COVID-19, and cell phone use and brain cancer development, among others. While epidemiological research aims to understand the strength of association in health outcomes, conveying the overall meaning and applicability of research results to stakeholders, and ultimately the general public is equally as important. In this presentation, various examples from real epidemiologic consulting work will be presented in order to demonstrate how evidence-based research can be used to communicate the state of knowledge on evolving or emerging epidemiological topics in public health to industry, government, and non-profit stakeholders alike. Examples will include the use of epidemiological principles such as using local data sources or translating national or regional data to local contexts, translating relative risks observed in occupational epidemiological studies to excess absolute risk among the general public, and using a weight of evidence approach to risk assessment. By actively communicating the meaning and relevance of research findings to those outside of the scientific community in a straightforward and evidence-based manner, epidemiologists can help prevent unnecessary fear-mongering and the spread of public health misinformation.

Screening

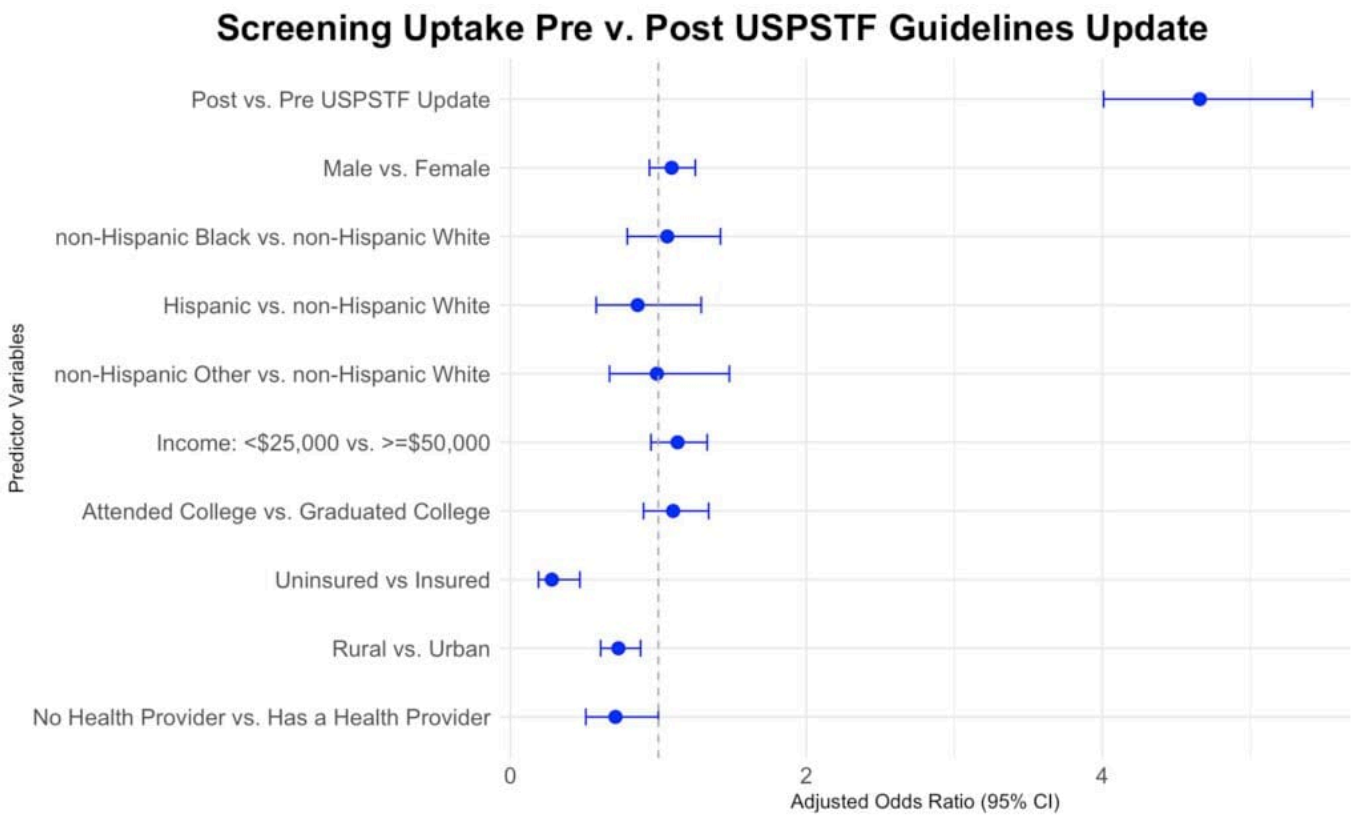
Impact of the 2021 us preventive services task force guidelines update on lung cancer screening adherence: disparities in marginalized and underserved communities LaShae D. Rolle* LaShae Rolle Coral Olazagasti Gilberto Lopes Estelamari Rodriguez Tracy E. Crane

Background: In 2021, the us preventive services task force updated lung cancer screening guidelines, expanding eligibility criteria to include adults aged 50 to 80 years with a smoking history of ≥20 pack-years, compared to the previous criteria of 55 to 80 years with ≥30 pack-years. This expansion aimed to increase access to early detection by including younger individuals and those with a lighter smoking history. Hence, this study evaluated the impact of these changes on screening uptake, with a focus on disparities among marginalized and underserved populations.

Methods: Data from the behavioral risk factor surveillance system for 2019-2020 (pre-guideline changes) and 2022-2023 (post-guideline changes) were analyzed. Multivariable logistic regression models estimated aor for lung cancer screening uptake and accounted for the behavioral risk factor surveillance system' complex survey design. Key predictors included sex, race, income, education, urban/rural status, health insurance, having a health care provider, and being up to date on lung cancer screening (yes/no).

Results: Lung cancer screening uptake increased significantly following the guideline update. The odds of screening were 4.66 times higher post-guideline changes compared to pre-guideline changes (aor = 4.66, 95% ci: 4.01-5.42, $p < 0.0001$). Lack of health insurance coverage (aor = 0.28, 95% ci: 0.19-0.42, $p < 0.0001$), being a rural resident (aor = 0.73, 95% ci: 0.61-0.88, $p < 0.001$) not having a health provider (aor = 0.71, 95% ci: 0.51-1.00, $p < 0.05$) decreased odds of screening compared to their counterparts.

Discussion: The updated us preventive services task force guidelines dramatically increased screening uptake but highlighted disparities among disadvantaged and underserved populations such as those living in rural areas, uninsured, and without a health provider. Targeted interventions addressing geographic and structural barriers are essential to ensure equitable access to screening.


Screening Uptake Pre v. Post USPSTF Guidelines Update
Post vs. Pre USPSTF Update
Male vs. Female
non-Hispanic Black vs. non-Hispanic White
Hispanic vs. non-Hispanic White
non-Hispanic Other vs. non-Hispanic White
Income: <$25,000 vs. >=$50,000
Attended College vs. Graduated College
Uninsured vs Insured
Rural vs. Urban
No Health Provider vs. Has a Health Provider
Predictor Variables
0
2
4
Adjusted Odds Ratio (95% CI)

Social

Indirect effects of receiving a Section 8 housing voucher on the prevalence of psychiatric disorders among boys and girls through aspects of neighborhood affluence and racial/ethnic composition Anna Krasnova* Anna Krasnova Dustin T. Duncan Jeremy Kane Keely Cheslack-Postava Sarah E. Tom Kara E. Rudolph

Background: The Moving to Opportunity (MTO) experiment randomized low-income predominantly Black and Hispanic families in high-poverty neighborhoods to a housing voucher, resulting in moves that changed neighborhood affluence and racial/ethnic composition. Unexpectedly, voucher receipt increased the risk of harmful mental health outcomes among boys but decreased it among girls. We utilized causal mediation to estimate the effect of voucher receipt in 1994-1998 on mental health outcomes in 2008-2010 through aspects of neighborhood racial/ethnic composition and affluence in 2001-2002, stratifying by sex.

Methods: Black and Hispanic adolescents 10-19 years at final follow-up were selected from the MTO. We estimated natural indirect effects of voucher receipt on past-year self-reported: 1) mood disorder, 2) externalizing disorder, and 3) post-traumatic stress disorder (PTSD) through a bundle of mediators, stratifying by sex. Mediators included the proportion of time spent in Census tracts with less than 20% poverty, share of college graduates, share of Black residents, and share of Hispanic residents. We used a recently developed nonparametric, multiply robust estimator.

Results: Voucher receipt increased time living in more affluent and slightly less segregated neighborhoods, which was protective against externalizing disorders, though not statistically significantly so, among boys (RD: -0.03, 95% CI: -0.09, 0.03) and girls (RD: -0.02, 95%: -0.05, 0.02), and mood disorders among girls (RD: -0.01, 95%: -0.04, 0.02). However, among boys, these neighborhood changes explained most of the harmful effect of voucher receipt on mood disorders (RD: 0.02, 95% CI: 0, 0.03).

Conclusions: These findings suggest that voucher receipt had a heterogeneous indirect effect on mental health outcomes through aspects of neighborhood affluence and racial/ethnic composition. (U.S. Census Bureau authorization Project P-7504667: CBDRB-FY24-CES018-008 and CBDRB-FY24-0355).

Social

The socio-economic characteristics and social determinants of health of a South African trans and gender nonbinary cohort Mary Carmody* Mary Carmody Rutendo Bothma Tonia Poteat Audrey Pettifor John Imrie

Background: Socio-economic status (SES) is often measured using individual indicators like education and income, representing possession of valued social and economic resources. This project describes participants' socio-economic environment using structural experiences such as economic, food, and housing insecurity, and neighborhood walkability and safety. This broader SES definition explores differential access to resources (e.g., education, medical care, quality nutrition) as a proxy for the social environment, hypothesizing that this differential access impacts health.

Methods: Baseline data were collected from 670 gender-diverse participants between 2023-2024 in a prospective study in South Africa (SA). Descriptive statistics were calculated for individual and neighborhood-level SES indicators.

Results: The majority of participants (73.9%) identified as Black, were born in South Africa (95.1%), and had a grade 11-12 education (64.0%). Due to purposeful sampling, almost two-thirds (67.2%) were HIV positive. Nearly one-fifth (18.1%) had full-time employment, and a majority (60.7%) reported a monthly income ≤ R499 ($26.6). Half (51.5%) worried about having enough food in the past 3 months, with 22.1% not eating for a whole day on some days. Most participants reported stable housing, with 93.4% having access to water and electricity, but only 11.9% had backup power. Most participants agreed they had access to stores and services within walking distance. Almost half (48.8%) strongly agreed there was a lot of crime in their neighborhood, with 33.7% somewhat agreeing there was too much crime to go outside during the day and 53.6% strongly agreeing there was too much crime to go outside at night. Participants generally described their neighborhoods positively, with many somewhat agreeing that their neighborhood was clean, free from bad smells, had beautiful views, and was free of pollution.

Conclusions: Traditional SES indicators describe participants' SES in one manner, while neighborhood quality and economic security provide additional insights. The cohort appears to have a marginally higher SES than typically found among persons living in rural communities in SA.. Future research should use a broader SES definition to proxy the social environment when examining health behaviors and outcomes.

Social

Creating a Comprehensive Framework for Structural Racism Measurement: Insights from a Modified Two-Phase Delphi Panel Ester Villalonga-Olives* Alisha Crump Yusuf Ransome Wendy Camelo Castillo Ichiro Kawachi Salene Jones Bryce B. Reeve Ester Villalonga-Olives

Aim:

Structural racism is a public health hazard. This study aimed to apply a theoretical foundation for identifying ecological level data that will contribute to developing a novel multilevel and multidimensional structural racism measure for use within Hispanic/Latino and Black communities.

Methods:

The National Institute on Minority Health and Health Disparities framework guided the selection of ecological level indicators for measure development. A content development team (N=4 social epidemiologists) pre-selected 68 ecological indicators from previous literature followed by a two-phase modified Delphi approach. A panel of health inequality experts, community members, economic inequality specialists and psychometricians participated in the process. In the initial Delphi round, indicators were categorized for inclusion, further discussion, or removal. In a subsequent Delphi session, panel members discussed indicators that did not have agreement from the first round and provided additional indicators. The content development team then evaluated these results to create a final selection based on criteria such as appropriateness for measuring structural racism. Lastly, the expert panel reviewed this finalized list and added weights to the indicators according to their importance.

Results:

We identified 71 ecological level indicators. The indicators spanned from educational metrics like high school graduation rates to financial measures such as credit loan access disparities, with economic and housing discrimination indicators receiving a stronger relevance score (Figure 1).

Conclusion:

This work serves as the foundation for a multilevel structural racism measure focused on Hispanic/Latino and Black populations, addressing a gap in epidemiologic research. Next steps include conducting community interviews to validate that selected indicators reflect lived experiences of racism and merging ecological level with individual level indicators to create the multilevel measure.

Figure 1. Results of the second round in-person Delphi panel weighting process

Note: * Bins 1-12 represent the domains within our modified NIMHD framework
** "nan" indicates that the indicator appears in a different category rather than the current bin

Social

Sense of community belonging associated with increased self-rated health and reduced barriers to health care among sex workers in Vancouver, Canada: Findings from 4 years of longitudinal cohort data Kaylee Ramage* Kaylee Ramage Wiebke Bartels Jennie Pearson Kate Shannon Andrea Krüsi Shira Goldenberg

Background: Community belonging is positively associated with general health and negatively associated with unmet healthcare needs. Sex workers often experience marginalization, discrimination, and criminalization, all of which may affect their sense of belonging within their geographical communities; however, this impact on health has not been investigated. Using the Brief Sense of Community Scale (BSCS), we examined the relationship between sex workers' sense of community and their health and healthcare access in Metro Vancouver, Canada.

Methods: Using data from a prospective, community-based cohort study of sex workers (09.2020–02.2024), we separately estimated the associations between the dichotomized BSCS (≥30 vs. <30) on health and healthcare access. We conducted complete case bivariate and multivariable logistic regression using generalized estimating equation modelling, controlling for race, age, education level, sexual and gender minority identity, immigration status, and marital status.

Results: Of 320 sex workers who responded to the BCSC, 55.6% reported moderate sense of belonging in their community at their first available observation. In bivariable and multivariable analyses, higher sense of community belonging was associated with higher self-rated health (aOR:1.29, 95%CI:1.01-1.65), increased access to health services when needed (aOR:3.47, 95%CI:2.19-5.48), and experiencing no barriers to receiving healthcare (aOR:2.02, 95%CI:1.54-2.63).

Conclusion: Higher levels of community belonging are associated with better health and reduced barriers to healthcare among sex workers. Strengths-based interventions which support increased sense of community and recognition of sex workers as community members, such as sex worker-led spaces and venues, may support improved health outcomes and health access for sex workers. Further research is needed to better understand the role of community belonging on health amidst other sources of structural marginalization.

Figure 1. Associations between sex workers' sense of belonging and health and health access outcomes in Vancouver, BC, 2020 – 2024: Unadjusted and adjusted odds ratios (ORs), 95% confidence intervals (95% Cis) and p-values from bivariate and multivariable logistic regression using generalized estimating equations.

Health & Healthcare Access	Unadjusted	Adjusted**
	OR (95% CI)	OR (95% CI)
Good self-rated health	**1.33 (1.05-1.69)**	**1.29 (1.01-1.65)**
Are able to access health services when needed	**2.60 (1.74-3.87)**	**3.47 (2.19-5.48)**
Recently saw a family doctor*	1.05 (0.80-1.37)	1.17 (0.88-1.56)
Have not experienced any barriers to receiving healthcare	**2.02 (1.57-2.59)**	**2.02 (1.54-2.63)**
Have sought care for any health concerns*	0.81 (0.62-1.04)	0.82 (0.63-1.06)

Note. OR = odds ratio; 95% CI = 95% confidence intervals,
*In the last 6 months
**Adjusted models controlled for race, age, education level, sexual and gender minority identity, immigration status, and marital status

Social

Does race moderate the relation between spirituality and well-being? Results from the mid life in United States (MIDUS) study, refresher sample, 2011-2014 Yusuf Ransome* Amparo Oliver Yusuf Ransome José Manuel Tomás

Spirituality is a key social determinant driving public health and wellbeing ecosystem (Ransome, 2020; WHO, 2012). There is evidence about its contribution to overall health and wellbeing (Oliver et al, 2015; Soto-Rubio et al, 2020; Torres et al, 2023) mostly in aging populations. When considering social ethnicity in the overall health-wellbeing measuring some paradoxical results arise. Black-White ratio of flourishing and free of any mental illness shows that more Blacks, before any adjustments for social inequality or discrimination, have better overall mental health than Whites (Keyes, 2007).
We aim to study the moderation or potential different contributions of spirituality to blacks' and whites' well-being.

Methodology
Data from MIDUS R (Midlife in the United States, 2011-2014) comprising 3577 participants aged 23 to 76 (M = 50.5, SD = 14.4), 51.9% females, 82.3% White, 7.7% Black and/or African American was analyzed. A MIMIC model was estimated with Mplus 8.11 using MLR methods analyzing Brief Multidimensional Measure of Religiousness/Spirituality (BMMRS) including spiritual mindfulness, coping styles and daily experiences plus Well-being measured by Ryff's scale with its 6 dimensions (7 items each): Autonomy, Environmental Mastery, Personal Growth, Positive Relations with Others, Purpose in Life, Self-Acceptance.
Results
The MIMIC model was first estimated in the overall sample. This model's fit was good ($\chi^2(29)=516.479$, $p<0.001$; RMSEA=0.08, 90% CI [0.074, 0.086]; CFI=0.941; SRMR=0.037) as it was its prediction of wellbeing ($R^2= .194$). Later this model was tested for ethnicity moderation with a multigroup routine (blacks and whites), with results showing the model did not change by ethnicity.
Discussion
This preliminary study testing model invariance by race provides an unbiased assessment supporting evidence on the similar importance of spirituality on well-being. Thus, spirituality-based initiatives could promote wellbeing in American society with equity.
Keywords: spirituality; well-being; moderation effect; race; MIDUS R survey

Social

The Association Between Racial Stereotypes and Mental Health in Asian Women Bhavana Ganduri* Yvette Cozier Bhavana Ganduri Uyen-sa Nguyen Michael Tang Yifan Xie Hyeouk Ham

Asian Americans (AA) face atypical racial and cultural stereotypes, including the false narrative that all AAs are a high-achieving racial minority that has assimilated well into American society through hard work. We explored this so-called “model minority myth” in relation to mental health in a cohort of AA women. The Epidemiology of Asian Women’s Action for Resilience and Empowerment study is a follow-up of 157 AA women aged 18-59 years (median=26 years) conducted between December 2019 and September 2022. An online questionnaire assessed participant’s experiences of racial and cultural stereotypes using 26 self-report items measuring “negative” stereotypes (e.g., “Someone wanted to date me only because of my race”), and 11 items measuring “positive” stereotypes (e.g., “Asian Americans are harder workers”)”). A summary score was created for each measure and grouped into low, moderate, or high. Self-reported poor mental health was categorized as present (fair/poor) or absent (excellent/very good/good). Logistic regression was used to estimate RRs and 95% CIs controlling for age, education, and body mass index. Thirty-one percent of participants reported high negative stereotype scores (>10; range: 11-24); 35% reported high positive stereotype scores (≥10; range: 10-22); and 39 % reported poor mental health. Compared to women reporting low levels of negative stereotypes, those reporting high levels were more likely to report poor mental health: OR: 2.59 (95% CI:1.07-6.28). Compared to those reporting high positive stereotype scores, the estimates for those reporting moderate and low scores were 0.47 (0.18-1.19) and 1.15 (0.50-2.66), respectively. Our data suggest that racial stereotypes can adversely affect mental health in AAs, although the association between positive stereotype scores and mental health was less clear. Further research is needed to understand the underlying mechanism(s) contributing to this association and to identify needed resources.

LATEBREAKER

Social

Avoidable hospitalizations among mothers by immigration status and admission category: a retrospective cohort study of births in Canada from 1993 – 2017 Rina Lall* Rina Lall Gabriel Shapiro Seungmi Yang

Hospitalizations for ambulatory care sensitive conditions (ACSCs), a group of acute, chronic, and vaccine-preventable conditions, are avoidable with adequate primary care. All immigrants face systemic barriers in accessing health care and utilize primary care less than their native-born counterparts. Factors associated with increased ACSC hospitalizations (e.g., low socioeconomic position, ethnic minority status, lack of health insurance) are also more prevalent among immigrants. However, immigrants are not a homogeneous group. Pre-migratory experiences combined with diverse socioeconomic and ethnocultural backgrounds create a heterogeneous population with distinct needs and health seeking behaviours. Additionally, international migrants in most host countries undergo varying selection and integration according to their migration pathway: economic migrants are chosen for their potential to contribute to the host country's economy, family reunification migrants are admitted to join relatives, and refugees are granted entry on humanitarian grounds. Disaggregating the immigrant population is thus essential to better understand health disparities between immigrants and native-born populations. It is plausible that limited health care access and utilization would translate into delays in diagnosis, management, and treatment of health conditions, which may in turn lead to increased hospital admissions for ACSCs among immigrants. Yet, studies on ACSC hospitalizations are scant and most have addressed those with migrant backgrounds as a single group. This work will examine maternal ACSC hospitalization rates in a nationally representative retrospective cohort of mother-newborn pairs for approximately 6 million births in Canada from 1993-2017. Specifically, we will report trends by delivery year, maternal duration of residence in Canada, and region (province/territory) in avoidable hospitalizations among mothers differentiated by their immigration admission category.

Social

Better understanding the social connection experiences of Americans: a latent profile analysis using the All of Us data set Omar* Omar Pedraza

Humans thrive on meaningful social relationships. Unfortunately, Americans are currently less socially connected than in the past, prompting the U.S. Surgeon General to release an advisory highlighting this as a critical public health issue. The current literature offers multiple, interconnected perspectives on social connection, framing it in terms such as loneliness, social isolation, and belonging. While each conceptualization provides different pieces of insight about an individual's social connection experience, research often focuses on just one or two constructs at a time. Using a broad range of constructs can both help better characterize the social connection experiences of individuals and can help elucidate which of those aspects might be most impactful to intervene on. Therefore, this study employs latent profile analysis to identify distinct profiles of social connection experiences among Americans, using survey data from the National Institutes of Health's All of Us Research Program. Specifically, the Social Determinants of Health survey data asks various questions to assess loneliness, social support, and neighborhood-level social cohesion, among others. The latent profile analysis will identify subgroups of social connection experiences among Americans, which will be cross-referenced with other demographic and neighborhood characteristics data to better understand the conditions that give rise to these experiences. This study aims to deliver critical insights into the dynamics of social connection in the United States, with a potential next step being a comparison of these subgroups concerning their health outcomes.

Social

Social Isolation and Cognitive Aging: Are Operational Definitions Creating a Reproducibility Crisis? Ruijia Chen* Ruijia Chen Dylan Tran Jingxuan Wang Peter T. Buto Erin Ferguson Mary Thoma Scott Zimmerman Ashwin Kotwal Jacqueline M. Torres M. Maria Glymour

A substantial body of research on the impact of social isolation on health has emerged; however, conflicting findings are common, even when using the same data. Discrepancies may arise from methodological choices, including operationalization of social isolation. We conducted multiverse analyses to investigate how varying definitions of social isolation influence associations with cognitive function and decline.

Using the 2010 to 2020 Health and Retirement Study (n=12,975), social isolation was defined using 16 items related to marital status, living arrangements, social interaction frequency, and participation in social activities. We created continuous and binary composite scores for social isolation based on all possible combinations of these items (n=196,587 combinations), using top tertile and quartile cutoffs for the binary definitions. Cognitive function was assessed by the Telephone Interview for Cognitive Status, with scores standardized to baseline mean and SD. Linear mixed-effects models evaluated associations of each definition with cognitive level and decline.

Across all model choices, most models suggested a negative association between social isolation and level of cognitive function: point estimates ranged from very large to close to the null (e.g. associations with binary social isolation measures ranged from -0.31 to 0.01 SD of average difference across all binary social isolation specifications, see Figure). Most models indicated that social isolation was associated with faster cognitive decline (e.g. from -0.001 to 0.03 standard deviations average annual difference across the range of binary social isolation specifications).

While social isolation appears associated with lower levels of cognitive function and faster cognitive decline, the magnitude of these associations varies widely depending on how social isolation is defined.

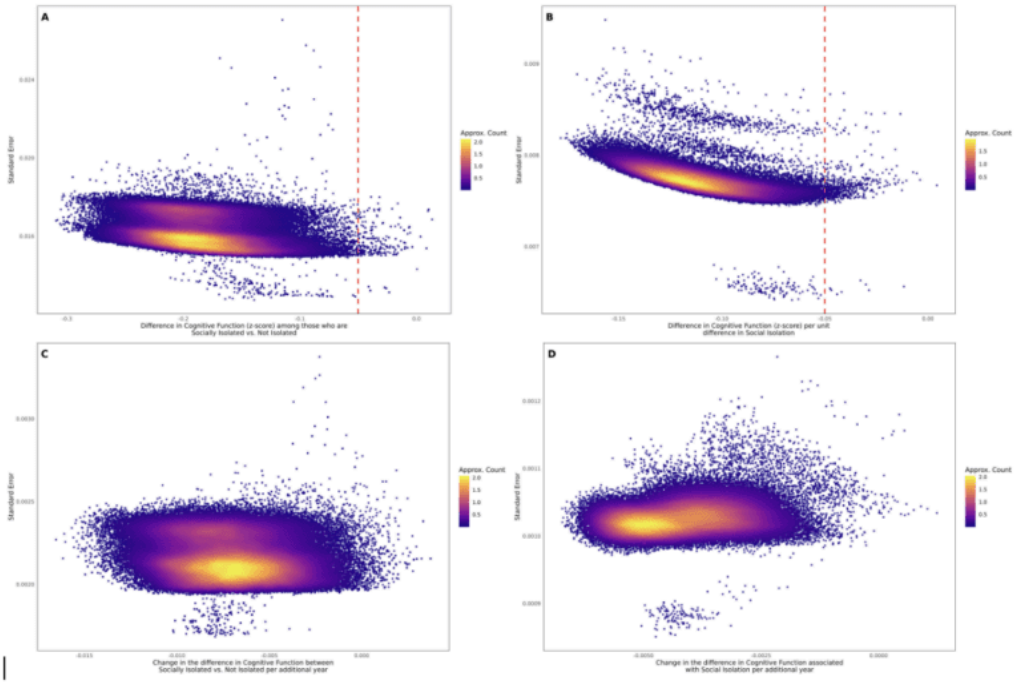


Figure. Scatter plots of the associations of social isolation with level and decline in cognitive function across multiverse analyses. Each dot represents the result of a single model, with the x-axis displaying the estimated coefficients and the y-axis representing the associated standard errors. The top two plots show the estimated coefficients of social isolation in binary (left) and continuous (right) forms for levels of cognitive function. The bottom two plots display the coefficients of the interaction terms between social isolation (binary on the left and continuous on the right) and time. For the models examining cognitive decline, time since baseline was used as the time scale, and models were adjusted for age, sex, race, education, and their interactions with time. The red dashed line represents the average difference in cognitive function scores by age.

Social

Demographic Correlates of Neighborhood Perception Among Mothers of Young Children in Philadelphia, PA Saiido Noor* Saiido Noor Stephanie Mayne

The social-ecological model elucidates the significance of our environment as pivotal factors influencing health. Grasping the underlying mechanics is crucial for our understanding of how social determinants affect health. This study posits that parents of young children with lower educational attainment and household incomes or elevated stress levels are likely to report worse perceptions of neighborhood collective efficacy and safety. These perceptions may in turn negatively impact pediatric healthcare access and child and family well-being. This cross-sectional study employed survey data gathered from October 2019 to August 2020, focusing on mothers or primary female caregivers of children aged 2–4 years and receiving primary care at the Children's Hospital of Philadelphia. The surveys documented sociodemographic attributes, stress levels, and perceptions regarding neighborhood safety and collective efficacy using validated scales. The analyses encompassed chi-square tests and linear regression models. The cohort comprised of 275 caregivers, primarily covered by Medicaid, aged 18 to 45. 50% of caretakers identified as Black, 30% as Hispanic, and 20% as White or belonging to other racial categories. The findings indicated a significant association between lower household income (below $25,000) and reduced educational attainment (highschool or less) with diminished perceptions of neighborhood safety and collective efficacy ($p<0.05$). Elevated stress levels exhibited an inverse relationship with both outcomes. The results highlight the profound influence of sociodemographic variables and stress on the perceptions of neighborhoods held by mothers of young children. Comprehending these perceptions is crucial for assessing their impact on pediatric healthcare accessibility and outcomes, in addition to formulating targeted, community-based interventions aimed at improving neighborhood conditions and tackling health disparities.

LATEBREAKER

Social

The Daily Life Experiences Scale: Factory structure, reliability, and validity for measuring experiences of microaggressions during prenatal care in a sample of Black postpartum women Sarah Haight* Sarah Haight Dawn Misra Lisa Miller Mercedes Price Jaime Slaughter-Acey

Objective: The Daily Life Experiences scale (DLE) measures the frequency of experiences of microaggressions. We assessed the factor structure, reliability, and validity of the scale for Black postpartum women in everyday life and specifically when receiving prenatal care.

Methods: Data were from the LIFE-2 cohort study of Black women delivering in metropolitan Detroit from 2023-2025. The 20-item DLE assessed past year experiences of microaggressions and a second scale (DLE-PNC) asked 17 of those items specifically in reference to prenatal care. Factor structure was determined with exploratory factor analysis (EFA) with a WLSMV estimator and varimax rotation. The correlation between the DLE and the DLE-PNC was calculated with Pearson's correlation coefficient. Internal consistency was determined with Cronbach's Alpha. Convergent and divergent validity were respectively determined using a scale that measured the same concept (Everyday Occurrences of Discrimination scale) and similar, but purportedly unique subscales of the Quality of Prenatal Care Questionnaire [QPNC].

Results: Among this sample of 401 postpartum women, a one-factor model had modest fit for the DLE (RMSEA=0.11; CFI/TLI=0.96/0.96) and the DLE-PNC (RMSEA=0.10; CFI/TLI=0.99/0.98); with stronger fit than higher order models. DLE and DLE-PNC were moderately correlated ($\rho=0.52$) and demonstrated strong internal consistency ($\alpha=0.97$ for both). Convergent validity with the Everyday Occurrences of Discrimination scale was observed for both the DLE ($\rho=0.59$; $p<0.01$) and the DLE-PNC ($\rho=0.40$; $p<0.01$). However, the DLE-PNC was not distinct from the QPNC's support/respect subscale ($\rho=0.40$; $p<0.01$), indicating that the DLE-PNC may not represent a distinct construct from this subscale.

Conclusions: The DLE is a reliable and valid tool for measuring Black postpartum women's experiences of microaggressions in daily life and within the context of prenatal care.

Social

Measuring multidimensional disadvantage of children in Australia using whole-of-population linked administrative data Anna Kalamkarian* Anna Kalamkarian Rhiannon Pilkington John Lynch Murthy Mittinty Catia Malvaso Catherine Chittleborough

Introduction:

Quantifying the size and characteristics of populations experiencing disadvantage is a pre-requisite for informed allocation of prevention resources. We used individual-level linked administrative data on children and their parents to describe the prevalence and distribution of multiple disadvantages that children are exposed to from the 12 months before birth to age 5.

Methods:

De-identified linked administrative data was used from the Better Evidence Better Outcomes Linked Data (BEBOLD) platform on all children born in South Australia between 2004-2011 (n=143,083) in addition to data on their parents.

Eleven domains were created to capture different forms of disadvantage: economic, education, access to services, mental health, substance misuse, smoking during pregnancy, domestic and family violence, health, child protection contact, justice system contact, and parental death.

Prevalence estimates of age-specific disadvantage were measured for each domain over the six-year period. Co-occurrence of the 20 most prevalent disadvantage domain combinations were investigated using UpSet Plots.

Results:

We present multi-dimensional disadvantage using a “dashboard approach,” where the proportion of the population experiencing disadvantage on each possible combination of domains was examined but not combined. One in two children (48%) experienced at least one disadvantage domain, and one in seven (14%) experienced 3 or more disadvantage domains before age 5. Economic disadvantage was most prevalent, affecting 27% of all children, and had high levels of co-occurrence with other disadvantages.

Conclusion:

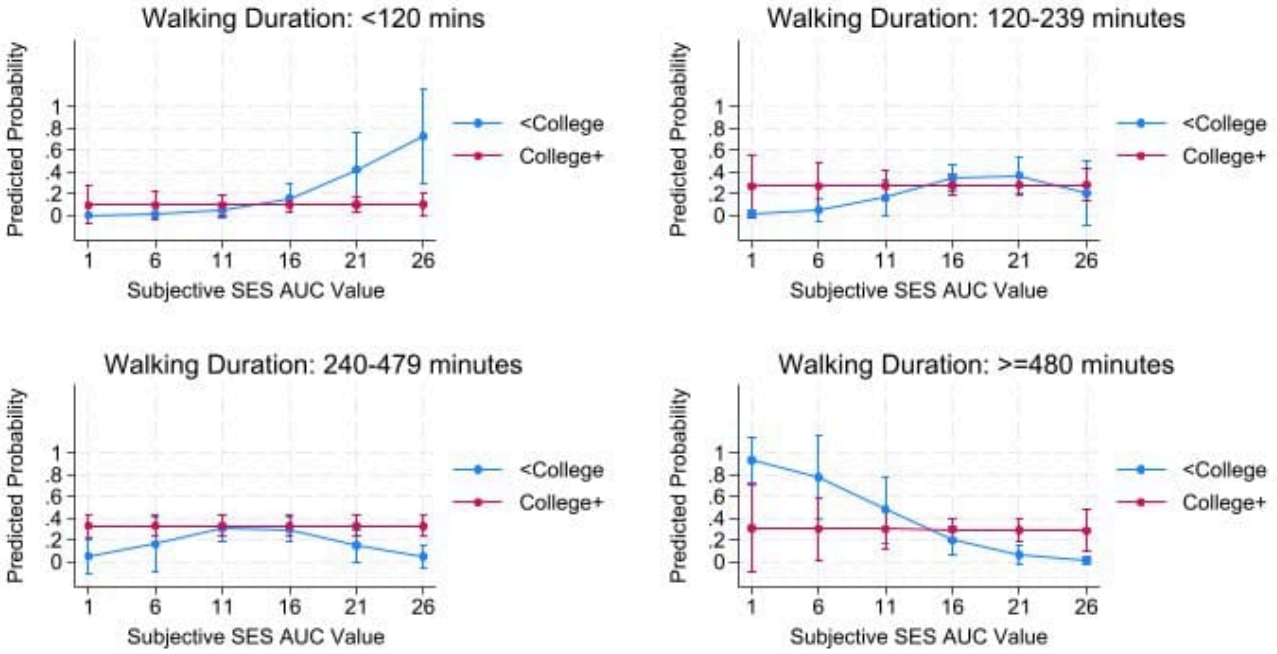
This study demonstrates the potential for administrative data collections to quantify individual-level multidimensional disadvantage. Given the whole-of-population linked data available, this study provides an alternative to the use of area-level disadvantage measures and highlights the experience of multiple disadvantages in families before age 5 in South Australia.

Social

Subjective socioeconomic status before and during pregnancy and prenatal physical activity Julia MP Bittner* Julia MP Bittner Stephen E Gilman Tonja R Nansel Zhen Chen Cuilin Zhang Mary Chong Fabian Yap Jerry Yen Tan Hian Shiao-yng Chan Yap Seng Chong Johan Eriksson Peter Gluckman Michael Meany Bobby K Cheon

Background: Pregnant individuals with lower socioeconomic status (SES) are less likely to meet physical activity guidelines than those with higher SES. Perceptions of one's SES compared to others ("subjective SES") may contribute to socioeconomic disparities in physical activity. We examined associations between subjective SES and prenatal physical activity and whether these associations differed across education levels. **Methods:** Data are from the Singapore Preconception Study of Long-Term Maternal and Child Outcomes (S-PRESTO). Women reported subjective SES before becoming pregnant and in each trimester (range: 1-10; n=102). Preconception-third trimester difference score captured if subjective SES changed after pregnancy. Area under the curve of subjective SES over time quantified how subjective SES changed during pregnancy. Physical activity (International Physical Activity Questionnaire score [IPAQ; inactive, minimally active, health enhancing physically active], weekly minutes walking [never, <120, 120-239, 240-479], weekly minutes of moderate physical activity [never, <150, >150]) was measured in the third trimester. We used ordinal logistic regression analysis to estimate the associations of preconception subjective SES and changes in subjective SES with physical activity. Effect modification by education level was examined. **Results:** Women with higher subjective SES throughout pregnancy had shorter walking duration (OR: 0.75 [95% CI: 0.60, 0.94]) and those whose subjective SES increased after becoming pregnant had a lower IPAQ score (OR: 0.69 [0.50, 0.96]). The relationship between subjective SES and walking duration was observed only among those with less than a college degree. **Discussion:** Contrary to our hypothesis, subjective SES was inversely associated with prenatal physical activity. This may be related to the high cost of car ownership in Singapore; those with higher status may drive for transportation and accumulate fewer minutes of physical activity.

Preconception-Prenatal Subjective SES Area Under the Curve (AUC) and Third Trimester Walking Duration by Education Level



Study Design

Assessing Equity in Pediatric Research Recruitment Using MyChart Amanda Luff* Amanda Luff Cheryl Lefaiver Huma Khan Darci Phillips Ileah Rios Aashima Chopra Yaojie Wang Rachel Zmora Rupali Gandhi Norrina Bai Allen

Background: Traditional recruitment methods often fail to reach diverse populations, limiting generalizability of findings and access to participation. Recruitment is especially challenging with special populations, such as children. The MyChart Recruitment Module offers a streamlined approach to engage pediatric patients and their guardians, but the representativeness of the populations reached is unclear.

Methods: This analysis included pediatric patients, ages 0-18, in a large Midwestern healthcare system contacted via the MyChart Recruitment Module to participate in a study. Interested guardians received a unique code to enroll children using an external platform. We assessed characteristics of children who received recruitment messages, those who engaged with messages (responded interested/not interested), and those who enrolled. We evaluated children's sex, age, race/ethnicity, language preference, and neighborhood traits (median income, adult educational attainment). We used log binomial regression to calculate adjusted risk ratios for 1) engaging with the MyChart message, and 2) among those who engaged, enrolling in the study.

Results: The MyChart message was sent to 123,218 patients, of whom 7,308 engaged (4,709 interested, 2,599 not interested) and 1,313 enrolled. Non-Hispanic Black patients were equally likely to engage as non-Hispanic white patients (RR 1.05, 95% CI 0.98, 1.13) but less likely to enroll (RR 0.75, 95% CI 0.63, 0.89). As age increased, engagement and enrollment decreased. Sex, language preference and neighborhood income were associated with engagement but not enrollment.

Conclusion: The MyChart Recruitment Module is an effective tool to recruit pediatric patients for research and should be used in conjunction with other strategies to ensure equity in research participation. Care should be paid to strategies used at both recruitment and enrollment touchpoints to ensure participation in research is accessible for patients of all backgrounds.

Study Design

Challenges in Evaluating the Impact of CGMs on Racial Disparities: Design Considerations for a Target Trial Emulation using All of Us Data Chloe R. Bennett* Chloe Bennett Robert Cavanaugh Louisa H. Smith

The burden of type 2 diabetes (T2D) disproportionately affects Black people, perpetuating health inequities. Continuous glucose monitors (CGM) improve glycemic control and reduce complications, potentially mitigating racial disparities in T2D outcomes.

This study uses the target trial framework to estimate the effect of CGM initiation on racial disparities in hospitalization. We specified a target trial in which non-Hispanic Black and white individuals with T2D and no prior CGM use are assigned to either initiate CGM use or continue standard monitoring.

We emulated the trial using data from the NIH All of Us Program, which includes electronic health record (EHR) and survey data. 17,507 participants had self-reported T2D, of which 13,360 had EHR data, and 83% of those had a T2D-related code appear in their EHR at any time. To emulate the target trial, eligible participants were 18+ with A1C measurement within 30 days and no CGM use within the past 6 months. 9298 participants met eligibility criteria at least once, 72% of whom were eligible for more than one iteration of the sequential emulated trial. We assessed time to hospitalization after meeting eligibility criteria (time zero).

In naïve analyses, both unadjusted and adjusted for sociodemographic characteristics, white participants consistently had higher hospitalization rates compared to Black participants, and the prescription of a CGM was strongly associated with hospitalization. Adjusting for diabetes-related characteristics and comorbidities reduced the effect estimate by approximately half, but a positive association with CGMs remained. We discuss possible origins of the presumed remaining bias and assess the effects of design choices. Specifically, we discuss definitions of eligibility criteria in survey and EHR data, confounding by indication, differences in monitoring by indication, as well as choices of time zero, a grace period for initiating treatment, and of outcome and censoring definition.

Substance Use

Does Onset of Problematic Substance Use and Externalizing Mental Health Problems Predict Cannabis Vaping Initiation Among U.S. Adults? Findings from the Population Assessment of Tobacco and Health (PATH) Study, Waves 5 and 6 Olatokunbo Osibogun*
Olatokunbo Osibogun Wei Li Ememgini Elo-Eghosa Olufemi Erinoso

Aim: Research has demonstrated that externalizing problems (i.e., aggression and impulsivity) are linked with substance use, including marijuana. However, the emergence of new consumption methods, like cannabis vaping, necessitates a focused examination of their relationship with externalizing behaviors and problematic substance use to identify susceptible groups. This study examines the longitudinal relationships between externalizing mental health problems, substance use problems (SUPs), and the initiation of cannabis vaping among US adults.

Methods: Data was drawn from the nationally-representative Population Assessment of Tobacco and Health (PATH) longitudinal Study Wave 5 (2018/19) and Wave 6 (2021). The analytic sample comprised cannabis vaping naïve adults (18+) at Wave 5 (baseline) who provided cannabis-vaping responses at Wave 6 (follow-up). We used weighted multivariable logistic regression models with adjusted odds ratios (AOR) to estimate associations between the onset of externalizing and substance use problems and the initiation of cannabis-vaping at follow-up (outcome), among adults with no history of these problems at baseline.

Results: The sample comprised mostly males (52.4%; 95% CI:50.2-54.6) and 25.5% (95% CI:23.4-27.7) were young adults aged 25-34 years. Participants who developed high externalizing mental problems had higher odds of initiating cannabis-vaping at follow-up (AOR:2.2; 95% CI:1.6-3.2). Similarly, those who developed moderate (AOR:1.7; 95% CI:1.3-2.3) and high substance use problems (AOR:2.7; 95% CI:1.5-4.8) had higher odds of cannabis-vaping at follow-up compared to those who remained without SUPs.

Conclusion: Our findings suggest interventions targeting externalizing problems and problematic substance use may be crucial for preventing the initiation of newer modes of substance use like cannabis-vaping.

Substance Use

Asking adults About Their Maximum Number Drinks in A single day to Screen for DSM-5 Alcohol Use Disorder – Comparison With Other Screening Strategies Rikki Fan* Rikki Fan Aaron White

Background: Screening adults for alcohol misuse is critical for closing the treatment gap for alcohol use disorder (AUD) in the United Sates. The US Preventive Services Task Force recommends using either the Alcohol Use Disorders Identification Test –Consumption (AUDIT-C) or a single screener developed by NIAAA, which asks how often an adult engaged in binge drinking (4+ for women or 5+ for men) in the past year. Additional research suggests that knowing the maximum number of drinks an adult consumed in a single day in the past year (MaxDrinks) helps identify risk of AUD, as well. Identifying optimal screening questions is important for helping clinicians connect people who need help with appropriate care. Here we compare MaxDrinks to other standard questions for identifying risk of AUD.

Methods: Using data from a large representative sample of U.S. adults (NESARC III), we conducted Receiver Operative Characteristics (ROC) analyses to compare MaxDrinks with AUDIT-C and binge frequency for discriminating AUD of different severities among current drinkers across gender and age groups.

Results. The screening performance of MaxDrinks was comparable with AUDIT-C in discriminating any DSM-5 AUD for both men and women among current drinkers. However, for discriminating moderate and severe forms of AUD, AUDIT-C appeared to perform better. The performance of frequency of binge drinking in discriminating DSM-5 AUD was inferior to MaxDrinks and AUDIT-C. Optimal cutpoints of MaxDrinks for discriminating AUD were higher for men (6 drinks) than that for women (4 drinks), and higher for discriminating more severe forms of AUD. Optimal cutpoints for MaxDrinks were more sensitive to age effects (younger drinkers had higher cutpoints than older drinkers) than AUDIT-C.

Conclusions: Findings support the value of all three simple screeners for identifying drinkers at risk of DSM-5 AUD. MaxDrinks is an ideal single-item screener that could be used in primary care settings to screen for AUD.

Substance Use

Associations of Fentanyl Polysubstance Use Patterns with Hepatitis C Virus and Skin and Soft Tissue Infections Among People Who Inject Drugs in New York City Mehrdad Khezri*
Mehrdad Khezri Sarah Kimball Chenziheng Allen Weng Courtney McKnight Don Des Jarlais

Background: Fentanyl's euphoric effects and short half-life may increase infectious disease transmission risks through frequent injecting and syringe sharing. We assessed whether fentanyl use and polysubstance use (PSU) patterns are associated with hepatitis C virus (HCV) antibody seropositivity and skin and soft tissue infections (SSTIs) among people who inject drugs (PWID) in New York City.
Methods: PWID, recruited using a modified respondent-driven sampling approach from October 2021 and July 2024, were tested for HCV and underwent urine toxicology screenings using the Premier Biotech 13-panel BioCup. Separate multivariable logistic regression models assessed the associations of fentanyl PSU patterns with HCV and SSTIs, adjusting for potential confounders.
Results: Of 502 PWID, the mean age was 48.6 years, and 74.4% were men. The prevalence of HCV antibody seropositivity and SSTIs was 44.6% and 10.4%, respectively. Fentanyl was detected in 82.5% of the sample. The most common fentanyl PSU combinations were with methadone (66.9%), opiates (65.9%), cocaine (64.9%), cannabis (44.8%), heroin (35.1%), benzodiazepines (32.1%), and alcohol (28.9%). Of 119 tested for xylazine, 36.1% co-used fentanyl and xylazine. Fentanyl use was significantly associated with increased odds of HCV seropositivity (aOR 2.28, 95%CI 1.32-4.04). Co-use of fentanyl with cocaine (aOR 2.71, 1.78-4.17), benzodiazepines (aOR 1.82, 1.18-2.81), and alcohol (aOR 2.01, 1.31-3.11) was also associated with HCV seropositivity. Co-use of fentanyl with cocaine (aOR 2.07, 1.03-4.55) and xylazine (aOR 4.57, 1.49-15.5) was associated with SSTIs.
Conclusions: Fentanyl use was associated with HCV and SSTIs. When combined with other psychoactive substances, fentanyl PSU may destabilize PWID and increase the risk for multiple infectious diseases, highlighting the need for tailored medication dosing for opioid use disorder and expanding access to syringe service programs and medical care for PWID in the fentanyl era.

Substance Use

Associations between county-level e-cigarette-inclusive Tobacco 21 law coverage and e-cigarette use behaviors among US adolescents in the Monitoring the Future Study James H. Buszkiewicz* James Buszkiewicz Catherine A. Vander Woude Yanmei Xie Steven Cook Bukola Usidame Megan E. Patrick Michael R. Elliott James F. Thrasher Nancy L. Fleischer

Background: State and local Tobacco 21 (T21) laws vary in their inclusion of e-cigarettes, which may inhibit their ability to reduce adolescent e-cigarette use and related disparities.

Methods: We used national, cross-sectional 2014-2020 Monitoring the Future Study data on US 8th, 10th, and 12th graders. Using grade-stratified, modified Poisson regression models, we examine associations between county-level e-cigarette and any T21 law coverage as a combined, dichotomized measure, E-cigarette T21 laws (100% vs. <100%), and past 30-day e-cigarette use and two-way interactions between these policies and sex, race and ethnicity, parental educational attainment, and college educational expectations.

Results: E-cigarette use was 1.8 percentage points (95% CI = -3.0%, -0.5%) lower among 8th graders, 2.5 percentage points lower (95% CI = -4.5%, -0.5%) among 10th graders, and 2.8 percentage points (95% CI = -5.4%, -0.3%) lower among 12th graders living in counties with 100% versus <100% e-cigarette and any T21 law coverage. We also found differences in these associations by sociodemographic subgroups. Higher (100% versus <100%) coverage was associated with lower e-cigarette use among male 8th, 10th, and 12th graders but not among females. Regarding racial and ethnic differences, we observed the greatest differences in use associated with higher coverage among Hispanic 8th graders and 12th and 10th graders of another race and ethnicity. By socioeconomic status, we found the greatest differences in use associated with higher coverage among 10th graders with at least one parent with a college degree or more and among 12th graders who said they probably will graduate from a four-year college.

Conclusions: E-cigarette T21 laws were associated with lower adolescent e-cigarette use. Our findings suggest that, given current e-cigarette use disparities, T21 laws may widen sex disparities in adolescent e-cigarette use but may narrow some racial, ethnic, and socioeconomic disparities.

Substance Use

Assessing associations between reduction in current substance use and HIV viral load in four diverse study populations using linear mixed models Ryan P. Kyle* Ryan Kyle Robin M. Nance Richard D. Moore Pamina M. Gorbach Brian S. Mustanski Shruti H. Mehta Marianna K. Baum Gregory D. Kirk Steven J. Shoptaw Laura Bamford Katerina A. Christopoulos George A. Yendewa Michael S. Saag Bridget M. Whitney Sonia Napravnik Joseph J. Eron Kenneth H. Mayer Peter W. Hunt Oluwaseun O. Falade-Nwulia Edward Cachay Geetanjali Chander Heidi M. Crane Joseph A.C. Delaney Raul N. Mandler Lydia N. Drumright

Background: Substance use is more prevalent among people with HIV (PWH) than in the general population, is associated with poor health outcomes, and is a barrier to effective care. PWH who use substances are less likely to achieve viral suppression, and are an important focus of efforts to control HIV transmission. Further, reduction, but not cessation, of substance use may be important to harm reduction efforts if it results in better HIV care.

Methods: In longitudinal analyses of data from the CNICS, JHHCC, RADAR, and mSTUDY cohorts, we assessed the association between HIV viral load, and use of methamphetamine, crack/cocaine, illicit opioids, marijuana, and alcohol using two-level linear mixed models to estimate relative viral load as a measure of the relative risk (RR) of exceeding varying thresholds for detection. Models clustered at the study and participant level to account for study heterogeneity and irregular data using an exchangeable correlation structure. All models were adjusted for baseline age, sex, race/ethnicity, study site, as well as time-varying frequency of other substance use.

Results: We identified 11,203 participants with at least two substance use measures. The mean follow-up was 3.8 years, 18% of participants were female, and the mean age was 45 years. Among PWH who reported illicit opioid use, PWH with reduced frequency of use had viral loads 39% lower than those not reporting stable or increased frequency of use (RR: 0.61; 95% CI: 0.39-0.94). Reduction in methamphetamine use was associated with 23% lower viral load (RR: 0.77; 95% CI: 0.60-0.99) on average relative to those with no reduction in current use. Quitting cocaine/crack (RR: 0.95; 95% CI: 0.79-1.15) or opioid use (RR: 0.91; 95% CI: 0.69-1.20) suggested an association with lower viral load. We did not find important associations between viral load and reductions in alcohol (RR: 0.99, 95% CI: 0.94-1.04) or cannabis use (RR: 1.05, 95% CI: 0.95-1.15).

Conclusions: Reduction in substance use over time among PWH was associated with lower relative viral load across all cohorts. As these analyses focused on frequency of use, and reasons for reductions in intensity of use were not explored, future work should also account for reasons PWH limit or cease use of substances, particularly in case of medication-assisted therapy and other interventions.

Substance Use

Exploring the mediating role of maternal functioning on the relationship between subjective stress and loneliness in postpartum individuals with opioid use disorder across acute and prolonged timeframes Arushi Chalke* Arushi Chalke Linnea Linde-Krieger Stacey Tecot Alicia Allen

Introduction: The “fourth trimester” (birth to 12 weeks postpartum) is a critical adjustment period, particularly for individuals with Opioid Use Disorder (OUD). Despite this, there is a lack of research on the links between stress, loneliness, and maternal functioning (ability to take care of self and infant) in this population. We investigated both the direct and indirect effects of stress on loneliness, focusing on maternal functioning as a mediator.

Methods: We enrolled pregnant people with OUD (n=50) and followed them through postpartum month 5. Subjective stress during the first postpartum month was a composite score from the following validated assessments’ total score: Postpartum Stressor Scale, Depression Anxiety Stress Scale, Adverse Childhood Events, and Stressful Life Events. Maternal functioning was assessed via Barkin Index of Maternal Functioning scale, and loneliness via the UCLA Loneliness Scale. SAS 9.4 was used to analyze mediation pathways for loneliness for acute (weeks 4-8) and prolonged (months 3-5) effects.

Results: Composite subjective stress score was significantly associated with maternal functioning (β=-0.55,p=0.002), which, in turn, was significantly linked to acute loneliness (β=-0.34,p=0.002). Maternal functioning mediated 60.8% of the effect of stress on acute loneliness. Stress was also significantly associated with maternal functioning (β=-0.42,p=0.02), which was not significantly associated (p=0.22) with prolonged loneliness, with only 18.8% mediated. For both pathways, the total effect of stress on loneliness was significant (β=0.37,p=0.02; β=0.36,p=0.01).

Conclusion: Maternal functioning’s stronger role in acute rather than prolonged loneliness, highlights the fourth trimester as an ideal time for targeted interventions for individuals with OUD. Future studies should employ larger samples and investigate biological or physiological mediators, such as cortisol levels or sleep patterns, to comprehensively understand stress effects.

Substance Use

Healthy Eating Index Modifies the Association Between Cannabis Use and Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD): A Cross-Sectional Analysis Using NHANES 2017-2018 Zhiyu Wu* Zhiyu Wu Amy Mahar Murray A. Mittleman

Introduction: Prior studies suggest protective associations of cannabis with metabolic dysfunction-associated steatotic liver disease (MASLD). However, the role of diet in modifying this relationship remains underexplored.

Methods: We analyzed NHANES 2017–2018 data. Participants aged 18-59 years were surveyed for cannabis use categorized as never, former, or current. Those missing liver elastography, cannabis data, diet data, and hepatitis B or C positive were excluded (n= 2,496). MASLD was determined using updated criteria and liver stiffness measurements (≥6.8 kPa) to identify clinically significant fibrosis (CSF). We examined the association between cannabis use and MASLD (none, MASLD with CSF, MASLD without CSF) using survey-weighted multinomial logistic regression adjusted for age, sex, self-reported race, BMI, education, and alcohol and included interaction terms for the Healthy Eating Index (HEI) to evaluate effect modification.

Results: The sample included 2,496 participants aged 18-59 (mean = 39 years); 45% never cannabis users, 18% current users, and 37% former users. We found that 65% had no MASLD, 13% had MASLD with CSF, and 22% had MASLD without CSF.

In our adjusted model, the conditional odds ratio (cOR) of having MASLD with CSF compared to no MASLD was:

- Current vs. never cannabis users: cOR=1.32 (95% CI 0.67–2.57, p=0.43)
- Former vs. never users: cOR=1.33 (95% CI 0.84–2.11, p=0.22).

The cOR of having MASLD without CSF compared to no MASLD was:

- Current vs. never users: cOR=1.34 (95% CI 0.60–2.99, p=0.48)
- Former vs. never users: cOR=1.23 (95% CI 0.64–2.39, p=0.53).

Table 1 shows that HEI score significantly modified the association between cannabis use (former vs. never) and MASLD status (MASLD without CSF vs. no MASLD) on the multiplicative scale (cOR 1.23 vs. 0.47 for those with HEI score ≤50 vs. >50, pinteraction=0.002).

Conclusion: HEI scores modify the association between cannabis use (former vs. never) and MASLD without CSF compared to no MASLD.

Table 1

	No MASLD [REF]							
	MASLD with CSF				MASLD without CSF			
	Odds Ratio 1 (Former vs Never Cannabis Use)	95% CI	Odds Ratio 2 (Current vs Never Cannabis Use)	95% CI	Odds Ratio 1 (Former vs Never Cannabis Use)	95% CI	Odds Ratio 2 (Current vs Never Cannabis Use)	95% CI
HEI = 0 (<=50)	1.332	0.840-2.113	1.310	0.667-2.574	1.234	0.638-2.387	1.339	0.600 - 2.990
HEI = 1 (>50)	0.810	0.560-1.172	1.142	0.382-1.715	0.466*	0.299-0.725	1.426	0.488-4.169

* Measure of effect modification on multiplicative scale (95% CI); P. 0.002

LATEBREAKER

Substance Use

Changes in community-level pedestrian stops after opening overdose prevention centers (OPCs) in New York City (NYC): an augmented synthetic control approach. Ignacio Bórquez* Ignacio Bórquez Bennett Allen Cale Basaraba Audrey Renson Brandi Moore Brandon D. L. Marshall Magdalena Cerdá

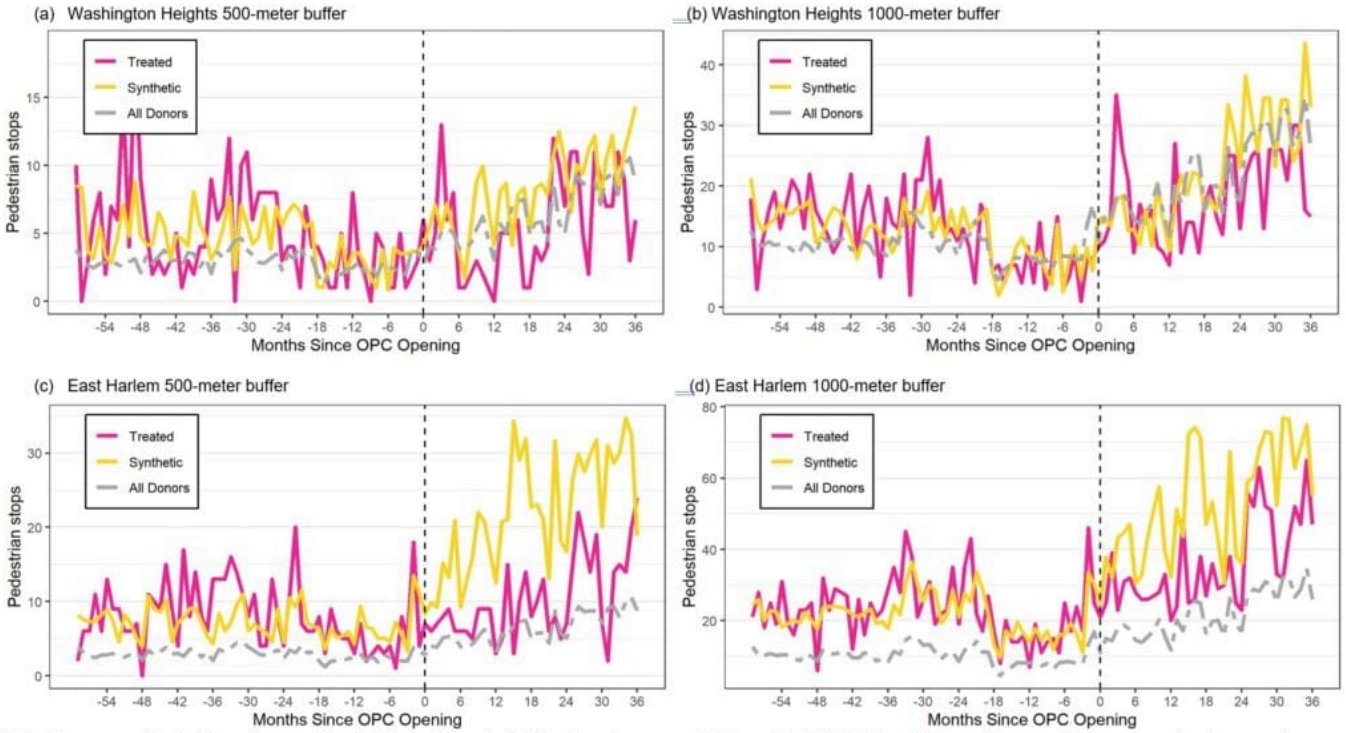
Background: Pedestrian stops are one of the main ways law enforcement enacts population surveillance. In the U.S., people who use drugs have been historically targeted with pedestrian stops. The opening of overdose prevention centers (OPCs) may decrease community-level policing by reducing public drug use. We assessed if opening two OPCs in November 2021 changed pedestrian stop practices in New York City (NYC).

Methods: We retrieved monthly pedestrian stop counts from the New York Police Department from January 2017 to December 2024. We created 500 (n=4,475 events) and 1000-meter (n=5,337 events) distance buffer zones around the two OPCs, using as comparison analogous buffers surrounding active syringe service (SSPs, n=10) and opioid treatment programs (OTPs, n=49). We used augmented synthetic controls to estimate the average monthly treatment effect on the treated (ATT) for each OPC site, both unadjusted and adjusted for covariates obtained from the American Community Survey's 5-year estimates. Permutation tests were employed for hypothesis testing.

Results: For the Washington Heights OPC site, there was no evidence of an effect on the average monthly pedestrian stop counts in both the unadjusted (500 meters: ATT=-0.958, p=0.948; 1000 meters: ATT=-1.093, p=0.724) and adjusted (500 meters ATT=-2.564, p=0.879; 1000 meters ATT=-4.06, p=0.776) models. In the East Harlem OPC site, there was no evidence of an effect on the average monthly pedestrian stop counts when using 500-meter buffers (ATT unadjusted=-12.206, p=0.138; ATT adjusted=-11.724, p=0.172). A decrease in monthly pedestrian stop counts was observed in the 1000-meter unadjusted model (ATT=-39.64, p=0.017), although after adjustment the effect size decreased and was approximately null relative to the available precision (ATT=-16.893, p=0.414).

Conclusion: This study found little evidence of an effect on pedestrian stops after opening two OPCs in NYC. Future mixed methods research should evaluate the effects of OPC implementation on other community-level policing practices affecting people who use drugs.

Figure 1: Augmented synthetic control (adjusted models)[1] for OPC sites using 500 and 1000-meter distance buffers



Note: Donors consist of active syringe services (SSPs, n=10) and opioid treatment programs (OTPs, n=49). [1]Adjusted for: total population; median age; percent male; percent non-Hispanic white; percent non-Hispanic black; percent Hispanic; percent employed; percent over 25 years old with less than high school; median income; median property value; median year of building; percent vacant units.

LATEBREAKER

Substance Use

Behavioral and Demographic Correlates of Cannabis Use Amy R. Mahar* Amy Mahar Murray A. Mittleman Jorge Chavarro

Introduction: Cannabis regulations have been changing at a state level in the United States since 1996. Currently, 24 states have regulations for recreational use, and 38 states for medical use. Past research shows cannabis use is associated with other negative health behaviors. Therefore, we sought to evaluate associations between cannabis use and demographics and other risky behaviors in a contemporary cohort of young- and middle- aged adults. We hypothesized that cannabis use is associated with negative health behaviors such as cigarette smoking, e-cigarettes, and higher alcohol intakes. **Methods:** We conducted a cross-sectional analysis of adults in the Growing Up Today Study (GUTS). The GUTS cohort were offspring of the Nurses Health Study II, and were recruited if between the ages of 9 and 14 in 1996 (n=16,882), with a second wave of recruitment in 2004 among children between the ages of 10 and 17 (n=10,923). We included crude descriptive and multivariable adjusted logistic regression models to evaluate correlates of cannabis use with demographics and other health related behaviors (cigarette smoking, alcohol use, supplement use) which were obtained by self-reported questionnaires. Cannabis use was classified as never, former, or current (use within the past year). We evaluated these behaviors in totality and stratified by sex. **Results**: 10,399 participants had survey data in 2021, and historical cannabis use data to classify them as never (n=5,744), former (n=1553) and current (n=3102) cannabis users. In the adjusted model those with initial enrollment living in the West had higher odds current cannabis among males (OR 1.7; 95% CI:1.3, 2.21) and females (OR 1.32; 95% CI 1.08, 1.61); those identifying as anything other than heterosexual had higher odds of cannabis use among males (OR 2.03; 95% CI 1.61, 2.56) and females (OR 2.99 95%CI 2.60, 3.43). e-cigarette use was associated with higher odds of current cannabis use among males (OR 3.1; 95% CI 2.4, 4.0) and females (OR 2.94; 2.33, 3.71), as was binge drinking among males (OR 2.9; 95% CI 2.30,3.64) and females (OR 2.54 95% CI 2.18, 2.97). **Conclusions**: Cannabis use may be associated with demographic and high-risk health behaviors. Careful consideration should be given when evaluating cannabis use and health effects to properly adjust for confounding.

LATEBREAKER

Substance Use

Exploring the Association between Mental Health Disorder and Substance Abuse Problem for Veterans across the Residential, and Employment Status in the United States: A Cross-sectional Study ADITYA CHAKRABORTY* ADITYA CHAKRABORTY Lagnajita Basu

Purpose: The goal of the study is to explore how serious mental illness and emotional disturbance (SMISED) are associated with substance abuse problem (SAP) for veterans across residential, and employment status.

Methods: Data came from 2021 BRFSS Mental Health Client-Level survey. The cross-sectional study included 885665 participants with a response rate of 60%. We investigated the effect of SAP on the SMISED for veterans across residential, and employment status using univariate and multivariable logistic regression models. The multivariable logistic regression model was performed to account for age, gender, ethnicity, marital status, education level, veteran status, residential status, and employment history.

Results: In the general population individuals with substance abuse problem (SAP) were found to have higher odds compared to their counterparts (AOR=1.21, 95% CI: [1.19, 1.22]). When stratified by the residential status, homeless veterans with SAP were found to have higher odds (AOR=1.19, 95% CI: [1.10, 1.40]) of falling under SMISED category compared to the veterans with SAP who live in private residence (AOR=1.13, 95% CI: [1.02, 1.19]). Unemployed veterans with SAP had higher odds (AOR=1.16, 95% CI: [1.07, 1.26]) of being categorized under SMISED compared to employed veterans without SAP (AOR= 0.98, 95% CI: [0.90, 1.08]).

Conclusions: This study addresses the larger impact of mental health disorder and substance abuse with associated risk factors on the veteran population. Understanding the association can inform targeted interventions, such as employment support programs, housing stability initiatives, and integrated mental health and substance abuse treatment. Policymakers and healthcare professionals can create more effective plans to improve veterans' health and quality of life by addressing these interrelated factors.

Substance Use

Trajectories and predictors of stimulant use among people who use drugs in the fentanyl era Leah Shaw* Seashore (Yu) Li Leah C. Shaw Katie B. Biello Scott E. Hadland Susan G. Sherman Brandon D.L. Marshall Julia E. Noguchi

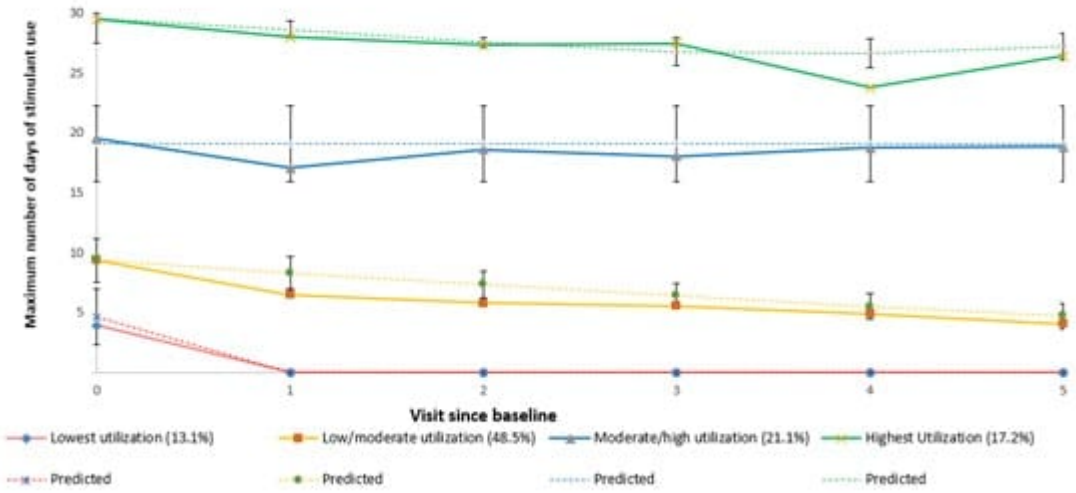
Background: Identification of trajectories and predictors of stimulant use are needed to understand rapidly evolving substance use patterns in the fentanyl era.

Methods: We used data from the Rhode Island Prescription and Illicit Drug Study (RAPIDS) at baseline and 5 subsequent follow-up visits through 12 months. We constructed group-based trajectory models based on the maximum days of any stimulant use in the past month involving four classes of stimulants to identify patterns of drug use among a subgroup of people who use stimulants. Generalized estimating equations (GEE) models were used to identify predictors of trajectory membership.

Results: Of 505 participants analyzed, the median age was 43 (IQR:35-53), almost ⅔ were cis-male and half were non-Hispanic White. Mean days of past-month stimulant use reported at baseline were extra-medical prescription stimulants (3.4); crystal methamphetamine (4.3); powder cocaine (3.9); and crack cocaine (13.1). Trajectory modeling identified four distinct trajectories of any stimulant use: lowest (12%), low/moderate (52%), moderate/high (19%), and highest (17%); Mean days of crack cocaine use were consistently the highest across the four groups (1.9, 8.1, 18.2, 27.7). Figure 1. In adjusted, multinomial GEE models, younger age, past month homelessness, more recent enrollment year (2022-2023), regular fentanyl use in the past month, and anxiety disorder were associated with significantly higher odds of membership in the highest utilization group compared to the low/moderate group.

Conclusion: People who use drugs who are younger, past month homelessness, regularly using fentanyl, and having been diagnosed with an anxiety disorder may be more likely to use stimulants frequently, and therefore may be at higher risk of unintentional overdose due to contamination of fentanyl in the illicit drug supply.

Figure 1. Group-based trajectories of maximum days of any stimulant use in the past 30 days



Teaching / education

Statistical software skills for graduate-level jobs in epidemiology: An analysis of U.S. job posting data Emily Goldmann* Emily Goldmann Ruby Barnard-Mayers M. Maria Glymour Megan A. Healey

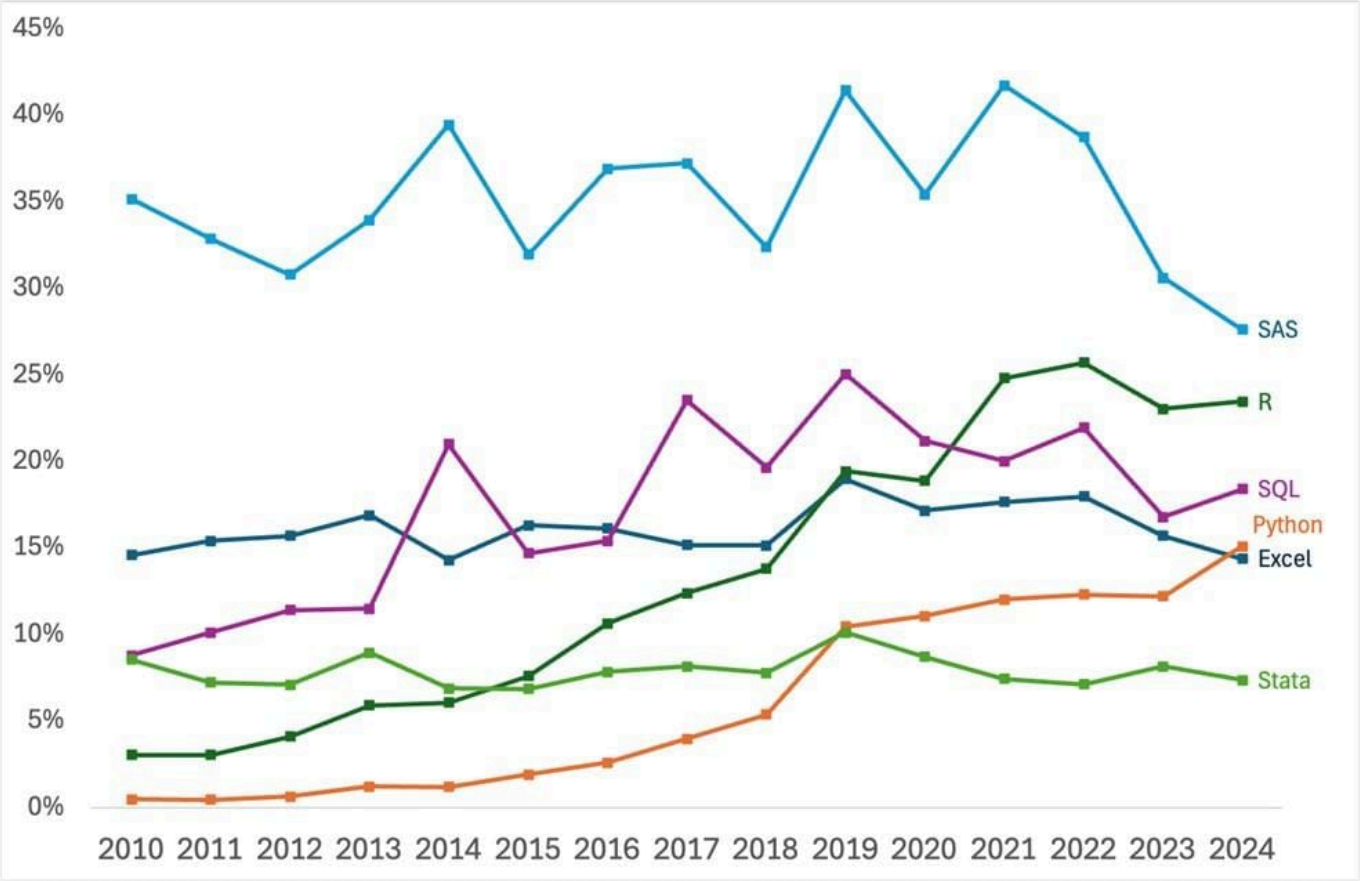
Background. Developing competency in statistical software is a core component of graduate-level epidemiology training. The most useful software packages to introduce in coursework is debated. Identifying the software skills most desired by potential employers may help guide this selection.

Methods. This study used data from Lightcast, a data vendor that collects, deduplicates, and codes job posting data scraped from websites globally. We conducted a search of unique U.S. job postings from January 2010-December 2024 that included a preference or requirement for a master's degree using "epidemiology" as a keyword (n=188,962). We examined yearly trends in the proportion of postings that mention specific software skills, overall and for the five most common job industries represented in these postings (academic 18%, pharmaceutical 11%, hospital 10%, government 9%, insurance 7%). We also analyzed job description text for 500 sample postings to evaluate overlap in demand for SAS Software and R Programming Language skills.

Results. Of the 15,950 unique postings from 2024, SAS was mentioned in the greatest proportion (28%), followed by R (23%), SQL (18%), Python (15%), and Microsoft Excel (14%). Of the 500 job descriptions that mentioned SAS or R (n=139, 28%), 58% mentioned both SAS and R, 29% mentioned SAS but not R, and 13% mentioned R but not SAS. Mentions of SAS decreased in proportion in recent years (Figure 1; from 42% in 2021 to 31% in 2023 and 28% in 2024), while mentions increased from 2010 to 2024 for R (3% to 23%), Python (1% to 15%), and SQL (9% to 18%). In 2024, SAS was the most commonly mentioned software skill in insurance (61%), government (28%), and hospital (22%) postings, while R was most commonly mentioned in pharmaceutical (23%) and academic (21%) postings.

Conclusion. While SAS skills remain frequently desired in epidemiology job postings, R has increased substantially in demand, particularly in academia and the pharmaceutical industry.

Figure 1. Proportion of graduate-level epidemiology job postings that mention specific statistical software, United States, 2010-2024



Veterinary Epidemiology

Paws for Thought: Neighborhood Effects on Canine Cognitive Dysfunction Christopher Pierson* Christopher Pierson Kendra Ratnapradipa Christopher Wichman Elizabeth VanWormer Edward Peters

BACKGROUND: In humans, people from socioeconomically disadvantaged areas are a higher risk of multiple health outcomes, including cognitive dysfunction and dementia. Because humans and pets share their neighborhood, a One Health paradigm would suggest that the neighborhood would have similar effects on both.

PURPOSE: To assess the impact of neighborhood disadvantage (ND) on canine cognitive dysfunction (CCD) and canine dementia.

METHODS: We analyzed data from 9,097 members of the Dog Aging Project (DAP) cohort, a nationally sampled cohort of dogs that annually asks owners to assess their dog's cognitive health and give information about the dog's general health and behaviors. CCD was measured using the Canine Social and Learned Behavior (CSLB) tool, which asks owners whether their dog is displaying behaviors associated with CCD and if those behaviors have increased in the past 6 months. Higher scores indicate increasing cognitive dysfunction and scores greater than 50 indicate a dog with dementia. The Area Deprivation Index (ADI) score for the dog's primary block group of residence was used as the measure for ND. We employed longitudinal logistic and linear regression models to examine the relationship between ND and CCD, adjusting for age, breed purity, rurality, and owner's income and age.

RESULTS: After adjustment, a 10 percentile increase in ADI was associated with a 0.04 unit decrease in CSLB score ($p < 0.05$). However, no relationship was observed between ND and dementia diagnosis.

CONCLUSION: While our findings suggest that ND is protective against cognitive dysfunction, the small effect size and lack of relationship between ND and dementia diagnosis suggests that the relationship may not be clinically relevant. The discrepancy between these results and known effects in humans warrants further investigation to deepen our understanding of neighborhood impacts on animal health and inform research into its impact on other health outcomes.

Women’s Health

Multimorbidity Burden, Physical Health Perception and Self-Efficacy Kristyne D Mansilla Dubon* Kristyne Mansilla Dubon Edward Peters

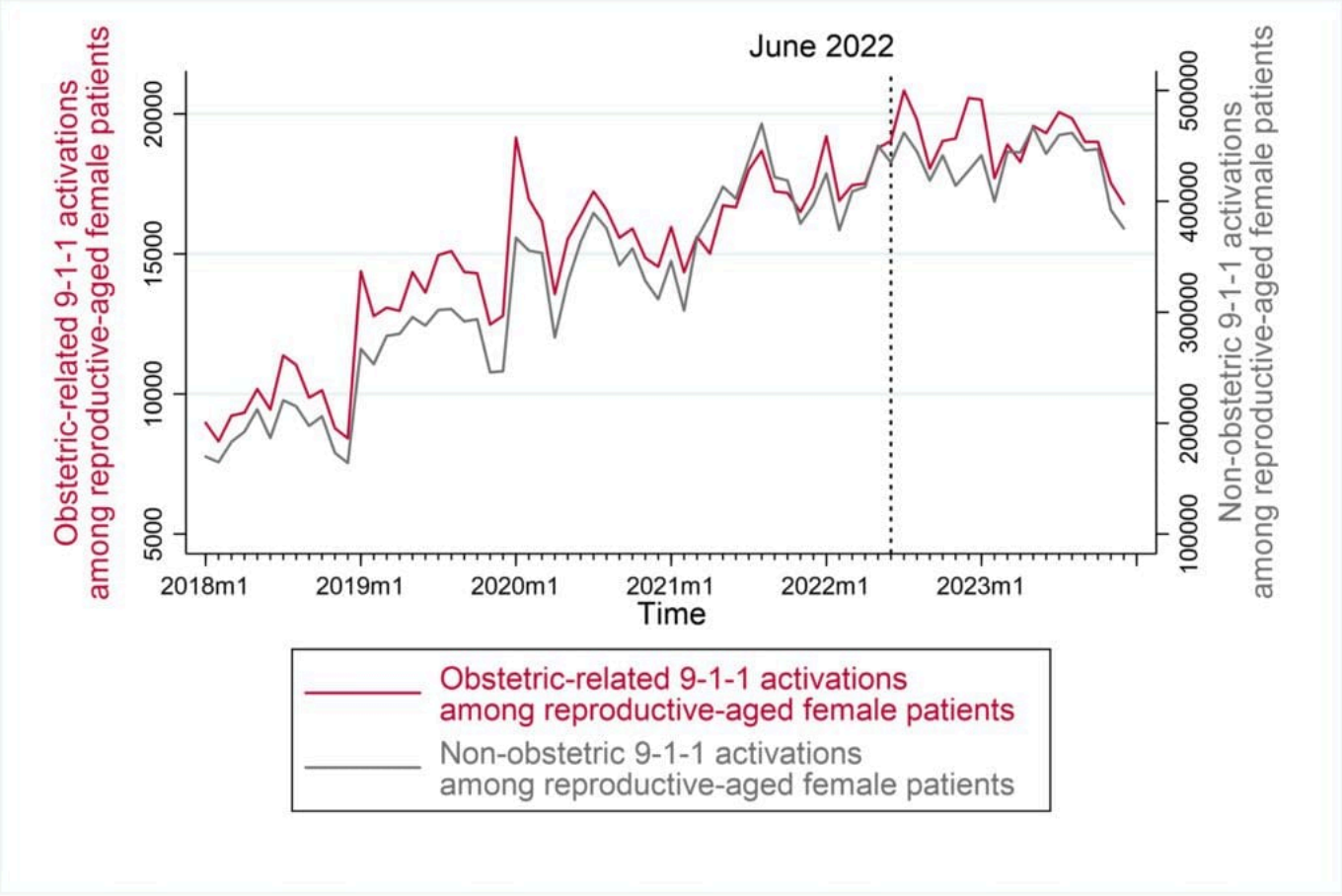
Multimorbidity is the presence of ≥2 chronic conditions in an individual and is increasingly common with the growing burden of chronic diseases. Multimorbidity is associated with premature death, poor quality of life, and declined physical function. We aimed to describe the overall multimorbidity burden and to examine the relationship between multimorbidity and self-rated physical health as well as the relationship between multimorbidity and self-efficacy. In this cross-sectional study, we used data from the prospective cohort of women, The Women and Their Children’s Health (WaTCH) conducted in southeast Louisiana from 2012-2014. We constructed our measure of multimorbidity by counting all chronic diseases participants reported. We captured self-rated physical health with a single item that asked individuals to rank their health as poor, fair, good, very good, or excellent. Each response had a score of 1-5, with the highest score indicating poor health. To measure self-efficacy, we used the 10-item General Self-Efficacy Scale, the total score ranges between 10-40, with a higher score indicating a greater sense of self-efficacy. We conducted descriptive analyses to describe overall multimorbidity and Poisson regression models to evaluate the relationship between multimorbidity, self-rated physical health and self-efficacy. We observed that of 2369 women who reported a chronic condition, 1502 (62%) had at least 2 chronic conditions. The mean number of chronic conditions per participant was 1.87 (SD: ±1.5) with a range of 0-15. The mean multimorbidity count was 2.95 (SD: ±1.3) with a range of 2-9. The most common condition found in women with multimorbidity was obesity (n=825, 59%). After adjusting for confounders, we observed positive associations between multimorbidity and self-rated health. (RR:1.1 95% CI:1.073-1.12), as the multimorbidity count increased, the self-rated physical health score increased. We also found that multimorbidity and self-efficacy had positive associations, (RR:1.1 95% CI:1.073-1.12), as the multimorbidity count increased, the self-efficacy score increased. In our study, we found that more than half of the women who reported a chronic illness had at least 2 chronic conditions. We observed that multimorbidity may affect the perception of health and, in contrast, may improve the sense of self-efficacy.

Women's Health

9-1-1 activations among reproductive-aged women following the Dobbs decision in the US

Parvati Singh* Parvati Singh Jonathan R. Powell Maria F. Gallo Payal Chakraborty Colleen Reynolds Morgan Anderson Parvati Singh

The United States Supreme Court's Dobbs v. Jackson Women's Health Organization decision in June 2022 may have preceded a surge in 9-1-1 activations for obstetric-related conditions. We used time-series analysis to examine whether the Dobbs decision corresponded with a proximate increase in obstetric-related 9-1-1 activations among reproductive-aged (15-49 years) female patients using national, monthly data from January 2018 to December 2023. Monthly national counts of obstetric-related emergent 9-1-1 activations with patient contact from January 2018 to December 2023 were retrieved from the National Emergency Medical Services Information System (NEMSIS) dataset. Monthly series of non-obstetric 9-1-1 activations among reproductive-aged female patients and all other 9-1-1 activations served as controls. Analysis was also stratified by three state groups per restrictiveness of state abortion policies (protective, mixed, and restrictive) within the first 3 months post Dobbs. A binary indicator of June 2022 with 0-to-3-month lags served as the exposure. Results from time series analysis showed 914 additional 9-1-1 activations for obstetric-related conditions one month following the Dobbs decision. States with protective abortion policies accounted for a about 50% of the national increase. Findings indicate an immediate surge in obstetric-related 9-1-1 activations following the Dobbs ruling, primarily in states with protective abortion policies.



Women’s Health

Contraceptive Effectiveness of Levonorgestrel Implant and Depot Medroxyprogesterone Acetate Injectable for Women Living with HIV on Dolutegravir-based Antiretroviral Therapy Katie R. Mollan* Katie Mollan Brian W. Pence Daniel Westreich Agatha Bula Clara Lemani John Chapola Sam Phiri Jane Chiwoko Michael G. Hudgens Lameck Chinula Mina C. Hosseinipour Karen Diepstra Jennifer Winston Jill M. Hagey Mackenzie Cottrell Michele Jonsson Funk Audrey Pettifor Jennifer H. Tang

Introduction: In Malawi, dolutegravir (DTG)-based antiretroviral treatment (ART) is broadly prescribed to treat HIV. Highly effective contraceptive methods are crucial for the health of women living with HIV (WLHIV). Herein, we compare the typical-use effectiveness of two common contraceptive methods, levonorgestrel (LNG) implant and Depot-Medroxyprogesterone-Acetate (DMPA) injectable, for WLHIV on DTG.

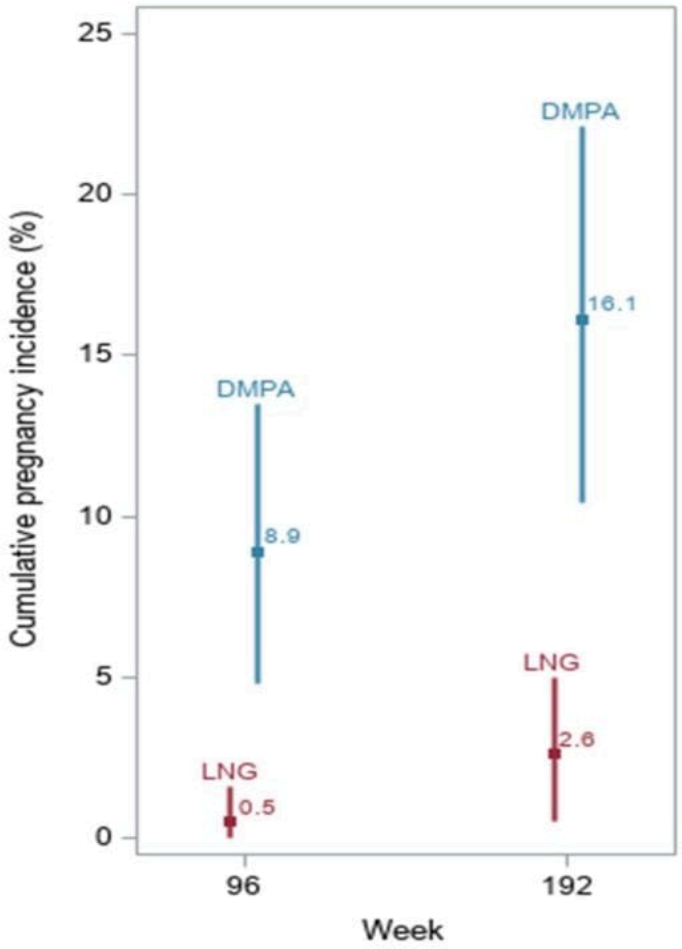
Methods: We analyzed a prospective cohort study conducted in Lilongwe, Malawi (2017-2021). Eligible participants were WLHIV ages 18-40 years who desired to not become pregnant for 4+ years and chose to initiate LNG implant or DMPA injectable 0-28 days before study enrollment. Incident pregnancies were measured by urine pregnancy testing and reported pregnancy diagnoses at study visits every 24 weeks. Analysis follow-up began at contraceptive initiation with right-censoring at the earliest of study dropout, 2+ consecutive missed visits, or no longer using LNG/DMPA contraception. The parametric g-formula was applied to estimate the contraceptive effectiveness of LNG implant vs. DMPA injectable if the entire study cohort used DTG-based ART throughout and everyone completed follow-up. Typical-use effectiveness was measured without requiring DMPA compliance.

Results: 1,359 eligible participants were enrolled and contributed 2,575 person-years (PY). At enrollment, median age was 30 (IQR: 26, 34) and 63% were lactating. Under the scenario of sustained DTG-based ART, the 192-week estimated probability of incident pregnancy was 2.6% for LNG implant and 16.1% for DMPA injectable (probability difference: -13.5%, 95% CI: -20.1%, -7.5%). The 96-week estimated probability of incident pregnancy was 0.5% for LNG implant and 8.9% for DMPA injectable (Figure).

Conclusions: For WLHIV on DTG-based ART who are seeking a reversible method to prevent pregnancy, the LNG implant is a highly effective option with better real-world effectiveness than typical use of provider-administrated DMPA.

Figure. Cumulative probability of pregnancy with LNG implant versus DMPA injectable under the scenario of sustained DTG-based ART

Legend: Estimated cumulative probability and corresponding 95% CIs by timepoint and contraceptive method.



Women’s Health

An estimation of sepsis and severe sepsis cases among patients with lactational mastitis in Optum claims data Ruchir Raman* Ruchir Raman Christina Ludema

Background and Justification: Lactational mastitis is an inflammatory breast disease associated with significant maternal morbidity. Its incidence varies from 2.5-20% in breastfeeding mothers, however these rates are generally thought to be underestimated. In a small number of cases, mastitis can progress to sepsis, a serious condition which requires hospitalization and treatment with antibiotics. Although a rare event, there is little information about how many with lactational mastitis postpartum develop or present with sepsis or other bacterial infections during hospitalizations. To this purpose, the current investigation aims to describe the incidence of sepsis among patients who have been hospitalized for lactational mastitis and describe treatment and assess sociodemographic predictors of sepsis.

Methods: We used data from Optum Clinformatics Data Mart from January 1, 2007 – March 31, 2022 for our analysis. Patients with lactation mastitis hospitalizations were identified through ICD 9 codes 675.1 (abscesses of breast associated with childbirth) and 675.2 (nonpurulent mastitis associated with lactation), and ICD-10 codes O91.13 (abscesses of breast associated with lactation) and O91.23 (nonpurulent mastitis associated with lactation). The subset of patients presenting with sepsis were further identified using ICD-9 and ICD-10 codes obtained from prior literature.

Results: We found 971 patients to be hospitalized with lactational mastitis in the above time period. 59 patients (6.1% hospitalizations) presented with sepsis or severe sepsis, with hospital stays ranging from 1-14 days and median and mean stay lengths of 3 and 3.2 days respectively. A comprehensive analysis of the sociodemographic and antibiotic use characteristics of these sepsis-mastitis patients is currently underway. Understanding these risk factors would be crucial to develop interventions and prevent severe complications in breastfeeding mothers.

Women’s Health

Differences in Dental Cleaning Rates During Pregnancy in 26 States: An Analysis of the Pregnancy Risk Assessment Monitoring System, 2022 Adit Doza* Adit Doza Lijing Ouyang Donatus U. Ekwueme Ada Dieke Shanna Cox

Background: This study explores the differences in dental cleaning rates during pregnancy across jurisdictions, examining its association with health insurance, dental insurance, race/ethnicity, income, education, and rural/urban status.

Methods: We analyzed data from the 2022 Pregnancy Risk Assessment Monitoring System (PRAMS) among women with a recent live birth. We modeled dental cleaning during pregnancy using a multivariate logistic regression as a function of race/ethnicity, age, education, insurance, income, rural/urban status, and state fixed effects among 26 states. In an additional analysis, we adjusted for dental insurance among jurisdictions containing dental insurance information for 19 states. All presented results are statistically significant at $p < 0.05$.

Results: Dental cleaning rates during pregnancy varied across jurisdictions, ranging from 35.75% in Kentucky to 57.81% in Rhode Island .The main regression model showed that dental cleaning during pregnancy varied by race/ethnicity (adjusted odds ratio [aOR] for non-Hispanic Blacks and non-Hispanic Asians were 0.822 and 0.648 vs. non-Hispanic Whites); age (20-24 years vs. <20 years [aOR=0.685]); health insurance (public vs. private insurance [aOR=0.683], no insurance vs. private insurance [aOR=0.548]); education (≥12 years vs. <12 years [aOR=1.407]); income (high-income vs. low-income [aOR=2.46]); and geographical area (rural vs. urban [aOR=0.783]). In additional analysis, women with dental insurance were more likely to have dental cleanings during pregnancy compared to those without dental insurance [aOR=3.272].

Conclusion: There is variation between states in the dental cleaning during pregnancy. Dental cleaning during pregnancy also varied by race/ethnicity, health insurance, dental insurance, education, income, and rurality. These data may inform the identification of structural barriers and evaluation of strategies to improve access and utilization of oral health care during pregnancy.

Women’s Health

Relationship Between Kidney Stones and risk of incident Hypertension Among Postmenopausal Women Mahsa H Javadi* Mahsa H Javadi Danielle J Harvey Bernhard Haring Nora Franceschini JoAnn E Manson Matthew Allison John Robbins Lorena Garcia

Background:

Kidney stones have been linked to an increased risk for hypertension. The relationship between hypertension and kidney stones is influenced by interconnected factors like obesity, diet, and sedentary lifestyle. However, existing data lacked adjustment for a wide range of confounding variables. Also, the role of obesity as a potential effect modifier in this relationship remains unknown.

Objectives:

To evaluate whether self-reported kidney stones are associated with incident hypertension in postmenopausal women in the Women’s Health Initiative (WHI).

Methods:

In a prospective cohort study of 89,769 postmenopausal women ages 50-79 years without hypertension (HTN) at baseline, data from the WHI observational study and clinical trials were analyzed to assess the association between kidney stones and incident HTN. Kidney stone status was self-reported at baseline and during follow-up, treated as a time-varying, dichotomous variable (with 4,524 women reporting kidney stones at some point and 85,245 reporting no kidney stones). Incident hypertension was identified based on self-reported diagnosis of hypertension, blood pressure (BP) >130/80 mmHg on at least two separate occasions, or use of anti-hypertensive medications. At baseline, demographic and health history information were self-reported, while dietary data were collected using a validated food frequency questionnaire. Key covariates included age, metabolic factors (osteoporosis, diabetes, high cholesterol, body mass index (BMI), waist circumference, and waist-to-hip ratio (WHR)), lifestyle risk factors (Dietary Approach to Stop Hypertension (DASH), total energy expended from recreational physical activity, history of alcohol use and smoking, sociodemographic conditions (race, ethnicity, neighborhood socioeconomic status (NSES), and region of residence).

Temporal changes in Systolic BP (SBP) and Diastolic BP (DBP) in relation to a history of kidney stones were examined. The analysis assessed how mean SBP and DBP levels varied over 28 years among participants reporting kidney stones at some point and without a history of kidney stones. Two-sample t-tests were applied to compare the mean differences of each continuous variable between participants with and without hypertension. Chi-square tests were used to compare the two groups on categorical variables. Cox proportional hazards models assessed the association of kidney stone and incident hypertension adjusting for potential confounders. Cox regression models was conducted with the following models: Model 1adjusted for age at baseline; Model 2 additionally adjusted for metabolic factors; Model 3 added lifestyle-related risk factors to Model 2; Model 4 additionally included sociodemographic covariates; Model 5 added use of thiazide diuretics to Model 4.

Results:

Mean age for all participants was 62.5 (±7.17). Mean WHR differed slightly between groups [0.81 (±0.81) in kidney stone, 0.79 (±0.07) in no kidney stone, p<0.0001]. The racial/ethnic distribution was similar between participants with and without a history of kidney stones. Additionally, participants with a history of kidney stones tended to have lower NSES, [73.4 (±8.5) in kidney stone, 75.2 (±7.3) in no kidney stone, p<0.0001]. Kidney stone history is associated with lower levels of dietary calcium intake (807 (±475.78) mg/day vs 837 (±464.88) mg/day), lower levels of Vitamin D intake (4.26 (±3.24) mcg/day vs 4.33 (±3.04) mcg/day), lower total energy expenditure (12.93 (±14.14) Met-hours/week vs 13.79 (±14.24) Met-hours/week), a higher rate of osteoporosis-related fractures (2.19% vs 1.54%), and a higher rate of hormone replacement therapy use (71.09% vs 69.19%) compared to those without a history of kidney stones.

Over a mean follow-up of 17.5 years for the no kidney stone group, 44.2% developed hypertension compared to 43.1% over 15.4 years in the kidney stone group. Systolic and diastolic BP increased by about 14 mmHg and 12 mmHg during follow-up, respectively, which were not significantly different by kidney stone group (p=0.3).

A report of kidney stones was associated with increased risk of hypertension. The crude hazard ratio (HR) for incident hypertension was 1.27, 95% CI (1.23, 1.32), p<0.0001. After adjustment for age, metabolic factors, lifestyle risk factors and sociodemographic conditions, the multivariable-adjusted HR was 1.21, 95% CI of (1.16, 1.25), p<0.0001].

Conclusion:

Kidney stones are associated with an increased risk of hypertension in postmenopausal women. Individuals with a history of kidney stones may represent a high-risk group that could be targeted for early lifestyle/behavioral and other hypertension-prevention strategies.

LATEBREAKER

Women’s Health

Cross-sectional Assessment of Experiences of Discrimination and Urinary Phthalate Metabolites Leah Martin* Leah Martin Emma Preston Marlee Quinn Tamarra James-Todd

Background

Previous studies investigating phthalates, a group of endocrine-disrupting chemicals, have revealed alarming disparities in exposure due to a litany of social and economic factors. Some minorities have been observed to experience increased exposure, with pregnant individuals among the most vulnerable in these populations. Still, no apparent study has examined associations between self-reported discrimination and urinary phthalate concentrations among pregnant individuals.

Objectives

To cross-sectionally examine associations between self-reported experiences of discrimination and urinary phthalate concentrations at mid-pregnancy and postpartum among individuals participating in the Environmental Reproductive and Glucose Outcomes (ERGO) Study.

Methods

Individuals seeking prenatal care at Boston-area hospitals from 2016 to 2020 self-reported experiences of racial discrimination using the Experiences of Discrimination (EOD) Scale at mid-pregnancy (~24-28 weeks) and ~6-12 weeks postpartum. Urinary phthalate concentrations (ng/mL) collected during study visits were specific gravity (SG) corrected and ln-transformed for analyses. Unadjusted geometric means of SG-corrected urinary phthalate metabolite concentrations (ng/mL) were estimated at each visit and p-values were computed to assess differences in mean concentration, comparing individuals who self-reported ever-experiencing discrimination (yes to any question) and individuals who self-reported never experiencing discrimination (no to all questions).

Unadjusted linear regression models were constructed to estimate beta coefficients and p-values. Beta coefficients were exponentiated to obtain percent differences.

Results

Among participants who reported ever-experiencing discrimination compared to those that self-reported never experiencing discrimination, geometric mean concentrations of MEP were significantly different (p=0.001). In our cross-sectional models, at mid-pregnancy, we observed a significant increase in MEP (172.12%, 95% CI:54.80, 378.35) and a nonsignificant but notable decrease in MCPP (-29.34%, 95%CI:-51.83, 3.64) among individuals who reported ever-experiencing discrimination compared to those that self-reported never experiencing discrimination. At postpartum, significant increases in MBzP (100.15%, 95% CI: 33.46, 200.17; p=0.001) and MEP (60.80%, 95% CI: 3.33, 150.22; p=0.035) were also observed.

Conclusion

Among individuals seeking prenatal care at Boston-area hospitals, reporting ever-experiencing racial discrimination was associated with increases in some urinary phthalate metabolite concentrations.

These findings bring to light potential differences in phthalate exposure among individuals who have experienced some form of racial discrimination during pregnancy or postpartum.

LATEBREAKER

Women's Health

Premature Menopause and Risk of Type 2 Diabetes in Postmenopausal Women Yu Du* Yu Du Juhua Luo Erin S LeBlanc Aladdin H. Shadyab Longjian Liu Hailey Banack Robert A Wild Nazmus Saquib Cassandra N. Spracklen

Background The association between premature (age <40 years) menopause (PM) and an increased risk of type 2 diabetes mellitus (T2DM) underscores complex mechanisms that are not yet fully understood. Hormonal changes during menopause, particularly reduced estrogen levels, affect glucose metabolism, insulin sensitivity, and body fat distribution, contributing to the development of T2DM. This study assessed how certain surgical procedures, hormone therapy (HT), and changes in body composition modified/mediated the relationship between PM and T2DM.

Method The study included 142,738 postmenopausal women from the Women's Health Initiative. Type (induced or natural) and age of menopause were determined using data on the last menstrual period, bilateral oophorectomy, hysterectomy, menopause symptoms, and HT timing. T2DM incidence was determined through self-reported initiation of diabetes treatment. Multivariable Cox models assessed the association between PM and T2DM, with interaction terms used to examine effect modification. Mediation analysis quantified the contribution of changes in BMI during midlife, which influenced the relationship.

Results The risk of T2DM was 7% higher (HR: 1.07, 95% CI: 1.03–1.13) among women with PM (n= 13,323; 9%) compared to women with menopause at age ≥ 50 years. The association was more pronounced among women with natural menopause (HR: 1.10, 95% CI: 1.02–1.19), in whom the usage of HT significantly modified the relationship between PM and T2DM (P for interaction = 0.04). The risk was higher in women who either never used HT (HR: 1.20, 95% CI: 1.01–1.43) or used combination HT (i.e., estrogen + progesterone) (HR: 1.33, 95% CI: 1.07–1.64) but not higher for women who used estrogen-only HT. PM was significantly associated with an increased risk of T2DM (HR: 1.21, 95% CI: 1.02–1.44) in women with a waist circumference <80 cm but not in those with ≥80 cm (P for interaction = 0.72). The association between PM and T2DM was significantly mediated by change in BMI, defined as the difference between BMI at age 50 and 35, with a proportion mediated of 33.8% (95% CI 25.6% – 59.1%).

Conclusion HT and changes in body composition significantly influence the link between PM and the risk of T2DM. These findings suggest regular body composition monitoring is essential to mitigating T2DM risk in women with PM.

Figure 1. Forest Plot of Hazard Ratios for the Association Between Premature Menopause and Risk of Diabetes Stratified by Induced and Natural Menopause

	Natural Menopause			Induced Menopause		
Subgroup	**Cases**	**Incidence***	**HR(95%CI)**	**Cases**	**Incidence***	**HR(95%CI)**
Age at Menopause						
50+ (Reference)	10165	10.16	1	10165	11.4	1
45-49	4128	10.26	1.01(0.97, 1.04)	4128	11.41	0.98(0.93, 1.04)
40-44	1448	10.72	1.00(0.94, 1.06)	1448	11.95	1.01(0.95, 1.07)
<40	749	12.8	1.10(1.02, 1.19)	749	13.14	1.04(0.98, 1.11)
HRs below represent the effect of premature menopause (Age at menopause < 40) in each stratum						
HT Usage						
Never	260	15.96	1.20(1.01, 1.43)	260	15.72	1.07(0.94, 1.23)
Unopposed estrogen	337	11.98	0.95(0.83, 1.08)	337	12.65	1.03(0.95, 1.11)
Estrogen + progesterone	90	11.41	1.33(1.07, 1.64)	90	12.71	1.01(0.65,1.56)
Waist Circumference						
< 80 cm	143	7.22	1.21(1.02, 1.44)	143	6.41	1.00(0.87, 1.16)
80.0 - 87.9 cm	155	10.45	1.14(0.96, 1.35)	155	11.11	1.03(0.90,1.18)
88+ cm	448	19.02	1.06(0.95, 1.17)	448	19.83	1.06(0.98, 1.14)
BMI						
Normal (18.5 - 24.9)	136	7.21	1.17(0.98, 1.39)	136	6.93	1.00(0.87, 1.16)
Overweight (25.0 - 29.9)	235	11.18	1.08(0.94, 1.24)	235	12.53	1.16(1.04, 1.29)
Obese(30+)	367	20.9	1.09(0.98, 1.22)	367	20.36	0.98(0.90, 1.08)

Note: The analyses are adjusted for the following covariates: age, race, ethnicity, BMI (measured at baseline/age 35/age 50), Hormone Therapy (HT), Calcium and Vitamin D (CAD), Dietary Modification (DM) intervention arm membership, physical activity, alcohol consumption, smoking history, education, family history of diabetes, waist-hip ratio, hypertension. The specific covariates adjusted for may vary depending on the stratification criteria.

* The incidence rate is expressed as cases per 1,000 person-years

Women’s Health

Outcomes of treatment resistance among women with postpartum depression Yufeng Chen*
Yufeng Chen Donghao Lu

Postpartum depression (PPD) affects millions of new mothers worldwide. While the conventional treatments are effective for many, emergence evidence indicates that treatment resistance (TR) in PPD is not uncommon. However, the clinical outcomes and health consequences in this venerable group are currently unknown. We conducted a nationwide register-based cohort study of all women who gave birth during 2006-2021 in Sweden and were diagnosed with PPD up to 12 months postpartum. TR is defined as use of either ≥3 distinct antidepressants, or add-on medications, or ECT, or rTMS in one year after PPD diagnosis. Information on demographics, pregnancy characteristics, treatments, and outcomes (included all-cause mortality, suicidal behavior, psychiatric disorder, and cardiovascular and autoimmune disease) were obtained from national registers. Associations between TRPPD and outcomes were assessed using multivariable Cox model. Of 58 618 patients with PPD (mean age 30.8, SD 5.3), 4 933 (8.5%) fulfilled the criteria for TRPPD. The all-cause mortality rate for patients with TRPPD was 1.6/1000 person-years (PYs), compared with 0.8/1000 PYs for patients without TRPPD (adjusted hazard ratio [HR] 1.87, 95% CI 1.42-2.47) over up to 16 years of follow-up. Compared with patients without TRPPD, patients with TRPPD were at a higher risk of suicidal behavior (incidence rate [IR]= 10.7/1000 vs. 3.7/1000 PYs; HR=2.41, 2.15-2.70) and psychiatric disorder (IR=244.0/1000 vs. 70.7/1000 PYs; HR=2.79, 2.69-2.89), cardiovascular disease (IR=8.3/1000 vs. 7.2/1000 PYs; HR=1.19, 1.05-1.34), and autoimmune disease (IR=19.0/1000 vs. 16.0/1000 PYs; HR=1.18, 1.09-1.28). This cohort study’s findings suggest that patients with TRPDD were associated with a higher risk of mortality, suicidal behavior, and mental and physical comorbidities. Better treatment and improved surveillance on comorbidities, particularly relapse of psychiatric episodes and suicidal behavior, are needed for these venerable patients.

Women’s Health

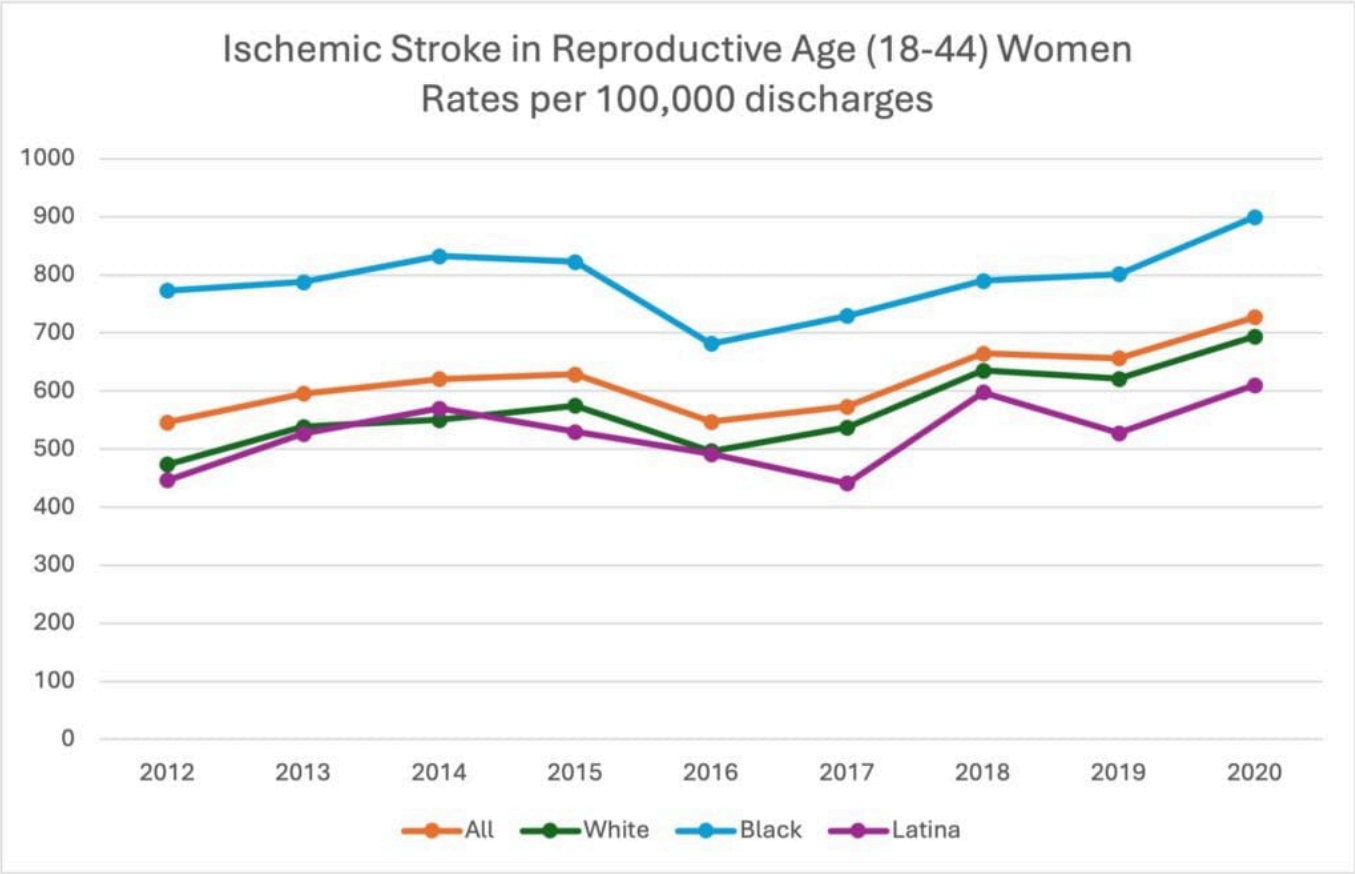
Racial Disparities in Ischemic Stroke in Women of Reproductive Age Kara Christopher* Kara Christopher Gunjanpreet Kaur Rachel Overberg Mollie Hoffmeyer Wilson Rodriguez

Background: Previous studies have found that women aged 18-44 have higher risk of stroke than men of the same age. However, few studies have examined trends and disparities in stroke rates in women of reproductive age. The objective of the current study was to examine trends and disparities in ischemic stroke among women of reproductive age.

Methods: In this cross-sectional study, we utilized the National Inpatient Sample from 2012-2020 to examine overall and stratified trends in ischemic stroke rates. Women with a pregnancy-related diagnosis were excluded from the sample. Rates per 100,000 discharges were calculated. Logistic regression was conducted for trend analysis, with 2020 as the reference year.

Results: Figure 1 shows the rates of ischemic stroke over time. There is an overall increase in rates of ischemic stroke between 2012 and 2020, with an absolute difference of 181 cases per 100,000 discharges between 2012 and 2020. Black women had significantly higher rates of ischemic stroke in all years compared to white women ($p<.001$). In the non-stratified trend analysis, the rate of stroke was significantly lower in all previous years compared to 2020. Further, in race stratified analysis, this trend continued for all racial groups. Black women had lower odds of stroke ($p<0.05$) in most years, apart from 2014 (OR=0.92, 95%CI 0.83, 1.02) and 2015 (OR=0.19, 95%CI 0.82, 1.02). Similarly, rates in Latinas were lower in most years apart from 2014, 2015, and 2018.

Conclusion: Rates of ischemic stroke among women of reproductive age, while low, have increased over time, especially in Black women. There are several possible explanations for this difference, including evaluation of socioeconomic factors and obesity rates, and increased amount of co-morbid conditions often seen in the Black population. It has also been shown that gender and racial bias within healthcare combined negatively impacts health, specifically among Black women. Longitudinal studies are needed to clarify the increasing trend of ischemic stroke in this population.


Ischemic Stroke in Reproductive Age (18-44) Women
Rates per 100,000 discharges
1000
900
800
700
600
500
400
300
200
100
0
2012
2013
2014
2015
2016
2017
2018
2019
2020
All
White
Black
Latina

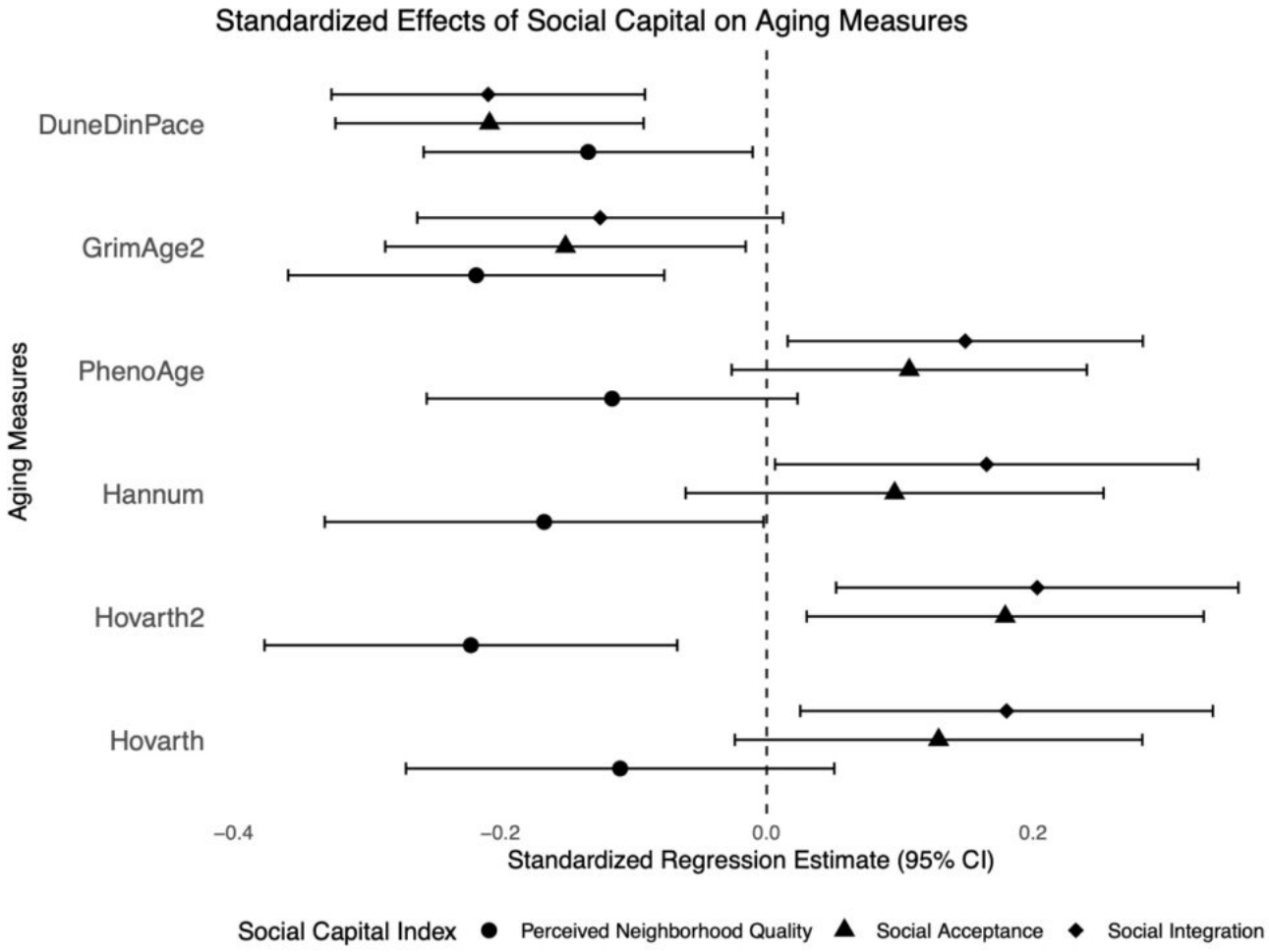
LATEBREAKER

Aging

Cognitive Social Capital Is Associated with Epigenetic Age Acceleration in the Midlife in the United States (MIDUS) Study Koichi Sakakibara* Koichi Sakakibara Agus Surachman

Introduction: Social capital, or social resources embedded within one's social relationships, is an important protective factor against age-related chronic health conditions. Nevertheless, the underlying biological processes that contribute to this relationship are not yet fully understood. This study investigated the relationship between cognitive social capital (i.e., individual-level perception or belief) and epigenetic age acceleration (EAA), a promising biological predictor of age-related chronic health conditions. Methods: We used cross-sectional data from the Midlife in the United States (MIDUS) wave 2 and Refresher, including 1,086 non-Hispanic (NH) Black and White adults (M age = 54, 55% female, 74% NH white). The cognitive social capital consists of three components: perceived neighborhood quality, perceived social integration, and perceived social acceptance. EAA was calculated using five epigenetic clocks (Horvath, Horvath2, Hannum, PhenoAge, and GrimAge; residuals obtained by regressing epigenetic clocks on chronological age) and one pace of aging measure (DunedinPACE). The analysis was adjusted for the Area Deprivation Index (ADI; country level, 2015) to control for objective neighborhood effects, along with sociodemographic, behavioral, and health-related factors. Additionally, a stratified analysis by racial groups (NH Whites vs. NH Blacks) is conducted. Results: Adjusted for age and sex, all components of cognitive social capital were significantly associated with EAA, especially Horvath2, GrimAge, and DunedinPACE. These significant associations mostly remained even after controlling for ADI and other covariates. The stratified analysis showed some significant associations, but only among the NH Black group. Conclusion: Findings from this study elucidated how cognitive social capital may influence biological aging, especially among Black adults, independent from objective neighborhood quality.

Chart. Standardized estimate for the association between accelerated aging and social capital indices adjusted for chronological age, sex, educational attainment, marital status, BMI, smoking history, and Area Deprivation Index (ADI).



LATEBREAKER

Aging

The Association Between Neighborhood Walkability and Alzheimer's Disease in Women: A Prospective Nested Case-Control Study Emma Walker* Emma Walker Fen Wu Simin Hua Andrew G Rundle James W Quinn Yelena Afanasyeva Karen L Koenig Anne Zeleniuch-Jacquotte Yu Chen

Background: Nearly two-thirds of patients with Alzheimer's disease (AD) are women. Much remains to be understood about how modifiable built environmental factors among women in midlife might reduce the risk of AD in the decades following.

Methods: The New York University Women's Health Study (NYUWHS) recruited 14,273 healthy women 35 to 65 years old between 1985 and 1991 with regular follow-up for over 30 years. We geocoded residential addresses for each participant and estimated a validated 4-item baseline neighborhood walkability (NW) measure and a 2-item average annual measure of NW across years of follow-up. We conducted a nested case-control study with 1,865 cases of AD identified via linkage to Centers for Medicare & Medicaid Services (CMS). Each case was matched to two controls on age, race/ethnicity, and Medicare coverage using risk-set sampling procedure. We used conditional logistic regression to estimate the odds ratios (ORs) for AD in relation to tertiles of NW measures, adjusting for potential confounders. We also assessed potential effect modification.

Results: Women who were diagnosed with AD during follow-up had lower education levels at baseline and a higher depression incidence than controls. Compared to women living in areas with the lowest baseline NW, women in the middle and highest tertiles of baseline NW had lower odds of AD diagnosis during follow-up, with an OR of 0.96 (95% CI: 0.82-1.11) and 0.83 (95% CI: 0.71-0.98), respectively (p-trend 0.037). The association was similar when we considered average annual walkability. This relationship did not differ appreciably by race/ethnicity, smoking history, education, depression history, or neighborhood poverty levels.

Discussion: These findings suggest that higher levels of NW in women's midlife might be protective against AD. This work highlights the importance of prioritizing walkable neighborhoods in future public health policy decisions to promote healthy aging.

LATEBREAKER

Aging

Informal Care Delivery Variation Between Women And Men: Gender Role Attitudes Or Institutional Context? Afshin Vafaei* Afshin Vafaei Eszter Zólyomi Cassandra Simmons Ricardo Rodrigues Susan P. Phillips Stefania Ilinca

Despite shifting attitudes towards men taking up more unpaid domestic works, there remains a persistent gender gap in informal caregiving for older adults. We investigated how individual gender role attitudes of women and men influence their provision of care to parents and whether this relationship is moderated by national public policies and gender equality indices such as female labour-force participation and percentage of women in parliament.

We analyzed data from the Generations and Gender Survey that includes information from diverse samples of nine European countries. Provision of informal care to a parent defined as personal care provided in the last 12 months and individual attitudes towards gender roles measured by levels of agreement with this statement “When parents are in need, daughters should take more caring responsibility than sons”. We constructed multiple logistic regression models to examine the relationship of interest adjusting for pertinent individual and country-level variables.

In all countries, a larger proportion of women than men provided informal care. Individual gender egalitarian views in women were associated with a significant decreased likelihood of providing care for women, while increased the probability in men (average marginal effects=-0.017 versus 0.014 respectively) confirming precedent results. However, we found no evidence for moderating effects of country contextual variables. While caution should be taken in placing too much hope on changing behaviours through shifts in individual gender role attitudes only, such attitudes may still contribute to narrowing the gender gap in informal care by influencing policy change through lagged generational change.

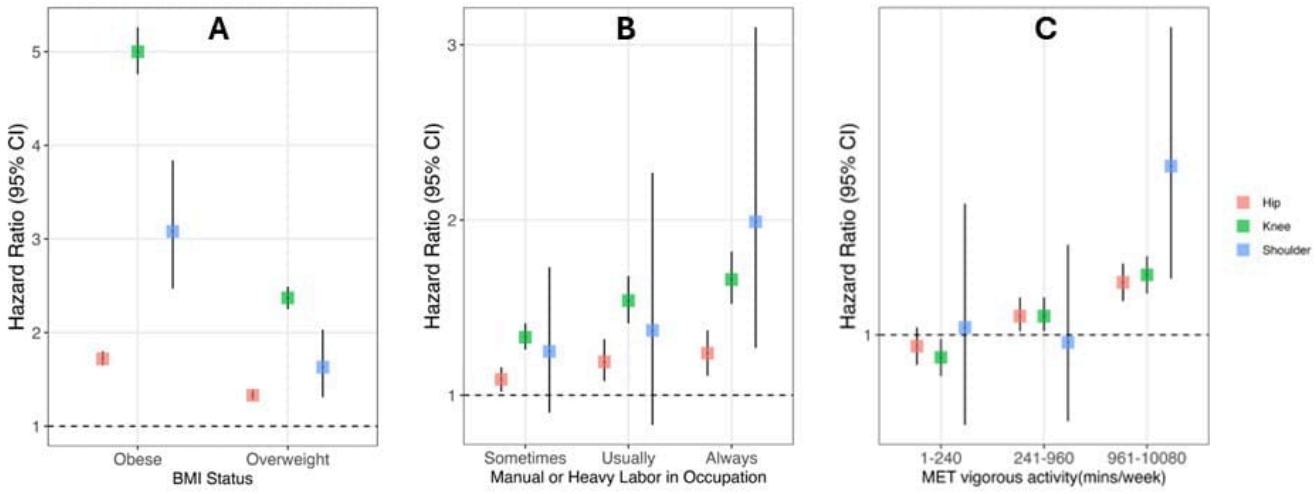
Aging

Identification of Risk Factors for Glenohumeral Osteoarthritis Requiring Shoulder Arthroplasty Elizabeth L. Yanik* Elizabeth Yanik Abigail G. Carey-Ewend Xiaoyi Xu Jay D. Keener Vy Pham

Glenohumeral osteoarthritis (OA) is a leading cause of disabling shoulder pain. Shoulder arthroplasty (SA) rates for OA in the US are increasing more rapidly than for hip or knee arthroplasty (THA/TKA). But understanding of the factors influencing glenohumeral OA risk is limited. We aimed to identify factors associated with OA-related SA, as a measure of end-stage glenohumeral OA, in the UK Biobank. The UK Biobank collects extensive data from surveys, interviews, and linked hospital records covering 10+ follow-up years. An OA SA case was defined as presence of a SA procedure code with an OA diagnosis before or at the time of the procedure. Age-adjusted Cox regression was used to estimate associations between each potential risk factor and OA SA. All factors with evidence of association based on age-adjusted models (P>0.10) were included in a final multivariable Cox model to evaluate independent associations. Factors included in the final model were also evaluated with OA-related THA/TKA using similar methods to compare the magnitude of associations across joints. Of the 494,203 people included, 652 underwent OA SA during follow-up. In the final multivariable model, each decade increase in age was associated with twice the OA-related SA risk. Higher BMI was strongly associated with higher risk, with obese individuals having over three times the risk of people with healthy BMI. BMI associations were weaker for THA and stronger for TKA (Fig.) OA SA risk increased consistently with increasing frequency of manual work, while vigorous physical activity was only associated with elevated risk at the very highest levels. The highest levels of manual work and physical activity were more strongly associated with OA SA than THA or TKA (Fig.). Similar factors may drive OA in the shoulder, a non-weight-bearing joint, as do weight-bearing joints, but the magnitude of associations differed by joint. Continued investigation of glenohumeral OA risk factors is critically needed to inform prevention approaches.

Figure. Associations of BMI (A), heavy manual labor (B) and physical activity (C) with OA-related shoulder, hip, and knee arthroplasty in the UK Biobank.

Based on multivariable Cox regression models including age, sex, race, education, income, BMI, frequency of heavy manual labor, and physical activity level. For BMI (A), the referent category was healthy BMI. For heavy manual labor (B), the referent category was 'Never/Rarely'. For physical activity (C), the referent category was 0 MET of vigorous activity (mins/week). BMI=body mass index, MET=metabolic equivalent tasks



Aging

Association of tailpipe-related and non-tailpipe-related air pollution exposure with neuroimaging outcomes in the Chicago Health and Aging Project Ryan M. Andrews* Ryan Andrews Stephanie T. Grady Neelum T. Agarwal Todd L. Beck Klodian Dhana Denis Evans Pauline Maillard Sarah Rothbard Elizabeth A. Stuart Adam A. Szpiro Saarika Virkar Sara D. Adar Charles S. DeCarli Joel D. Kaufman Kumar B. Rajan Jennifer Weuve

Background: Long-term exposure to air pollution has been associated with MRI measures of brain injury and reduced cognitive ability. A major source of air pollution is vehicle traffic, which is modifiable. In this study, we estimated associations between four traffic-related air pollutants and five neuroimaging biomarkers.

Methods: We analyzed data from a subset (N=817; 61% female; 60% Black) of participants in the Chicago Health and Aging Project (1993-2012) who underwent a structural MRI scan between 2002-2012, which is when MRI scans were offered as part of the study. Using validated fine-scale spatiotemporal models, we predicted participant-level exposure to the tailpipe pollutants oxides of nitrogen (NOX) and nitrogen dioxide (NO2), plus the non-tailpipe pollutants copper and zinc found in coarse particulate matter (PM10-2.5,Cu and PM10-2.5,Zn, respectively) over the three years prior to each participants' first MRI scan date. Using linear regression, we estimated cross-sectional, covariate-adjusted associations between each pollutant with total cerebral volume, total hippocampal volume, total lateral ventricle volume, total white matter hyperintensity volume, and cortical thickness. These models incorporated inverse probability weights to account for potential selection biases driven by differences between participants who did and did not undergo an MRI scan after being offered one.

Results: Exposure to NOX and NO2 was associated with smaller cortical thinning on average (-0.06 mm, 95% CI: -0.09 to -0.02 per 1 SD [7.8 ppb] NOX; -0.04 mm, 95% CI: -0.07 to -0.01 per 1 SD [2.7 ppb] NO2). All other estimated associations were consistent with no effect.

Conclusion: Overall, these results are not indicative of large adverse associations between traffic-related air pollution exposures and indicators of brain injury in this biracial cohort.

Aging

Plasma homocysteine level and trajectories and their association with longitudinal increase in plasma neurofilament light among urban middle-aged adults May A. Beydoun* May Beydoun Nicole Noren Hooten Michael F. Georgescu Hind A. Beydoun Marie T. Fanelli-Kuczmarski Jordan Weiss Michele K. Evans Alan B. Zonderman

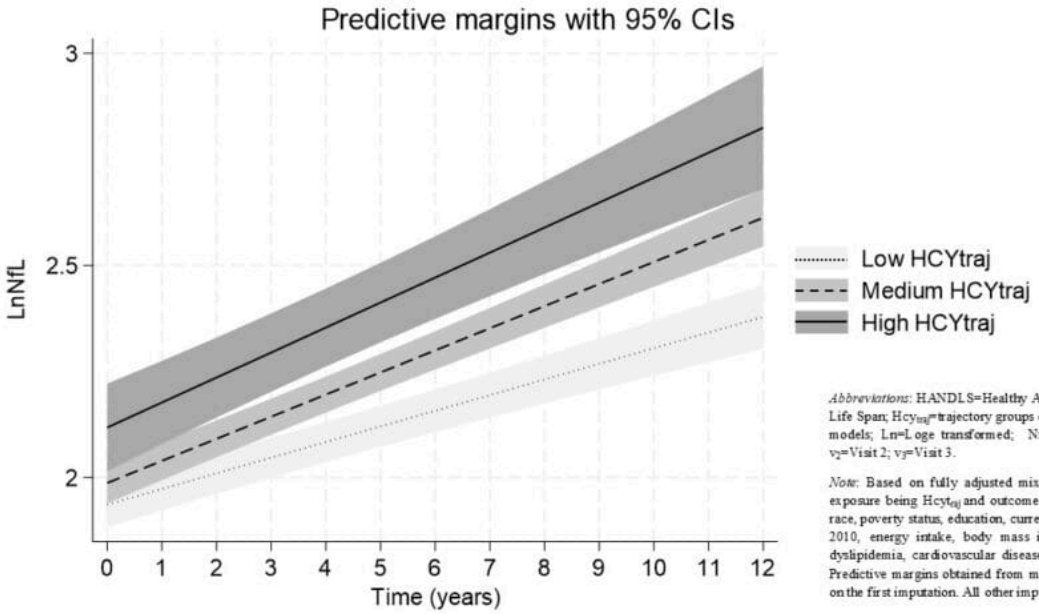
Background and Objectives: Plasma neurofilament light (NfL) is a non-specific marker of axonal degeneration which may be linked to elevated blood concentrations of homocysteine (Hcy). Such associations may be differential across sex and race. Therefore, we tested whether Hcy was linked to longitudinal change in plasma NfL overall and differentially across sex and race in a sample of middle-aged urban adults.

Methods: We used data from the Healthy Aging in Neighborhoods of Diversity across the Life Span (HANDLS) study [n=690, Age at visit 1 (v1:2004-2009): 30-66y, 42.1% male, 55.4% African American] to evaluate relationships between NfL levels and both visit 1 Hcy (Hcyv1) and time-dependent Hcy concentrations (Hcytd). Specifically, we examined the relationship between these measures and visit 1 NfL (NfLv1) as well as annualized change in NfL (δNfL) over the study period of ~8y [2004-2009 (v1), 2009-2013 (v2) and/or 2013-2017 (v3)] using mixed effects linear regression models.

Results: Hcyv1 was positively associated with NfLv1, but not with δNfL. However, when Hcytd was considered along with time-dependent covariates on multiple-imputed data, both NfLv1 and δNfL were associated with Hcytd, with some significant sex difference in the longitudinal association, whereby this relationship was stronger among males. The Hcy exposure obtained from group-based trajectory models, indicated that individuals belonging to the “High increasing” group were consistently associated with both higher NfLv1 and faster increase in NfL (overall, fully adjusted, High vs. Low: γ0gbtm=+0.226±0.058, P<0.001; γ1gbtm= +0.022±0.007, P<0.010).

Discussion: Dynamic Hcy exposures (Hcytd and Hcygbtm) were associated with faster rate of increase in NfL over time, reflecting potentially faster rate of axonal degeneration. Further studies are needed in comparable populations to replicate our findings.

FIGURE 3. Predictive margins of LnNfL over follow-time vs. group-based trajectories of LnHcy: HANDLS 2004-2017



Abbreviations: HANDLS=Healthy Aging In Neighborhoods of Diversity Across the Life Span; Hcy_{traj}=trajectory groups of LnHcy obtained using group-based trajectory models; Ln=Loge transformed; Nfl =plasma Neurofilament Light; v_1=Visit 1; v_2=Visit 2; v_3=Visit 3.

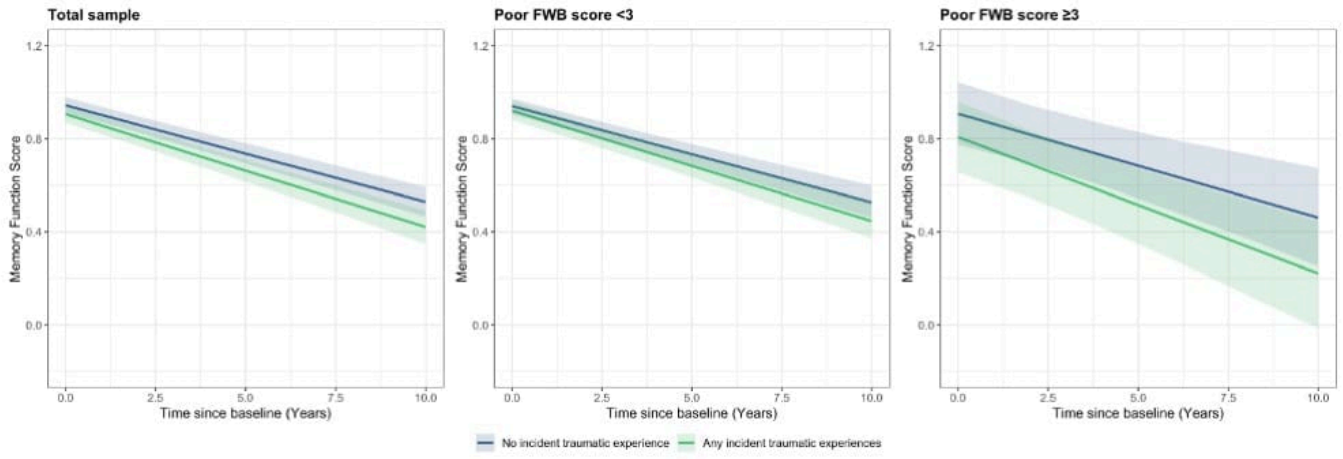
Note: Based on fully adjusted mixed-effects linear regression model with main exposure being Hcy_{traj} and outcome being LnNfL. Model is adjusted for age, sex, race, poverty status, education, current smoking status, current drug use status, HEI-2010, energy intake, body mass index, allostatic load, hypertension, diabetes, dyslipidemia, cardiovascular disease and the total CES-D score, measured at v_1. Predictive margins obtained from mixed-effects linear regression model conducted on the first imputation. All other imputation gave a similar pattern of association.

Aging

Incident traumatic experiences and poor financial wellbeing: a double hit for cognitive aging? Katrina Kezios* Katrina Kezios Eleanor Hayes-Larson

Traumatic experiences and financial hardship may affect cognitive aging through shared stress-related pathways, amplifying their impact when experienced together. Using data from the Health and Retirement Study (N=3432), we quantified the effect of incident traumatic experiences (ITE, occurring 2006-2010 or 2008-2012), defined as ≥1 event from the Lifetime Traumas index (death of a child, being in a major natural disaster, firing or being fired upon in combat, spouse/partner/child addicted to drugs/alcohol, victim of serious physical attack/assault, life-threatening illness/accident, and life-threatening illness/accident in spouse/child). We examined effect modification by poor financial wellbeing (FWB), defined as reporting ≥3 of 7 subjective (financial dissatisfaction, low financial control, difficulty paying bills, taking less medication because of money) and objective (low income, low non-housing wealth, no housing wealth) indicators of financial hardship. Memory was assessed biennially from 2010/2012 to 2020 via a composite score computed from direct memory assessments and proxy reports. We used linear mixed effects models with random intercept and slope to estimate the effect of ITE on ~10-year memory decline overall and within strata of FWB. Models used follow-up time as the timescale and adjusted for baseline age, practice effects, sex/gender, race, educational attainment, parental education, Southern birth, childhood SES, marital status, self-rated health, and interactions between covariates and time. Overall, having ≥1 ITE was associated with accelerated memory decline (βanyITE*time=-0.007, [95% CI:-0.012, -0.002], **Figure**). The magnitude of this association was larger in the presence of poor FWB (βanyITE*time|FWB≥3=-0.014, [-0.030, 0.003] vs. βanyITE*time|FWB<3=-0.006, [-0.012, -0.001]). Our results suggest financial wellbeing may modify the effects of traumatic experiences and may be a policy intervention point to delay memory decline in older adults.

Figure. Predicted 10-year memory decline for the total sample and within strata of poor financial wellbeing.[1]



[1]Figure predictions are made for a 65 year old at baseline, white, male, with 12 years of education, parents with 12 years of education, no practice effect, and who was not born in the South, had the sample mean childhood SES index score, was married/partnered, and reported good/very good/or excellent self-rated health.

Aging

Unmeasured Confounding in Studies on GLP-1 Receptor Agonist Initiation and Incident Dementia Sarah Ackley* Sarah Ackley Jingxuan Wang Kaley Hayes Andrew Zullo Minhyuk Choi Peter Buto Andrew Stokes Maria Glymour

Glucagon-like peptide-1 and glucose-dependent insulinotropic polypeptide receptor agonists (GLP-1 RAs) are new, effective drugs for diabetes and weight management. GLP-1 RAs reduce the incidence of diabetes-related complications associated with dementia (e.g., stroke) and may have direct effects on the brain. Randomized-controlled-trial evidence on GLP-1 RAs and dementia is limited. Observational studies suggest that GLP-1 RAs reduce incident dementia, but omit potential confounders like education and genetic factors. Using current and retrospective electronic health record data from All of Us cohort participants with a diabetes diagnosis (n=37,821), we evaluated whether these known dementia risk factors are associated with GLP-1 RA initiation (n=7,419 initiators). Logistic regression models for initiation of any GLP-1 RA were adjusted for age at liraglutide approval (12/23/14), sex, race/ethnicity, BMI, and genetic ancestry (only for genetic risk). Compared to those with less than a high school degree, GLP-1 RA initiation was associated with completion of high school (OR=1.14, 95% CI (1.03, 1.26)), some college (OR=1.36, 95% CI (1.24, 1.50)), and college or above (OR=1.39, 95% CI (1.26, 1.53)). Compared to non-APOE-ε4 carriers, one and two APOE-ε4 alleles were associated with 0.88, 95% CI (0.82, 0.95), and 0.93, 95% CI (0.76, 1.15), respectively, times the odds of GLP-1 RA use. A one standard deviation increase in non-APOE-ε4 Alzheimer’s disease genetic risk did not appreciably change the odds of GLP-1 RA use (OR=1.02, 95% CI (0.98, 1.05)). In conclusion, education is associated with increased risk of GLP-1 RA use, while APOE-ε4 carriers have decreased risk. These associations suggest that education and APOE-ε4 are plausible confounders that may account for a portion of GLP-1 RA-dementia associations, reducing credibility of observational studies to date.

Aging

Assessing the Causal Impact of Leisure-Time Physical Activity and Screen Time on Lifespan: A Mendelian Randomization Study Zhu Liduzi Jiesisibieke* Zhu Liduzi Jiesisibieke Zhu Liduzi Jiesisibieke C Mary Schooling

Objectives. Observational studies have consistently shown physical activity associated with lower mortality. However, randomized controlled trials to confirm the value of physical activity for lifespan in the general population are infeasible. To address this gap, we conducted a Mendelian Randomization (MR) study, using the largest available suitable studies and control outcomes.

Method. We conducted a two-sample MR study. We used single nucleotide polymorphisms strongly ($p < 5\times 10-8$) and independently ($r2<0.001$) predicting more than 30 minutes per week of moderate to vigorous intensity physical activity during leisure time and conversely predicting leisure screen time to obtain inverse-variance weighted estimates. We adjusted for household income using multivariable MR. We used waist circumference and whole-body fat mass as control outcomes. Sensitivity analyses included the weighted median, MR-Egger, MR-PRESSO and MRlap.

Results. Physical activity was associated with longer lifespan, which remained evident after adjusting for household income (1.71 years, 95% CI: 0.43 to 2.99 years) with similar estimates for men (1.79 years, 95% confidence interval (CI) 0.09 to 3.5 years) and overall. Conversely, leisure screen time was associated with shorter lifespan, which was less evident after adjusting for household income. As expected, physical activity reduced and screen time increased waist circumference and whole-body fat mass, which remained evident for whole-body fat mass after adjusting for household income.

Conclusions. Physical activity may extend lifespan, while the role of leisure screen time is less clear. Questions remain about the optimal type, duration, intensity, and frequency of physical activity.

Aging

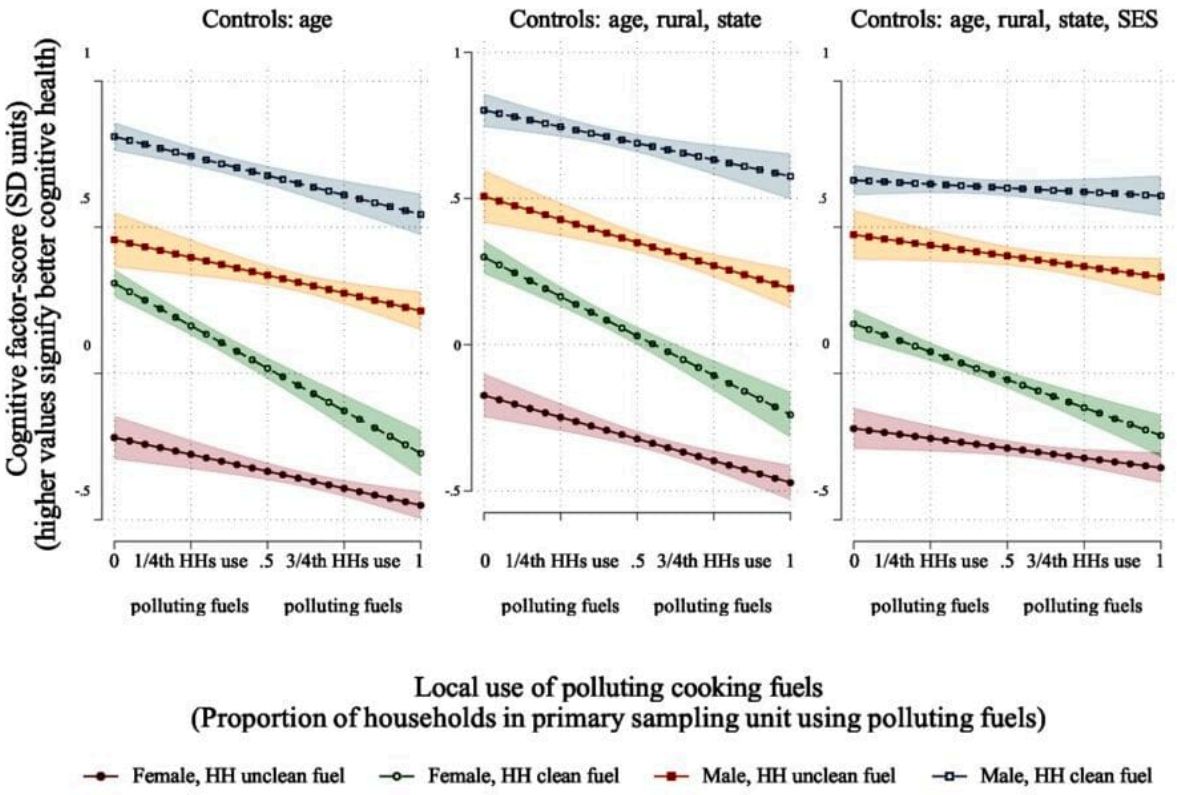
Polluting Cooking Fuel Use and Adult Cognitive Health: Externalities and Gender Disparities in LMICs Sneha Sarah Mani* Sneha Sarah Mani Aashish Gupta Irma T Elo

Scientific understanding of how environmental hazards affect cognitive health in older adults, particularly in low- and middle-income countries (LMICs), remains limited. As Alzheimer's disease and related dementias become an escalating public health concern, the need to address contributing factors becomes ever more urgent. By 2030, over 80% of individuals aged 60 and above are expected to live in LMICs, where household use of polluting fuels for cooking and heating is widespread. This reliance on polluting fuels is a major contributor to global ambient air pollution—accounting for nearly one-sixth of total emissions—and is predicted to increase the number of adults at risk of cognitive impairment and dementia.

Using two data sources from LMICs that measure household-level polluting cooking fuel use and cognitive function, this study examines the role of polluting cooking fuel use at the household and community level on cognitive function as well as gender differences in these associations. The analysis uncovers a clear pattern: cognitive health tends to be poorer among individuals from households that rely on polluting fuels and among residents of neighborhoods where such fuel use is more common. Additionally, we also observe that local use of polluting fuels has a greater negative impact on cognitive health among members of households that use clean fuels. These relationships persist even after accounting for individual socioeconomic status and local economic differences, suggesting a robust association between polluting fuels and cognitive outcomes. Moreover, the study highlights gender disparities in these associations. Women living in households where polluting fuel use prevails exhibit the lowest predicted cognitive scores. This result is consistent with women being the primary cooks in households and consecutively having the greatest exposure to polluted cooking fuel use.

Our findings reveal the substantial direct influence and negative externality of polluting fuel use in LMICs and help understand why overall cognitive health may be poor in these settings. Moving away from polluting fuels toward clean fuels may not only reduce individual risk but also community-level exposure to air pollution, contributing to better cognitive health in older ages.

Figure 1: Higher own and local use of polluting fuels is associated with lower cognition, especially for females using clean fuels in LASI (2017-19)



Notes: Each graph shows predicted values of the cognitive score factor index from a linear regression interacting local and household use of polluting cooking fuels and dummy variable for female. The left panel includes controls for age dummies. The middle panel controls for age dummies, state dummies, and rural or urban residences. The right panel controls for deciles of the value of assets a household owns (as dummies), dummies for the caste and religious categories a household belongs to, whether the household owns the land, the proportion of households in a primary sampling unit that owns land or local land ownership, household electricity use, local electricity use, household consumption expenditure, and average local household expenditure.

Local use of polluting fuels is measured as the proportion of households in a primary sampling unit that a household lives in who use polluting fuels and ranges from 0 to 1.

HH: Household. SES: Socioeconomic Status

Source: Longitudinal Aging Study of India 2017-19. N= 32,256 females and 28,135 males

Aging

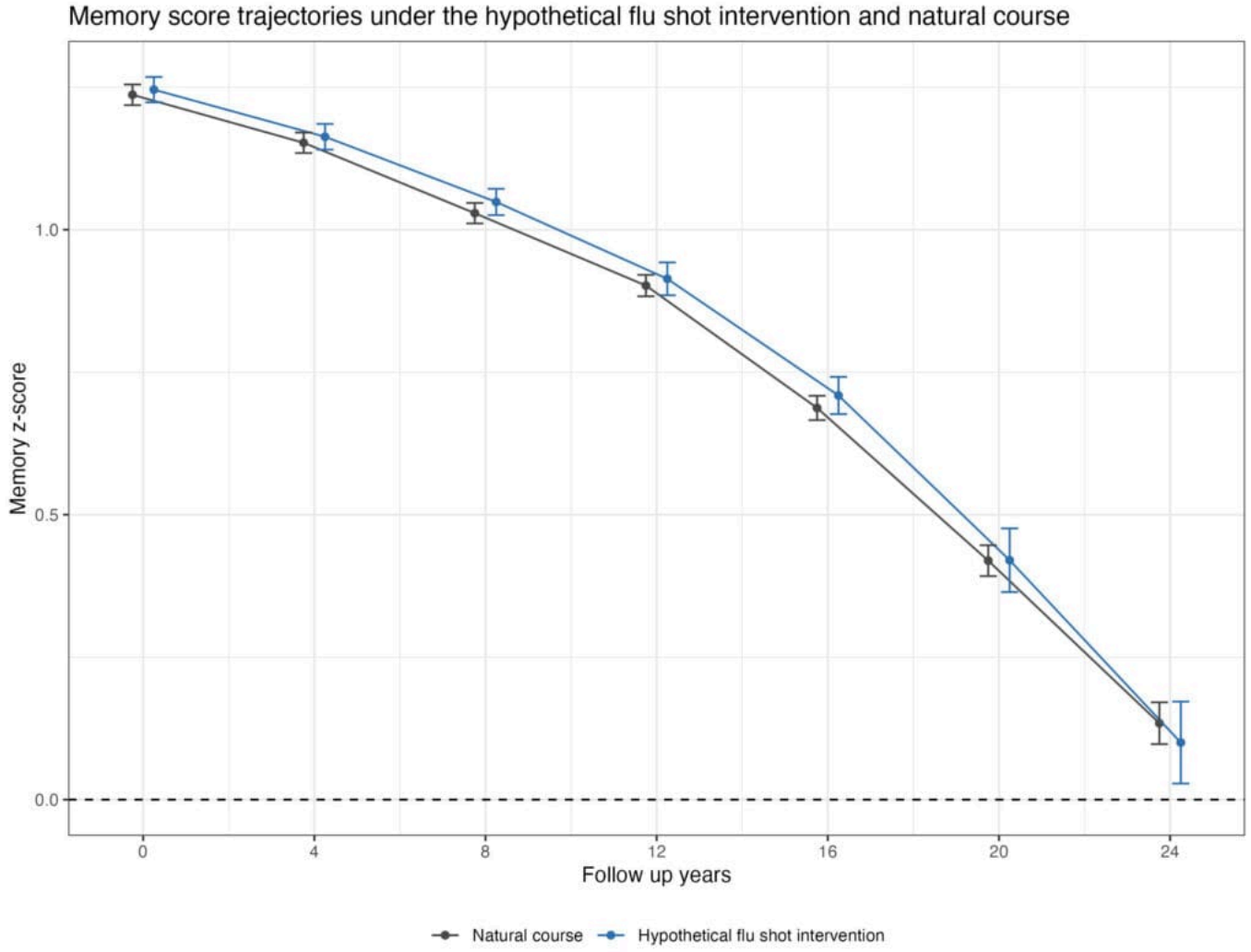
The association of change in obesity across mid and late-life with late-cognitive decline in a diverse cohort Claire Meunier* Claire Meunier Paola Gilsanz Kristen M. George Michelle C. Odden Brandon Gavett Alexander Ivan B. Posis Rachel Whitmer

The impact of late-life obesity on cognitive decline remains unclear, especially in racially diverse cohorts. Further, estimates of this association may be biased due to the competing risk of mortality. We pooled data from 1136 participants in the LifeAfter90 and Kaiser Healthy Aging and Diverse Life Experiences studies to explore whether change in weight status between mid- and late-life is associated with cognitive decline. Race-specific body mass index (BMI; kg/m2) cutoffs categorized participants into groups: 1) no obesity (no obesity at mid- and late-life), 2) obesity onset (obesity at late-life), 3) obesity resolution (obesity at midlife), and 4) consistent obesity (obesity at mid- and late-life). Midlife BMI was defined as the first clinical measure between ages 40-60, and late-life BMI as the first measure starting at age 65. BMI between ages 60-65 were excluded as part of the transition period. Cognitive decline in executive function (EF) and verbal episodic memory (VM) were assessed using the Spanish English Neuropsychological Assessment Scale with up to 4.3 years of follow-up. Joint models were used to account for competing risk of mortality, combining Cox proportional hazards for mortality and linear mixed models for cognitive change. At the start of cognitive follow up, participants had a mean age of 80, with 66% categorized as no obesity, 16% obesity onset, 3% obesity resolution, and 16% consistent obesity. Obesity onset was associated with faster decline in EF compared to no obesity (β(95% CI) = -0.04(-0.07, -0.004)). There were no differences in decline in VM (consistent obesity: -0.02(-0.07, 0.04), obesity resolution: 0.04(-0.07, 0.16), and obesity onset: -0.03(-0.07, 0.02)). Findings were similar to models not accounting for mortality. In this diverse cohort, obesity onset in late-life was associated with accelerated decline in EF, underscoring the importance of interventions targeting late-life obesity as a strategy to mitigate cognitive decline.

Aging

Emulating a Target Trial of Flu Shots and Memory Decline Among Older Adults in the United States Yingyan Wu* Yingyan Wu Ryo Ikesu Roch Nianogo Beate R. Ritz Elizabeth Rose Mayeda

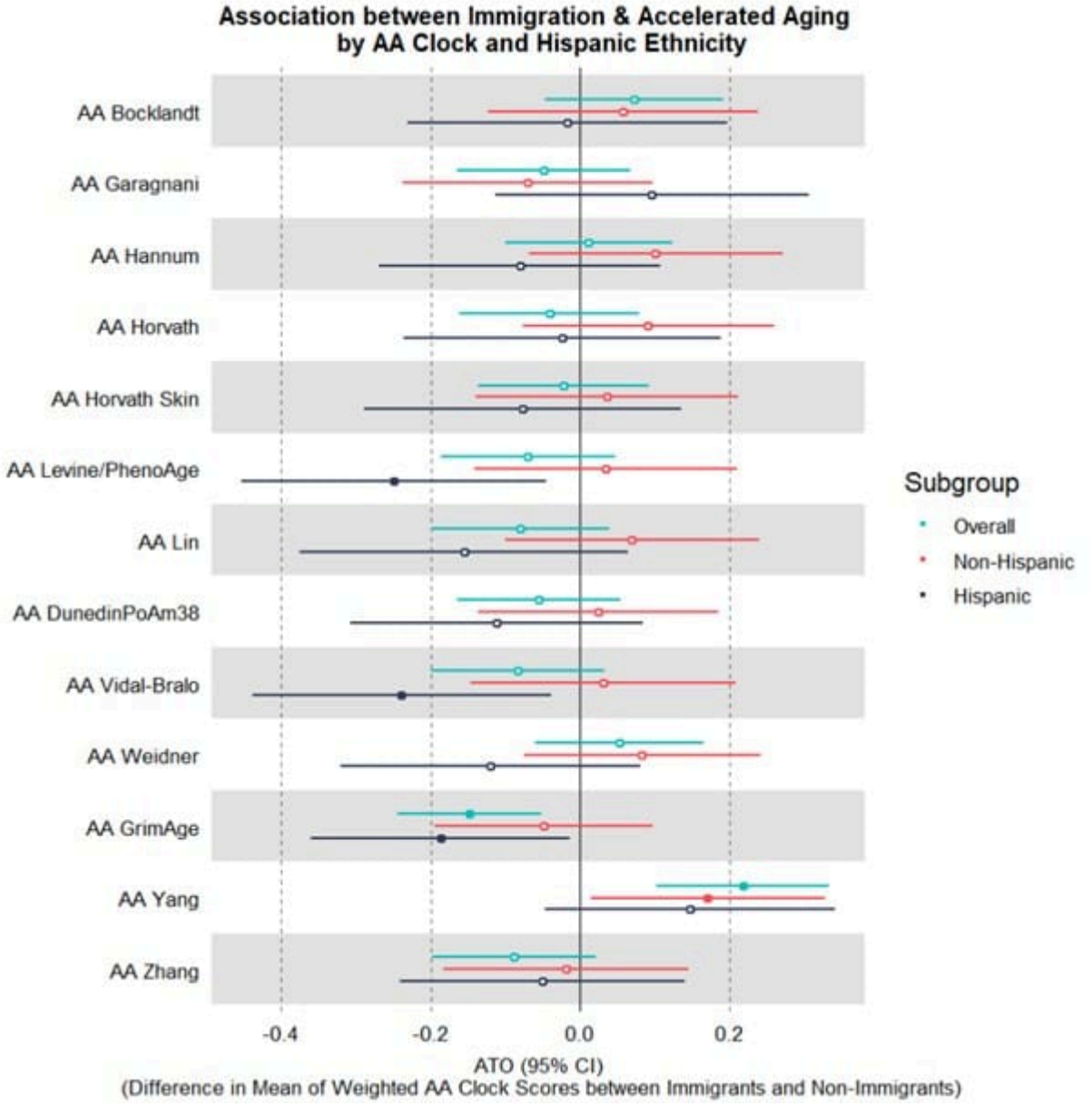
Annual flu shots have been suggested to prevent dementia among older adults, but prior studies were limited by short follow-up periods and residual confounding. We used the U.S. representative Health and Retirement Study (1996-2020) to emulate a trial to assess memory decline under a hypothetical flu shot intervention of receiving a flu shot at least once every 4 years over 24 years, compared to the natural course (no specified intervention). Every 4 years, participants self-reported whether they took a flu shot at least once over the prior 2 years. Memory was measured every 4 years using a composite memory score (z-scored to baseline distribution) integrating direct and proxy memory assessments. We used targeted maximum likelihood estimation to simulate memory scores over the study period under the two hypothetical intervention scenarios while addressing time-invariant (baseline age, sex/gender, race/ethnicity, education) and time-varying confounders (marital status, household income, medical insurance, loneliness, chronic disease conditions, depression, and daily functioning). We applied sampling weights, used multi-level multiple imputation to address missing exposure and covariate data, and inverse probability of censoring weights to account for loss to follow-up and death. The analytic sample included 12,362 participants (mean baseline age 59.4 years; 54% women; mean number of flu shots reported during the study period = 3, range 0-7). Average memory decline over 24 years was -1.14 SD units [95% CI: -1.21, -1.07] under the hypothetical flu shot intervention and -1.11 SD units [95% CI: -1.14, -1.07] under the natural course (**Figure**). Compared to the natural course, the flu shot intervention was not associated with better memory function over follow-up (mean difference at 24 years of follow-up: -0.04 SD units [95% CI: -0.10, 0.03]). Our study suggests flu shots may not prevent memory decline.


Memory score trajectories under the hypothetical flu shot intervention and natural course
Memory z-score
1.0
0.5
0.0
0
4
8
12
16
20
24
Follow up years
Natural course
Hypothetical flu shot intervention

Aging

Effect of Immigration to the US on Accelerated Aging in the Health and Retirement Study: Differences between Hispanic & Non-Hispanic Immigrants. Antonio J. Bustillo* Antonio Bustillo Adina Zeki Al Hazzouri Kaylie N. Moropoulos Xuexin Yu M. Maria Glymour Katrina L. Kezios

The effect of immigration on accelerated aging is understudied, and it is unclear if this relationship differs for Hispanic vs. non-Hispanic immigrant groups. Using the 2016 Venous Blood Study subsample of the Health and Retirement Study and data on immigration from 1995-2016, we assessed the effects of immigration to the US on accelerated biological aging, separately for 398 Hispanic (N=266 Immigrant & N=132 Non-Immigrant) and 2857 non-Hispanic (N=167 Immigrant & N=2690 Non-Immigrant) participants. Immigration was defined as being born outside vs. in the US. Accelerated aging (AA) was defined as the residual of models which regressed each of the 13 epigenetic clocks on chronological age. Residuals were standardized for ease of comparison between clocks. Positive AA scores indicate age acceleration. We modeled propensity scores (PS) for immigration status using the following confounders of immigration and AA: gender, race, education (years), parental education (years), ever smoked, and ever married. Separate PS models were created for Hispanic & non-Hispanic participants. We used overlap weighting to estimate the ATE in the overlapping population (ATO) as the mean difference in weighted AA scores between immigrants vs. non-immigrants. We calculated 95% CIs using the delta method. In general, Hispanic immigrants tended to show equal or decelerated aging compared with their non-immigrant counterparts, but often with wide CIs (ATO_AA Levine/PhenoAge = -0.25, 95% CI: -0.45., -0.05; ATO_AA Vidal-Bralo = -0.24, 95% CI: -0.44, -0.04; ATO_AA GrimAge = -0.19, 95% CI: -0.36, -0.01). Among non-Hispanic participants, ATOs suggested either equal or accelerated aging for immigrants vs. non-immigrants, although only one clock reached statistical significance (ATO_AA Yang = 0.17, 95% CI: 0.01, 0.33). Immigration to the US may contribute to aging, but the direction (acceleration/deceleration) may vary by Hispanic ethnicity and larger samples are needed for precise conclusions.


Association between Immigration & Accelerated Aging
by AA Clock and Hispanic Ethnicity
AA Bocklandt
AA Garagnani
AA Hannum
AA Horvath
AA Horvath Skin
AA Levine/PhenoAge
AA Lin
AA DunedinPoAm38
AA Vidal-Bralo
AA Weidner
AA GrimAge
AA Yang
AA Zhang
-0.4
-0.2
0.0
0.2
ATO (95% CI)
(Difference in Mean of Weighted AA Clock Scores between Immigrants and Non-Immigrants)
Subgroup
Overall
Non-Hispanic
Hispanic

Aging

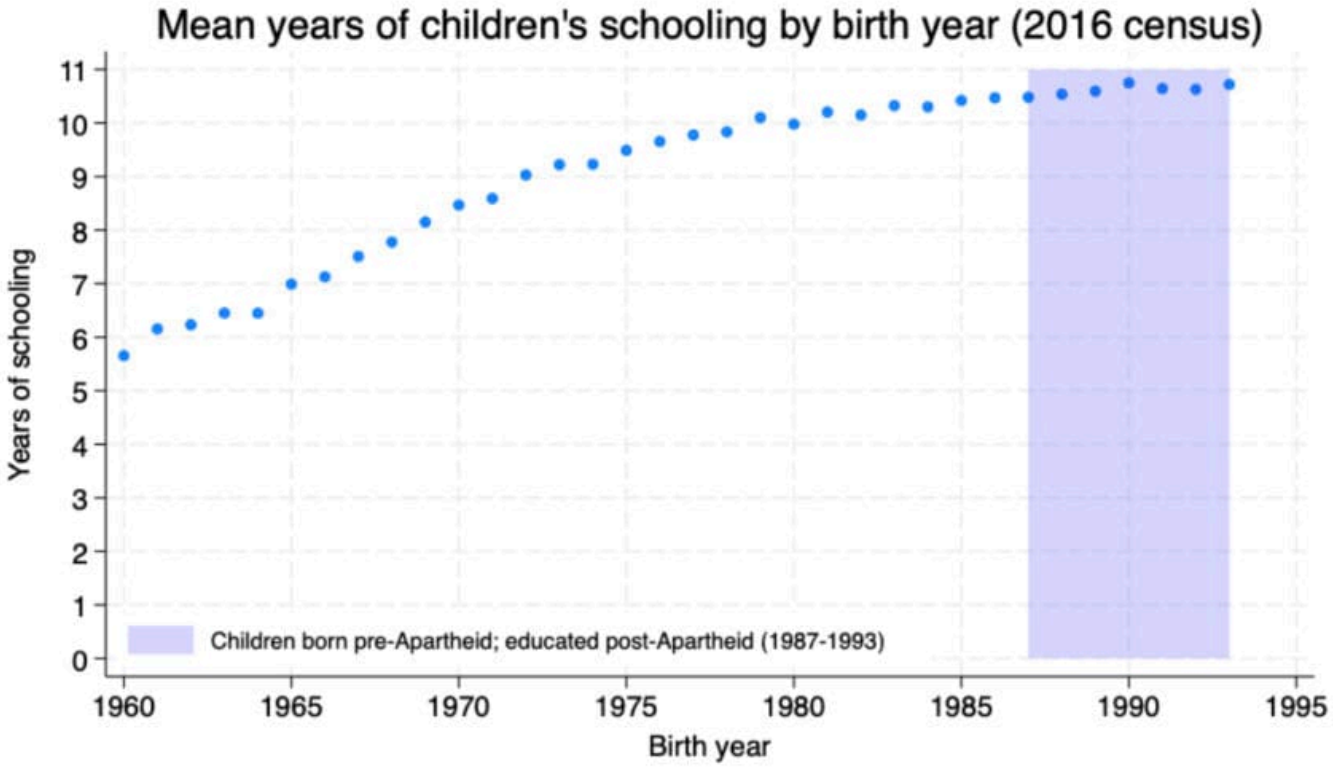
Children’s Expected Educational Attainment and Depressive Symptoms Among Parents in a Rural Cohort of Older Black South African Individuals David Kapaon* David Kapaon Paul Ayernor Darina T. Bassil Jacqueline M. Torres Thomas Gaziano Kathleen Kahn Stephen Tollman Lisa F. Berkman M. Maria Glymour

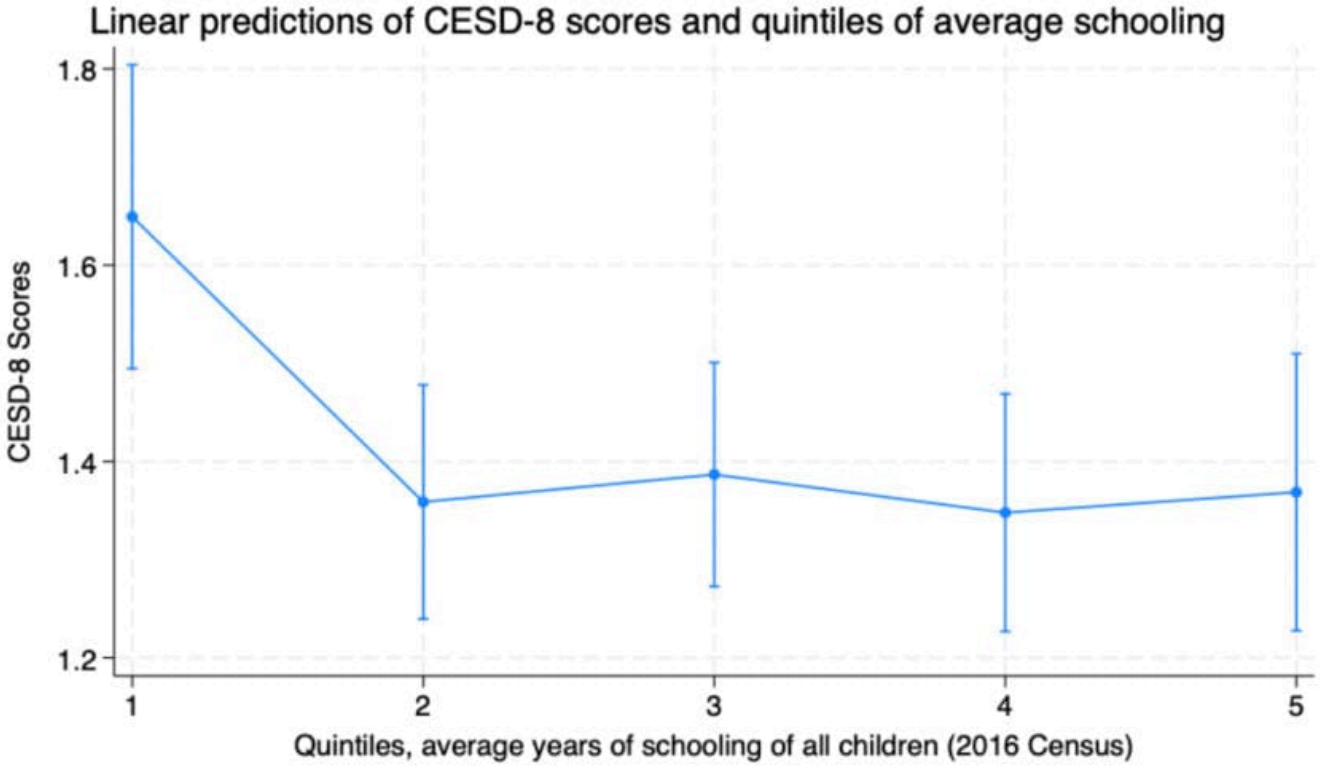
Introduction: The impact of children’s education on the health of their parents is not well studied, especially in settings with rapid educational changes like South Africa. Under Apartheid, educational opportunities for Black South Africans were profoundly restricted. However, the transition to democracy brought new educational prospects for millions. We hypothesized that expanded educational opportunities for Black children after Apartheid benefited the mental health of their parents.

Methods: Health and Aging in Africa: Longitudinal Studies in South Africa (HAALSA) is a longitudinal cohort study of 5,059 Black South African individuals aged 40+ living in rural Mpumalanga Province, South Africa. Using the 2016 South African census, we calculated mean years of schooling for Black South Africans living in Mpumalanga by birth year (1960-1993), and merged them to children of parents in HAALSA by the birth year of each child. Years of schooling were averaged across all children of each HAALSA respondent and grouped into quintiles. Depressive symptoms (CESD-8) were reported by HAALSA participants in 2014-2015. We estimated GEE models, grouped by household, for associations between quintiles of children’s expected educational attainment and parents’ depressive symptoms, adjusting for number of children, as well as parental country of origin, years of education, and age.

Results: Children born in Mpumalanga between 1960-1986 averaged 8.66 (SD: 1.57) years of schooling, compared to 10.62 (SD: 0.09) for children born 1987 or later. Parents in the lowest quintile of children’s expected years of schooling [5.65 to 9.22 years] had higher (worse) CESD-8 scores than parents of children in the highest quintile (10.55 to 10.75 years; $\beta = -0.33$; 95% CI: [-0.56,-0.09]).

Discussion: Increased educational opportunities for children may have benefited the mental health of older parents, though more research is needed to evaluate other pathways and outcomes.


Mean years of children's schooling by birth year (2016 census)
Years of schooling
0
1
2
3
4
5
6
7
8
9
10
11
Children born pre-Apartheid; educated post-Apartheid (1987-1993)
1960
1965
1970
1975
1980
1985
1990
1995
Birth year


Linear predictions of CESD-8 scores and quintiles of average schooling
CESD-8 Scores
1.2
1.4
1.6
1.8
1
2
3
4
5
Quintiles, average years of schooling of all children (2016 Census)

Aging

Cardiometabolic health and dementia risk: A prospective cohort study of 0.5 million adults in China Clara Bueno Lopez* Clara Bueno Lopez Fiona Bragg Andri Iona Zhengming Chen

Introduction

China faces one of the largest dementia-associated economic and healthcare burdens globally, accounting for approximately one-fourth of dementia cases worldwide. However, risk factors for dementia are poorly understood in the Chinese population. We investigate the relevance of markers of cardiometabolic health for risk of dementia.

Methods

China Kadoorie Biobank is a prospective cohort study involving 512,724 adults aged 30-79 years, recruited in 2004-2008 from 10 diverse regions. During ~12 years' follow-up, 1,099 cases of dementia were recorded, including 173 vascular and 344 Alzheimer's dementia, through linked death registries and health insurance databases. Cox regression yield adjusted hazard ratios (HRs) for incident dementia associated with markers of cardiometabolic health.

Results

At recruitment, 34.5% of participants had hypertension, 6.0% diabetes, 3.1% IHD and 1.8% stroke/transient ischaemic attack (TIA). By 2018, an additional 26,652 incident cases of hypertension, 23,747 of diabetes, 56,504 of IHD, and 64,744 of stroke/TIA were recorded. The incidence rate for dementia was 19.0 (95% CI: 17.9-20.1) per 100,000 person-years, higher at older ages, among men and in rural regions. There were positive associations of prior hypertension (HR 1.21 [95% CI 1.05-1.39]), diabetes (1.36 [1.13-1.65]), stroke/TIA (2.52 [2.14-2.96]) and, less clearly, IHD (1.17 [0.97-1.41]) with dementia, driven by notably strong associations with vascular dementia. Systolic blood pressure (SBP) showed a log-linear positive trend with dementia risk, with 9% higher risk (1.09 [1.03-1.15]) per 10 mmHg higher usual SBP.

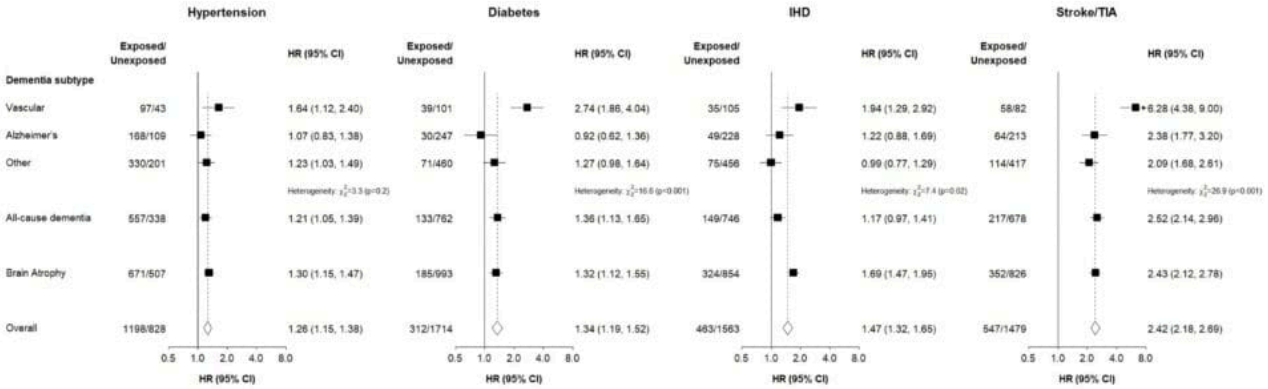
Conclusion

In this population with a high vascular disease burden, markers of cardiometabolic health are important risk factors for dementia.

Conflict of interest: None disclosed

Funding: Wellcome Trust, National Institutes of Health, NIHR, MRC, BHF, CR-UK, Kadoorie Foundation, MoST, NSFC

Associations of markers of cardiometabolic health with dementia and brain atrophy



Hazard ratios (HR) stratified by age-at-risk, sex and study region and adjusted for smoking, alcohol consumption, education, physical activity, healthy diet score, and BMI. Exposed/Unexposed: Number of participants who develop dementia or brain atrophy by exposure status. Exposure is self-reported or screen-detected at recruitment or first instance of exposure identified by ICD-10 codes recorded at hospitalization or in disease registries at least one year prior to incident dementia or brain atrophy. Horizontal lines represent 95% confidence intervals (CI). IHD: ischaemic heart disease. TIA: transient ischaemic attack.

Aging

Causal estimands for cognitive change in the presence of truncation by death L. Paloma Rojas-Saunero* L. Paloma Rojas-Saunero Yixuan Zhou Joan A. Casey Lan Wen Elizabeth Rose Mayeda

Alzheimer’s disease and Alzheimer’s disease-related dementias present a growing public health burden. Research efforts that aim to identify causal mechanisms and potential targets of intervention to reduce dementia risk often estimate the effect of the exposure of interest on the rate of change in cognitive function. A major challenge in these studies is that death acts as a truncation event, and cognitive function becomes unobservable. There is limited work defining causal estimands in this setting, and current literature relies on linear mixed models, generalized estimating equations with inverse probability of censoring weights, or joint longitudinal-survival models, with little attention to interpretation of “rate of change” in the context of truncation by death. This work aims to discuss potential estimands for cognitive change as the outcome of interest in the presence of truncation by death, including causal effects under the hypothetical scenario where death is prevented, the survivor average causal effect, causal separable effects, and the estimand conditional on survival (i.e., “while alive”). We outline identifiability assumptions and identification strategies, and clarify the interpretation of estimates. To illustrate and compare estimated effects, we conducted a case study using data from the U.S. Health and Retirement Study and U.S. life tables to simulate alternative data generation mechanisms based on directed causal graphs, using effects of early-life and late-life environmental exposures on cognitive change over 20 years

Aging

‘Til death do us part? Marital status and excess mortality among older adults during the COVID-19 pandemic Michelle A DeVost* Michelle DeVost Yea-Hung Chen Marie-Laure Charpignon Whitney M Wells M Maria Glymour Ruijia Chen

Background

Despite extensive research on social factors affecting health outcomes during the COVID-19 pandemic, the role of marital status in influencing older adults’ mortality remains underexplored. This study aimed to fill this gap by examining the relationship between marital status and excess mortality among older Californians during the pandemic, assessing potential heterogeneity by place of death.

Methods

Using California death records for decedents aged 65+, we estimated the expected number of deaths during the pandemic (Mar. 2020–Jul. 2023) based on pre-pandemic trends (Jan. 2015–Feb. 2020). ARIMA time series models stratified by marital status (married, widowed, divorced, never married) and place of death (home, hospital, nursing home/long-term care, other) yielded monthly and cumulative estimates of absolute pandemic-era excess mortality overall and by subgroup, per 100,000 using American Community Survey population data.

Results

Among California decedents aged 65+ (n=1,595,862), married individuals had lower excess mortality overall and across age, sex, and education groups. In nursing homes, married individuals had a relative mortality risk ratio of 0.69 (0.65, 0.73), 31% lower than expected based on pre-pandemic trends. Never-married individuals had a ratio of 0.86 (0.83, 0.89), 14% lower than expected. The difference (0.17) between the relative risk ratios of married vs. never-married in nursing homes was nearly twice as large as that observed for home deaths (1.15 vs. 1.24) and six times larger than for hospital deaths (1.22 vs. 1.25).

Conclusions

Marriage was associated with lower excess all-cause mortality among older adults during the COVID-19 pandemic, particularly in nursing homes. These findings suggest that marital status–possibly through mechanisms such as social support and advocacy–may play a critical role in mitigating mortality risk during public health crises, especially in institutional care settings.

Behavior

Predicting COVID Vaccine Uptake Using Machine Learning Zichao Li* Zichao Li

Background

Vaccination has always been a controversial and dividing topic. The anti-vaccine movement resurged in 1970s in UK and grew rapidly in the past 20 years with a focus on child vaccines (Dubé et al., 2015). The COVID-19 pandemic has fueled this intense debate. According to a national survey fielded in Oct. 2021, only 38% of the respondents are vaccinated or very likely to get vaccinated, indicating the majority of individuals in the U.S. are hesitant about getting vaccinated to a certain degree (OSF Preprints | The COVID States Project #35, n.d.).

Scholars further suggest that there is a discrepancy between attitudes toward vaccination and the actual vaccine uptake behavior (Dubé et al., 2013), posing challenges for policymakers and healthcare professionals to more effectively and accurately intervene on vaccine uptake behaviors. Despite research using a machine learning approach to investigate attitudes and beliefs on COVID vaccines (Lincoln et al., 2022), there lack of academic efforts in predicting the COVID vaccine behavioral outcomes. Previous studies have investigated using machine learning to shed light on COVID-related behavioral outcomes, for instance, predicting the likelihood of following the CDC health guidelines (Hajdu et al., 2022; Van Lissa et al., 2022a). This study uses supervised machine learning methods to predict individual COVID vaccination uptake behaviors, which could further provide implications for future vaccine promotion health campaigns and interventions, allowing for a more optimal allocation of resources.

Data

I used COVID-19 Behavior Determinants Database, data from a three-way survey fielded in the US and Canada for this paper (Song et al., 2022). This is a web-based survey administered to 8070 English-speaking respondents above the age of 18. 5326 of the respondents reside in four states of the US: New York, California, Florida, and Texas; the subsample in Canada include all provinces except Quebec (Song et al., 2022). The first two waves of the survey were conducted in 2020 before the COVID-19 vaccine was approved by the FDA, so I only used the data from the third wave (n=3024) fielded in March 2021 for this project. There are no missing values in the outcome from the third wave of the survey, so data from all 3024 respondents were used for data analysis.

Method

In data pre-processing, I conducted principle component analysis (PCA) on several scales, including Brief Locus of Control Scale, General Trust Scale (GTSQ) and Multidimensional Iowa Suggestibility Scale (SSSQ), to compute one score that represents the whole scale. After data preprocessing, 98 predictors were used for modeling training and selection. Then I applied supervised machine learning methods for categorization to develop models that predict the individual COVID vaccine uptake, including logistic regression, KNN, LDA, QDA and tree-based methods. To effectively

manage the variance bias tradeoff, I used 10-fold cross-validation, with 80% of the data as the training set.

Results

Logistic regression performs the best among all models, showing its advantage in high accuracy and relatively low false negative rate. The logistic regression model has an accuracy of 79.01%. A side note is that for the logistic regression models discussed above, I also raised the threshold for predicting positive cases from a 0.5, the default value, to 0.8 and 0.9, the model performances do not improve.

In a nutshell, the logistic regression model yields the strongest model, indicating that machine learning could be used in predicting vaccination behaviors at an individual level. This study could offer practical implications to the design of vaccine promotion campaigns. In the future public health crisis, this tool can be powerful to identify vaccine hesitant individuals that vaccine promotion programs intend to intervene on. Especially because COVID-19 was a novel vaccine, public opinion on the vaccine could be quite versatile and risk-sensitive. In preparation for the occurrence of such challenge, this machine learning approacg could contribute to a deeper understanding in vaccine hesitant groups and then develop persuasive campaign messages for them.

LATEBREAKER

Behavior

Assessing characteristics and outcomes of interventions designed to mitigate the effects of adverse childhood experiences: A Scoping review Maribel Dominguez* Maribel Dominguez Christine M. Markham Andrew E. Springer Louis D. Brown

Background: Adverse childhood experiences (ACEs) are traumatic and distressing events that occur under the age of 18 to a child or a child's family and social environment. Objective: The primary purpose of this study is to describe characteristics of interventions rigorously evaluated in randomized controlled trials (RCT) and assess their effectiveness in mitigating the negative outcomes of ACEs by ACE category. Methods: The project utilizes a comprehensive and transparent synthesis of existing evidence utilizing the ROBIS and GRAMMS tools to help minimize bias and error.

Progress update: The data collection and analysis phases are underway. Anticipated Outcomes: Initial findings indicate that interventions tested in RCTs have included counseling, psychodynamic, and cognitive behavior therapy, with outcomes evaluated that include mental health, physical health, and behavior-focused outcomes. Still, comprehensive conclusions cannot be drawn yet. However, the challenges encountered include effectively synthesizing different outcomes, including patient-reported outcomes, biomarkers, or other clinical endpoints of intervention effectiveness. We are resolving this by modifying the review method that allows us to characterize rigorously evaluated interventions.

Relevance to patients: The significance of this research lies in the contribution of the methods and the potential contributions of the description of study designs, measures, specific outcomes, and theoretical foundations for future intervention development. Conclusion: Upon completion, the findings will provide valuable insights into the characteristics and outcomes of effective interventions focused on mitigating the impact of ACEs by the ACE category. Future work will focus on developing recommendations to replicate, disseminate, and inform on strategies that effectively mitigate the impact of ACEs by ACE category and inform the design of future interventions based on the lessons learned and limitations from the studies reviewed.

Behavior

Association of Cancer Information Seeking and Literacy Level with Preventable Cancer Risk Factors: A Cross-Sectional Analysis from a Nationally Representative U.S. Adult Survey Beomyoung Cho* Beomyoung Cho Sukwon Lee Sericea Stallings-Smith

Introduction

The literacy level of cancer information seekers (CISs) can significantly impact their prevention efforts. While studies highlight the importance of cancer information seeking as a means of preventing cancer risk factors (CRFs), there is a need to understand the extent of literacy level among CISs. We examined the association of cancer information seeking and literacy level with preventable CRFs.

Methods

We used the Health Information National Trends Survey-6, 2022. CISs who have looked for cancer information from any source were asked to answer four subsequent questions: whether they had challenges in locating information, frustration during the search, concerns about information quality, and comprehension difficulties. We considered CISs who had ≥1 of the four characteristics as having lower literacy. We classified all participants into three groups based on cancer information seeking and literacy level: non-seekers, CISs with higher literacy, and CISs with lower literacy. Five CRFs were dichotomized: cigarette smoking (have smoked ≥100 cigarettes and currently smoke every day/some days); binge drinking (≥5 [male] or ≥4 [female] alcoholic drinks on one occasion/past 30 days; being overweight/obese (≥25 body mass index [kg/m2]); physical inactivity (≤150 minutes/week); and experiencing sunburn (≥1 times/past 12 months). We conducted multinomial logistic regression analysis to examine the association of cancer information seeking/literacy level with cumulative CRFs, adjusting for covariates (n = 4,684 adults).

Results

CISs with higher literacy had lower odds of having single CRF (AOR: 0.58, 95% CI: 0.36, 0.95) and ≥2 CRFs concurrently (AOR: 0.60, 95% CI: 0.39, 0.91) compared to non-seekers, while there was no significant difference between non-seekers and CISs with lower literacy.

Conclusions

Disseminating easily accessible and understandable cancer information may help reduce disparities in preventable CRFs between individuals with and without lower literacy.

Behavior

Cancer Risk Behaviors in Quito: A Cross-Sectional Survey of the Adult Population in 2024
Harold Alexander* Harold Alexander María Fernanda García Mateo Bernal Mellany Torres Jahel Castellanos Paula Pauta

Introduction: Cancer is a leading global health issue, with over 23 million new cases worldwide in 2019. Risk behaviors such as smoking, physical inactivity, alcohol misuse, and inadequate sun protection contribute to cancer development. Identifying these behaviors in specific populations is key for prevention. Quito, Ecuador, with its cultural and socioeconomic diversity, presents a unique setting for studying these factors. Between 1985 and 2017, over 93,000 new cancer cases were diagnosed in Quito, showing a rising trend. This study aims to assess cancer risk behaviors in the adult population of Quito between April and June 2024.

Methods: This observational, cross-sectional study was approved by an ethics committee, and participants provided electronic informed consent. A locally adapted, validated survey was based on the HINTS and BRFSS instruments, with additional questions tailored for the local context. Data were collected through social media and electronic platforms from adults residing in the Metropolitan District of Quito. Due to the convenience sampling, a descriptive analysis was conducted.

Results: A total of 405 surveys were analyzed. The median age was 29 years (IQR 22–42), with 64.4% of respondents being female. Regarding risk behaviors, 38.77% reported not drinking alcohol, while 39.26% consumed alcohol excessively at least once in the past month. Physical inactivity was reported by 16.30%, and 21.73% had smoked at least 100 cigarettes in their lifetime. Additionally, 48.15% had used e-cigarettes, 11.12% used sunscreen three or more times daily, and 27.16% had no sunburn in the past year.

Conclusion: The results highlight key cancer risk behaviors in Quito’s adult population, pointing to the need for targeted public health interventions. These findings will inform strategies to reduce cancer risks, promote prevention, and address health disparities in the community.

Keywords: Cancer risk behaviors, Quito, tobacco use, alcohol consumption, physical activity, public health.

Big Data/Machine Learning/AI

A validated transformer-based model to identify transgender and gender diverse people in electronic health records Qi Zhang* Qi Zhang Yuting Guo Mohammed Al-Garadi Timothy L. Lash Lee Cromwell Abeed Sarker Michael Goodman

Background: Natural language processing (NLP) of free-text information from electronic health records (EHR) holds promise for efficient large-scale identification of hard-to-reach populations, including transgender and gender diverse (TGD) people.

Objective: To develop and validate NLP models for automated creation of a large de-identified TGD cohort from EHR across multiple institutions.

Methods: Free-text EHR data were collected from the Study of Transition, Outcomes, and Gender (STRONG), including individuals enrolled in multiple sites of the Kaiser Permanente healthcare network between January 1, 2006, and February 28, 2022. This research protocol included two studies: 1) model development and evaluation, using TGD keyword-containing text excerpts pertaining to 11,529 previously confirmed TGD individuals; and 2) assessment of model validity, involving model application to a larger group (n=371,909) of TGD candidates, with a stratified random sample validated by trained reviewers. The validation strata were based on NLP predicted class, geographic location and additional evidence (TGD-specific diagnostic codes and/or self-reported gender identity). Performance of models was assessed using sensitivity, and positive and negative predictive values (PPV and NPV) and F1 score.

Results: In the first study, the transformer-based RoBERTa outperformed other models, achieving an F1 score of 0.95, with a sensitivity of 0.97 and a PPV of 0.94. In the validation study, when participants had TGD evidence beyond keywords, RoBERTa predictions showed a high PPV of 0.92–1.00, despite a low NPV of 0.11–0.59. Conversely, the model yielded a high NPV (0.98–0.99) but a low PPV (0.20–0.36) among candidates with keywords alone.

Conclusion: NLP models provide an efficient and scalable approach for identifying TGD individuals in EHR. Transformer-based models outperformed other algorithms and showed potential for transportability to external populations with additional TGD evidence.

Big Data/Machine Learning/AI

A framework for collecting data for public health research from the web using large language models Thomas Berkane* Thomas Berkane Marie-Laure Charpignon Maimuna S. Majumder

Many public health researchers rely on using data from the web in their work, from epidemiological reports and vaccination statistics published by governments to public sentiment on health topics discussed in news and social media. However, these data are typically scattered across the web, becoming useful for longitudinal or cross-sectional studies only after compilation into structured datasets. Further, manually searching for data points is time-consuming and prone to human error.

We propose a framework that automates web-scale collection of research data end-to-end, leveraging large language models (LLMs). Given a user-provided description of the target dataset, our framework generates search queries, navigates the web to find relevant pages, selectively extracts data, performs quality control, and produces a structured dataset. The framework operates in a human-in-the-loop manner, allowing users to inspect and adjust the data collection process at each stage to ensure alignment with their goals. In addition to mitigating LLM hallucinations through grounding, we correct for two types of bias introduced by search engines: webpage recency and user geographical location. The framework maintains transparency by linking each data point to its original source. The quality control step automatically flags potentially anomalous data points for user review, such as outliers and duplicates.

After validating each step of our framework, we present three case studies illustrating its application to collecting diverse types of public health data from the web: (1) time series of cholera cases globally, (2) US state-level COVID-19 contact tracing app downloads, and (3) timelines of natural disasters — events often leading to disease outbreaks — in Haiti and Cameroon. The dataset derived for case study (3) is shown in Fig. 1.

Future research will expand our framework to handle the extraction of public health data from more modalities than text, such as images and PDFs.

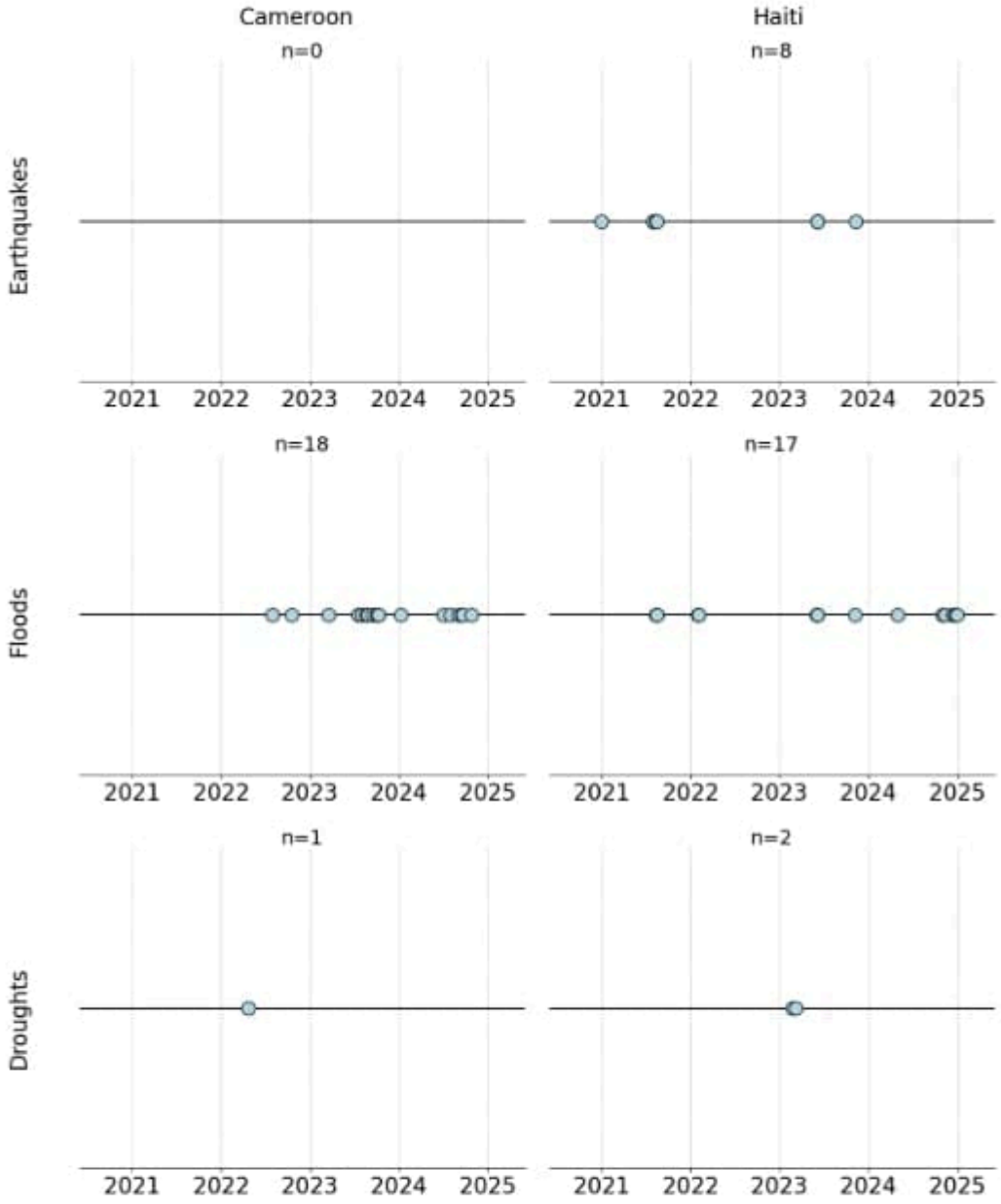


Figure 1: Timelines of earthquakes, floods, and droughts in Cameroon and Haiti from 2021 to 2025, as extracted by our LLM-based framework. Each dot represents an event extracted from a web page, after removal of duplicate events. While earthquakes are typically well-documented in established databases, floods and droughts often lack standardized reporting due to varying definitions. Our framework helps capture such events, which may be reported in regional sources but missed by global databases. The derived dataset suggests many floods in both countries, but only a few droughts and earthquakes, and no earthquakes in Cameroon during the considered period.

Big Data/Machine Learning/AI

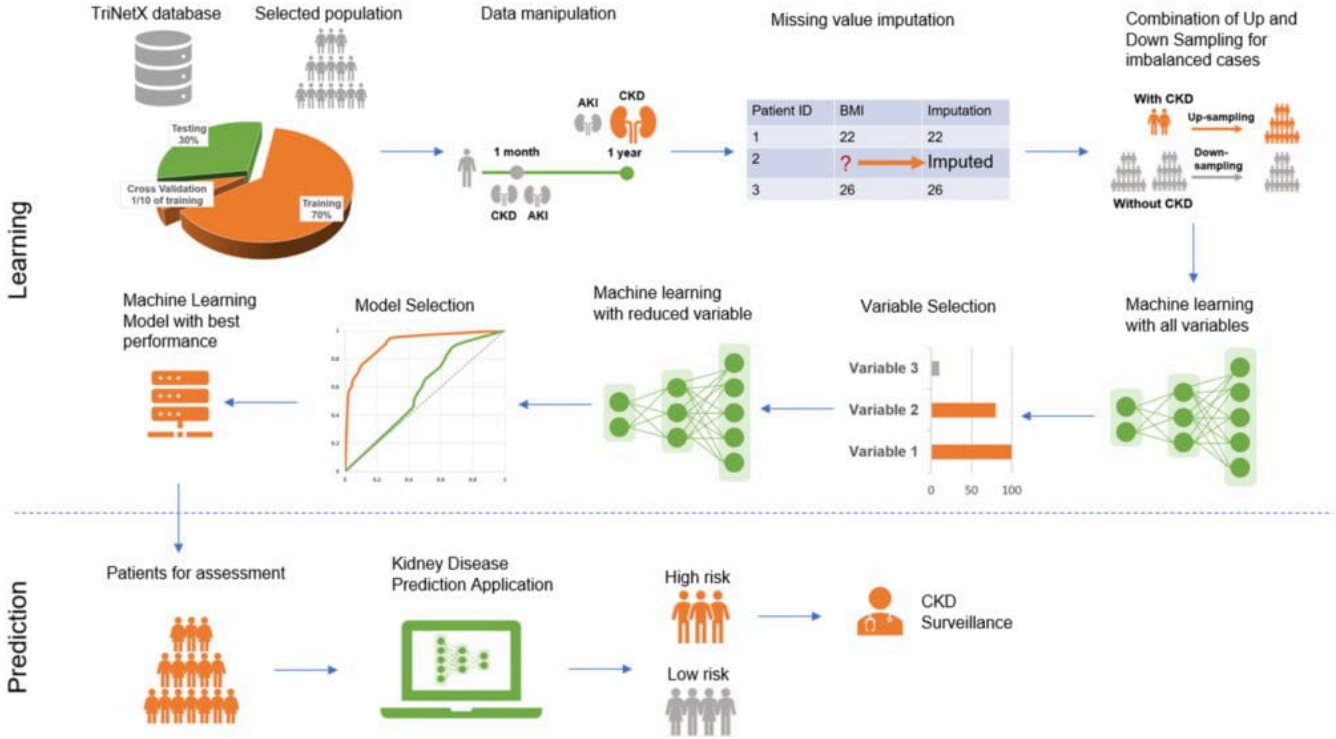
Prediction of Acute and Chronic Kidney Diseases During the Post-COVID-19 Pandemic with Machine Learning Models: Utilizing National Electronic Health Records in the US Yue Zhang* Yue Zhang Nasrollah Ghahramani Vernon M. Chinchilli Djibril M. Ba

Background: COVID-19 infections have been demonstrated to impact acute kidney injury (AKI) and chronic kidney disease (CKD). However, the application of machine learning (ML) algorithms to predict the risk of AKI and CKD during the post-pandemic period is lacking. We aimed to leverage large electronic health records (EHR) and ML algorithms to predict the risk of incident AKI and CKD in both the short and long term during the post-pandemic period and to translate our ML models into a practical webpage application.

Methods: National EHR data from TriNetX were used, emulating a prospective cohort from 07/01/2022 to 03/31/2024, which was separated into training and testing datasets. A total of 69 baseline variables were included, with demographics, comorbidities, lab test results, vital signs, medication histories, hospitalization visits, and COVID-19-related variables. Two prediction windows, 1 month and 1 year from the index dates, were defined to identify the incidence of AKI and CKD. Eight machine learning models, primarily including adaptive boosting (AdaBoost), extreme gradient boosting (XGBoost), neural network (NN), and random forest (RF), were applied. Cross-validation and model tuning were conducted during the training process. Six evaluation metrics, including the area under the receiver-operating-characteristic curve (AUROC), were used to compare model performance. A combination of model-driven, data-driven, and clinical-driven methods was employed to identify the final models. An application with the final models was built using the R Shiny framework.

Results: A total of 104,565 patients were included in this study. The final models, incorporating 9 variables—primarily including eGFR, inpatient visit number, and COVID-19 infection counts—were selected. XGBoost demonstrated the best performance for predicting the incidence of AKI in 1 month (AUROC = 0.803), AKI in 1 year (AUROC = 0.799), and CKD in 1 year (AUROC = 0.894). Random Forest (RF) was selected for predicting the incidence of CKD in 1 month (AUROC = 0.896). Number of COVID-19 infections was shown to be a critical factor for inclusion in the prediction model. The final models were translated into a convenient tool to facilitate their use in clinical settings.

Conclusions: Our study demonstrates the applicability of using large national EHR data in developing high-performance machine learning models to predict AKI and CKD risks in the post-COVID-19 period. Incorporating the number of COVID-19 infections in the past year showed improved prediction performance and should be considered in future models for kidney disease prediction. A user-friendly application was created to support clinicians in risk assessment and surveillance.



Overall machine learning and prediction strategy flow (Example: Incidence of chronic kidney disease in 1 year)

Big Data/Machine Learning/AI

Development of Self-Assessment Tools for Osteoporosis among Postmenopausal Vietnamese Women: A Machine Learning Approach Thuy Trang Nguyen* Tunglam Nguyen Christine Pallota My Hanh Bui Khuong Quynh Long

Development of Self-Assessment Tools for Osteoporosis among Postmenopausal Vietnamese Women: A Machine Learning Approach

Authors: TungLam Nguyen1, Christine Pallotta2, My Hanh Bui2, Thuy Trang Nguyen2, Quynh Long Khuong3

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Background

Osteoporosis is a major health concern in Vietnam due to a rise in aging rates. However, cost-effective early screening tools tailored to the Vietnamese population are lacking. In this study, we applied a machine learning approach to develop self-assessment tools for osteoporosis in menopausal women.

Methods

We used retrospective data from 16,516 postmenopausal Vietnamese women extracted from electronic medical records. Bone mineral density (BMD) measurements of the lumbar vertebrae (L1–L4) and the left and right femoral necks were obtained using the dual-energy X-ray absorptiometry (DXA) system. Osteoporosis was defined as a BMD T-score of < -2.5. Eight algorithms (Logistic Regression, Decision Trees, Random Forest, XGBoost, K-Nearest Neighbors, Neural Networks, Lasso and Ridge regressions, and Naïve Bayes) were utilized to develop prediction algorithms for each anatomical site. The main predictors included age, menopause age, weight, height, lifestyles, and comorbidities. Cross-validation was employed to prevent overfitting.

Results

The prevalence of osteoporosis, as determined by BMD, varied across anatomical sites, ranging from 37% to 51% in the lumbar vertebrae and from 19% to 21% in the left and right femoral necks, respectively. The performance of the models varied slightly across algorithms, though the differences were not substantial. Considering the balance between performance and simplicity, logistic regression was selected as the final algorithm. The final models were developed using four predictors: age, menopause age, height, and BMI, with the area under the curve (AUC) ranging from 0.75 at lumbar vertebrae L4 to 0.84 at right femur. Our models demonstrated superior performance compared to existing tools, such as OSTA, which were developed for the general Asian population.

Conclusion

The newly developed self-assessment tools were shown to be simple and effective in predicting osteoporosis among postmenopausal Vietnamese women. These tools have the potential to serve as early screening instruments for osteoporosis, particularly in resource-limited settings.

LATEBREAKER

Big Data/Machine Learning/AI

The Crucial Role of Predictive Models in Childhood Asthma care: Improving Outcomes Through Data-Driven Insights ADITYA CHAKRABORTY* ADITYA CHAKRABORTY AKMR. Bashar Sikta Das

Introduction: Asthma is the most prominent chronic disease in children and one of the most challenging ailments to diagnose in infants and preschoolers in the United States. Predictive models can be instrumental in offering a data-driven approach to improve early diagnosis, personalize treatment strategies, and disease progression. By utilizing nationalized data, this study focuses on building, and comparing high performing analytical predictive models based on the 28 associated risk factors and identifying the most contributing factors influencing childhood asthma.

Method: Data came from the BRFSS (2011-2020) Asthma Call Back Survey (ACBS). The cross-sectional study included 9813 participants with a response rate of 65% (current asthma status positive). Respondents were randomly divided into training and testing samples. The grid-search mechanism was implemented to compute the optimum values of the hyper-parameters of the analytical eXtreme Gradient Boosting (XGBoost) model. The fitted XGBoost model was compared with four competing ML models including support vector machine (SVM), random forest, LASSO regression, and GBM. The performance of all the models was compared using accuracy, AUC, precision, and recall. Variable importance plot (VIP) was used to measure the percentage of contribution of the predictors to the response, and SHapley Additive exPlanations (SHAP) plot was used to understand how the predictors are related to the outcome. Chi-square test was used to measure the association between the predictors and the outcome.

Results: Asthma diagnosis was found to vary by age group, with the highest prevalence in kindergarten age (31.44%). Of the five predictive models, the XGBoost was found to be the best performing model with AUC: 0.95, followed by random forest (AUC: 0.9345), GBM (AUC: 0.9341), SVM (AUC 0.9304), and LASSO (AUC 0.88); however, the random forest model was found to have the highest sensitivity (0.9786), and hence preferred for initial screening of asthma. The top two contributing predictors were overnight hospitalization visits, and time since the last asthma medication, accounting for 24.62%, and 20.92% respectively to the asthma status, from the VIP.

Conclusion: The analytical methodology of the model development was found to be instrumental in the discovery of behavior health-risk knowledge and to visualize the significance of predictive modeling from a multidimensional behavioral health survey. These insights can be instrumental to predict different types of chronic lung diseases affecting people of all ages and can be useful for clinicians to diagnose asthma at an early stage, allowing for early intervention and proactive management.

Big Data/Machine Learning/AI

Comparing Extreme Gradient Boosting and Multi-Layer Perceptron algorithms for the prediction of neonatal mortality Renan Moritz VR Almeida* Renan Moritz VR Almeida Nubia Karla de Oliveira Almeida Renan Moritz Varnier Rodrigues de Almeida

Objective: To apply eXtreme Gradient Boosting (XGBoost) and Multilayer Perceptron (MLP) models to the prediction of neonatal mortality.

Methods: The study used 167.928 singleton births in Rio de Janeiro State (Brazil), 2019-20, obtained from a national administrative information system (Datasus). The outcome was neonatal mortality, and the predictors were 15 variables pertaining to characteristics of the mother, the pregnancy and the newborn.

Data were randomly split into a training (70% of data) and a testing set, after what an MLP with one hidden layer and an XGBoost model were developed in the training set. Backpropagation MLPs are the “classical” machine-learning models, introduced in the 1970s and popularized in the 80s; while XGBoost is widely regarded for its efficiency and robustness, and is now one of the most preferred methods for machine-learning applications. Performance was evaluated in the testing set by the usual metrics AUC, Accuracy, Precision, Sensitivity, F1-score and Specificity. Two classification thresholds were tested: The usual “0.5” and an empirical threshold that maximized sensitivity. All analyses were done with the R language.

Results: The identified threshold for sensitivity maximization was 0.01. Regardless of threshold or metric, both models did not differ much in their outcomes, with the main XGBoost x MLP differences: AUC: 0.83 x 0.88, Precision: 0.28 x 0.54, F1-score: 0.11 x 0.13 (threshold 0.5); AUC: 0.83 x 0.88, Sensitivity 0.68 x 0.72, F1-score: 0.07 x 0.10 (maximizing sensitivity; no change in other metrics).

Conclusions: Both models were good classifiers for the studied data. In fact, despite its alleged advantages, XGBoost performed slightly worse than the classical MLP model. Threshold definition also did not have a marked effect on outcomes.

Overall, these results once more indicate that the most important factors for the application of machine learning models to epidemiologic data are model specification and data quality.

Big Data/Machine Learning/AI

Machine learning for predicting hospital mortality in cervical cancer patients Audêncio Victor* Audêncio Victor Fabiano Barcellos Filho Sancho Xavier Pedro Alexandre Dias Porto Chiavegatto Filho

Introduction: Cervical cancer (CC) is a leading cause of cancer mortality among women in low- and middle-income countries, especially in regions with limited healthcare infrastructure. This study utilizes machine learning (ML) models to predict hospital mortality in patients hospitalized with CC from 2011 to 2023 in Mato Grosso, Brazil.

Methods: Hospital data on cervical cancer patients were obtained from the Hospital Information System (SIH) of the SUS, covering 2011–2023. Five ML algorithms Logistic Regression, Random Forest, CatBoost, LightGBM, and XGBoost were used to predict hospital mortality based on demographic, clinical, and hospital variables. Performance metrics included AUC-ROC, accuracy, sensitivity, specificity, precision, F1, and Matthew's correlation coefficient (MCC).

Results: All models achieved AUC-ROC above 0.87, indicating high predictive performance. XGBoost demonstrated the best overall performance, with an AUC-ROC of 0.89, 88% accuracy, and 95% specificity, with an MCC of 0.28. Tree-based models such as Random Forest and XGBoost showed high specificity with 94% and 95%, respectively, while CatBoost also performed well with an accuracy of 88% and specificity of 94%. SHAP value analysis identified medical procedure type, hospitalization cost, and service complexity as the main mortality predictors.

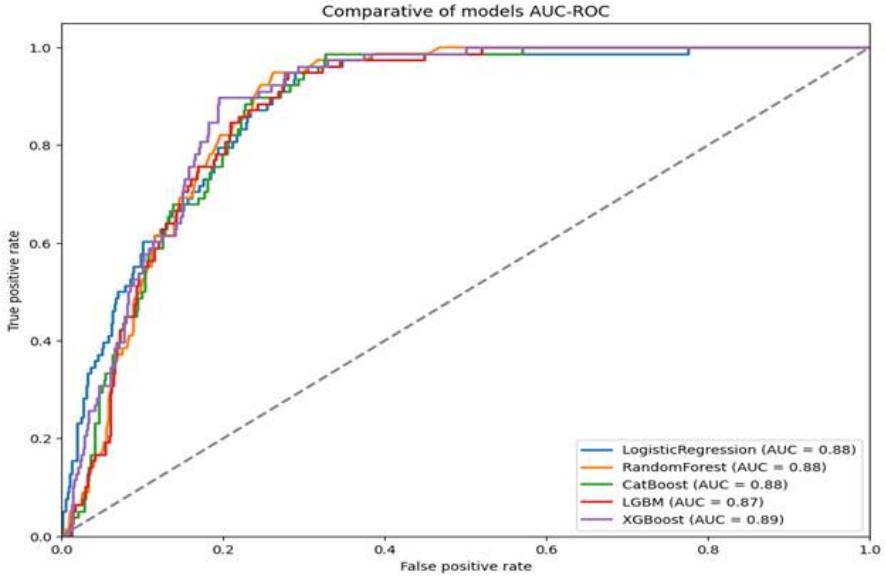
Conclusion: ML was found effective for predicting hospital mortality in CC patients in Mato Grosso, providing valuable insights into risk factors and facilitating clinical decision-making. These models can be integrated into healthcare systems to optimize resource allocation and improve survival in areas with limited infrastructure.

Keywords: Cervical cancer, hospital mortality, machine learning, oncology, Brazil

Predictive performance on test data of the best algorithm for each outcome with hyperparameter tuning.

Model	AUC-ROC	Accuracy	Recall	Specificity	Precision	F1	Threshold	MCC
Logistic Regression	0.88	0.79	0.81	0.79	0.29	0.43	0.5	0.4
Random Forest	0.87	0.88	0.32	0.94	0.36	0.34	0.5	0.27
CatBoost	0.88	0.88	0.33	0.94	0.38	0.36	0.5	0.29
LGBM	0.88	0.87	0.22	0.94	0.28	0.25	0.5	0.18
XGBoost	0.89	0.88	0.31	0.95	0.39	0.34	0.5	0.28

Predictive performance on test data of algorithms for each model in terms of AUC-ROC.



Big Data/Machine Learning/AI

Machine Learning to Predict Tuberculosis Treatment Abandonment in São Paulo, Brazil

Marcela Quaresma Soares* Marcela Soares Fabiano Barcellos Filho Alexandre Dias Porto Chiavegatto Filho

Tuberculosis (TB) treatment abandonment is a significant public health challenge, contributing to increased disease transmission and worsening patient outcomes. This study aimed to develop and compare machine learning models to predict treatment abandonment, using data from the Brazilian Unified Health System (SUS) in São Paulo, covering the period from 2013 to 2023. We included a total of 232,809 TB cases, of which 34,034 (14.6%) were classified as treatment abandonment. The analysis considered a wide range of independent variables, including demographic, clinical, and contextual factors, with missing data grouped into 'ignored' categories. Popular machine learning algorithms for structure data such as Random Forest, XGBoost, LightGBM, CatBoost, and TabNet were evaluated. All models were optimized through hyperparameter tuning and validated using 5-fold cross-validation to enhance robustness and generalizability. Performance was assessed using AUC-ROC, precision, recall, and F1-score metrics. CatBoost achieved the highest performance, with an AUC-ROC of 0.912, followed by LightGBM (0.911) and XGBoost (0.910). CatBoost also demonstrated the best balance between precision (0.73) and F1-score (0.61), significantly outperforming other models in identifying cases of treatment abandonment. Hyperparameter tuning notably enhanced the performance of the boosting algorithms, particularly in improving precision and recall. These results highlight the potential of machine learning not only to predict treatment abandonment but also to inform evidence-based decision-making. The ability to identify high-risk patients can enable health authorities to design targeted interventions, prioritize resources, and ultimately reduce TB-related morbidity and mortality. This study reinforces the importance of integrating advanced analytical methods into public health strategies, especially in resource-limited settings where TB remains a critical health issue.

Big Data/Machine Learning/AI

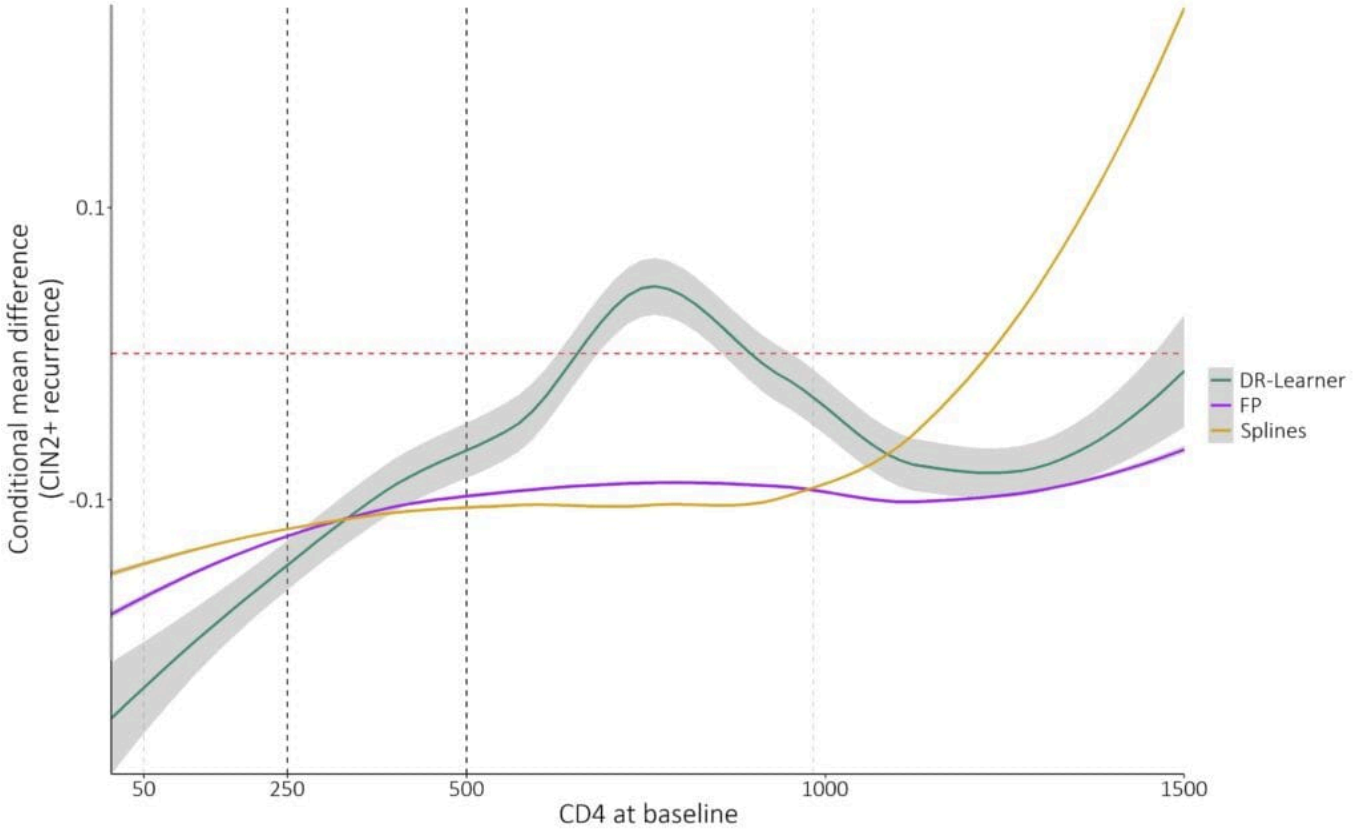
Leveraging Nonparametric Machine Learning to Assess Effect Modification of Cervical Precancer Treatment in Women Living with HIV Nazha Diwan* Nazha Diwan Michael H. Chung Sharon A. Greene Judith Lukorito Samah R. Sakr Nelly R. Mugo Gabriel Conzuelo Rodriguez

Background: Ablation is currently a standard treatment for cervical precancer (CIN2+) in low-resource settings. While its efficacy in non-HIV populations is established, evidence suggests suboptimal effects in women living with HIV (WLWH). It is hypothesized that the elevated risk of recurrence among WLWH depends on the level of immunosuppression. However, most studies assessing this treatment effect modification rely on subgroup analyses of categorized CD4 count, which results in substantial loss of information and statistical power. Flexible parametric models address these limitations by avoiding categorization of continuous modifiers, but still rely on restrictive assumptions about the data-generating mechanism. Alternatively, nonparametric machine learning approaches (e.g. DR-learner) avoid parametric assumptions and provide flexibility to capture effect modification.

Methods: We used data from a randomized trial conducted at the Coptic Hope Center in Nairobi, Kenya (2011-2016), which assessed differences in CIN2+ recurrence over 24 months in WLWH assigned to ablation (cryotherapy [n = 172]) or excision (LEEP [n = 167)]. Effect modification by CD4 count at treatment was modeled using generalized linear models that incorporated either restricted cubic splines or fractional polynomials, as well as the DR-learner.

Results: Overall, LEEP is superior to cryotherapy in treating CIN2+ lesions among WLWH. However, as CD4 count increased, the risk difference for CIN2+ recurrence between cryotherapy and LEEP decreased.

Conclusion: While excisional treatments like LEEP are superior, they are impractical in low-resource settings. Ablation is a viable alternative for some WLWH, with eligibility guided by immunological factors. The DR-learner could be leveraged to more effectively model complex relationships between factors such as ART duration, viral load, and HPV type, enhancing risk stratification and enabling more targeted and evidence-based treatment strategies for WLWH.


Conditional mean difference
(CIN2+ recurrence)
0.1
-0.1
50
250
500
1000
1500
CD4 at baseline
DR-Learner
FP
Splines

Big Data/Machine Learning/AI

Auditing Models: Machine Learning for Early Detection of Prediction Errors Kevin Anderson Ruperto Mateo Panduro* Kevin Anderson Ruperto Mateo Panduro Roberta Moreira Wichmann Alexandre Chiavegatto Filho

The ability to anticipate prediction errors in clinical models is essential for improving decision-making and optimizing resource allocation, especially in high-pressure scenarios such as the COVID-19 pandemic. This study aimed to develop and evaluate machine learning algorithms to predict errors in a base model designed to classify critical outcomes, specifically mortality and ICU admission, in patients diagnosed with COVID-19. Data from 8,477 hospitalized patients were obtained through the Artificial Intelligence for COVID-19 in Brazil (IACOV-BR) network, covering 18 hospitals across the country. A base predictive model was built using XGBoost, achieving an AUC of 0.852 for mortality and 0.928 for ICU admission. Auxiliary models were subsequently developed to predict type 1 (false positives) and type 2 (false negatives) errors. The XGBoost algorithm demonstrated superior performance, with AUCs ranging from 0.662 for type 1 error prediction in mortality to 0.870 for type 2 error prediction in ICU admission. Group analysis identified intersections where the base model’s predictions exhibited higher-than-average error rates, particularly among groups with high predictive probabilities in the auxiliary models. These findings underscore the importance of integrating auxiliary models to detect high-risk prediction errors, contributing to more reliable clinical decision-making and improved patient management during healthcare emergencies.

Cancer

Symptom burden and health-related quality of life in pediatric cancer after treatment completion Krishtee Napit* Krishtee Napit Don Coulter Daisy Dai Katrina Cordts Evi Farazi Shinobu Watanabe-Galloway

Background

With advanced treatments, survivors are living longer. However, they often experience symptom burden after treatment completion, which deteriorates their health-related quality of life (HRQoL). The association between HRQoL and symptom burden in pediatric cancer after treatment completion remains understudied.

Methods

We conducted a cross-sectional study of 136 pediatric cancer survivors aged 10-25 who completed treatment within 8 years from 2 major hospitals in Nebraska. We used a survey to collect data during their hospital visit, the validated Memorial Symptom Assessment Scale tool to collect information on the presence, frequency, severity, and distress of 30 symptoms, and the PedsQoL instrument to measure the HRQoL. At least for one symptom, the distress level should be '1-4' to be considered for symptom burden. The burden was categorized as higher and lower if the total symptoms were 13-30 and 1-12, respectively. We conducted a multiple linear regression model to find the association between HRQoL and symptom burden at a significance level with a p-value of less than 0.05 and an adjusted beta coefficient.

Results

The mean age, year since diagnosis and treatment completion were 14.91, 4.66, and 3.05, respectively, and the mean symptoms number was 6.06. Around 79% experienced symptom burden. Difficulty concentrating (48.53%), lack of energy (45.59%), and feeling drowsy (45.59%) were the most common symptoms. The mean HRQoL score was 80.84 out of 100. The presence of a higher symptom burden negatively influenced HRQoL in bivariate analysis. The adjusted model, which included co-variates based on literature, showed that higher symptom burden (β= -4.66, p-value=0.0004) and education of father high school vs less than high school (β= -4.46, p-value=0.0147) were associated with HRQoL.

Conclusion

Even after the treatment completion, symptom burden is prevalent in pediatric cancer survivors, and the prevalence of a higher symptom burden degrades the HRQoL.

Cancer

Leveraging Cross-Modality Interactions of DNA Methylation and Gene Expression for Insights Into Tumorigenesis in Lung Adenocarcinoma Shaira Kee* Shaira Kee Michael Aaron Sy Panayiotis V. Benos

Lung adenocarcinoma (LUAD) is the most common lung cancer in the United States. While treatment has improved, LUAD remains the leading cause of cancer death in the US. Studies show that conventional staging alone is insufficient in predicting LUAD prognosis and guiding treatment. Gene expression (GE) is among the instrumental tools in cancer research. Additionally, Aberrant DNA methylation (DNAm) is considered a hallmark of tumorigenesis and is associated with multiple malignancies.

Clinical Proteomic Tumor Analysis Consortium (CPTAC) is a cancer research initiative that utilizes molecular data and matched pairs of tumor and normal tissue extracted from the same patient, which better assesses inter-patient variability and tumor-specific alterations. RNA-seq data from 96 CPTAC-LUAD participants were used in the study. Firstly, we extracted 10 distinct groups from the RNA-seq data (n = 15,314 genes) using ward linkage hierarchical clustering to reduce complexity. Subsequently, cross-modality interactions were analyzed using causal graph modeling of combined normalized clinical, GE, and DNAm.

We found a distinct separation of tumor and non-tumor omics data using causal graphs (see Fig. 1C), suggesting that certain gene groups are more indicative of tumor characteristics. The predictive classification using a random forest classifier achieved high performance with an accuracy of 99%, underscoring its robustness in differentiating tumors from normal samples.

In summary, this study proposes a new approach to determining gene signatures relevant to LUAD prognosis using causal graph approaches and machine learning prediction. Through causal graphs, we were able to identify direct interactions between omics data of LUAD, furthering the potential clinical utility of multimodal omics data for prognostic biomarkers.

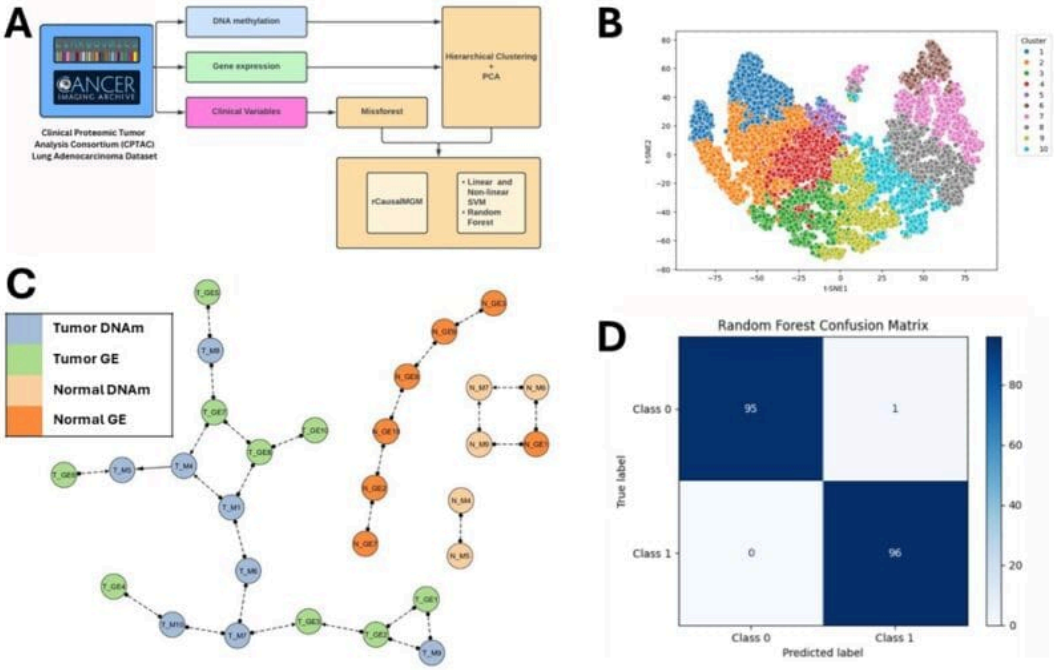


Figure 1. Summary of the analysis. (**A**) Overall pipeline workflow. (**B**) t-SNE Visualization of Omics Data. (**C**) Causal Graph with tumor and normal clinical, GE program, and DNAm program variables. (**D**) Confusion Matrix of Random Forest.

Cancer

Association Between Dietary Intake of Advanced Glycation End-Products and Aggressive Prostate Cancer Among Black and White Men in the North Carolina-Louisiana Prostate Cancer Project Hadi Rashidi* Hadi Rashidi David P Turner Joseph Su Lenore Arab Jeannette T Bensen Ebonee N. Butler Laura Farnan Victoria Findlay James L. Mohler Tyler-Stukes, Gayle Susan E Steck

Background

Prostate cancer is the most common cancer and second leading cause of cancer-related mortality among men in the United States. Advanced glycation end-products (AGEs) are reactive metabolites formed endogenously but also consumed in processed food and foods that are cooked at high temperatures. Evidence from experimental animal studies show that AGEs are related to pathogenesis of various chronic diseases including cancer. However, the association between dietary AGEs and aggressive prostate cancer has yet to be examined.

Method

We analyzed data from the North Carolina – Louisiana Prostate Cancer Project (PCaP), a cross-sectional study of Black and White men diagnosed with prostate cancer. We included 1900 men, (901 Black and 991 White) in the analyses and defined aggressiveness as “high” (n=332) or “low/intermediate” (n=1568) based on clinical stage, Gleason grade, and prostate specific antigen at diagnosis. Dietary intake of AGEs was estimated from responses to the NCI-Diet History Questionnaire linked to the Uribarri et al. dietary AGE database. Multivariable logistic regression was used to determine the adjusted odds ratios and 95% confidence intervals for high-aggressive prostate cancer by tertile of AGE intake.

Result

Among dietary sources of AGEs, red meat products were major contributors, representing 23.4% of total AGE intake. In race-stratified analyses, a positive association between AGEs intake and high aggressive prostate cancer was observed for Black men (OR2nd vs 1st tertile= 1.42; CI, 0.88-2.29 and OR3rd vs 1st tertile=1.68; CI, 0.96-2.91) but not for White men (OR2nd vs 1st tertile = 0.88; CI, 0.56-1.38, OR3rd vs 1st tertile =0.75; CI, 0.39-1.41).

Conclusion

Based on study results, it appears that higher dietary AGEs intake is associated with increased odds of high aggressive prostate cancer among Black men. Future prospective studies are warranted to confirm this finding

Cancer

Racial Disparities and Physical Activity in the Pathways Study, A Prospective Cohort Study of Breast Cancer Survivors Tanvi Srivastava* Tanvi Srivastava Lia L D'addario Janise M Roh Lawrence H Kushi

Physical activity (PA) is widely recognized for its numerous health benefits, including improved survival and quality of life in breast cancer (BCa) survivors. However, disparities in PA levels among different racial and ethnic groups have been documented. Understanding these disparities among BCa survivors is crucial for developing targeted interventions to promote PA among underserved populations. The diverse prospective cohort of BCa survivors in the Pathways Study at Kaiser Permanente Northern California (KPNC) provides a unique opportunity to explore these disparities in a comprehensive manner. A cohort of 4,504 women was enrolled soon after diagnosis from Jan 2006 to May 2013 with data collected through surveys, electronic health records, and other KPNC databases. Self-reported PA was assessed at baseline (~2 months post-diagnosis). Follow-up surveys were collected at around 6 and 24 months after baseline. The cohort is followed for outcomes such as recurrence, overall mortality, and cause-specific mortality. PA levels were defined as low, medium, and high based on MET-hour tertiles. Among 4,386 survivors with baseline PA data, 21% were foreign-born. Asian Americans (AA) had the highest percentage (48%) of college-educated patients and highest household incomes, with 41% earning $90,000+, while Non-Hispanic Blacks (NHB) had the lowest incomes, with 38% earning <$50,000. Poisson regression in the exploratory phase of this project showed that AA and NHB survivors were more likely to have lower PA levels (adj. RR for AA = 1.69 (1.42, 2.01); adj. RR for NHB = 1.24 (1.02, 1.51)) compared to NHW patients. AA survivors were less likely to have higher PA levels (adj. RR = 0.64 (0.53, 0.77)) compared to NHW patients. The next phase of this ongoing project is to investigate the associations of PA on BCa recurrence, BCa mortality, and mortality due to cardiovascular disease in this cohort across different racial and ethnic groups.

LATEBREAKER

Cancer

Associations of Plasma C-Peptide and IGFBP-1 With Chemotherapy Completion and Adverse Events in Patients with Colon Cancer: Results from CALGB/SWOG 80702 Adhirai Muthukumar* Adhirai Muthukumar Qian Shi Anthony F. Shields Chaoyuan Kuang Ardaman P. Shergill Chao Ma Katherine A. Guthrie Felix Couture Philip Kuebler Pankaj Kumar Benjamin Tan Smitha S. Krishnamurthi Kimmie Ng Eileen M. O'Reilly Justin C. Brown Edward L. Giovannucci Philip A. Philip Jeffrey A. Meyerhardt En Cheng

Background: Hyperinsulinemia and the insulin-like growth factor (IGF) pathway play important roles in colon cancer development and progression, but their impact on colon cancer chemotherapy tolerance is largely unknown. To fill this gap, we assessed the associations of C-peptide (a marker of insulin resistance and secretion) and IGF binding protein 1 (IGFBP-1) with colon cancer chemotherapy completion and adverse events.

Methods: Among an NCI-sponsored adjuvant chemotherapy trial for patients with stage III colon cancer enrolled between 2010 and 2015 (CALGB/SWOG 80702), we assayed C-peptide and IGFBP-1 using blood samples collected after surgery but before chemotherapy. We focused on relative dose intensity (RDI; an indicator for chemotherapy completion associated with early colon cancer recurrence and death) and severe adverse events (AE; chemotherapy toxicities associated with worse colon cancer prognosis). We estimated odds ratios (OR) for the associations of C-peptide and IGFBP-1 with reduced RDI (RDI <85%) and the occurrence of severe AE using multivariable logistic regression.

Results: Of 1342 patients included in this study, the mean age was 61.0 years, 82.5% were White, and 53.2% were male. The medians (interquartile) were 4.8ng/mL (3.2-7.2ng/mL) for C-peptide and 1.3ng/mL (1.0-1.9ng/mL) for IGFBP-1. Compared to the lowest quintile (Q1), the highest quintile (Q5) in C-peptide was significantly associated with higher risk of reduced RDI (OR [95% CI]: 1.50 [1.02, 2.21]; *P*trend = 0.05), but not for severe AE (OR [95% CI]: 1.33 [0.92, 1.93]; *P*trend = 0.12). Compared to the lowest quintile (Q1), the highest quintile (Q5) in IGFBP-1 was significantly associated with higher risk of severe AE (OR [95% CI]: 1.60 [1.08, 2.36]; *P*trend = 0.02), but not for reduced RDI (OR [95% CI]: 1.30 [0.87, 1.94]; *P*trend = 0.13).

Conclusions: These findings suggest C-peptide and IGFBP-1 may have the potential to identify patients at higher risk of poor chemotherapy tolerance.

Table 1. Adjusted Associations (OR [95% CI]) of C-peptide and IGFBP-1 with Reduced RDI and Severe AE

Biomarkers	Q1	Q2	Q3	Q4	Q5	P_{trend}
C-peptide						
Reduced RDI						
# of events/at risk	107/268	120/268	115/269	116/269	126/268	
OR	1.00 (Ref)	1.15 (0.79, 1.66)	1.03 (0.71, 1.51)	1.19 (0.81, 1.74)	1.50 (1.02, 2.21)	0.05
Severe AE						
# of events/at risk	134/268	146/268	146/268	148/269	149/268	
OR	1.00 (Ref)	1.12 (0.79, 1.61)	1.12 (0.78, 1.62)	1.23 (0.85, 1.78)	1.33 (0.92, 1.93)	0.12
IGFBP-1						
Reduced RDI						
# of events/at risk	98/266	115/271	114/268	128/269	129/268	
OR	1.00 (Ref)	1.04 (0.71, 1.52)	0.97 (0.66, 1.42)	1.17 (0.79, 1.74)	1.30 (0.87, 1.94)	0.13
Severe AE						
# of events/at risk	123/266	144/271	140/268	149/269	167/268	
OR	1.00 (Ref)	1.12 (0.78, 1.61)	1.01 (0.70, 1.45)	1.07 (0.73, 1.57)	1.60 (1.08, 2.36)	0.02

Abbreviations: AE, adverse event; CI, confidence interval; IGFBP-1, insulin-like growth factor binding protein 1; OR, odds ratio; Q1, quintile 1; Q2, quintile 2; Q3, quintile 3; Q4, quintile 4; Q5, quintile 5; RDI, relative dose intensity.

Adjustment: Age (years), sex (male, female), race (Asian, Black, White, Others), ethnicity (Hispanic, Non-Hispanic), ECOG performance status (0, 1-2), T stage (T1/T2, T3, T4), N stage (N1, N2), tumor location (left side, right side, multiple), BMI (<18.5, 18.5-24.9, 25.0-29.9, ≥30 kg/m^2), randomization arm (celecoxib, placebo), chemotherapy cycles (6 cycles, 12 cycles), and diabetes (yes, no, unknown).

Cancer

Ambient air pollution and survival among Black women with epithelial ovarian cancer across diverse geographical regions of the United States Ekaterina Chirikova* Ekaterina Chirikova Courtney E. Johnson Anke Huels Pushkar P Inamdar Elisa V. Bandera Lawrence H. Kushi Jennifer A. Doherty Joellen M. Schildkraut Melissa Bondy Edward S. Peters Kendra Ratnapradipa Salma Shariff-Marco Scarlett L. Gomez Andrew Lawson

Ovarian cancer is a leading cause of gynecologic cancer mortality, with Black females experiencing five-year survival rates of only 41%. Disproportionate air pollution exposure may impact survival, but this relationship remains understudied. We evaluated associations of fine particulate matter (PM2.5) and nitrogen dioxide (NO2) exposure with survival among Black females diagnosed with epithelial ovarian cancer (EOC) using data from the California Cancer Registry (CCR) and the multi-state African American Cancer Epidemiology Study (AACES).

Annual PM2.5 and NO2 levels were estimated at a 1 km resolution using well-validated ensemble-based prediction models derived from the Socioeconomic Data and Application Center. Average PM2.5 and NO2 exposures during the year of diagnosis (2004-2016) were assigned to the participants' residential addresses. We used adjusted Weibull accelerated failure time models to assess air pollutant exposure associations with overall survival, addressing unobserved confounding by including participant-level frailty.

The study included 1,286 Black females with primary EOC. Average PM2.5 and NO2 exposures were 11.3 μg/m³ and 25.8 ppb in CCR, and 9.7 μg/m³ and 17.5 ppb in AACES. Associations between PM2.5 or NO2 exposure and overall survival were not statistically significant, with event time ratios in CCR analysis of 1.08 (95% CI: 0.97–1.20) per 1 μg/m³ PM2.5 and 1.07 (95% CI: 0.99–1.15) per 10 ppb NO2, and in AACES analysis of 1.00 (95% CI: 0.93–1.07) per 1 μg/m³ PM2.5 and 1.04 (95% CI: 0.91–1.19) per 10 ppb NO2. Replication analysis of prior CCR studies confirmed that our results differed due to variations in methods and exposure measures.

Using precise exposure measures and robust methods addressing unobserved confounding, we found no evidence of associations between PM2.5 or NO2 exposure and overall survival in Black females with EOC in a geographically diverse U.S. area. These results emphasize the need to explore other contextual factors.

Cancer

Quantifying the impacts of social determinants of health on survival among Black women with epithelial ovarian cancer in the United States Theresa Hastert* Courtney Johnson Theresa Hastert Anthony Alberg Andrew Lawson Lauren Peres Joellen Schildkraut

Survival among Black women with epithelial ovarian cancer (EOC) is poor and investigating unique contributors of these poor outcomes can be considered through a social determinants of health (SDOH) framework. Using survey response and geocoded data from a population-based study of Black women with EOC (N=433), we quantified 5 SDOH domains: economic stability, education access and quality, health care access and quality, neighborhood and built environment, & social and community context. We classified relevant variables into each domain and conducted a factor analysis to identify the sufficient principal components. We ran hierarchical clustering on these principal components, creating one categorical variable per SDOH domain. To measure the association with survival, we then fit Cox proportional hazards models for each domain, adjusting for stage and age at diagnosis and allowing the baseline hazard to vary by histotype. The strongest predictor of survival among Black women with EOC was economic stability, clustered into 3 levels: (1) low income & high proportions receiving disability, (2) middle income & high proportions of retired women, (3) high income & high proportions employed full time. Compared to the low-income group, survival was better among women in the second/middle income group (HR: 0.74, 95% CI: 0.55, 1.00) and those in the third/ high income group (HR: 0.68, 95% CI: 0.49, 0.93; p-trend=0.02). Living in a more densely populated area, regardless of SES, was associated with about 20% better survival (p=0.09), and survival was about 35% worse for women with incomplete/infrequent health insurance than for women with privately funded health insurance (p=0.08). The relationships between the social context or education and survival were null. The use of dimension reduction enabled us to quantify SDOH into easily interpretable single variables. Economic stability was the SDOH most strongly associated with survival among Black women with EOC in this study.

Cancer

Nutritional supplements and survival outcomes in patients with multiple myeloma Jiarui Yang* Jiarui Yang Bei Wang Benjamin Derman Jade Mason Andrzej Jakubowiak Brian C. Chiu

Nutritional supplements and mortality or survival have been investigated in several solid tumors. However, there remains a comparative paucity of data in multiple myeloma (MM). In a cohort of 429 patients with MM, we examined whether the pre-diagnostic nutritional supplement use was associated with overall-survival (OS) and progression-free survival (PFS). Nutritional supplement use was collected using a questionnaire at enrollment. After excluding supplements used by less than 5% of participants, 11 supplements were included in the current report. Patients self-reported never used any of these supplements were defined as “never users” and served as the referent group. Important prognostic variables were collected from electronic medical records. Proportional hazard models were used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for OS and PFS. A total of 148 deaths occurred in the patient cohort over a median follow-up period of 51.4 months. Compared with never users of any nutritional supplement before diagnosis, users of chondroitin had a worse OS (HR ever vs. never = 2.1 [1.0-4.5]) after controlling for prognostic factors. In addition, ever used B vitamins (HR ever vs. never = 1.7 [1.0-2.8]) and vitamin C (HR ever vs. never = 1.6 [1.0-2.6]) was associated with worse PFS. No association with OS or PFS was detected for all other nutritional supplements evaluated. In conclusion, our data suggest that the use of most nutritional supplements prior to diagnosis is not associated with OS and PFS in patients with MM. Our findings on chondroitin, B vitamins, and vitamin C are novel and require confirmation.

Cancer

Civic engagement and cancer screening among US citizens Jordan Baeker Bispo* Jordan Baeker Bispo Jingyi Tian Ahmedin Jemal Farhad Islami

Background: Civic engagement may influence health behaviors through social pathways, but little is known about its relationship to utilization of preventive care services like cancer screening. In this study, we examine relationships between civic engagement and screening for breast cancer (BC) and colorectal cancer (CRC) in a representative sample of US citizens.

Methods: Data are from the 2023 National Health Interview Survey. Measures of civic engagement included binary indicators of voting in the last local election, past year attendance at a public meeting, and past year participation in volunteer activities. Up-to-date screening was defined according to US Preventive Services Task Force recommendations. Associations were evaluated using survey-weighted logistic regression models with adjustment for multiple sociodemographic characteristics, health insurance status, and self-rated health.

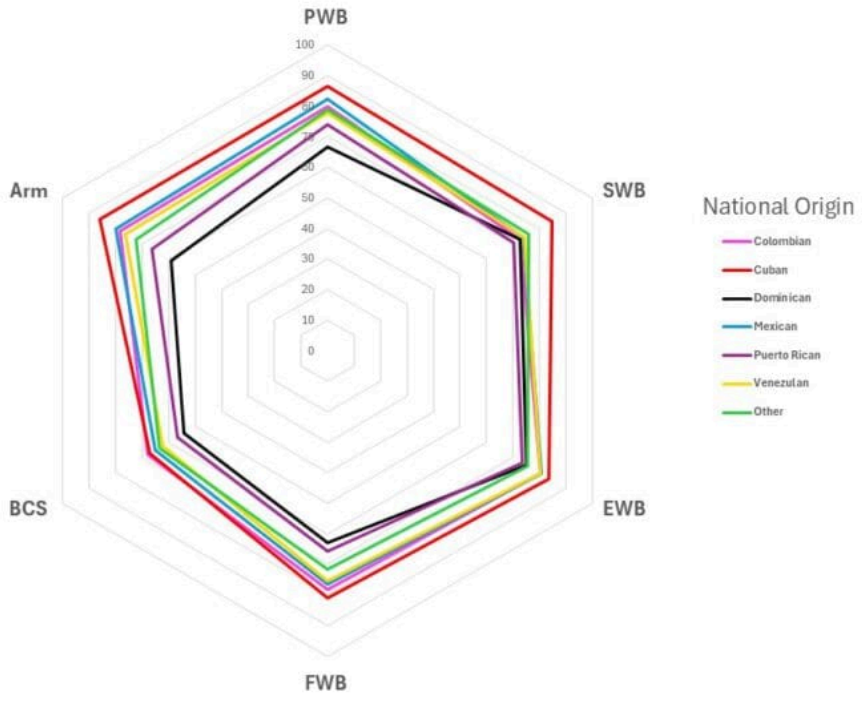
Results: Analyses included 5,733 and 12,849 adults eligible for BC and CRC screening, respectively. In adjusted models, the prevalence of up-to-date screening was higher among those who voted (adjusted prevalence ratio [aPR]=1.12, 95%CI=1.08-1.16 for BC; aPR=1.13, 95% CI=1.10-1.17 for CRC), attended a public meeting (aPR=1.07, 95% CI=1.02-1.11 for BC; aPR=1.05, 95%CI=1.01-1.09 for CRC), or volunteered (aPR=1.08, 95%CI=1.05-1.11 for BC; 1.07, 95%CI=1.04-1.10 for CRC) relative to those who did not. Associations were strongest for those who participated in ≥2 measures of civic engagement relative to none (aPR=1.19, 95%CI=1.14-1.24 for BC; aPR=1.17, 95%CI=1.13-1.22 for CRC).

Conclusions: Cancer screening is higher in civically engaged adults. More research is needed to understand the mechanisms (e.g., social integration) that underlie this relationship, but the findings support efforts to advance cancer control through paired public health and civic health programming.

Cancer

Evaluating health-related quality of life among Hispanic breast cancer survivors Eunkyung Lee* Eunkyung Lee Maria Eduarda de Azevedo Daruge Jongik Chung Jaeyoung Park Robert B. Hines Victoria Loerzel

Background: Hispanic breast cancer survivors report worse health-related quality of life (HRQOL) compared to non-Hispanic counterparts. Due to large intercultural diversities, little is known about intra-Hispanic disparities that could guide culturally tailored interventions. This study assessed intra-Hispanic disparities and the independent factors associated with HRQOL among Hispanic breast cancer survivors.
Methods: Eligible participants were Hispanic women >20 years old, diagnosed with breast cancer at least six months ago, alive and resident of Central Florida, and able to read/speak either English or Spanish, who were recruited following the Florida Cancer Registry recruitment procedure. The Functional Assessment of Cancer Therapy – Breast (FACT-B+4) was utilized to assess HRQOL total and six domains' scores: physical, social, emotional, and functional well-being, as well as breast cancer and arm symptoms. Multivariable linear regression analysis was conducted to identify independent factors associated with the FACT-B+4 total score, adjusting for potential confounders. Radar charts were constructed to examine the dynamics of domain scores.
Results: 411 women have participated, including 36 Colombians, 25 Cubans, 31 Dominicans, 23 Mexicans, 213 Puerto Ricans, 24 Venezuelans, and 59 others. The mean total score was the highest among Cubans (134.7±18.6) and the lowest among Dominicans (108.3±29.5). The significant factors included national origin, age at diagnosis, body mass index, income, and comorbidities. Radar charts showed that breast cancer symptoms were the worst, while arm symptoms had the most significant variation among the six domains according to national origin.
Conclusions: There were significant intra-disparities in HRQOL among Hispanic breast cancer survivors. The differences in sociodemographic and clinical characteristics by national origin could explain these disparities and be used to develop culturally tailored intervention programs.



Cancer

Perceptions of the health care system as mediators in the association between experiences of discrimination, communication from providers, and gaps in mammography. Hannah Cohen-Cline* Hannah Cohen-Cline Megan Holtorf Monique Gill

Background: Breast cancer is a leading cause of cancer death among women, and early detection is critical for positive outcomes. However, there are well documented disparities in the completion of regular preventive mammography, and understanding what drives gaps in mammography remains a critical area of focus. Negative healthcare experiences contribute to decreased utilization of health services, influence perceptions of the system, and damage relationships between patients and providers, but there is limited knowledge of how they interact with each other to shape use of screening mammography.

Objective: This study aimed to assess if perceptions of the healthcare system mediate the relationships between patient-centered communication and healthcare discrimination and gaps in mammography.

Methods: We fielded a survey about healthcare experiences, healthcare perceptions, and mammogram history to 20,000 female Providence Health System patients aged 50-74 in Oregon and Washington, of whom 7,473 (37.3%) responded. We constructed structural equation models to assess the direct effects of patient-centered communication and healthcare discrimination on mammogram completion, as well as the extent to which each effect was mediated by healthcare perceptions.

Results: Approximately 89% of respondents were current on mammography. Women who reported patient-centered communication were significantly more likely to be current (RR = 1.16; $p<0.001$), while those who experienced healthcare discrimination were less likely to be current (RR = 0.94; $p<0.001$). Both effects were partially mediated by perceptions of the healthcare system (28% mediated for patient-centered communication; 19% mediated for healthcare discrimination).

Conclusion: Patient-centered communication, discrimination, and perceptions are key contributors to disparities in mammography, and healthcare systems must take action to ensure that solutions improve access to and quality of care for all.

Cancer

Collider Bias in Estimating the Effects of Pre-Incident-Cancer Exposures on Post-Incident-Cancer Outcomes Matthew M Coates* Matthew Coates Danica Anukam Zuo-Feng Zhang Onyebuchi A. Arah

Studies estimating the effects of exposures before incident cancer on post-incident-cancer outcomes, such as cancer progression, cancer recurrence, or cancer mortality, are restricted to people with incident cancer or pre-cancer malignancies, potentially creating selection bias. This study identifies examples of this bias in literature, explains the structural causal mechanisms underlying this bias with causal diagrams, and quantifies the potential impact of this bias through simulations. In a causal diagram, incident cancer is (i) a mediator between pre-incident exposure and post-incident cancer consequences and (ii) a potential collider between pre-incident exposure and risk (e.g., genetic, infectious, or environmental) factors that lead to both higher cancer risks and outcomes of interest such as tumor aggressiveness. Estimating the direct effect of pre-incident exposures on post-incident outcomes (e.g., the effect of cancer screening on cancer survival that conditions on cancer diagnosis) requires adjustment for this mediator-outcome confounding, even under a randomized exposure. We simulated data using causal diagrams and parameters informed by published literature to quantify the degree of bias in estimates of the effects of pre-incident exposures on post-incident outcomes for a set of exposures of interest identified from the literature. In simulations based on results from published studies, a combination of pre-incident exposure causing cancer and strong uncontrolled confounding of cancer incidence and the post-incidence outcome could create substantial, varying bias in the estimated effects. Studies estimating the effect of pre-incident exposures on post-incident outcomes among people with cancer should adjust for common causes of cancer incidence and subsequent cancer outcomes, use bias analysis to assess potential collider bias, or, if relevant, target alternative estimands that do not depend on measurement of such common causes.

Cancer

Association of fast-food consumption with colorectal cancer (CRC) incidence among Louisville Environmental Assessments Pilot Study in Colorectal Cancer (LEAPS-CRC): a clinical case-control study. Jeevan Adhikari* Jeevan Adhikari Sandy Kavalukas Allie Jin Olufunmilayo Babarinde Natalie DuPre

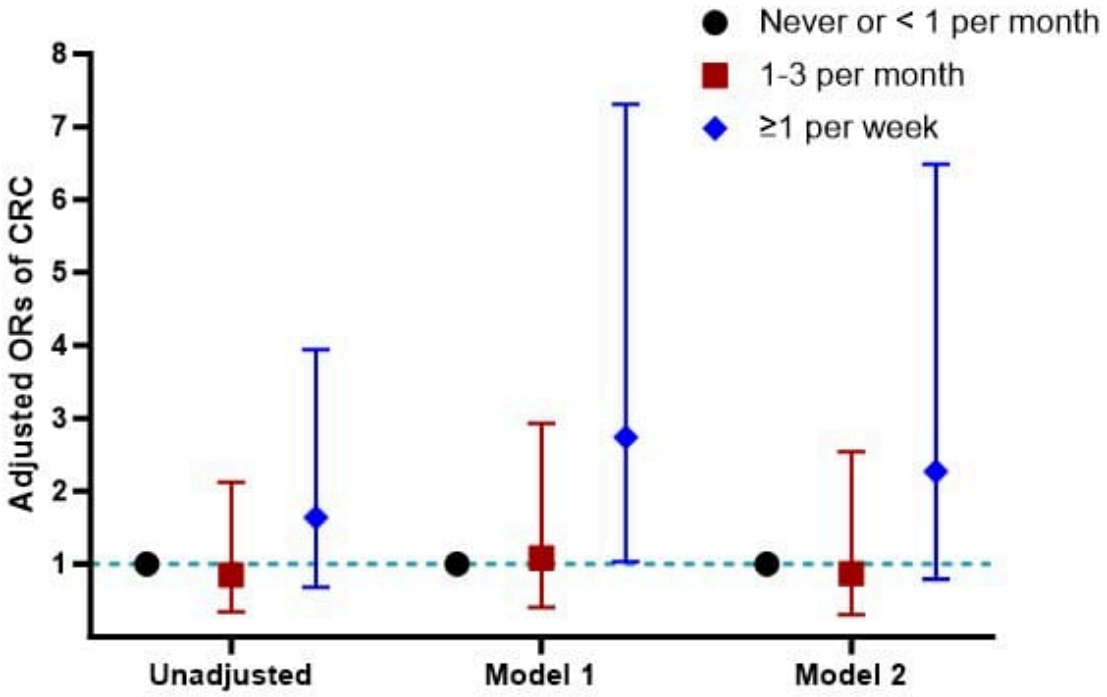
Background: Colorectal cancer (CRC) is the 3rd most common cancer in the US with Kentucky reporting the 2nd highest incidence rate of CRC. Fast-food consumption is associated with CRC risk factors (ex. obesity, physical inactivity), and its nutritional components (ex. red and processed meats) contribute to CRC risk. Studies suggest that higher fast-food consumption increases CRC incidence; however, most studies were outside of the US.

Hypothesis: Regular fast-food consumption increases CRC incidence.

Methods: The Louisville Environmental Assessments Pilot Study in CRC (LEAPS-CRC) is an ongoing clinical case-control study that started in August 2023. Consented participants were recruited in a surgical clinic, where CRC cases and controls underwent a surgical CRC treatment or screened negative on a colonoscopy, respectively. Participants completed a questionnaire that captured information on several CRC risk factors. Participants were asked how often they ate food from McDonald’s, KFC, Taco Bell, Pizza Hut etc., on average in the last year. We categorized fast-food consumption into never or <1 per month, 1-3 per month, and ≥1 per week. A multivariable logistic regression model estimated the odds ratios (ORs) with 95% confidence intervals (CI) of CRC incidence for fast-food consumption categories. A two-sided p-value of <0.05 was considered statistically significant and analyses were conducted using SAS version 9.4.

Results: Among 156 participants (46 cases; 110 controls), CRC risk factors were more prevalent in cases than controls (ex. older, men, obese, family history). Among the controls, 31.8% consumed fast food ≥1 per week, 40.9% consumed fast food 1-3 times per month, and 27.3% never consumed or consumed fast food <1 per month. Compared to never or <1 per month fast food consumers, the odds of CRC incidence among those who consumed fast food ≥1 per week were 2.74 (95% CI: 1.03-7.31) times higher after adjusting for age, gender, race, and family history. Results were no longer statistically significant after additional adjustment for physical activity and education (OR=2.27 95% CI: 0.79-6.46).

Conclusion: Based on preliminary data, daily to weekly fast-food consumption may be associated with higher risk of CRC in LEAPS-CRC participants. As enrollment continues, we will adjust for additional confounders.



Model 1 Adjusted for age (in years), gender (man, woman), and race (White,Black/Asian/Others), and Family History of CRC (Yes,No)

Model 2 Adjusted for Model 1 plus Physical activity (<7.5 MET-hr/week, 7.5 to <21 MET-hr/week, and >=21MET-hr/week') and education (High School or Less, Some college/Vocational, and Bachelor's or higher)

Fig.1. The ORs with 95% CIs for colorectal cancer by categories of fast-food consumption.

Cancer

Area Deprivation as a Risk Factor for Distant-Stage Breast Cancer in South Korea (2012–2019): A Multilevel Study Jeehyun Kim* Jeehyun Kim Eunhye Park

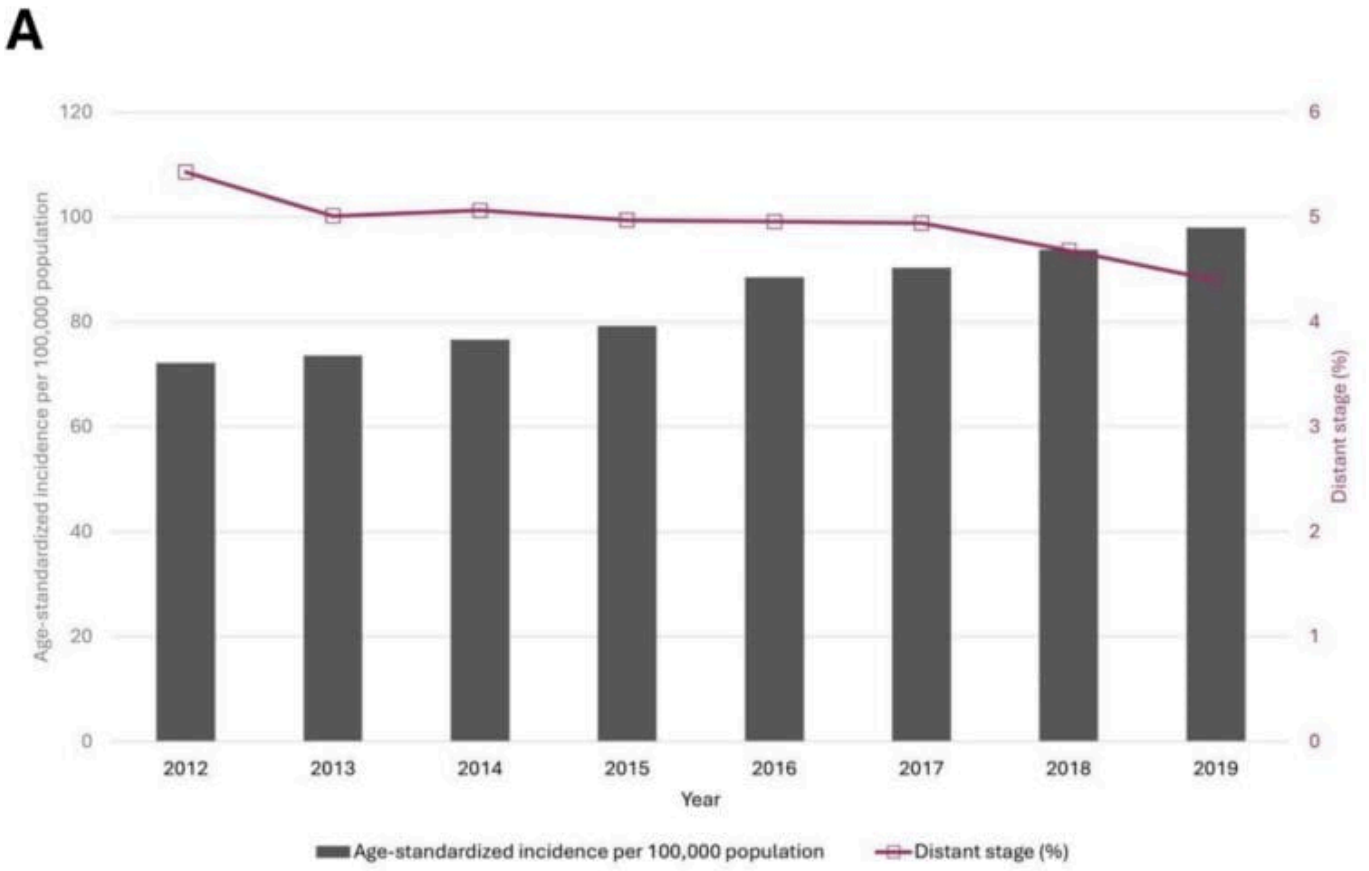
Background: Breast cancer is the most common cancer in women globally, with rising incidence in South Korea. Regional disparities in breast cancer show higher incidence in affluent areas but higher mortality in deprived ones, likely due to delayed diagnosis and limited health access. Few studies adjust for individual-level risks, leaving gaps in understanding how the areal deprivation index (ADI) affects distant-stage breast cancer.

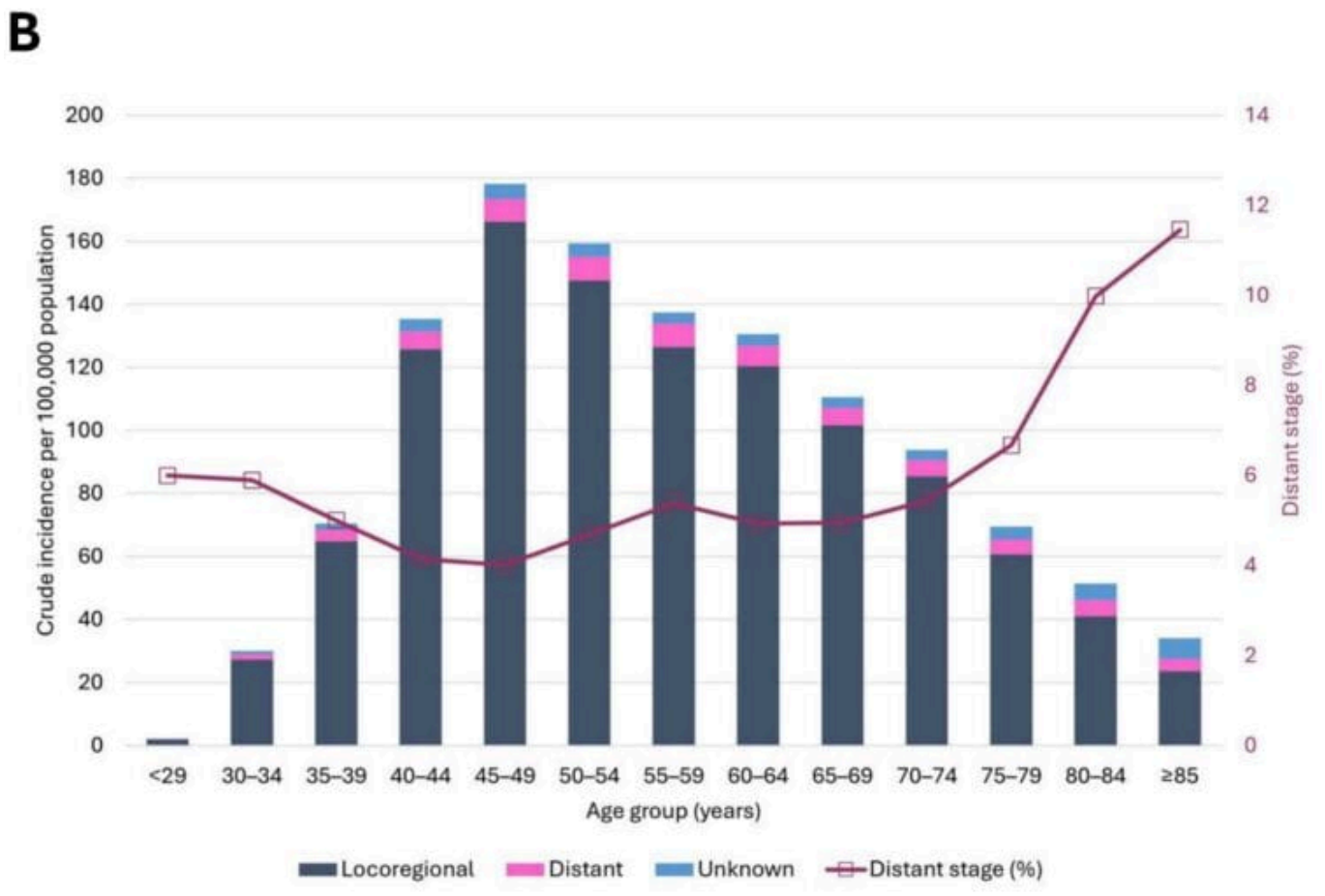
Objective: To determine how ADI increases distant-stage breast cancer incidence, beyond individual factors

Methods: Data from the Korea Central Cancer Registry linked to the National Health Information Database (2012–2019) were analyzed. Breast cancer stages were classified using SEER summary stages: Localized, Regional, and Distant. Age-standardized incidence rates were calculated using Segi's world population. Regional variables, including ADI and mammography devices, were sourced publicly. Multilevel analysis evaluated individual- and regional-level impacts on distant- versus local-stage incidence.

Results: Of 164,292 cases, 163,152 were includedThe 45–49 age group had the highest prevalence (N= 31,568, 19.3%), while distant-stage proportions were highest in the youngest (<29 years, 6.0%) and oldest (≥85 years, 11.5%). Multilevel analysis showed higher odds of distant-stage cancer in younger and older individuals, those with higher BMI, lower insurance premiums, severe disabilities and residents in areas with higher deprivation (OR=1.06, p<.001) or fewer mammography devices (OR=0.93, p=.003).

Conclusions: Regional socioeconomic characteristics significantly influence breast cancer stage at diagnosis, even after accounting for individual factors. Addressing healthcare disparities through early detection and equitable access to quality care is essential to improve breast cancer outcomes.


A
120
100
80
60
40
20
0
6
5
4
3
2
1
0
Age-standardized incidence per 100,000 population
Distant stage (%)
2012
2013
2014
2015
2016
2017
2018
2019
Year
Age-standardized incidence per 100,000 population
Distant stage (%)


B
200
180
160
140
120
100
80
60
40
20
0
14
12
10
8
6
4
2
0
Crude incidence per 100,000 population
Distant stage (%)
<29
30–34
35–39
40–44
45–49
50–54
55–59
60–64
65–69
70–74
75–79
80–84
≥85
Age group (years)
Locoregional
Distant
Unknown
Distant stage (%)

Cancer

Determinants of Survival in Cervical Cancer: The Critical Role of Early Detection and Treatment in Resource-Limited Settings Citlalli Lopez* Citlalli Lopez Sithembiso S. Msibi Joseph L. Su

Eswatini has one of the highest prevalence rates of HIV at 25.9% and only recently implemented an HPV vaccine in 2023.1 The country also reported the highest incidence and mortality rates of cervical cancer in 2021, estimated at 84.5 and 55.7 per 100,000 female population, respectively. 2 This study aimed to examine the impact of clinical and demographic factors on cervical cancer survival outcomes. The Eswatini Cancer Registry was screened for participants from 2016-2024, yielding a total of 2,210 cervical cancer patients, of whom 561 deaths were analyzed using the Cox proportional hazards model. The primary analysis assessed the association between cancer stage at diagnosis and survival, adjusting for potential confounders (age, smoking status, HIV status, treatment, and basis of diagnosis). The models were stratified by Stage at diagnosis and Basis of diagnosis to uphold proportional hazards assumptions. Interaction terms were introduced to evaluate whether the effect of treatment and cancer stage on survival varied by HIV status. Advanced cancer stages (Stages 3 and 4) were significantly associated with increased hazard of death, with diagnosis at Stage 4 lowering the chance of survival by approximately 4.4-fold compared to Stage 1, highlighting the importance for early detection and screening. Treatments (chemotherapy, radiation, surgery) reduced the hazard of death by 17% (HR: 0.83, 95% CI: 0.68-0.99, $p < 0.001$). Interaction analysis revealed no statistically significant difference in treatment or cancer stage effects by HIV status. However, we observed a marginally significant lower risk of death for HIV-positive patients diagnosed at Stage 1 (HR = 0.24, 95% CI: 0.06-1.24, $p = 0.05$), likely due to increased clinical attention. Despite the uncertainty of this confidence interval, it warrants further investigation. Our findings confirm that diagnosis at advanced cancer stages significantly worsens survival outcomes, underscoring the importance of screening, early detection, and access to effective treatment options for patients.

LATEBREAKER

Cancer

Are Individuals Diagnosed with Asthma More Likely to Undergo Cancer Screening? Results from a US 2016-2022 National Level Study Odele Rajpathy* Odele Rajpathy S. Cristina Oancea

Cancer remains the second leading cause of death in the U.S., with an estimated 610,000 cancer-related deaths in 2023. Cancer screening (CS) reduces cancer mortality by enabling early detection and treatment. While socioeconomic factors are known to influence CS, less is known about the impact of chronic health conditions like asthma on CS. This study examines the association between having asthma and undergoing prostate, breast, cervical, and colorectal CS in a nationally representative sample of US adults, using the BRFSS 2016-2022 data. Weighted, adjusted multivariable logistic regression models were applied to sex&age-based groups per the official CS guidelines. Results showed significantly higher CS adherence among individuals with asthma across all 4 CS types when Compared with their Counterparts Without Asthma (CCWA). Males (55–69 years old (YO)) with asthma had 15% significantly higher weighted and adjusted odds (WAO) of prostate CS (95% CI: 1.04–1.27) when CCWA. Women (50–74 YO) with asthma had 16% significantly higher WAO of breast CS (95% CI: 1.01–1.32) when CCWA. Not depressed, heavy drinking women with asthma had a 300% significantly higher WAO (95% CI: 2.20–7.22) of breast CS when CCWA. Women (21–65 YO) with asthma had 9% significantly higher WAO (95% CI: 1.02–1.17) of cervical CS when CCWA, with education significantly modifying this association (WAOR for college educated women=1.23, 95% CI: 1.11–1.36). Men (50-75 YO) with asthma had 36% significantly higher WAO of colorectal CS (95% CI: 1.24–1.49) and women (50-75 YO) with asthma had 24% significantly higher WAO of colorectal CS (95% CI: 1.15–1.33) when CCWA. These findings suggest that having asthma is significantly associated with a greater CS adherence. Strong associations in drinking and education subgroups highlight crucial points of targeted public health intervention via low-literacy CS materials, mobile CS units, physician-led counseling during asthma visits, and community outreach programs.

LATEBREAKER

Cancer

The Association between Dental Care and Screening for Cancer among US Adults: results from a 2016- 2022 National Level Study Nishat Sultana* Nishat Sultana S. Cristina Oancea

Regular dental care plays a vital role in maintaining oral health and may serve as an indicator of broader preventive healthcare engagement. Cancer screening (CS) is essential for early detection and improved health outcomes. However, limited research has examined the association between dental care and CS participation.

This study examines the association between dental care and undergoing breast, cervical, prostate, and colorectal CS in a nationally representative sample of US adults, using the BRFSS 2016-2022 data. Weighted and adjusted multivariable logistic regression models were applied to sex and age-based groups per the official CS guidelines.

Among males, 14% of 50-75 YO and 14% of 55-69 YO, and among females 10% of 50-75 YO, and 8% of 21-65 YO, visited the dentist 5 or more years ago or never. The weighted and adjusted odds (WAO) of breast (ages 50-74 years old (YO), N=262,967), cervical (ages 21-65 YO, N=315,218), and colorectal (ages 50-75 YO, N=270,439) CS among females who visited the dentist more than 5 years ago or never, were 59% (95% CI: 0.36,0.46), 29% (95% CI: 0.65,0.77), and 55% (95% CI: 0.41,0.48) significantly lower, respectively, than the WAO of CS among females who had their last dental visit within the last year. The WAO of prostate (ages 55-69 YO, N=120,336), and colorectal (ages 50-75 YO, N=243,994) CS among males who visited the dentist more than 5 years ago or never, were 41% (95% CI: 0.54,0.64), and 54% (95% CI: 0.43,0.49) significantly lower, respectively, than the WAO of CS among males who had their last dental visit within the last year.

This study results indicate that the longer the gap since the last dental visit, the lower the odds of CS participation. Future research should explore systemic barriers, behavioral factors and targeted interventions to promote preventive health engagement among populations at higher risk for delayed CS.

LATEBREAKER

Cancer

Diabetes and Cancer Incidence among Adults in the Hispanic Community Health Study/Study of Latinos (HCHS/SOL) Humberto Parada* Humberto Parada Lakshna Manoharan Benjamin Aceves Corinne McDaniels-Davidson Pragnya Wanjerkhede Ilir Agalliu Margaret S. Pichardo Daniela Sotres-Alvarez Olga Garcia-Bedoya Christina Cordero Sylvia E. Rosas Frank J. Penedo Bharat Thyagarajan Martha Daviglus Gregory A. Talavera Linda C. Gallo

Purpose: We examined the association between diabetes and cancer risk among adults in the Hispanic Community Health/Study of Latinos (HCHS/SOL).

Methods: HCHS/SOL is a multi-site cohort study of 16,415 Hispanic adults. Incident cancers diagnosed from baseline (2008-2011) through 2021 were identified through state cancer registry linkages. Baseline diabetes measures included diabetes status defined using ADA guidelines (no diabetes, pre-diabetes, and diabetes) and HbA1c levels (<7.0%, ≥7.0%), diabetes medication use (no medication use, metformin use, or insulin use), and insulin resistance estimated using the Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) index (<3.0, ≥3.0). Survey-weighted Cox proportional hazards models estimated covariate-adjusted hazard ratios (HRs) and 95% confidence intervals (CIs) for each diabetes measure and overall cancer risk as well as obesity-related cancer (ORC) risk, a composite measure of 13 cancers. We also examined effect measure modification by sex and Hispanic heritage.

Results: Diabetes (vs. no diabetes) was associated with an 11% (HR=1.11, CI=0.76-1.62) increase in overall cancer risk and with a 35% (HR=1.35, CI=0.67-2.70) increase in ORC risk. ORC risk was also elevated among those with diabetes+HbA1c levels ≥7.0% (HR=1.91, CI=0.77-4.75); among those who used metformin (HR=2.45, CI=1.13-5.34); and among those who had pre-diabetes+HOMA-IR index ≥3.0 (HR=1.53, CI=0.86-2.72). The association between diabetes status and cancer risk was elevated among women (HR=1.64; CI=0.72-3.74), but not among men (HR=0.91, CI=0.34-2.45; PInt.=0.59) and among those of South American descent (HR=1.70, CI=0.37-7.82), but not among the other heritage groups (HRs ≤1.00; PInt.=0.04).

Conclusion: Diabetes measures were associated with an increase in cancer risk; however, estimates were imprecise and most CIs contained the null value. These findings suggest the need for additional and pooled investigations among Hispanic adults.

LATEBREAKER

Cancer

Military Exposures to Per- and Polyfluoroalkyl Substances (PFAS) and Breast Cancer Risk among Active-Component Service Members Barbara Fuhrman* Barbara Fuhrman Michelle Mellers Stephanie Silsby Caroline A. Hoffman Celia Byrne

Previous studies have indicated higher rates of early-onset breast cancers among women in the U.S. Military compared to the U.S. population. The impact of the endocrine disrupting chemicals, Per- and Polyfluoroalkyl Substances (PFAS) on breast cancer in younger women (<50 years of age) remains uncertain. Many industrial and consumer products contain PFAS, but long-term intensive use of Aqueous Film Forming Foam for firefighting was a major source of contamination of drinking water on a number of US military installations.

We carried out a nested case-control study among women in the active-component of the U.S. military who entered service in or after 1990, to test the association of years of service on 22 military installations with very high drinking water PFAS levels (>70 ppt) with incident breast cancer. Between 2000-2022, there were 828 women diagnosed while in the active-component with invasive breast cancer (BC, N=708) or ductal carcinoma in situ (DCIS, N=120). We selected 1655 controls matched on age, race, and time from the same population and without a reported breast cancer diagnosis at the time of the cases' diagnosis. Of the cases, 85% were under the age of 45 and 56% were non-White. Odds ratios estimated the rate ratio (RR) with 95% confidence intervals (CI) using conditional logistic regression.

Compared to women never assigned to the 22 identified installations, those assigned for three or more years had an RR=1.34 (95% CI:1.05-1.72) for invasive BC or DCIS. The RR increased for invasive BC only (RR=1.50; 95% CI:1.14-1.97), those diagnosed with invasive BC before 2016, (OR=1.57; 95% CI:1.05-2.32), and those diagnosed with invasive BC before the age of 45 (RR= 1.71; 95% CI:1.25-2.32).

These findings may provide an explanation for higher rates of breast cancer reported among women serving in the U.S. Military.

Cancer

Associations between Posttraumatic Stress Disorder and Cancer Prevalence in a Cohort of Vietnam-Era Women Veterans Hannah M. Burns* Hannah Burns Kelsey N. Serier Kathryn M. Magruder Rachel Kimerling Avron Spiro Anica Pless Kaiser Brian N. Smith

The role of Posttraumatic Stress Disorder (PTSD) as a risk factor for various cancers is unclear, with mixed results in the extant literature. One study found that PTSD was a risk factor for ovarian cancer, but other studies have found no such association with ovarian and other cancers (e.g., breast and lung); however, evidence is sparse, including no studies to date focused on women Veterans.

Utilizing data from a cohort of Vietnam-era women Veterans (N=4219, Mage=67), weighted logistic regression analyses were conducted to examine the association between PTSD and likelihood of reproductive (cervical, uterine, ovarian), breast, lung, and colon cancers. Lifetime PTSD was assessed by phone interview with the Composite International Diagnostic Interview, while cancer diagnoses were self-reported. Analyses excluded cases with missing PTSD/cancer diagnoses, age of onset, or a cancer diagnosis preceding PTSD.

The prevalence of reproductive, breast, lung, and colon cancers were 6.4%, 8.6%, 0.4%, and 1.1% in Veterans with lifetime PTSD, and 4.6%, 11.0%, 0.8%, and 1.8% in Veterans without PTSD. PTSD was not associated with increased odds of reproductive (OR= 1.42 [95% CI 0.94; 2.14]), breast (OR= 0.80 [95% CI 0.57; 1.11]), lung (OR= 0.58 [95% CI 0.13; 2.66]), or colon (OR= 0.64 [95% CI 0.25; 1.61]) cancer when adjusting for demographics, military characteristics, and health behaviors. Unadjusted models also yielded nonsignificant results.

PTSD was not associated with cancers examined in this study of women Veterans. These findings are consistent with other studies investigating PTSD with breast and lung cancer but are inconsistent with some previous findings on PTSD and ovarian cancer. We may not have observed an association between PTSD and reproductive cancer in part due to the sample size, survival bias, and retrospective cross-sectional nature of the data. Prospective research would help determine if PTSD is an important consideration for cancer risk in women Veterans.

*Table 1. Likelihood of Cancer Diagnosis as a function of Lifetime Posttraumatic Stress Disorder (PTSD)**

	Odds Ratio [95% Confidence Interval]			
	Reproductive Cancer (n=4092)	Breast Cancer (n=4115)	Colon Cancer (n=4102)	Lung Cancer (n=4099)
Model 1	1.42 [0.98; 2.04]	0.76 [0.56; 1.02]	0.65 [0.28; 1.48]	0.48 [0.11; 2.11]
Model 2	1.44 [0.99; 2.10]	0.84 [0.63; 1.14]	0.84 [0.35; 2.00]	0.58 [0.13; 2.69]
Model 3	1.45 [0.99; 2.13]	0.85 [0.63; 1.15]	0.83 [0.33; 2.08]	0.59 [0.12; 2.83]
Model 4	1.42 [0.94; 2.14]	0.80 [0.57; 1.11]	0.64 [0.25; 1.61]	0.58 [0.13; 2.66]

*Reference group = No Lifetime PTSD
Model 1: Unadjusted
Model 2: Adjusted for demographic characteristics
Model 3: Adjusted for demographic and military service characteristics
Model 4: Adjusted for demographic/military service characteristics, and health-related habits and behaviors

Cancer

Mechanisms underlying the effect of adiposity on risk of postmenopausal estrogen receptor-positive breast cancer: an interventional mediation analysis in the Melbourne Collaborative Cohort Study Frances Albers* Frances Albers Makayla Lou Ghazaleh Dashti Christopher Swain Sabina Rinaldi Vivian Viallon Amalia Karahalios Kristy Brown Marc Gunter Roger Milne Dallas English Brigid Lynch

Background: Adiposity increases the risk of postmenopausal estrogen receptor (ER)-positive breast cancer. Inflammation, insulin and insulin-like growth factors, and sex-steroid hormones may explain this effect. We performed interventional mediation analysis to estimate the effects of hypothetical interventions targeting these pathways in postmenopausal women with obesity on reducing their excess risk of ER-positive breast cancer relative to postmenopausal women with normal weight.

Methods: The mediation analysis included 1,260 postmenopausal women (352 ER-positive breast cancers) from a case-cohort within the Melbourne Collaborative Cohort Study. A Monte Carlo g-computation approach with non-parametric bootstrapping was used to estimate risk differences (RDs) and 95% confidence intervals (CIs) for interventional direct and indirect effects of hypothetical interventions that would shift the joint distribution of inflammation, insulin and sex-steroid hormone biomarkers in postmenopausal women with obesity to that observed in postmenopausal women with normal weight.

Results: The RD for the total effect of obesity versus normal weight on postmenopausal ER-positive breast cancer was 16.1 (95% CI: 3.3, 30.4) additional cases per 1,000 women. RDs for interventional indirect effects through inflammation, insulin and sex-steroid hormones were 16.4 (95% CI: 4.3, 27.2), -8.4 (95% CI: -23.4, 1.2) and 13.0 (95% CI: 3.3, 23.7) additional cases per 1,000 women, respectively. The RD for the interventional direct effect not via any pathway was -5.3 (95% CI: -17.4, 10.6) additional cases per 1,000 women.

Conclusion: Inflammation and sex-steroid hormones, but not insulin, may contribute to the detrimental effect of adiposity on risk of postmenopausal ER-positive breast cancer and may be targets for intervention.

Cancer

The effects of working conditions on the risk of breast cancer: a cohort study Bernadette van der Linden* Bernadette van der Linden Joy Sudan Arnaud Chiolero Stéphane Cullati Salvatore Vaccarella Cristian Carmeli

Background Breast cancer is the most commonly diagnosed cancer among women worldwide. While unhealthy lifestyle behaviors have been established to increase the risk of breast cancer, the effect of working conditions is not well known. We aimed to quantify the effects of working-related physical activity and long working hours on breast cancer risk using a large-scale longitudinal cohort study.

Methods Data were from the UK Biobank and included 161,673 women between 40 and 69 years old without breast cancer at baseline (2006) and followed until the end of 2016. Exposures were heavy physical/manual work (yes, sometimes, no), walking/standing work (yes, sometimes, no), and working hours per week (<15, 16-30, 31-48, >49), all self-reported at baseline. Incident breast cancer diagnoses (outcome) were verified through linkage with cancer registries. We calculated the cumulative risk differences/ratios of breast cancer, standardized by age at baseline, attained education, history of illnesses and number of live births.

Results There were 5092 (3.1%) women diagnosed with breast cancer during the 9 years of follow-up. Heavy physical/manual work led to 680 (95% CI: 281 to 1054) fewer breast cancer cases per 100 000 women compared to no heavy physical/manual work. That corresponded to a risk ratio (RR) of 0.79 (95% CI: 0.67 to 0.95). Walking or standing work led to 325 (95% CI: 77 to 596) fewer breast cancer cases per 100 000 women compared to not walking or standing work (RR: 0.90; 95% CI: 0.79 to 0.98). Negligible differences in breast cancer risk were found for number of working hours.

Conclusion Heavy physical/manual and walking or standing work reduced breast cancer risk in women among the UK Biobank participants. This is in contrast to the known higher risk of cardiovascular diseases conferred by high levels of occupational physical activity. Further studies are needed to assess the transportability of these findings to other populations.

Cardiovascular

Comparison of objective coagulation parameters between clopidogrel resistant vs non-resistant patients Adriana Araceli Rodriguez Alvarez* Adriana Rodriguez Alvarez Adriana Araceli Rodriguez Alvarez Isabella Cieri Shiv Patel Mounika Boya Jang Jeongin Anahita Dua

Background: While aspirin and clopidogrel are the mainstay of therapy to prevent thrombosis post revascularization in patients with peripheral artery disease (PAD), 25% of patients are resistant to clopidogrel. Hence, identifying factors contributing to clopidogrel resistance is critical to improving patient outcome post revascularization.

Objective: To assess differences in objective coagulation parameters between clopidogrel-resistant and non-resistant patients.

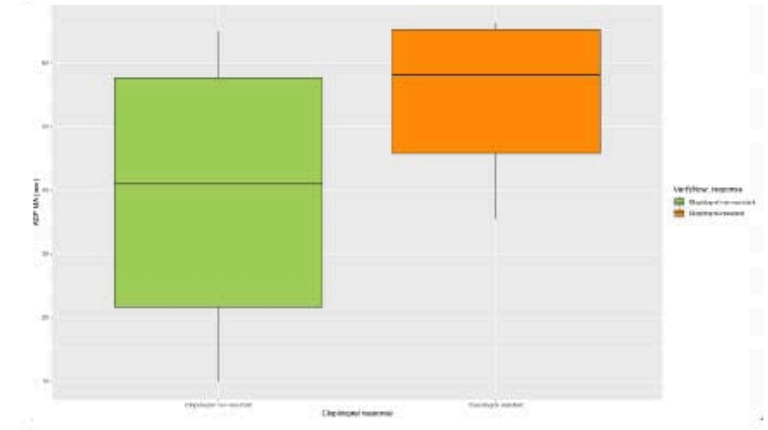
Methods: Patients with PAD undergoing revascularization and taking clopidogrel between 2022 and 2024 were evaluated. Coagulation profiles were assessed using thromboelastography (TEG) on whole blood samples collected perioperatively and up to six months postoperatively. VerifyNow testing was performed at one timepoint to identify clopidogrel resistance. Patients were categorized based on their clopidogrel response: clopidogrel-resistant (>180 P2Y12 Reaction Units (PRU)) and non-resistant (<180 PRU). Descriptive statistics were calculated, and group comparisons were performed using Fisher’s exact and Wilcoxon tests.

Results: A total of 53 patients were analyzed, 70% were male, and 23% were clopidogrel-resistant. Compared to the non-resistant group, the clopidogrel-resistant cohort was older, had a higher mean BMI, and exhibited higher platelet reactivity. Clopidogrel-resistant patients demonstrated faster clot formation (1.14min vs. 1.22, $p<0.0001$), stronger clots (54.9mm vs. 39.8, $p<0.0001$), and reduced clot lysis (0.97min vs. 0.69, $p<0.05$). These patients also showed a higher platelet aggregation (74.0% vs. 44.0%, $p<0.0001$) and a lower platelet inhibition (26.0% vs. 56.0%, $p<0.0001$), indicating a diminished response to clopidogrel and an increased risk of thrombosis.

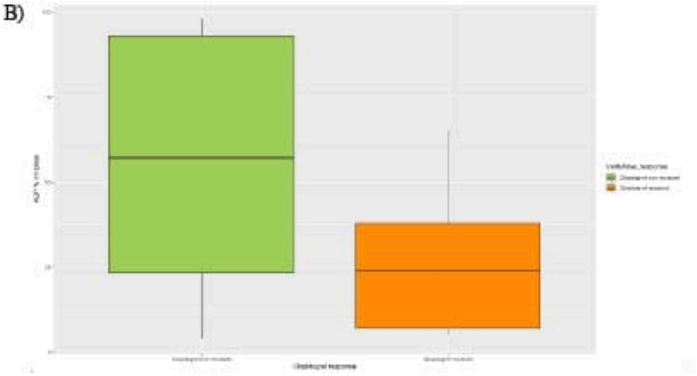
Conclusion: Clopidogrel-resistant group exhibited faster clot formation, greater clot strength, and higher platelet aggregation. Incorporating TEG into clinical practice could help identify patients at risk of inadequate clopidogrel response.

Figure. Platelet function – (A) Maximum Amplitude with Adenosine Diphosphate and (B) Adenosine Diphosphate Percentage of platelet inhibition

A)



B)



Cardiovascular

Associations Between Long-Term Methylmercury Exposure from Fish Consumption and Blood Pressure in Older Women Sally Thurston* Sally Thurston Gary Myers Matthew Conrad Shamlaye Emelyn Shroff JJ Strain Alison Yeates Emeir McSorley Maria Mulhern Edwin van Wijngaarden

Background: Fish contains many beneficial nutrients, but also contains methylmercury (MeHg), a known neurotoxicant at sufficiently high doses. Studies have reported beneficial effects of fish intake on blood pressure (BP) but whether MeHg alters this relationship is unclear.

Methods: We estimated associations of long-term fish intake and MeHg exposure on BP in a high fish-eating cohort of 608 middle-aged to older women (mean age in 2021: 58 years, range: 45-77 years). Their MeHg exposure and fish intake were determined at enrollment in 1990 as part of the Seychelles Child Development Cohort and again in 2013 and 2021. Maternal fish intake (number of fish dishes consumed) was obtained from questionnaires and MeHg was measured in hair. A long-term average of each variable was estimated as the mean over the three time periods. Associations of fish and MeHg with systolic and diastolic BP in 2021 were estimated from linear regression in separate, joint and interaction models adjusted for relevant covariates.

Results: Mean fish intake was 10.4 dishes/week (range: 3.0 – 24.0) and mean MeHg was 6.93 ppm (range: 1.3-19.7). Each additional fish dish eaten was associated with 0.96 mmHg (95% CI: 0.42, 1.50) increase in systolic BP and 0.50 mmHg (95% CI: 0.18, 0.81) increase in diastolic BP without adjustment for MeHg; associations were similar with MeHg adjustment. MeHg was not associated with systolic or diastolic BP, with or without adjustment for fish intake. In interaction models that allowed the fish intake slope to differ by tertile of estimated average MeHg, associations with fish intake were most adverse in the highest MeHg tertile. In the highest tertile each fish dish was associated with 1.89 mmHg (95% CI: 0.66, 3.11) increase in systolic BP and 0.82 mmHg (95% CI: 0.13, 1.51) increase in diastolic BP.

Discussion: Results suggest that eating many fish dishes with high average MeHg levels over many decades may be adversely associated with blood pressure.

Cardiovascular

The long term trend incidence of Stroke in Benign Prostatic Hyperplasia patients: a population-based descriptive study in Taiwan Wei-Ting Wang* Wei-Ting Wang Fu-Huang Lin Yu-Ching Chou

The long term trend incidence of Stroke in Benign Prostatic Hyperplasia patients: a population-based descriptive study in Taiwan

Wei-Ting Wang1 , Fu-Huang Lin1 , Yu-Ching Chou1*

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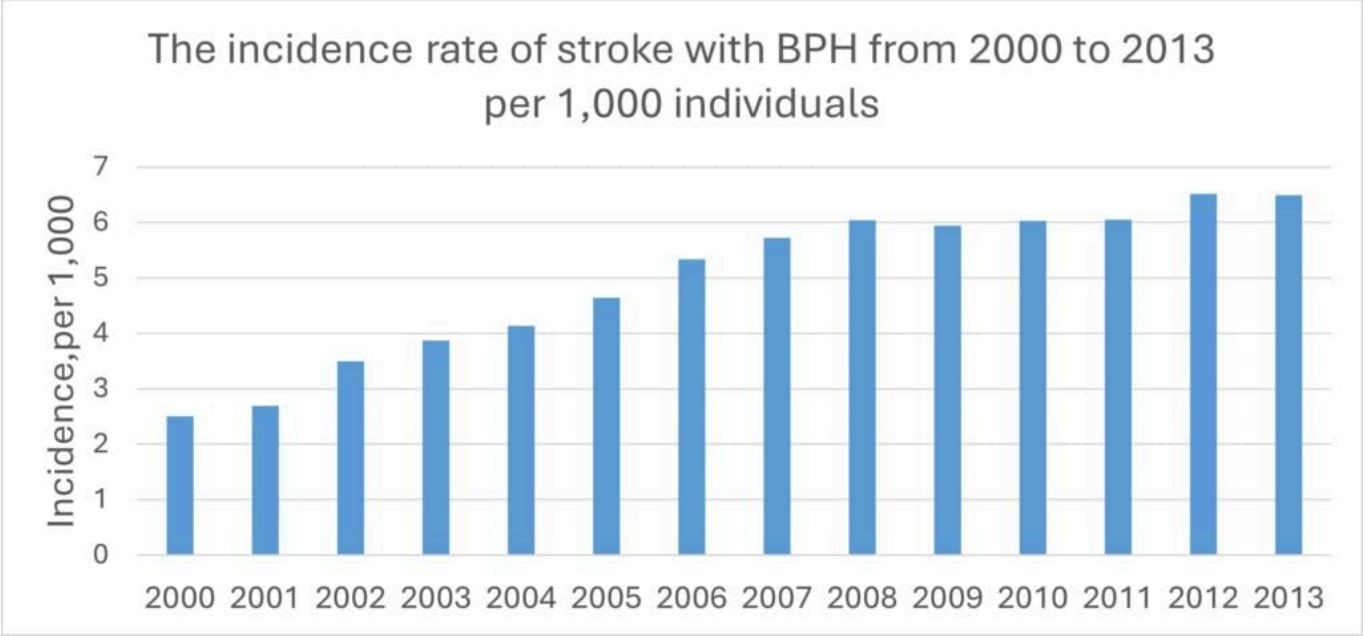
Background: Stroke is one of the top ten causes of death in Taiwan, while benign prostatic hyperplasia (BPH) is the most common urological disease among aging men. Studies have shown a potential association between BPH and cardiovascular diseases. However, there is a lack of research targeting the Taiwanese population. This descriptive study utilized the Taiwan National Health Insurance Research Database to investigate the incidence of stroke with BPH in a large, population-based Taiwanese cohort.

Methods: A descriptive study was conducted using data from Taiwan's National Health Insurance Research Database between 2000 and 2013. A total of 44,533 new cases of BPH were identified . Chi-square tests were used to evaluate the incidence of stroke among BPH patients across different age groups and time periods. For long-term trends, changes in incidence over the 14-year period were assessed using linear trend analysis.

Results:. The incidence of Stroke among BPH patients increased from 2.5 per 1,000 person-years in 2000 to 6.49 per 1,000 person-years in 2013, with an average incidence of 4.96 per 1,000 person-years.. After dividing the cohort into four age groups, the stroke incidence rates per 1,000 person-years were as follows: 1.18 for ages 40-49, 1.95 for ages 50-59, 4.34 for ages 60-69, and 6.52 for ages ≥70. The incidence of stroke increased with age.

Conclusion: Over the past 14 years, the incidence of Stroke with BPH has significantly impacted daily life. Using big data, our findings revealed that the incidence of stroke among BPH patients is steadily rising. Future studies are needed to test our hypothesis and further evaluate the association between BPH and stroke.

Keywords: Benign prostatic hyperplasia (BPH), National Health Insurance Research Database (NHIRD).


The incidence rate of stroke with BPH from 2000 to 2013 per 1,000 individuals
Incidence,per 1,000
0
1
2
3
4
5
6
7
2000 2001 2002 2003 2004 2005 2006 2007 2008 2009 2010 2011 2012 2013

Cardiovascular

Joint Association of Food Insecurity and Overweight/Obesity on Hypertension Risk among Guatemalan Women Paola Arevalo, MSc* Paola Arevalo Amy Auchincloss, PhD, MPH Fernanda Kroker, PhD, MSc Felice Le-Scherban, PhD, MPH

Objective: Examine the association between food insecurity and overweight/obesity (OWT/OB) on hypertension among Guatemalan women. **Methods:** Data came from Guatemala's 2018-2019 Health and Nutrition Epidemiological Surveillance System Survey (SIVESNU), including 1538 women aged 15-49 years. Blood pressure was measured and classified as normo-tension, pre-hypertension and hypertension, according to standard protocols. Food security was assessed via the 8-item Food Insecurity Experience Scale and dichotomized (yes/no). Using measured weight and height, OWT/OB was classified as yes/no. The exposure was a 4-category cross-classification of food insecurity and OWT/OB. Multinomial logistic regression was used, adjusting for confounders. **Results:** Mean age was 30 years, with nearly 40% of the sample having elevated blood pressure (28% pre-hypertension/11% hypertension). About 44% experienced the 'double burden' of OWT/OB and food insecurity. Significant positive associations with pre-hypertension and hypertension were found for 'only OWT/OB' and 'double burden'. Women experiencing 'double burden' had 66% (OR=1.66 [1.05-2.62]) and 297% (OR=3.97 [1.53-10.30]) higher odds of pre-hypertension and hypertension, respectively, compared to those experiencing none. **Discussion**: Food insecurity alone may not independently increase hypertension risk, but its interaction with metabolic factors like OWT/OB could exacerbate cardiovascular risk. While OWT/OB alone had a stronger association with hypertension, the increased risk observed in the 'double burden' group, along with the high prevalence of elevated blood pressure in our sample, reinforces the need for targeted preventive health strategies. **Conclusion**: OWT/OB and its 'double burden' with food insecurity are associated with increased odds of hypertension. Future research should explore longitudinal trends to better understand its causal pathways and design culturally appropriate interventions for low-income settings.

Table 2. Adjusted association between food insecurity and overweight/obese status, and outcomes for hypertension stage and systolic blood pressure (N= 1538)

	Outcome 1: Hypertension (JNC-8)*								Outcome 2: SBP *			
	Prehypertensive vs. normotensive				Hypertensive vs. normotensive				mm Hg (continuous)			
		95% CI				95% CI				95% CI		
	OR	Low	High	P-value	OR	Low	High	P-value	β coeff.	Low	High	P-value
Model 1: Unadjusted												
Neither	Referent				Referent				Referent			
Only Food Insecure	0.81	0.51	1.29	0.38	1.32	0.49	3.56	0.59	1.67	-0.75	4.08	0.18
Only Overweight/Obese	2.23	1.38	3.60	**0.00**	5.35	2.02	14.18	**0.00**	6.64	3.99	9.29	**<.0001**
Food Insecure + Overweight/Obese (double burden)	2.09	1.36	3.21	**0.00**	6.56	2.61	16.51	**<.0001**	8.43	6.10	10.76	**<.0001**
Model 2: Adjusted for individual-level variables †												
Neither	Referent				Referent				Referent			
Only Food Insecure	0.84	0.52	0.13	0.46	1.25	0.46	3.46	0.66	1.54	-0.81	3.88	0.20
Only Overweight/Obese	2.02	1.23	3.31	**0.01**	3.99	1.47	10.85	**0.01**	5.28	2.68	7.87	**<.0001**
Food Insecure + Overweight/Obese (double burden)	1.67	1.07	2.63	**0.02**	3.99	1.55	10.29	**0.00**	6.21	3.88	8.53	**<.0001**
Model 3b: Adjusted for model 2 variables and household variables ¶												
Neither	Referent				Referent				Referent			
Only Food Insecure	0.78	0.48	1.12	0.30	1.19	0.43	3.29	0.74	0.68	-1.67	3.03	0.57
Only Overweight/Obese	2.19	1.33	3.62	**0.00**	4.24	1.55	11.56	**0.00**	5.92	3.34	8.51	**<.0001**
Food Insecure + Overweight/Obese (double burden)	1.66	1.05	2.62	**0.03**	3.97	1.53	10.30	**0.05**	5.80	3.47	8.12	**<.0001**

* **Outcome 1** was modeled with multinomial logistic regression based on JNC-8 2014 guidelines (pre-hypertension SBP 120-139 and DBP 80-89, hypertension SBP≥140 or DBP≥80). **Outcome 2** used continuous systolic blood pressure (SBP), modeled using linear regression. Its adjustment list also included hypertension medication (takes oral prescription medicine to control hypertension).

† **Individual-level covariates:** age group, physical activity (tertiles of min/week), lactating status (yes/no).

¶ **Household-level covariates:** socio-economic position (tertiles of low, middle and high), total children birthed (0, 1-2, ≥3), total adults in the houshold (1-2, 3-4, ≥5), and urbanicity (urban vs rural).

Cardiovascular

Impact of Blood Flow Patterns on Cardiac Surgery Outcomes: Pulsatile vs Non-Pulsatile Flow Ayse Ulgen* Ayse Ulgen Ercan Kahraman Sirin Cetin

Non-physiological blood flow during cardiopulmonary bypass (CPB) may contribute to postoperative complications. This study evaluates pulsatile vs non-pulsatile flow impacts on cardiac surgery outcomes.

30 coronary artery bypass patients at Amasya University, Turkey, were retrospectively assigned to non-pulsatile or pulsatile CPB flow. Mean age: 61±11 years, 62% male. The following were compared: (1) Lactate levels at CPB onset and in intensive care unit (ICU) (2) Intubation duration, CRP levels (postop days 1-2); (3) pre/postop albumin and GFR level using 2-tailed t-test or Wilcoxon Rank Sum Tests.

No significant preop GFR/albumin differences ($p>0.005$) (Cl: 0.19-1.36 and -32.11;-9.62) was observed. Postop day 2: pulsatile group had higher GFR/albumin ($p<0.005$) (Cl -2,07-;-3.04) levels. Pulsatile group had shorter intubation times ($p<0.005$) (Cl 0.65-.5.89). No significant differences in lactate levels during CPB/ICU or postop CRP ($p>0.005$) (Cl -33.51;-1.48) was observed.

Pulsatile flow positively influenced recovery post-coronary bypass. Debate continues on pulsatile vs non-pulsatile flow effects on ICU stay, morbidity, mortality. Pulsatile flow may optimize organ perfusion, enhancing hemodynamic stability. A Turkish study found preop low albumin increased post-cardiac surgery renal replacement need. Further research on pulsatile flow's physiological benefits could inform strategies to prevent organ failure in critical patients. This study aligns with previous research showing pulsatile perfusion's benefits. Pulsatile flow preserves microcirculation better than non-pulsatile, potentially reducing systemic inflammation during CPB. High lactate (≥4 mmol/L) during CPB correlates with increased postop morbidity/mortality. While this study found no significant lactate differences, monitoring remains crucial. Pulsatile flow's higher circuit pressures may increase hemolysis risk, requiring careful management. Future research should standardize pulsatile flow definitions and explore its impact on specific patient subgroups.

Clinical and Biochemical Parameters Between Two Patient Groups

	Group 1 (n=15)	Group 2 (n=15)	
	(Mean ± Std)	(Mean ± Std)	*p*
Lactate levels during emergence from cardiopulmonary bypass (mmol/L)	2.36 ± 1.22	2.37 ± 1.05	0.966
Initial lactate levels measured in the intensive care unit (mmol/L)	1.40 ± 0.81	1.82 ± 0.88	0.060
C-reactive protein levels on Day 1 (mg/L)	78.59 ± 35.28	90.87 ± 31.88	0.323
C-reactive protein levels on Day 2 (mg/L)	205.3 ± 53.59	183.98 ± 57.38	0.303
Intubation time (hours)	10.63 ± 6.35	7.24 ± 3.05	**0.015**
Preoperative glomerular filtration rate (ml/min)	74.46 ± 17.01	86.61 ± 14.87	0.070
Glomerular filtration rate levels on Day 2 (ml/dk)	66.18 ± 26.56	84.51 ± 20.35	**0.043**
Preoperative albumin levels (g/L)	39,5 ± 2.42	39,22 ± 5.06	0.970
Albumin levels on Day 2 (g/L)	27.35 ± 3.14	30.37 ± 2.61	**0.009**

Cardiovascular

Insufficient Sleep Elevates Stroke Risk: a meta-analysis János Tibor Fekete* Janos Tibor Fekete Zoltan Ungvari Mónika Fekete Andrea Lehoczki Gyöngyi Munkácsy Virág Zábó György Purebl Péter Varga Anna Ungvari Balázs Győrffy

Background: The relationship between abnormal sleep duration and stroke outcomes remains controversial. This meta-analysis aims to quantify the impact of both short and long sleep durations on stroke incidence and mortality.

Methods: A comprehensive search of PubMed, Web of Science, Cochrane Library, Embase, and Google Scholar was conducted up to November 1, 2024, to identify cohort studies examining the relationship between sleep duration and stroke outcomes. The meta-analysis was carried out using MetaAnalysisOnline.com.

Results: A total of 43 studies (35 on stroke incidence, 8 on stroke mortality) were included in the analysis. Short sleep duration (≤5–6 hours) was associated with a 29% increased risk of stroke incidence (HR: 1.29, 95% CI: 1.19–1.40, $p<0.01$) and a modest 12% increase in stroke mortality (HR: 1.12, 95% CI: 1.01–1.25, $p=0.03$). Long sleep duration (>8–9 hours) showed stronger associations, with a 46% increase in stroke incidence (HR: 1.46, 95% CI: 1.33–1.60, $p<0.01$) and a 45% increase in stroke mortality (HR: 1.45, 95% CI: 1.31–1.60, $p<0.01$). Significant heterogeneity was observed in studies on stroke incidence (I^2 = 74–75%), whereas studies on stroke mortality displayed moderate to low heterogeneity (I^2 = 35–40%).

Conclusions: This meta-analysis highlights a U-shaped association between sleep duration and stroke risk, with both short and long sleep durations linked to higher stroke incidence and mortality.

Cardiovascular

Longitudinal assessment of the time-dependent association between cigarette smoking and incident atrial fibrillation in the Atherosclerosis Risk in Communities (ARIC) study Oluseye Ogunmoroti* Oluseye Ogunmoroti Ashely I. Naimi David Benkeser Elsayed Z. Soliman Lin Yee Chen Faye L. Norby Alanna M. Chamberlain Alvaro Alonso

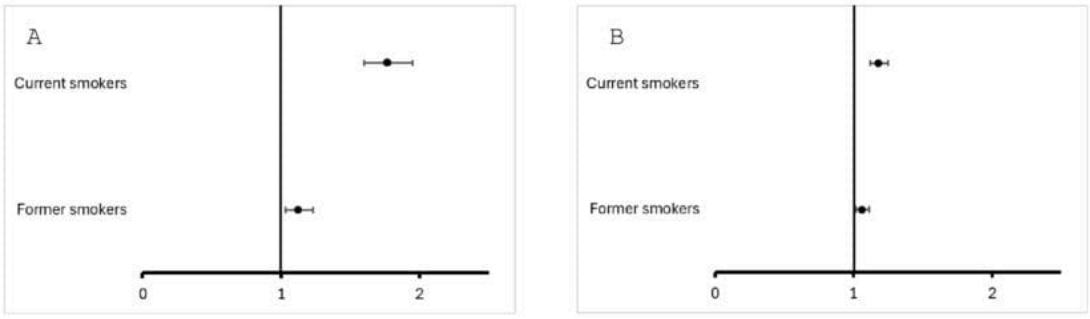
Background: Prior research investigating the link between cigarette smoking and atrial fibrillation (AF) does not account for the complex history of cigarette smoking overtime and the influence of time-dependent confounding. This study estimates the longitudinal time-dependent association between cigarette smoking and AF.

Methods: The analytical study sample comprised 13,201 adults aged 45-64 years enrolled between 1987 and 1989 and followed up until 2019. Cigarette smoking status was measured at 7 visits by self-report questionnaire and categorized as current, former and never. Incident AF was identified by ECG, hospital discharge records and death certificates. We compared estimates from 2 cox regression models. The standard model estimated the association of baseline cigarette smoking with AF, adjusting for time-fixed confounders (Figure). The time-dependent model estimated the association of cigarette smoking at multiple visits with AF, adjusting for both time-fixed and time-dependent confounders.

Results: At baseline, 55% of participants were women with mean age (SD) of 54.1 (5.7). After a median (IQR) follow-up of 28 (20, 31) years, 3,094 AF cases (23.4%) were identified. Compared with never smokers, estimates from the standard model showed that current and former smokers had an increased AF risk (HR: 1.77 [95% CI: 1.60, 1.95] and 1.12 [1.03, 1.23], respectively). While the time-dependent model showed an increased AF risk for current and former smokers, the magnitude of risk was lower (1.18 [1.12, 1.25] and 1.06 [1.02, 1.11], respectively).

Conclusion: The time-dependent cox model, accounting for the complex history of cigarette smoking and time-dependent confounding, showed an attenuated risk of AF among current and former cigarette smokers. These findings suggest that the estimates from the standard cox model may be biased. Further analysis using more advanced methods such as the parametric g-formula may be warranted to confirm and quantify the bias.

Figure: Longitudinal assessment of the time-dependent association between cigarette smoking and atrial fibrillation in the Atherosclerosis Risk in Communities study.



Reference = Never smokers

Panel A: Multivariable standard cox regression model was adjusted for the following baseline time-fixed covariates: age, sex, race-center, educational attainment, physical activity, stroke, heart failure, use of anti-hypertensive medication, body mass index, alcohol consumption, diabetes, systolic blood pressure, diastolic blood pressure and coronary heart disease.

Panel B: Multivariable time-dependent cox regression model was adjusted for the following baseline time-fixed covariates: age, sex, race-center, educational attainment, physical activity, stroke, heart failure, use of anti-hypertensive medication and the following time-dependent covariates: body mass index, alcohol consumption, diabetes, systolic blood pressure, diastolic blood pressure and coronary heart disease.

Causal Inference

Benchmarking observational analysis against registry-based trials: estimands, assumptions and estimators Camila Olarte Parra* Camila Olarte Parra Anita Berglund Issa Dahabreh

To increase our confidence in observational analyses, we can compare real trials with observational emulations of target trials designed to be similar. Obtaining equivalent results could make observational analyses more trustworthy to evaluate other (long-term) outcomes outside the scope of the real trial and to assess treatment heterogeneity. Here, we outline a framework for formal benchmarking in an ideal setting of a registry-based trial, where the real trial is embedded in a nationwide registry. We describe the conditions required for valid comparisons and propose methods to evaluate the implications of these conditions on the observed data. We evaluate the proposed methods through plasmode simulations which allow us to generate datasets that mimic the features of real-world observational data while embedding known causal effects as found in trials. These simulations are designed to resemble a large cardiovascular trial nested in a large Swedish registry, where we have follow-up data for patients who did not enrol in the trial. Well-performing methods in simulations are subsequently applied to the real data from the Swedish registry, exploiting the rich variables available from the linkage of different population registers that contain clinical and socio-economic variables.

Causal Inference

Transparent Reporting of Observational Studies Emulating a Target Trial: The TARGET Statement Harrison* Harrison Hansford Aidan Cashin Sonja Swanson Matthew Jones Nazrul Islam Issa Dahabreh Barbra Dickerman Matthias Egger Xabier Garcia-Albeniz Robert Golub Sara Lodi Margarita Moreno-Betancur Sallie-Anne Pearson Sebastian Schneeweiss Jonathan Sterne Melissa Sharp Elizabeth Stuart Hopin Lee Miguel Hernán James McAuley

Aim

To develop international, consensus-based guidance for reporting studies that use the target trial framework to estimate the effect of interventions using observational data.

Methods

The TARGET (Transparent Reporting of Observational Studies Emulating a Target Trial) guideline was developed following methodological guidance from the EQUATOR Network. This included a systematic review of reporting practices in studies that explicitly aimed to emulate a target trial; a 2-round online survey (Aug 2023-Mar 2024; 18 expert participants) to identify and refine items selected from previous research; an expert consensus meeting (Jun 2024; 18 panellists) to refine the scope of the guideline and draft the checklist; and an external piloting activity with stakeholders (n=66; Sept 2024-Dec 2024). The checklist was revised based on piloting feedback.

Results

The TARGET guideline is focussed on observational studies of interventions that explicity emulate a target trial. The 27-item TARGET checklist is organized into 7 sections (abstract, introduction, methods, results, discussion, open science, and patient & public involvement). Key recommendations are (1) the causal question should be stated, including the reason for emulating a target trial, (2) the target trial protocol should be clearly defined (ie. causal estimand, identifying assumptions, data analysis plan) and how these components were mapped to the observational data should be thoroughly described, and (3) for each causal estimand, the estimate obtained and its precision should be reported along with findings from additional analyses to assess robustness to potential violations of assumptions and design and analysis choices.

Discussion

The TARGET guideline provides recommendations on reporting of studies explicitly emulating a target trial. Use of the guideline should facilitate transparency in their reporting to improve peer review, and help researchers, clinicians and other readers interpret and use the results

Causal Inference

Long-term cardiovascular outcomes following bariatric surgery: Reconciling seemingly conflicting evidence. Sebastien Haneuse* Sebastien Haneuse Luke Benz Valerie A. Smith Matthew L. Macejewski David Arterburn

To-date there have been no randomized trials of the impact of bariatric surgery on incident cardiovascular disease (CVD). Nevertheless, a large body of observational evidence exists in support of bariatric surgery being associated with reduction in risk of CVD, as well as a wide range of other adverse outcomes. Two recent studies, however, with one based on claims data from Optum and another based on electronic health record (EHR) data from the Veterans Administration (VA), found no evidence of benefit regarding CVD, arguing that much of that prior work suffers from various sources bias, including confounding, information bias and surveillance bias, and from design decisions that compromise whether one can conceive of a corresponding target trial. In turn, renewed calls for randomized trials have been put forward. In this work, we first present new results based on a target trial emulation that mimics the emulation employed in the VA study but with EHR data from Kaiser Permanente. The results provide evidence of a protective effect of bariatric surgery in relation to risk of CVD and, therefore, are consistent with the majority of the literature. We then examine possible mechanisms by which the discrepant results can be reconciled, including issues of statistical validity that arise from small samples and whether recent work on transportability indicates that we should not expect results to always be concordant. We conclude with a discussion of the role of conservatism associated with “clinical trial thinking”, what standards we should be using as we consider the work of others in the literature and the role that evidence triangulation may play in the future.

Causal Inference

Estimating the impact of Shigella vaccines on growth outcomes and implications for clinical trial design Allison Codi* Allison Codi Elizabeth Rogawski-McQuade Razieh Nabi David Benkeser

Shigella vaccines could prevent growth faltering in children in low-resource settings, prompting interest in trials to demonstrate a vaccine effect (VE) on linear growth. However, the population-level VE on height-for-age z-score (HAZ) is expected to be small (<0.01) because most participants won't experience shigellosis, such that the effect is diluted by children who were not at risk for Shigella-attributable growth faltering. Thus, standard VE estimation methods are likely to be underpowered at realistic trial sizes and at risk of producing null or inverse results.

We use causal inference to develop an alternative estimand that quantifies VE for HAZ in the subset of children with Shigella. We adjust for confounders of infection and growth and include children for whom the vaccine prevented infection. These children would be expected to experience the largest VE but would be excluded in a naïve comparison of children observed to have shigellosis in the trial (i.e., a comparison of growth among unvaccinated cases and vaccinated breakthrough cases). We compare power of our estimand to the population-level measure through trial simulations using data from recent observational studies of shigellosis for parameterization.

Simple population-level comparisons of HAZ by vaccine arm showed extremely limited power (<5%) and a negative point estimate for VE in more than 40% of simulated trials of realistic size (n=10,000-20,000). Analysis of VE for HAZ in the subset of children with vaccine-preventable Shigella has improved power (~20-30%) and decreased likelihood of demonstrating negative VE (<10% of simulated trials). While our method offers dramatic improvement over the population-level comparison, realistically sized trials will still likely be underpowered. Nevertheless, these novel methods may be relevant beyond the specific application to Shigella vaccines for studying other post-infection endpoints in a broad range of vaccine trials.

Causal Inference

Causal Effects of Mobility Patterns on Pollution Exposure Mai Waziry* Mai Waziry

Purpose

Individuals move daily, and during this movement, they are exposed to air pollution. Most previous studies relied on static measurements to infer pollution exposure. Individuals' mobility patterns differ based on lifestyles and the longevity of their activities. This paper focuses on filling the gap in understanding the causal effects of exposure to PM2.5 on the outcome of individuals' mobility patterns, focusing on outdoor activities. The mobility dataset from Spectus, offered through the Data for Good program, includes almost 8 million observations in Boston and Chicago.

Method

This paper uses a framework with two main steps. First, an instrumental variable analysis is used to close the backdoor between exposure and outcome. Two instrumental variables are used: wind speed and elevation. The second step in the framework is causal mediation analysis, which infers direct and indirect effects between exposure to PM2.5 and the outcome of outdoor activities through the mediator, which is the distance from an individual's home to the activity location.

Findings

The results from the instrumental variable (IV) analysis using wind speed show that increased daily wind speeds reduce individuals' PM2.5 exposure, with the relevance and validity assumptions for wind speed as an IV being satisfied. However, elevation, initially considered as an IV, was found to act as an interaction term with pollution exposure rather than a valid IV. The findings for the IV analysis are consistent across both cities. The results provide an understanding of the spatiotemporal patterns of mobility and shed light on how and why responses can play a critical role in disaster mitigation and prevention.

COVID-19 Pandemic

Estimates of SARS-CoV-2 infections and population immunity after the COVID-19 pandemic in Austria: Analysis of national wastewater data Uwe* Uwe Riedmann Alena Chalupka Lukas Richter Martin Sprenger Wolfang Rauch Hannes Schenk Robert Krause Peter Willeit Herbert Oberacher Tracy Beth Høeg John PA Ioannidis Stefan Pilz

Background:

Post-pandemic surveillance data on COVID-19 infections may help inform future public health policies regarding SARS-CoV-2 testing, vaccinations or other COVID-19 measures. We estimate the total SARS-CoV-2 infections in Austria after the end of the pandemic (May 5, 2023, per WHO) up to May 2024 from wastewater data. Those estimates are used in an agent-based model (ABM) to estimate average national levels of SARS-CoV-2 infection protection (IP) and COVID-19 death protection (DP).

Methods:

We use a previously published model estimating total infections in Austria from wastewater data and extrapolate the approach up to May 2024. Utilizing those estimates in an ABM, we estimate daily national average IP and DP. These estimates are based on waning immunity estimates of previous literature and incorporate documented vaccinations.

Findings:

We estimate approximately 3·2 million infections between May 6, 2023, and May 23, 2024, with a total of 17·8 million infections following May 12, 2020. The ABM estimates that 95% of people in Austria were infected with SARS-CoV-2 at least once. It also shows very high levels of national average DP a year after the end of the pandemic. National IP remained relatively low after the onset of Omicron.

Interpretation:

The estimated high number of SARS-CoV-2 infections since the end of the COVID-19 pandemic in Austria has kept the national average DP very high. These findings should be considered for public health decisions on SARS-CoV-2 testing practices and vaccine booster administrations.

COVID-19 Pandemic

Obesity and Long-term Cardiovascular Outcomes after COVID-19 Infection among Children and Young Adults: Findings from the RECOVER Ting Zhou* Ting Zhou Bingyu Zhang Dazheng Zhang Jiajie Chen Yiwen Lu Qiong Wu Jiayi Tong Yuqing Lei Lu Li Christopher B. Forrest Yong Chen

Background

Current research is focusing on the link between pre-COVID-19 elevated BMI or obesity and long-term cardiovascular issues after infection, especially in children. Obese children, who are at higher risk for severe COVID-19, may face greater long-term cardiovascular complications due to chronic inflammation and metabolic stress. Understanding this association is crucial for developing targeted interventions and improving health outcomes in this vulnerable group.

Methods

To tackle this issue, we utilized one of the largest pediatric Electronic Health Record (EHR) cohorts in the U.S., the pediatric RECOVER program by the National Institutes of Health (NIH). This program studies the long-term effects of COVID-19 and includes data from a national network of academic medical centers, covering approximately 10% of the U.S. pediatric population. Our analysis considered various covariates, including demographic characteristics (age, sex, race/ethnicity), virus-variant predominant periods, healthcare utilization metrics, severity of acute phase COVID-19, Pediatric Medical Complexity Algorithm (PMCA) index, and vaccination status. We fitted a Poisson regression model to estimate relative risks (RRs) and 95% confidence intervals (CIs) and conducted comprehensive sensitivity analyses. To ensure the robustness and generalizability of our findings, we selected a negative control outcome unrelated to pre-COVID-19 BMI or obesity, specifically “foreign body in ear.” This helped us detect residual biases, validate our methods, and strengthen our conclusions, confirming that the associations between elevated BMI and post-acute cardiovascular sequelae are genuine.

Results

Before fitting the model, we applied a cutoff incidence value of 0.1% to avoid overfitting for rare cardiovascular outcomes. Before fitting the model, we applied a cutoff incidence value of 0.1% to prevent overfitting for rare cardiovascular outcomes. This led us to identify six cardiovascular symptoms and disorders from the predefined cardiovascular outcomes provided by clinicians: chest pain, palpitations, syncope, hypertension, ventricular arrhythmias, and thromboembolism, occurring during the post-acute phase (28 to 179 days after cohort entry). Among the 139, 320 participants, 71,901 (51.6%) were female, and 729,52 (52.4%) were non-Hispanic White. Compared to participants with a healthy weight, the risk increased in those with severe obesity for chest pain (RR, 1.180; 95% CI, 1.003-1.388), hypertension (RR, 3.681; 95% CI, 2.651-5.111), composite outcomes, i.e., any cardiovascular disorders (RR, 2.562; 95% CI, 1.928-3.407), and any cardiovascular symptoms or disorders (RR, 1.185; 95% CI, 1.042-1.346).

Conclusion

In this large, retrospective pediatric cohort study, elevated BMI is associated with long-term cardiovascular outcomes after COVID-19 infection in the pediatric population. The takeaway is that thorough consideration of BMI is crucial when assessing the long-term health impacts of COVID-19 in children.

COVID-19 Pandemic

Health, Healthcare, and Psychosocial Experiences among Latine and non-Latine Iowans during the COVID-19 Pandemic (March – September 2021) Crystal Garcia-Auguste* Crystal Garcia-Auguste Breanna Blaess Miriam Velez-Bermudez Jonathan Platt Ryan Carnahan Jacob Oleson Natoshia Askelson Mary Charlton Nicholas Rudzianski Brian Gryzlak Elizabeth Chrischilles

Background: The COVID-19 pandemic disproportionately affected racialized minorities and urban/rural areas in the United States (US). We compared COVID-19 perceptions, behaviors, psychosocial experiences, and healthcare disruptions between Latine and non-Latine residents in Iowa.
Methods: Bilingual surveys were mailed March 2021 to 2,500 households from 32 Latine-majority census block groups in 4 rural (n=1,251) and 5 urban (n=1,249) counties. Age-adjusted means/frequencies were calculated using linear regression for continuous/binary variables and logistic regression for categorical variables with direct age standardization (Latine subsample as reference).
Results: Among 536 respondents (53% rural, 21% Latine), Latine individuals were younger, more often employed, born outside the US, living in multigenerational homes, and less likely to be health insured. Latine respondents reported greater COVID-19 exposures (e.g. household member test positive: 43.9% vs 16.7%, p<.001), longer test result waits (41.6 vs 5.6 days, p=.012), greater community concern about COVID-19 (53.2% vs 35.8%, p=.012), stronger social distancing support (85.56% vs 52.08%, p<.001), and more risk-reducing behaviors (e.g. staying home: 90.4% vs 70.7%, p<.001; masking inside: 98.8% vs 94.2%, p=.030). Latine reported greater anxiety symptoms (p<.001), disruptions to daily activities and social interactions (p=.044), financial hardship (p=.006), and psychological benefits (p<.001). They were also more likely to report weight loss (p<.001) and less likely to report increased alcohol use (p=.014) or smoking (p<.001) compared to pre-pandemic. No significant differences emerged in cancer screening delays.
Conclusion: Latine residents experienced more COVID-19 exposures, greater positive and negative psychosocial impacts, and practiced more risk-reducing behaviors than non-Latine residents. Investing in Latine communities in public health emergencies may bolster positive outcomes and address disparities.

COVID-19 Pandemic

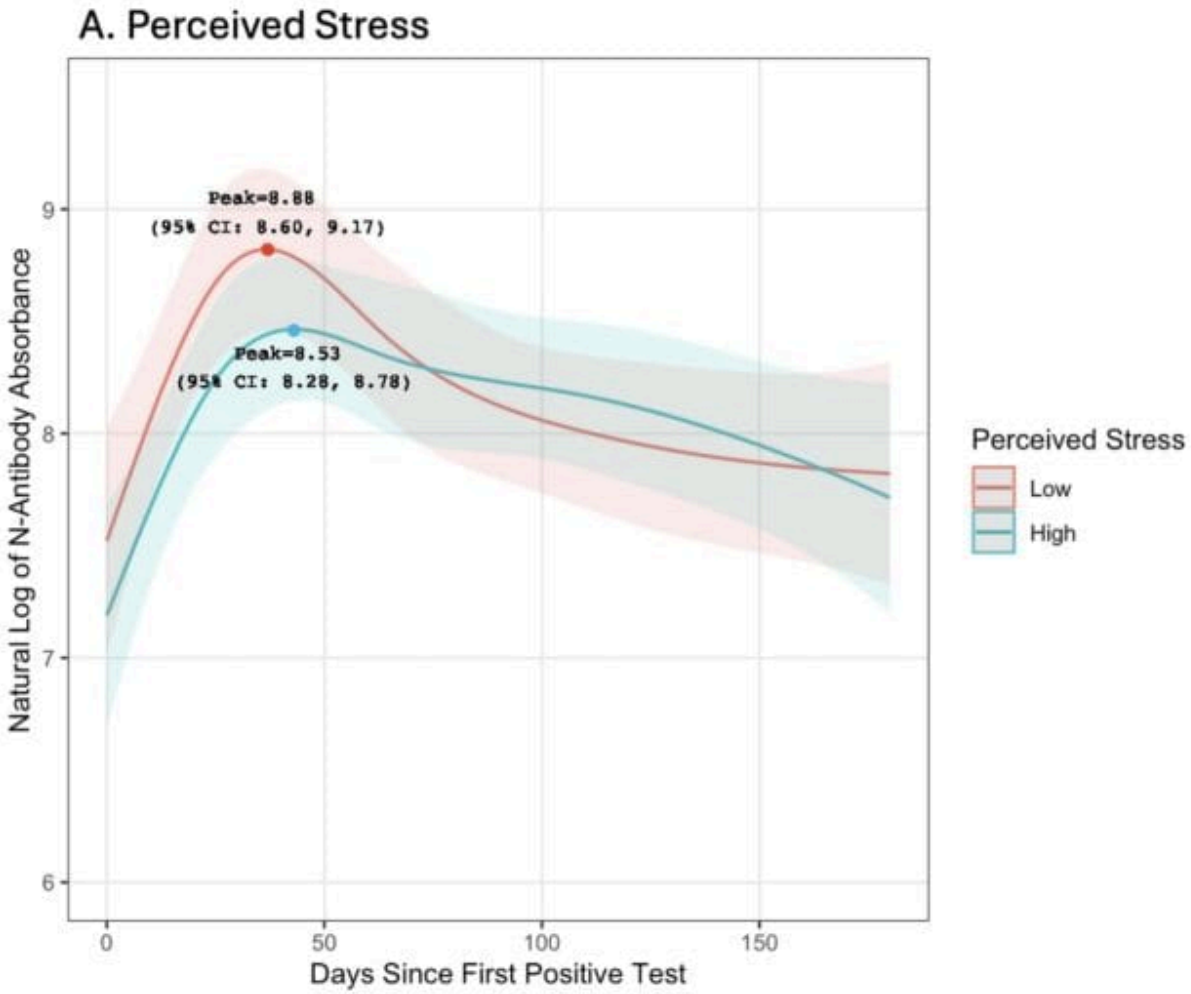
The relationship between stress and SARS-CoV-2 Antibody Response after Natural Infection: Longitudinal Findings from the Aegis Study Erika Beidelman* Erika Beidelman Ashley Judge David B. Allison Stephanie Dickinson Lilian Golzarri Arroyo Anna L.M. Macagno Jon Macy Christina Ludema Kevin C. Maki Molly Rosenberg

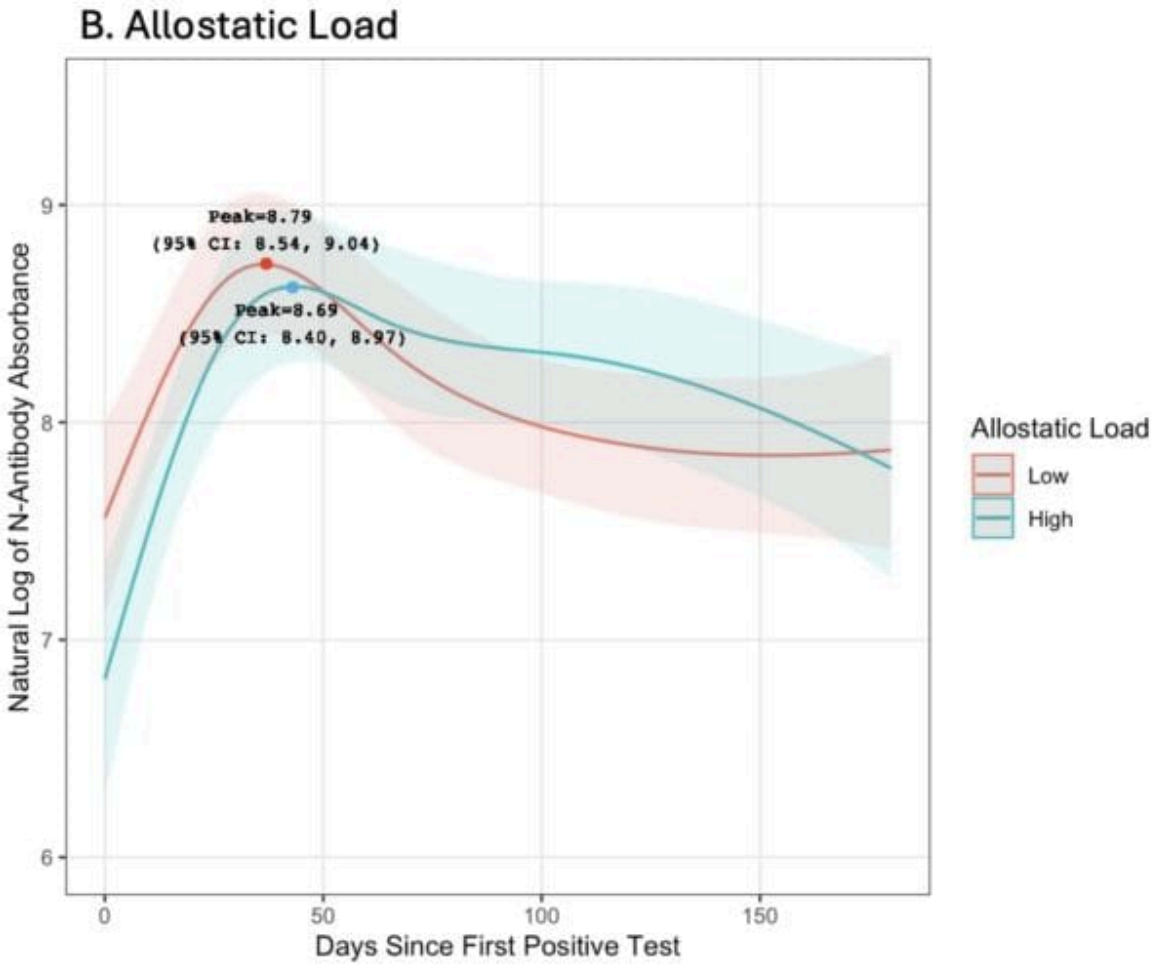
Introduction: Psychological stress can cause diminished immune response to infectious challenges. The extent this holds true during SARS-CoV-2 infection and the modifying effect of vaccination status is to date untested. We explored these relationships in a sample of adults sourced across nine clinical sites, standardizing our results to the U.S. adult population.

Methods: Out of 2178 participants in the Aegis Study (2021-2022) we identified 445 adults with a laboratory-confirmed SARS-CoV-2 infection. We estimated the natural log of nucleocapsid-binding antibody (N-antibody) absorbance at each study visit following a positive SARS-CoV-2 test. Linear mixed effects models were fit to estimate the association of each perceived stress and allostatic load, both measured prior to infection, with N-antibody trajectories up to 260 days post-positive SARS-CoV-2 test. Standardization was performed using NHANES data and a post-stratification weighting approach.

Results: Lower stress groups had higher peak antibody response, with consistent results across standardized and unstandardized analyses. Differences were greater for perceived stress compared to allostatic load. Low perceived stress was associated with greater antibody response up to 31 days post-positive test (0.418, p=0.0493) while low allostatic load was associated with greater antibody response up to 20 days post-positive test (0.374, p=0.0443). Pre-infection vaccination status (full vaccination = 73%) appeared to modify the relationship between stress and N-antibody trajectories where the observed estimates attenuated to the null for individuals with full vaccination.

Discussion: In this longitudinal analysis linking two robust stress measures and longitudinal antibody data, we found consistent evidence that high stress was associated with reduced N-antibody response following SARS-CoV-2 infection. We also observed that full vaccination may equalize the antibody response between high and low stress groups.


A. Perceived Stress
Peak=8.88
(95% CI: 8.60, 9.17)
Peak=8.53
(95% CI: 8.28, 8.78)
Natural Log of N-Antibody Absorbance
9
8
7
6
0
50
100
150
Days Since First Positive Test
Perceived Stress
Low
High


B. Allostatic Load
Peak=8.79
(95% CI: 8.54, 9.04)
Peak=8.69
(95% CI: 8.40, 8.97)
Natural Log of N-Antibody Absorbance
9
8
7
6
0
50
100
150
Days Since First Positive Test
Allostatic Load
Low
High

COVID-19 Pandemic

COVID-19 Hospitalization Rate and Mortality Rate by Respiratory Season in Tennessee.
Magdalena Dorvil-Joanem* Chaitra Subramanya Jennifer Jain Sarah Waldo Kelly Squires Jane Yackley

BACKGROUND: As of March 2024, the Centers for Disease Control and Prevention stated that vaccinations, effective treatment, and population immunity have caused fewer hospitalizations and deaths due to COVID-19 compared to previous years. Tennessee trends are similar; approximately 50% of COVID-19 hospitalizations and deaths in Tennessee occurred during the 2020-2021 respiratory season. Hospitalization and mortality declined over subsequent years. The Tennessee Department of Health aimed to evaluate the statistical significance of these trends.
METHODS: Data from the National Electronic Disease Surveillance System were used to calculate 7-day rolling averages and rates per 100k population for COVID-19 hospitalizations and deaths from March 5, 2020, through September 30, 2024. Data was divided into 5 respiratory seasons from 2019-2024. Each respiratory season started October 1 and ended September 30 of the following year, except for the respiratory season 2019-2020 due to data limitations. A one-way ANOVA was performed to compare COVID-19 hospitalization and mortality rates across respiratory seasons.
RESULTS: The one-way ANOVA shows a statistically significant difference in mean hospitalization rates ($F(4,1656) = [407.67]$, $P = <0.001$) and mortality rates ($F(4,1650) = [245.43]$, $P = <0.001$) across all respiratory seasons. Tukey's HSD test found that mean hospitalization rates and mortality rates between all respiratory seasons were statistically significant for 2019-2020, 2020-2021, and 2021-2022.
CONCLUSIONS: There were statistically significant differences in the mean COVID-19 hospitalization and mortality rates in Tennessee over the respiratory seasons from 2019-2024. Further analysis needs to be conducted to explore potential causes and associations in trends between COVID-19 hospitalizations and deaths by respiratory seasons.

COVID-19 Pandemic

Genomic Epidemiology Reveals Multiple SARS-CoV-2 Introductions in a Long-Term Care Facility Outbreak Magdalena Dorvil-Joanem* Magdalena Dorvil-Joanem Jyoti Narayana Pamela Obodoechina Shoana M Anderson Emily J Gateley Jane Yackley

The COVID-19 pandemic significantly advanced whole genome sequencing (WGS) technologies and expanded the application of genomic epidemiology. Analyzing SARS-CoV-2 genomic data offers valuable insights into outbreaks, including viral introductions and transmission patterns. Combined with traditional epidemiological methods, this data enhances disease prevention and control strategies. This study examines SARS-CoV-2 genetic sequences from a COVID-19 outbreak in a long-term care facility (LTCF) in Tennessee.

Between December 2023 and January 2024, an LTCF experienced a COVID-19 outbreak involving 46 cases. Collaboration between outbreak response and genomic epidemiology teams facilitated timely specimen retrieval, sequencing, and analysis. Nine remnant SARS-CoV-2-positive specimens were sent to the state laboratory for WGS; seven were successfully sequenced. Lineage assignment using Pangolin and GISAID databases, followed by NextStrain phylogenetic analysis, revealed two distinct SARS-CoV-2 lineages circulating during the outbreak.

Four cases belonged to the HV.1 parent lineage, including three from sublineage EG.5.1.6, while three cases were associated with the JN.1 parent lineage, all from sublineage JN.1.8.1. The presence of two lineages indicates multiple virus introductions rather than a single-source transmission event. These findings align with the lineages circulating in the surrounding community, underscoring the role of community transmission in seeding LTCF outbreaks.

This study emphasizes the critical role of integrating genomic surveillance with public health measures to manage outbreaks in high-risk settings like LTCFs. Combining genomic and epidemiological data clarified transmission dynamics and informed interventions such as testing, patient cohorting, and infection control measures. Limited sample availability remains a challenge, highlighting the need for active surveillance and robust support systems to enhance data collection. Continuous genomic monitoring is essential for providing insights into outbreak responses and enabling LTCFs to adapt effectively as SARS-CoV-2 reporting guidelines evolve.

Cultural

ePi art: A new paradigm for epidemiologic research as an art practice Hiroshi Habu* Hiroshi Habu Naoki Kondo

Epidemiologic research, central to public health, aims to enhance well-being addressing health determinants. However, its processes often prioritize linear objectives, external evaluations, and competition, overlooking the well-being of those involved. Research must transcend technical goals, aligning methods with its purpose. The COVID-19 pandemic exposed critical challenges, such as a gap between evidence producers and the public, resistance to top-down policies, and insufficient cross-cultural dialogue. These challenges highlight the need for methods embracing plurality and collaboration. Art uniquely addresses these issues and reimagines epidemiologic research. Art, defined here as an unexchangeable act of mutual communication where means and ends are inseparably intertwined, emphasizes play and the value of process and relationships. Creative activities such as playing music or painting directly enrich lives and foster well-being. To explore this potential, we developed ePi Art as a life practice, a framework integrating art paradigms into epidemiologic research. The term ePi represents epidemiology and evidence. The capital P symbolizes process, play, poetry, and others. In ePi Art, participants craft themes inspired by their aspirations and use them as material for creation, and expression through their expertise or interests. These processes remain deeply tied to their aspirations. Unlike community- or arts-based research, ePi Art uniquely integrates art and research as inseparable. In its pilot phase, ePi Art brought diverse participants into collaborative sessions to explore shared themes and build relationships. The next step is to create multidimensional outputs. Mitigating biases from active participation, however, requires meticulous planning to ensure quantitative evaluation. By aligning methods with well-being, ePi Art offers a fresh perspective on epidemiologic research, integrating artistic paradigms to address challenges and foster co-creation.

Diabetes

Trends and Risk of Melioidosis in Diabetic Patients: A Population-Based Study Using Taiwan's National Health Insurance Database Chia-Chi Chien* Chia-Chi Chien Fu-Huang Lin Chien-An Sun Yu-Ching Chou

Trends and Risk of Melioidosis in Diabetic Patients: A Population-Based Study Using Taiwan's National Health Insurance Database

Chia-Chi Chien1, Fu-Huang Lin1, Chien-An Sun2, Yu-Ching Chou1*

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Background: Melioidosis, caused by Burkholderia pseudomallei, is a Category IV notifiable disease in Taiwan with high mortality rates, reaching 90% without treatment and 10–50% with treatment. Predominantly found in tropical regions, it is closely linked to diabetes, with about 50% of patients affected. Data on its incidence among diabetic patients in Taiwan is limited. This study uses the National Health Insurance Research Database to analyze melioidosis incidence in diabetic patients and the broader Taiwanese population.

Methods: From 2000 to 2013, trends and risks of melioidosis in diabetic patients were analyzed using Taiwan's National Health Insurance Database. Eligible cases were identified, and chi-square tests were employed to evaluate differences in the incidence rates of melioidosis across sex, age groups, and time periods. Additionally, long-term changes in the incidence rates of melioidosis among diabetic patients were assessed using linear trend analysis to reveal potential trends and associated risk factors.

Results: In men, diabetes incidence dropped from 1.43 to 0.34 per 1,000 individuals between 2000 and 2013, and in women, from 1.59 to 0.33. Overall, it declined from 3.02 to 0.67 per 1,000. In contrast, melioidosis incidence rose from 0.92 to 1.60 per million, with an annual increase of 4.3% in women and 0.9% in men. Among diabetic patients, melioidosis incidence per 10,000 increased across age groups (30–39, 40–49, 50–59, ≥60 years) from 0.89 to 4.04 ($P < 0.001$), and was higher in females (3.02) than males (1.91) ($P = 0.012$).

Conclusion:

In the past 14 years, the incidence of melioidosis among diabetic patients have shown significant trends. Utilizing big data from the Taiwan National Health Insurance Research Database, our findings suggest a steadily increasing incidence of melioidosis in this population. Therefore, further studies are required to confirm the association between diabetes and melioidosis and to explore potential preventive strategies.

Keywords: Melioidosis□Diabetes mellitus

LATEBREAKER

Diabetes

Estimating the Association between Neighborhood Walkability and Type 2 Diabetes Mellitus after Gestational Diabetes: A Longitudinal Study in New York City Bohao Wu* Bohao Wu Natalie Boychuk Katharine McCarthy Frances M. Howell Andrew G. Rundle Teresa Janevic

Background: Neighborhood walkability is associated with decreased risk of gestational diabetes (GDM). We estimated the association between walkability and type 2 diabetes mellitus (T2DM) after GDM to understand neighborhood environment's role in life-course cardiometabolic health. We also explored the race/ethnicity-walkability interaction given potential contextual factors affect walkability and T2DM after GDM.

Methods: Using 2009-2021 linked New York City birth, hospital discharge, and NYC A1c Registry data, we identified GDM cases in birth/hospital data. We excluded women with pre-pregnancy diabetes. We used a previously published neighborhood walkability index in quartiles, with the 4th group indicating the highest walkability. T2DM was ascertained as two A1c results ≥6.5% after 12 weeks postpartum. We used Cox proportional hazards models to estimate the association between walkability and T2DM after GDM, adjusting for maternal age, race and ethnicity, education, nativity, parity, and neighborhood economic opportunity. We tested the interaction between race-ethnicity and walkability.

Results: Among n=12,403 women with GDM at baseline, the 12-year cumulative incidence of T2DM after GDM was 20.6%. Compared with the walkability 4th group, only the 3rd group had decreased risk of T2DM after GDM (1st group: HR=0.96, 95% CI 0.83-1.10; 2nd group: HR=0.92, 95% CI 0.83-1.03; 3rd group: HR=0.90, 95% CI 0.82-0.98). Multivariable estimates were similar. The walkability-race-ethnicity interaction was not significant. However, in the multivariable model, the lowest walkability group had an increased risk of T2DM compared with the highest walkability group in Black women only (aHR=1.42, 95%CI=1.11-1.81).

Discussion: Little association was found between neighborhood walkability and T2DM after GDM. An important exception to the overall null findings was found among Black women, warranting further exploration of mechanisms and potential interventions.

Diabetes

Insulin-like growth factor-1, lean mass and fat mass in type 2 diabetes prevention: Mendelian randomization study in East Asian populations KWOK Man Ki* Man Ki KWOK Parco Ming Fai SIU C Mary SCHOOLING

Background: Differences in body composition by ethnicity and gender have been implicated in susceptibility to type 2 diabetes mellitus (T2DM). However, few sex-specific assessments of body composition and its biological drivers, insulin-like growth factor-1 (IGF-1), on T2DM have been conducted. This study assessed the role of IGF-1 in T2DM, and examined whether any mediation by lean mass and/or fat mass, in men and women in East Asian settings.

Methods: In a two-sample Mendelian randomization (MR) study, genetic variants predicting IGF-1 and body composition (fat mass or lean mass) were obtained from young Chinese (aged ~17.6 years) from the Hong Kong "Children of 1997" Biobank (n=3,443). Genetic associations with T2DM in men and women of East Asian descent (aged 60.8 years for cases and 55.8 years for controls) were from the largest available East Asian GWAS (n=433,540). Univariable and multivariable MR were used to obtain total and direct effects of IGF-1 and fat mass or lean mass on T2DM. Mediation analyses were conducted to obtain the indirect effects (via the mediator) using the product method.

Results: Genetically predicted higher IGF-1 was associated with a higher risk of T2DM in both sexes [odds ratio (OR) 1.06 per 1 standard deviation (SD) of IGF-1, 95% confidence interval (CI): 1.01 to 1.12]. Fat and lean mass were unrelated to T2DM. Genetically predicted IGF-1 was associated with more lean mass (in men), but not fat mass. After allowing for lean mass or fat mass, IGF-1 was no longer associated with T2DM. No indirect effects of lean mass or fat mass were found for the associations of IGF-1 with T2DM were found.

Conclusions: IGF-1 directly affected T2DM, independent of body composition, in both men and women. Neither fat mass nor lean mass was related to T2DM risk, consistent with a higher T2DM risk despite a lower prevalence of obesity among East Asians.

Diabetes

Composite risk of cardiovascular disease comorbidity in people living with diabetes in Africa Divine-Favour Chichenim Ofili* Divine-Favour Chichenim Ofili Regina Idu Ejemot-Nwadiaro Stephen Chukwuma Ogbodo Henshaw Okoroiwu Ugochinyere Vivian Ukah

Aim: Diabetes mellitus (DM) and cardiovascular diseases (CVD) share similar risk factors, thereby increasing the likelihood of comorbidity. However, the risk of CVD, based on the interaction of key risk factors, among people living with DM is poorly understood. Thus, this study quantified the composite CVD risk and its association with socio-demographic characteristics in people living with DM in Africa.

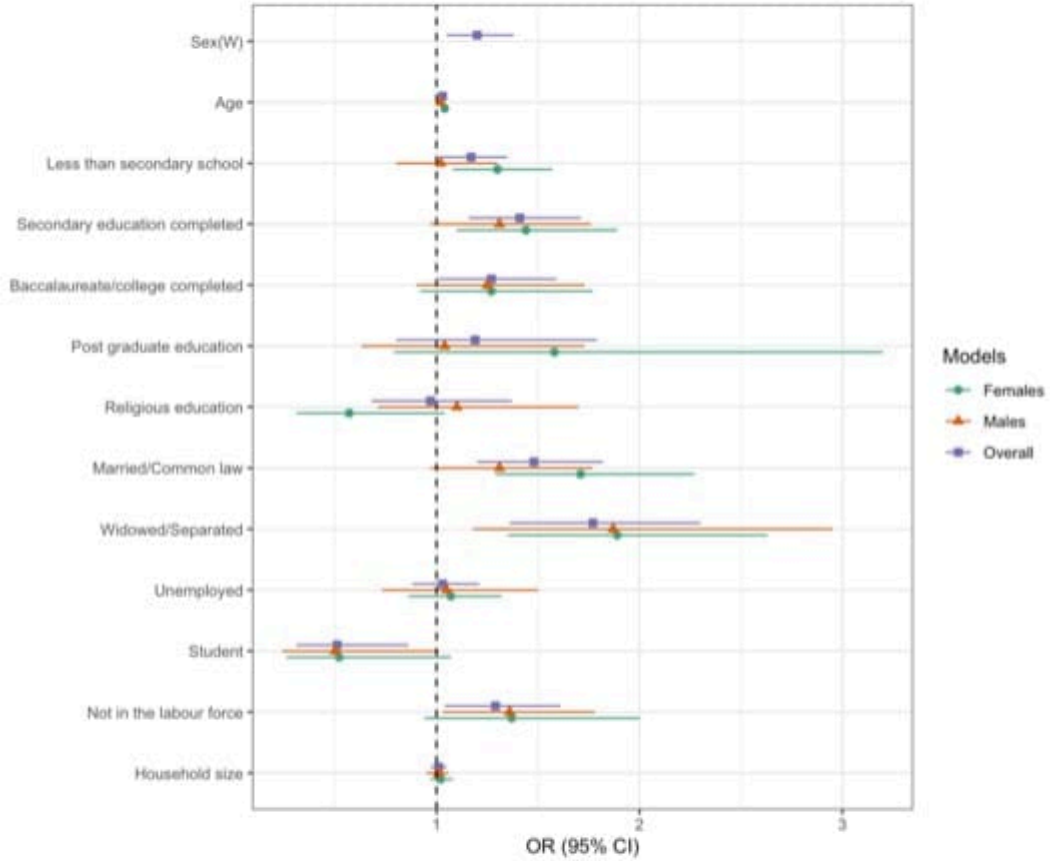
Methods: Using data from the World Health Organization STEPwise approach to non-communicable diseases risk factor Surveillance (STEPS), and generalized linear mixed models for clustered ordinal responses, we assessed the association between CVD risk and socio-demographic characteristics in non-pregnant African adults living with diabetes. CVD risk was measured using a composite score (STEPS-CARDIO index) of five key CVD risk factors – smoking, overweight/obesity, hypertension, physical activity, and diet.

Results: In this sample of 4738 individuals, most respondents were at medium risk of developing CVD (country level mean STEPS-CARDIO score ranged from 2 to 3·22). Older age was significantly associated with higher CVD risk (OR, 1.03; 95% CI, 1.02-1.04), and this was consistent for both sexes, and women had 1.20 times higher CVD risk than men (OR, 1.20; 95% CI, 1.05-1.38). Although education, marital status, occupation, and household size, were generally positively associated with CVD risk, being a student (OR, 0.51; 95% CI, 0.31-0.86) or religious education graduate (OR, 0.97; 95% CI, 0.68-1.37) was protective; the latter presented an increased CVD risk for men.

Conclusion: The findings highlight gendered and social differences in CVD risk among people with DM in Africa. Tailored preventive interventions are therefore required to address the specific needs, and significantly reduce the CVD risk, of populations living with diabetes in Africa.

Keywords: Diabetes, Cardiovascular Diseases, CVD risk, DM-CVD comorbidity, Africa, Risk stratification, STEPS-CARDIO index

Odds ratio plot for the overall and sex-specific models



Reference groups: sex, men; education, no formal education; marital status, single; occupation, employed

Diabetes

Discoveries and challenges in identifying GLP-1 RA-associated phenotypes using real-world data Maxwell Salvatore* Maxwell Salvatore Bingyu Zhang Yiwen Lu Dazheng Zhang Ting Zhou Marylyn Ritchie Yong Chen

Objective:

To investigate the utility and challenges of using real-world electronic health record (EHR) data to identify downstream phenotypes associated with GLP-1 RA use compared to other second-line diabetes therapies.

Methods:

We analyzed EHR data from the All of Us Research Program, including 15,146 participants with a type 2 diabetes diagnosis and one of three second-line diabetes therapies. We used phenome-wide propensity score-matched intention-to-treat (ITT) and per-protocol (PP) Cox proportional hazard models and restricted mean survival time (RMST) to identify phenotypes associated with GLP-1 RA use (n=6,020) versus sodium-glucose cotransporter-2 inhibitors (SGLT2i; n=3,897) and dipeptidyl peptidase-4 inhibitors (DPP4i; n=5,229).

Results:

We found one significant phenotype associated with GLP-1 RA use compared to SGLT2i:·

- ITT: Reduced risk of optic neuropathy (HR: 0.33, 95% CI: 0.20, 0.54)
- PP: Increased risk of vomiting (HR: 1.67, 95% CI: 1.31, 2.14)

In comparisons with DPP4i, 83 and 4 phenotypes were significantly associated under ITT and PP analyses, respectively. Comparing significant phenotypes with their 5-year RMST difference 95% CI, we found:

- ITT: 11% of significant HR associations had RMST differences >30 days.
- PP: All 4 significant phenotypes showed RMST differences >30 days.

A positive association of GLP-1 RA use with morbid obesity was an artifact likely due to confounding factors like under coding, billing practices, and drug indication, as this result contradicts the known action of GLP-1 RAs.

Conclusions:

Our study highlights phenotypes associated with GLP-1 RA use, generally in line with published findings. These findings demonstrate the benefits and pitfalls of using real-world EHR data for agnostic scanning for impacts of GLP-1 RAs. Future work will focus on validating these results across independent datasets and comparing GLP-1 RA-associated phenotypes with those of other anti-obesity medications in individuals with obesity without diabetes.

Disability

The Association Between Obstructive Sleep Apnea and Dementia in Adults with Down Syndrome Alianna Higgins* Alianna Higgins Eric Salina

Background

People with Down syndrome are predisposed to Alzheimer dementia due to the triplication of the 21st chromosome and are also at increased risk for obstructive sleep apnea (OSA) due to airway morphology. OSA is a known risk factor for Alzheimer dementia in the general population; yet, how OSA impacts Alzheimer dementia in Down syndrome has not been examined. We aimed to document the prevalence of OSA in adults with Down syndrome in the United States and examine the association between OSA and dementia in this population.

Methods

We used Medicaid claims data from 2011-2019 that included a sample of 118,539 adults with Down syndrome. We identified OSA and Alzheimer dementia by ICD-9 and ICD-10 codes. We used Cox proportional hazards models to assess the relationship between OSA and time to dementia.

Findings

20.1% of our cohort had OSA, with 13.4% of those with OSA also having Alzheimer dementia. Of those with at least one OSA claim, 55% were male and 40% were aged 18-25 in their first year in our cohort. Of those with no OSA claims, 50% were male, and 34% were aged 18-25 in their first year of our cohort. Race, ethnicity, eligibility type, and dual enrollment were similar comparing those with and without OSA claims. In our unadjusted model, those with OSA were not at more risk of dementia compared to those without OSA (HR 1.01, 95% CI 0.97-1.05), among those aged 35 and older. After adjusting for age and dual enrollment, those with OSA had 1.16 times the hazard of developing dementia compared to those without OSA (95% CI 1.11-1.21), among participants aged 35 and older.

Conclusion

OSA and Alzheimer dementia are burdensome conditions for people with Down syndrome and our results highlight that OSA could impact Alzheimer dementia development. Further, the link between OSA and Alzheimer dementia has implications for healthcare practice and policy for people with Down syndrome.

Disaster Preparedness

The effects of Disasters on Access to Healthcare and Services in Houston Willie Rajvong*
Willie Rajvong Wilford Robinson Roger Zoorob Christine Walther Jacqueline Hirth

Introduction: Disasters, such as flooding or the COVID-19 pandemic, have caused delays in the provision of medical supplies, medication, and treatment. This study assessed the effects of flooding and COVID-19 on access to healthcare and related services.

Methods: This pilot study surveyed adults attending community clinics and libraries in areas of Houston prone to flooding from 3/1/2022 – 10/7/2022 and assessed how access to health and support services were affected by the COVID-19 pandemic and flooding. Comparisons were made between those who have been diagnosed with COVID-19 and those who were not, and those affected by flooding (homes/vehicles damaged) and those who were not with chi-square analyses, t-tests, and unadjusted and adjusted logistic models for either comorbidities or race/ethnicity. Significance was assessed at $p<0.05$ for logistic regression analyses and $p<0.10$ for all other analyses.

Results: Among 206 adults, 20.39% had lost homes or vehicles due to flooding, and 33.5% were diagnosed with COVID-19. Those affected by flooding were more likely to have delayed access to medical care (OR: 7.52; 95% CI: 2.94 – 19.22), delays filling prescriptions (OR: 5.47; 95% CI: 1.18 – 25.49), the closest hospital closed (OR: 3.45; 95% CI: 1.00 – 11.91), their doctor’s office closed (OR: 3.04; 95% CI: 1.25 – 7.38), the closest grocery store closed (OR: 4.60; 95% CI: 2.10 – 10.09), were unable to get food (OR: 3.28; 95% CI: 1.34 – 8.05), and could not get needed medical care (OR: 6.45; 95% CI: 1.73 – 24.07). Those with COVID-19 had reduced access to the nearest hospital (OR: 2.05; 95% CI: 1.06 – 3.98).

Conclusion: These findings highlight the community level needs for planning related to expanded access to care and support services during emergency situations. Plans for communities that flood frequently in Houston should include how to expand access for those with comorbidities who may have restricted ability to get needed services.

Education-teaching epidemiology in post secondary settings

An evaluation of the impact of an ‘authentic learning’ cumulative case study assignment in an undergraduate health science introductory epidemiology course Whitney Qualls* Whitney Qualls Travis Salway

Background:

Epidemiology is increasingly a part of undergraduate health science curricula, as described in recent articles in the American Journal of Epidemiology. Goldman, et al. recently proposed case studies as an appropriate pedagogical tool for undergraduate-level teaching; however, the effectiveness of this approach has not been evaluated. Case studies are particularly appealing because they can create ‘authentic learning’, i.e., relating content to students’ everyday lives.

Methods:

In an undergraduate introductory epidemiology course of 179 students (fall 2024), we developed a cumulative case study assignment with a topic of students’ choosing to better understand how the application of ‘authentic learning’ principles impacts their: a) learning of foundational epidemiology concepts and b) perceived relevance of epidemiology to future health science careers. Students are grouped by shared interests to collaborate on a semester-long cumulative case study.

We conducted a survey (Nov 2024) to measure perceived personal connections to the case study topics. We will conduct interviews (Jan-Feb 2025) with a subset of students purposefully sampled for a range of felt personal connection. Lastly, we will analyze reflections from instructors and TAs.

Results:

Most survey respondents (N=130) felt a personal connection with the case study (83%) and indicate that establishing a personal connection with course materials is important (84%) and that it helps them retain what they learned (90%). Interview and reflection data analyses are in progress.

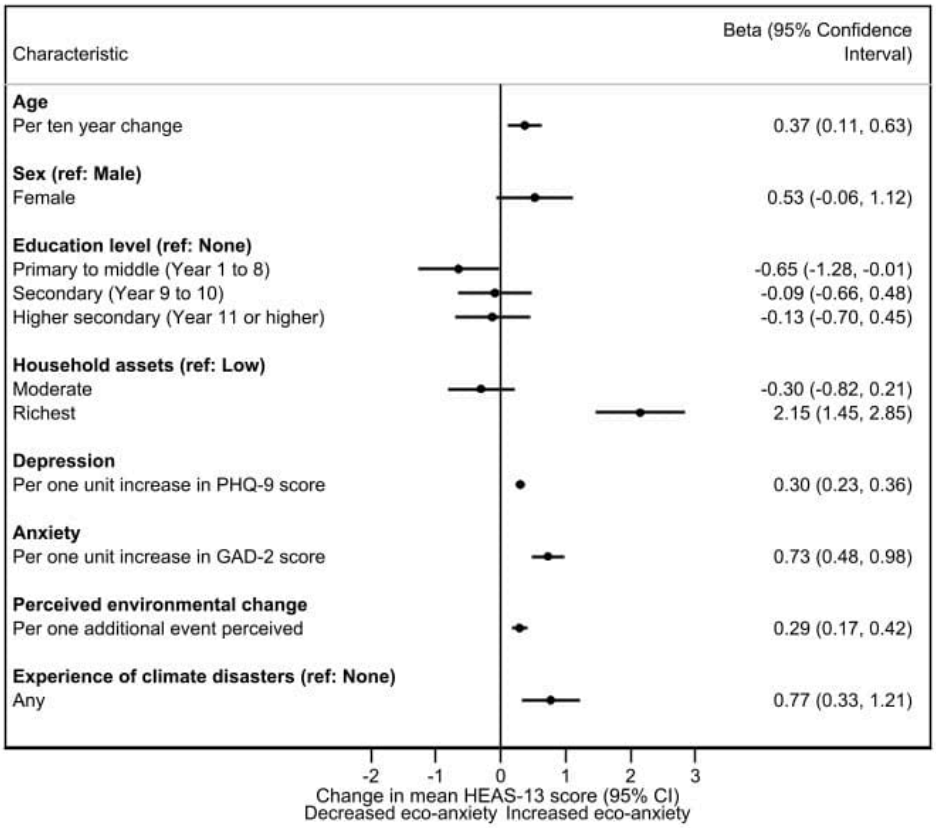
Discussion:

Findings will be used to inform pedagogical innovation in instruction of epidemiology.

Environment/Climate Change

Validation of the Urdu language Hogg Eco-Anxiety Scale and Associated Factors of Eco-Anxiety in Gilgit-Baltistan, Pakistan Rohini R. Datta* Rohini R. Datta Falak Madhani Daniel S. Farrar Muhammad Yasin Shahirose S. Premji Nazia Jabeen Shariq Paracha Imran Ahmed Faisal Ali Sher Hafiz Khan Masood Ali Khan Muhammad Karim Lisa G. Pell Adria Rose Dr. Saleemuddin Sajid B. Soofi Monica Taljaard Rachel F. Spitzer Sifat Wali Zulfiqar A. Bhutta Shaun K. Morris

Eco-anxiety is a distinct mental health event that refers to climate change-related distress. Gilgit-Baltistan (GB), a territory in northern Pakistan, is highly vulnerable to the impacts of climate change. We aimed to validate the Urdu version of the Hogg Eco-Anxiety Scale (HEAS-13) and identify factors associated with eco-anxiety in GB. We conducted a cross-sectional household survey in GB from July–September 2024 during the endline phase of a cluster randomized trial. One adult aged 15–49 years was randomly selected per household. Eco-anxiety was evaluated using an Urdu-translated HEAS-13, and depression and anxiety were assessed using translated versions of the Patient Health Questionnaire (PHQ-9) and the short-form Generalized Anxiety Disorder Scale (GAD-2) respectively. Internal consistency was assessed using Cronbach's alpha, and convergent validity of HEAS-13 with PHQ-9 and GAD-2 was assessed using Spearman's rank correlation coefficients. Multivariable linear regression was conducted to identify factors associated with increased eco-anxiety. In preliminary analysis (n=1140 participants), 48% experienced floods in the past five years, 45% reported increased hot weather, and 41% reported decreased water quality. The median HEAS-13 score was 3 (out of 39, IQR 0–6). In the past two weeks, ≥1 eco-anxiety symptom was experienced by 56.8% for several days and by 18.4% nearly everyday. The translated scale showed good internal consistency (α=0.81) and moderate convergent validity with PHQ-9 (ρ=0.62) and GAD-2 (ρ=0.43). Older age, greater household wealth, higher PHQ-9 and GAD-2 scores, more perceived environmental changes, and experience with climate disasters were significantly associated with increased eco-anxiety (Figure). Preliminary findings suggest the presence of mild eco-anxiety in GB and that the Urdu-translated HEAS-13 can be used to assess eco-anxiety. Future analysis will explore subscale structure and test-retest reliability of the Urdu HEAS-13 in GB.



Perceived environmental change events (increased dry/cold/hot weather, change in precipitation level, increased pollution, etc.) in the previous five to ten years. Experience of climate disasters (avalanche, flooding, landslide, wildfire) in the past five years. Generalized Anxiety Disorder-2 (GAD-2), Hogg Eco-Anxiety Scale (HEAS-13), Patient Health Questionnaire-9 (PHQ-9).

Figure. Coefficient plot of factors associated with eco-anxiety in Gilgit-Baltistan, Pakistan.

Environment/Climate Change

Impact of population size denominators for census-tract level cancer incidence hotspot identification Johnnie Newton* Johnnie Newton Natalie DuPré

Background: Getis-Ord Gi* was used to map hotspots of cancer rates at the county-level. The impact of population size changes over time on this method is not clear. We investigate the sensitivity of population size denominator selection for this hotspot methodology at a smaller geographical unit (census tract) to identify cancer hotspots.

Methods: To calculate age-standardized colorectal cancer (CRC) and lung cancer (LC) rates in KY's 1,115 census tracts, we used KY Cancer Registry case counts from 1995-2021 and age-specific population-size denominators from the 2018 American Community Survey (Method 1) and by summing annual tract estimates from the National Historical GIS 2000-2019 (Method 2). We excluded tracts designated as special use (n=10). The Getis-Ord Gi* statistic identified census-tract level hotspots of high CRC and LC rates. The Kappa (K) statistic assessed method agreement.

Results: The CRC analysis detected 1050 concordant census tracts; 44 hotspots were identified by both Methods, Method 1 uniquely identified 42 hotspots, and 13 were unique to Method 2. For the LC analysis, 1052 tracts were concordant non-hotspot tracts; 61 hotspots were identified by both methods, 43 hotspots were unique to Method 1, and 10 were unique to Method 2. CRC agreement was moderate (K= 0.59; 95% CI 0.49, 0.69) and LC agreement was substantial (K= 0.67; 95%CI 0.59, 0.75). Visually, the hotspots were in the same general geographic areas regardless of method. Method 1 detected predominantly urban hotspots (CRC 85% urban; LC 70% urban, 30% rural). Method 2 detected fewer hotspots with a higher proportion being rural than Method 1 (CRC 68% urban; LC 59% urban, 41% rural).

Conclusion: Single year population size denominators identified more hotspot census tracts, particularly in urban areas, than using estimated population sizes summed across nearly two decades. Public health practitioners should use both methods to best detect the extent of cancer incidence at small geographies.

Environment/Climate Change

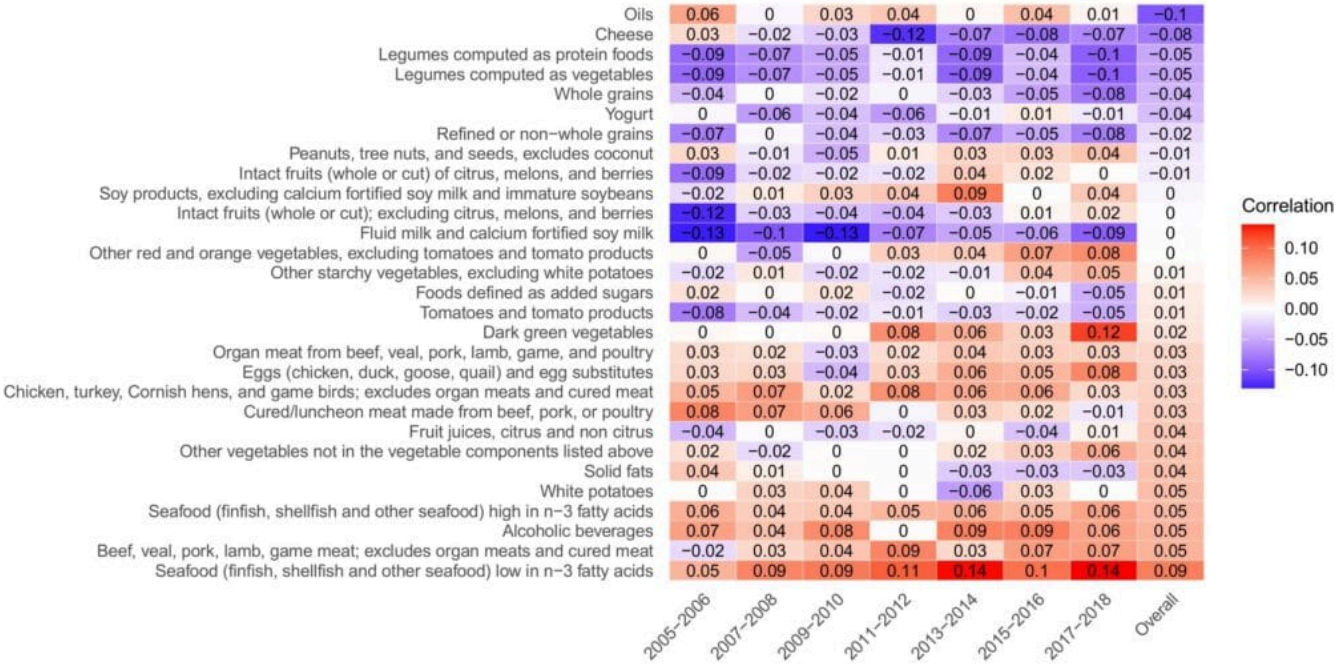
Food Groups and Circulating Per- and Polyfluoroalkyl Substances Levels: Cross-Sectional and Trend Analyses in NHANES 2005–2018 Longgang Zhao* Longgang Zhao Xinyuan Zhang Aimin Chen Xuehong Zhang

Objectives: Diet is considered a primary source of per- and polyfluoroalkyl substances (PFAS) exposure in non-occupational populations, yet studies on the diet-PFAS relationship and its trend across time remain limited. We examined correlations between food intake and serum PFAS levels and evaluated temporal trends in associations of food groups with PFAS levels in US adults between 2005 and 2018.

Methods: We analyzed data from seven cycles of National Health and Nutrition Examination Survey (NHANES) (2005–2018) with diet and PFAS data (N=9063, ≥20 years). Partial Spearman rank correlation coefficients between intake of 29 predefined food groups (in servings/day) and serum concentrations of total and seven specific PFAS compounds were used to evaluate the cross-sectional associations with adjustments of age, sex, race, smoking status, total energy intake, body mass index, and physical activity.

Results: Correlations between food groups and PFAS levels varied by compound. Seafoods with low omega-3 fatty acids (n-3 FA), red meat, alcoholic beverages, seafoods with and high n-3 FA , and other starchy vegetables were associated with total PFAS (γSpearman=0.05-0.09), while seafood with low or high n-3 FA, alcoholic beverages, dark green and other vegetables were associated with PFUA (γSpearman=0.11-0.21). Over time, seafood with low or high n-3 FA and alcoholic beverages were consistently correlated with total PFAS (γSpearman=0.04-0.14). For PFHxS, associations with dark green (γSpearman from 0.04 to 0.10) and other vegetables (γSpearman from 0.02 to 0.07) strengthened in recent cycles (P trend≤0.05).

Conclusions: Seafood, meat intake, and alcoholic beverage were top food groups correlated with serum PFAS levels. The trend of stronger correlations between vegetables and PFHxS levels over time highlights shifting exposure patterns. Our findings emphasize the need for targeted interventions to reduce contamination and guide future research on mitigating dietary exposure.


Oils 0.06 0 0.03 0.04 0 0.04 0.01 −0.1
Cheese 0.03 −0.02 −0.03 −0.12 −0.07 −0.08 −0.07 −0.08
Legumes computed as protein foods −0.09 −0.07 −0.05 −0.01 −0.09 −0.04 −0.1 −0.05
Legumes computed as vegetables −0.09 −0.07 −0.05 −0.01 −0.09 −0.04 −0.1 −0.05
Whole grains −0.04 0 −0.02 0 −0.03 −0.05 −0.08 −0.04
Yogurt 0 −0.06 −0.04 −0.06 −0.01 0.01 −0.01 −0.04
Refined or non−whole grains −0.07 0 −0.04 −0.03 −0.07 −0.05 −0.08 −0.02
Peanuts, tree nuts, and seeds, excludes coconut 0.03 −0.01 −0.05 0.01 0.03 0.03 0.04 −0.01
Intact fruits (whole or cut) of citrus, melons, and berries −0.09 −0.02 −0.02 −0.02 0.04 0.02 0 −0.01
Soy products, excluding calcium fortified soy milk and immature soybeans −0.02 0.01 0.03 0.04 0.09 0 0.04 0
Intact fruits (whole or cut); excluding citrus, melons, and berries −0.12 −0.03 −0.04 −0.04 −0.03 0.01 0.02 0
Fluid milk and calcium fortified soy milk −0.13 −0.1 −0.13 −0.07 −0.05 −0.06 −0.09 0
Other red and orange vegetables, excluding tomatoes and tomato products 0 −0.05 0 0.03 0.04 0.07 0.08 0
Other starchy vegetables, excluding white potatoes −0.02 0.01 −0.02 −0.02 −0.01 0.04 0.05 0.01
Foods defined as added sugars 0.02 0 0.02 −0.02 0 −0.01 −0.05 0.01
Tomatoes and tomato products −0.08 −0.04 −0.02 −0.01 −0.03 −0.02 −0.05 0.01
Dark green vegetables 0 0 0 0.08 0.06 0.03 0.12 0.02
Organ meat from beef, veal, pork, lamb, game, and poultry 0.03 0.02 −0.03 0.02 0.04 0.03 0.03 0.03
Eggs (chicken, duck, goose, quail) and egg substitutes 0.03 0.03 −0.04 0.03 0.06 0.05 0.08 0.03
Chicken, turkey, Cornish hens, and game birds; excludes organ meats and cured meat 0.05 0.07 0.02 0.08 0.06 0.06 0.03 0.03
Cured/luncheon meat made from beef, pork, or poultry 0.08 0.07 0.06 0 0.03 0.02 −0.01 0.03
Fruit juices, citrus and non citrus −0.04 0 −0.03 −0.02 0 −0.04 0.01 0.04
Other vegetables not in the vegetable components listed above 0.02 −0.02 0 0 0.02 0.03 0.06 0.04
Solid fats 0.04 0.01 0 0 −0.03 −0.03 −0.03 0.04
White potatoes 0 0.03 0.04 0 −0.06 0.03 0 0.05
Seafood (finfish, shellfish and other seafood) high in n−3 fatty acids 0.06 0.04 0.04 0.05 0.06 0.05 0.06 0.05
Alcoholic beverages 0.07 0.04 0.08 0 0.09 0.09 0.06 0.05
Beef, veal, pork, lamb, game meat; excludes organ meats and cured meat −0.02 0.03 0.04 0.09 0.03 0.07 0.07 0.05
Seafood (finfish, shellfish and other seafood) low in n−3 fatty acids 0.05 0.09 0.09 0.11 0.14 0.1 0.14 0.09
2005−2006
2007−2008
2009−2010
2011−2012
2013−2014
2015−2016
2017−2018
Overall
Correlation
0.10
0.05
0.00
−0.05
−0.10

Environment/Climate Change

Effect of bike sharing system on pollution expsoure Mai* Mai Waziry

Introduction

Travel behavior has changed in recent years, with more people working from home, shorter commute trips, and more individuals using sustainable modes of transportation, such as bike-sharing systems (BSS). Two drivers of these changes have been post-pandemic attitudes about work and a more acute interest in mitigating climate change.

Purpose

This investigation explores the following mechanisms: travel time, bike ridership, and pollution exposure, with two primary objectives. The first is to examine the relationships among these mechanisms, and the second is to investigate causal mediation processes, including both direct and indirect effects, that influence bike ridership. In order to examine these objectives, the study proposes two key hypotheses. First, bike ridership is associated with shorter travel times, primarily because bikes are often used for first- and last-mile commuting and due to the proximity of bike stations to individuals' locations. Second, pollution exposure is mediated by travel time, directly and indirectly affecting ridership.

Findings

The main findings of this case study focus on identifying causal mediation effects, which provide deeper understanding into the relationship between bike-sharing system ridership and health. There is an indirect effect on health between ridership and pollution through travel time, suggesting that cyclists may be exposed to air pollution during their rides, with the duration of their commute potentially influencing this exposure. Built environment factors could mitigate or exacerbate the air quality conditions experienced during the trip. Second, working from home might negatively decrease BSS ridership, although the results are not significant, this could provide insight into understanding the change in travel behavior post-pandemic. Third, shorter travel time increases BSS ridership, which further supports the fact that BSS users use bikes for first and last-mile trips.

Environment/Climate Change

Identifying Climate Vulnerability Profiles of U.S. Cities through Cluster Analysis Andrea Titus and Lorna Thorpe* Hanxue Wei Ben R Spoer Andrea Titus Alex Azan Anna Bershteyn Lorna E Thorpe

Background and Objectives: Understanding patterns of vulnerabilities to climate risk is critical for targeted climate adaptation and public health interventions. However, city-level clustering analyses for climate vulnerability in the U.S. are limited. This study employs data-driven methods to group U.S. cities into distinct climate vulnerability profiles, facilitating the identification of shared challenges and collaborative solutions.

Methods: We analyzed annual city-level data from 1,103 U.S. cities from 2015 to 2021 obtained from the City Health Dashboard and other public sources, focusing on baseline weather variables (e.g., temperature, humidity, precipitation, and air pollution) and climate-driven extreme weather events (e.g., extreme heat days, drought frequency, tornado events, and coastal or riverine flood hazards). We employed K-means clustering and latent trajectory modeling to identify city typologies, with sensitivity analyses using hierarchical clustering and longitudinal trend analysis.

Results: Analyses using K-means clustering based on multi-year mean values suggest 3 main climate risk typologies of U.S. cities, with clear regional differentiation. The first cluster, located predominantly in the Southeast region, faced significant tornado and flood risk, higher precipitation, higher humidity, and elevated maximum temperatures. The second, predominantly in the Northeast and Midwest, had lower flood risk, lower maximum and minimum temperatures, and lower humidity. The third, predominantly in the Southwest and West, faced higher drought frequency, more extreme heat days, higher PM2.5 concentrations, and lower precipitation.

Conclusion: The current analyses show that US cities have three distinct climate risk profiles that correspond well to geographic regions. Identified city profiles can guide tailored adaptation strategies, enabling cities with similar challenges to collaborate on effective solutions.

Environment/Climate Change

Comparative Effect of Subjective and Objective Green Space on Children's Mental Health and Cognitive Function Brooke Ury* Brooke Ury Jue Yang Samantha R. Rosenthal David H. Barker John E. McGeary Shira I. Dunsiger Diana S. Grigsby-Toussaint

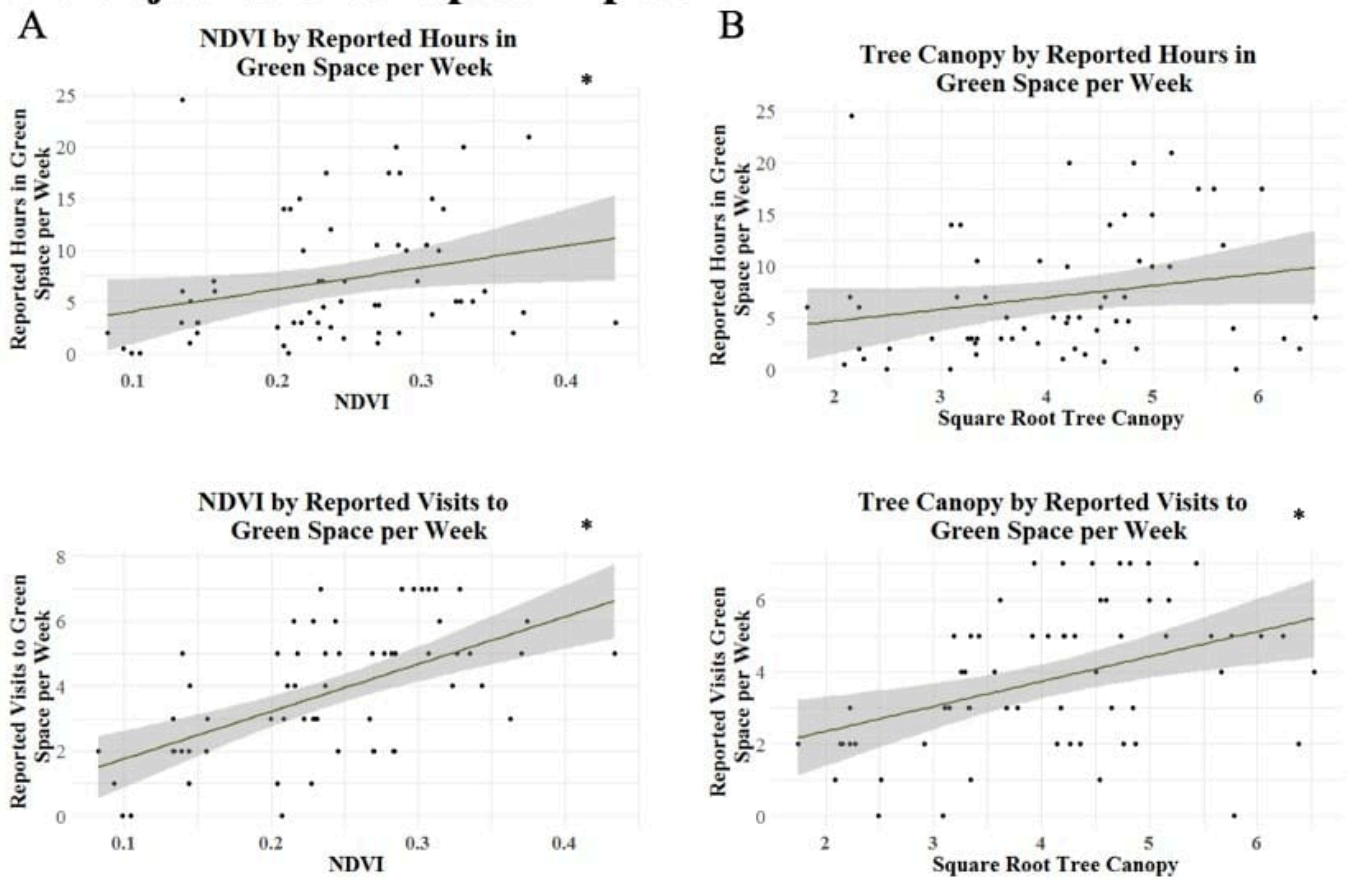
Previous literature has linked green space exposure to improved mental health and cognitive function outcomes in children, but these studies vary in their measurements of green space. We examined the associations between subjective and objective green space and the ability of these measures to predict mental health outcomes.

Data came from the ongoing cross-sectional study Project Green Space, Sleep, and Mental Health (G-SPACE) in Rhode Island, United States. Survey data provided insights into subjective green space and mental health, while GPS data collected over 7-days objectively captured individual green space exposure in real-time. To determine the associations between green space measures, Pearson's correlation coefficients and t-tests were used. Based on green space exposure, multivariate logistic regression models predicted binary health outcomes, i.e., below or above normal limits for positive affect, anger, stress, and cognitive function.

Eighty percent of the subjective green space measures were significantly positively correlated with objective green space, including caregiver-reported weekly visits to green space, perceived sufficiency, and perceived quality of green space (rs 0.347 to 0.571 and p-values < 0.01). Green space and mental health outcomes were generally positively correlated, with green space and cognitive function ($p = 0.016$) and perceived green space quality and stress ($p = 0.025$) being statistically significant.

Caregiver green space perception and caregiver-reported green space are important indicators of objective green space exposure in children and highlight the differential green space needs of pediatric populations. Additional research is required to assess the ability of green space measures to predict health outcomes.

Comparison of Caregiver Neighborhood Green Space Perception and Objective Green Space Exposure



This figure illustrates the relationship between caregiver-perceived green space and objective green space for **A** Normalized Differential Vegetation Index (NDVI) and **B** tree canopy cover. * indicates a p-value less than 0.05 for an independent two-sample t-test.

Environment/Climate Change

Assessing the Relationship Between Indoor Air Pollution and Sleep Quality in Disadvantaged Communities Tianjun Lu* Tianjun Lu Yisi Liu

Indoor air pollution poses a significant but underexplored threat to sleep quality, particularly in disadvantaged communities. We used low-cost PurpleAir monitors to continuously measure indoor PM2.5 (fine particulate matter) data over 22,836 hours from 11 households across disadvantaged communities in South Los Angeles from June to September 2022. We administered five bi-weekly surveys per household, collecting information on sleep quality (e.g., time taken to fall asleep, bedtime, and overall sleep quality). Using mixed-effect linear models, we analyzed the association between hourly PM2.5 concentrations and sleep latency, adjusting for confounders such as temperature, relative humidity, perceived stress. We tested the impact of daily PM2.5 concentrations on time taken to sleep, and the lag effect of exposures during the 1-6 hours before bedtime. We found that concentrations peaked at 9:00 am, with higher weekend levels before noon and higher weekday levels after noon. For each 10μg/m3 increase in 24-hour indoor PM2.5 concentrations, the time taken to fall asleep increased by 0.11 min (95% CI: 0.04, 0.17). Notably, we found that PM2.5 concentrations around 3 hours before bedtime held the greatest impact, that time taken to fall asleep increased 0.22 min (95% CI: 0.03, 0.41) for each 10μg/m3 increase in PM2.5. Adjusting for additional confounders slightly impacted the sleep latency results. These results underscore the need for targeted interventions to reduce indoor air pollution and its impact on sleep health, particularly in vulnerable populations. Our work highlights the importance of precise, community-specific approaches to mitigate environmental health disparities.

Environment/Climate Change

Ambient temperature and indicators of overweight during infancy and early childhood: a population-based historical cohort study Raanan Raz* Raanan Raz Neora Alterman Ronit Calderon-Margalit Iaroslav Youssim Itai Kloog Michael Hauzer Daniel Nevo

Background

The global rate of obesity has risen sharply in past decades reaching 14% of adults. High anthropometric measurements during childhood and infancy are predictive of later adiposity. Preliminary evidence links prenatal and postnatal ambient temperatures with rapid infant weight gain. We assessed the association between ambient temperature exposure during the first year of life and high weigh-for-length at age 1-1·5 years and overweight at age 2-2·5 years.

Methods

We carried out a population-based historical cohort study of 968,534 infants born 2011-2019. Using a satellite-based spatiotemporal model we assessed daily mean and minimum temperatures at the family's residence and calculated weekly averages throughout the first year. High weight-for-length at age 1-1.5 years was defined as ≥85th percentile according to WHO-standardization and overweight at age 2-2.5 years was defined as BMI ≥85th percentile. Weekly and cumulative relative risks were assessed using distributed lag nonlinear models.

Results

We found a positive association between ambient temperatures during the entire first year of life and high weight-for-length at age 1-1·5 years. The relative risk for cumulative exposure to the highest temperature quintile compared to the lowest was 1·82 (95% CI 1·63-2·04) for mean temperature and 1·50 (95% CI 1·36-1·66) for minimum temperature. We also observed an association with overweight at age 2-2·5 years with a relative risk of 1·67 (95% CI 1·46-1·91) and 1·19 (1·07-1·33) for mean and minimum temperatures, respectively.

Conclusions

Exposure to warmer temperatures during the first year of life is associated with high weight-for-length in infants and overweight in toddlers.

Environment/Climate Change

Wildfire smoke PM2.5 and cancer prevalence in the US: a national cross-sectional analysis

Hiwot Zewdie* Hiwot Zewdie Seigi Karasaki Malia Cortez Jiayu Lin Amanda Phipps Trang VoPham

Introduction: Climate change has contributed to increasing incidence of wildfires. The composition of fine particulate matter (PM2.5) from wildfire smoke may be more harmful to human health than other sources of PM2.5, due to its higher carbon content and oxidative potential. Little is known about the role of wildfire smoke PM2.5 in cancer burden.

Methods: Census tract-level wildfire smoke PM2.5 exposure, estimated for the contiguous US using ground monitors and satellite-based smoke plumes, was aggregated to a cumulative annual average (2006-2020). Smoke PM2.5 data was linked with tract-level cancer prevalence (% of adults in 2022 ≥18 years diagnosed with cancer excluding non-melanoma skin cancer) using national data. Robust Quasi-Poisson models estimated prevalence ratios (PRs) and 95% confidence intervals (CIs) for associations between tract-level smoke PM2.5 and cancer prevalence. Models were adjusted for tract-level sociodemographics and population density as confounders, and health conditions and behaviors as precision variables. We examined effect modification using stratified models.

Results: Average estimated tract-level cancer prevalence was 7.4% (SD 2.7; n= 81,838 tracts). Smoke PM2.5 exposure was not associated with cancer prevalence (PR per IQR [0.13-0.32 µg/m3]: 1.00; 95% CI 0.99-1.00) in fully adjusted models. There was statistically significant effect modification by age, racial composition, and region ($p < 0.01$). However, the magnitude of the interactions was modest (region: PR per IQR in Northeast: 1.04, 95% CI 1.02-1.06; West: 0.99, 95% CI 0.99-0.99; South: 1.02, 95% CI 1.01-1.03; Midwest: 0.99, 95% CI 0.97-1.00).

Conclusion: Wildfire smoke PM2.5 was not associated with cancer prevalence at the tract-level, although there may be potential effect modification by region. Further investigation using individual-level data on wildfire smoke PM2.5 exposure and cancer incidence are needed to better understand the potential health implications of wildfires.

Environment/Climate Change

Associations between Oil and Gas Development and Asthma Emergency Department Visits in California Erin Polka* Erin Polka Jonathan Buonocore Erin Campbell Mary Willis

Background: Oil and gas development (OGD) emits hazardous air pollutants associated with a range of respiratory diseases and are often sited near established communities. However, few studies have analyzed the association between OGD activity and asthma exacerbations. Our objective was to estimate the association between asthma emergency department (ED) visits and proximity to OGD in California.

Methods: We obtained aggregated data on total asthma ED visits at the zip code level for each year 2013-2020 from California Health and Human Services Agency (n= 1,304,897 visits). Using a novel publicly-available database on active OGD sites, we assessed exposure to OGD for each zip code, operationalized as density of OGD activity nearby (i.e., new sites/km2 in a given zip code-year). We implemented negative binomial regression models to estimate incidence rate ratios (IRR) and 95% CI, adjusting for spatial-temporal variation and an offset for population size.

Results: IRRs across tertiles of OGD density were 0.89 (95% CI: 0.78, 1.00), 0.93 (95% CI: 0.82, 1.05), and 1.11 (95% CI: 0.98, 1.25), respectively.

Discussion: After controlling for spatial-temporal variation and population size, our preliminary results showed that zip codes with highest OGD density were associated with an increased rate of asthma hospitalizations compared to zip codes with no OGD density. However, contrary to our hypothesis, preliminary results also showed that zip codes with lowest OGD density had reduced rates of asthma hospitalizations. Future analyses will explore environmental co-exposures (e.g., wildfire smoke) and economic changes (e.g., resource extraction booms) to better understand this complex association.

Environment/Climate Change

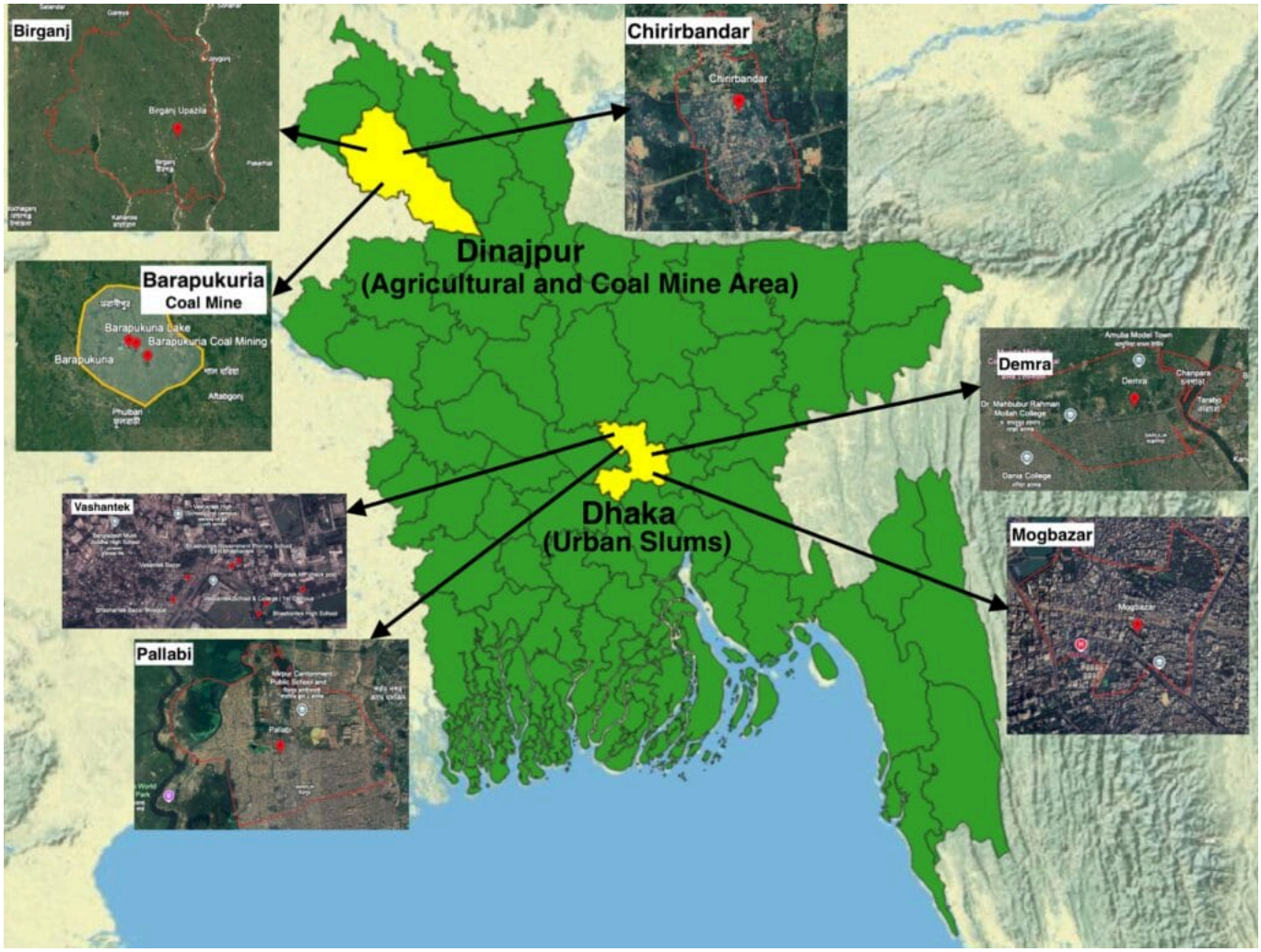
A Systematic Review of Residential Green Space Exposure and Cognition in Children: Insights from Individual-Level Research Mozhgan Naji* Mozhgan Naji Amy E. Kalkbrenner

Exposure to green space, defined as open, natural areas with vegetation, may benefit child cognition by promoting physical activity, reducing stress, and lowering exposure to environmental factors such as air pollution and noise. Several systematic reviews report that green space surrounding schools supports cognition, but residential exposure has not been reviewed. Residential green space exposures vary from school-based, perhaps in duration, frequency, and relevant pathways of impact, and would call for different public health response. We conducted a review of studies of children (< 18), residential green space exposure, and cognition measured at the individual level. We searched PubMed, CINAHL Plus, and Web of Science up to October 1, 2024, identifying 567 publications, of which 17 met our criteria. 16 took place in Europe and 1 in Canada (Ns from 307-27,372).11 measured green space using a satellite-derived measure, the Normalized Difference Vegetation Index (NDVI), which does not differentiate between types of greenness (e.g. trees vs. grass) and 2 focused on tree cover. 12 reported a positive association between residential green space exposure and cognition measured as enhanced working memory, attention and overall IQ, 3 reported near-null associations, and 2 reported an inverse link. Some reported evidence that noise and air pollutants acted as partial mediators, with one reporting modification where less impoverished neighborhoods exhibited stronger associations. Next steps of this project involve assessing the included studies for risk of bias with regard to the inconsistent findings, and further evaluating whether green space at home, which is likely correlated with school exposure, exerts an independent influence on child cognition. Ultimately, understanding the potential impact of green space on cognition, including the vegetation characteristics and location with the most impact, may suggest actions to promote optimal child development.

Environment/Climate Change

The Bangladesh Longitudinal Child-Adolescent Development, Education, and Environment Study (BLADES) Juwel Rana* JUWEL RANA Ridwana Nahrin Sadia Katha U S Rokeya Akhter Toufica Sultana Rakib Islam Abdus Salam Jay S Kaufman

Concurrent exposures to environmental and climate-related factors, inadequate living conditions, poor nutrition, psychosocial stress, and structural inequities adversely affect child-adolescent development, academic attainment, and health outcomes. Yet a few studies have comprehensively analyzed how multiple exposures shape health outcomes in urban slums, agricultural regions, and coal mine areas with complex social and environmental conditions. To address this gap, the South Asian Institute for Social Transformation (SAIST) launched the Bangladesh Longitudinal Child-Adolescent Development, Education, and Environment Study (BLADES) in 2021 across Dhaka and Dinajpur districts. Adopting a community-level exposomics framework, BLADES aims to examine the concurrent, prospective, and lifetime exposures, including environmental, climate-sensitive, psychosocial, lifestyle, and structural factors—and their effects on child development, academic performance, and maternal-child health. BLADES enrolled 2,331 households with children aged 0–18 and mothers from 2022 to 2024, following them annually. Baseline phases I–III and follow-up I measured household, school, and ambient air pollutants (PM1, PM2.5, PM10, SO_2, CO, NO_2, O_3, heavy metals, PAH), climate-sensitive variables (greenness/NDVI, temperature, humidity, rainfall, floods, storms, cyclones, drought, heat waves, nighttime light), and socioeconomic data. Outcomes span growth, development, school attendance, academic performance, blood pressure, lung function, mental health, functional difficulties, behavioral issues (SDQ), quality of life, and maternal well-being. Blood samples will be collected for biomarkers—heat shock proteins, DNA methylation, inflammatory markers, oxidative stress markers, fluid balance indicators, and hormones associated with heat and air pollution. Early data show that 25% of participants were under six, 40% were aged 11–15, and 45% of households were in the poorest wealth quintile. Median PM2.5 is higher in Dhaka (104 µg/m^3) than in Dinajpur (70 µg/m^3). BLADES will produce critical evidence on how community-level exposomics affect child-adolescent development and long-term health outcomes for children and their mothers, guiding interventions for marginalized communities.


Birganj
Birganj Upazila
Chirirbandar
Chirirbandar
Dinajpur
(Agricultural and Coal Mine Area)
Barapukuria
Coal Mine
Barapukuria Lake
Barapukuria Coal Mining
Barapukuria
Phulbari
Altabgonj
Demra
Amulia Model Town
Demra
Dr Mahbubur Rahman Molla College
Dania College
Dhaka
(Urban Slums)
Vashantek
Mogbazar
Mogbazar
Pallabi
Pallabi

Environment/Climate Change

The National Flood Insurance Program (NFIP): spatial distribution of who can be covered and who is covered across the US Lauren Wilner* Lauren Wilner Joseph Dieleman Joan Casey

Introduction.

Floods accounted for the majority of climate change attributable mortality in the 21st century, and are predicted to increase further in frequency and severity. In the US, one program aimed at mitigating the impacts of floods on individuals is the Federal Emergency Management Agency's (FEMA) National Flood Insurance Program (NFIP). NFIP's goal is to minimize losses after a flood by (1) identifying flood hazard areas and disincentivizing building homes there, and (2) providing monetary relief in the event of flood damage to existing homes. By preventing financial loss and facilitating housing security after floods, NFIP may improve health outcomes following floods. There are limited studies on the health effects of this program, in part because there is no single dataset that contains information on NFIP availability, policies held, or claims filed.

Methods.

In the US, NFIP availability varies. In addition, when available, NFIP coverage varies in terms of individuals who hold policies or file claims. Such availability and use likely impact post-flood health. To generate a comprehensive spatial NFIP dataset we combined several federal- and state-level data sources to identify NFIP (1) designations, (2) policies held, and (3) claims filed across the US from 2000–2024.

Results.

In a preliminary analysis of this dataset in the Pacific Northwest, we map differences in coverage across the region. In Washington, only 6,800 people had no option to acquire NFIP, which means that almost 100% of the population had access to NFIP. On the other hand, approximately 1% of the population in Idaho (17,000 people) could not acquire NFIP.

Conclusions.

We developed a new nationwide spatial dataset of NFIP. It will facilitate the study of the potential program effects on the relationship between floods and health in the US.

LATEBREAKER

Environment/Climate Change

Distribution of urinary lead concentrations and exploration of socioeconomic predictors in a cohort of Ugandan adolescent girls and young women Kristen Upson* Kristen Upson Julio Landero Juhee Lee Renee Heffron Andrew Mujugira Flavia Matovu Kenneth Mugwanya Robert O. Wright Michael Yin Anne Marie Jukic Quaker Harmon

Given the adverse health effects of lead, biomonitoring data are critical. Yet, these data are sparse in low-income and middle-income countries, particularly in Africa. We examined the distribution of urinary lead (uPb) concentrations and explored socioeconomic predictors in a cohort of Ugandan adolescent girls and young women. We conducted a cross-sectional analysis using baseline data (years 2018-2020) from the Kampala Women's Bone Study, which enrolled 499 HIV-negative women ages 16-25 years in Kampala, Uganda; none were pregnant, lactating, nor recent users of hormonal contraception. We measured uPb by inductively-coupled plasma-mass spectrometry (detection limit (DL) 0.188 µg/l; n=5 (1%) <DL). uPb concentrations were specific gravity-adjusted to account for urinary dilution. In non-smokers (n=494), we conducted multivariable linear regression to estimate the percent change in uPb concentrations and 95% CIs in relation to socioeconomic factors (collected by questionnaire), adjusting for age and education. In this Ugandan cohort, the median uPb concentration was 2.30 µg/l (interquartile range (IQR): 1.47, 3.53 µg/l). For comparison, this concentration is 14 times higher than the median uPb in US women ages 16-25 years (0.160 µg/l, IQR: 0.122, 0.252 µg/l, National Health and Nutrition Examination Survey 2017-2020). We observed higher uPb concentrations with fewer years of educational attainment. Compared with 12-16 years of education, uPb concentrations were 25% higher (95% CI: 2%, 54%) and 20% higher (95% CI: -1, 45%) with 8-10 years and 11 years of education, respectively. uPb concentrations were 31% higher for participants receiving financial/material support from partner (95% CI: 2%, 70%) and 22% higher for participants reporting job loss worries in the past 3 months (95% CI: 2%, 46%). This study contributes critical uPb data in a non-occupational, general Ugandan population and suggests higher uPb with indicators of lower socioeconomic status.

LATEBREAKER

Environment/Climate Change

Characterize the nasal mycobiome of infants who were born in a post-hurricane setting

Ruochen Wang* Ruochen Wang Leyao Wang

Objective: Hurricanes are associated with an increase in indoor fungal species, and infants are particularly susceptible to respiratory illnesses due to exposure to these fungi. This study examined the effects of Hurricane Maria on the nasal fungal profiles of infants in Puerto Rico, aiming to characterize the variations in fungal composition over time. Our goal was to advance understanding of post-disaster fungal impacts on infant health, thereby enabling early detection and preventive interventions for respiratory conditions triggered by fungal exposure.

Methods: We recruited 63 infants aged 2-6 months, whose mothers had resided in Puerto Rico throughout their pregnancies. Of these, 61 infants had quality fungal sequencing data—28 were recruited one year after Hurricane Maria and 33 two years post-hurricane. Nasal swab samples from these infants were collected and analyzed using ITS rRNA gene sequencing to profile the mycobiome composition.

Results: At the community level, the two groups exhibited significant differences in beta-diversity (p-value = 0.002), which indicated distinct mycobiome compositions by year. At the taxa level, infants in the first-year group were found to have more pathogenic species, including Alternaria (p-value = 0.003) and Eutypella (p-value = 0.003), compared to those in the second-year group. Phenotypic analysis revealed that infants younger than 16 weeks were more susceptible to the impacts of the hurricane, with significant differences in both the Shannon index (p-value = 0.04) and the number of observed ASVs (p-value = 0.05) across the two years.

Conclusion: Our findings reveal that infants are particularly vulnerable to pathogenic fungal exposures in the first year following Hurricane Maria. This study underscores the profound and enduring impact of hurricanes on infant respiratory health. Further research is needed to assess the long-term effects of extreme weather events on the nasal mycobiome and respiratory health of infants.

Key words: Infant nasal mycobiome; Hurricane Maria; respiratory health; post-disaster impact; environmental changes

Environment/Climate Change

Long-term Ambient Air Pollution Exposures in Relation to Glaucoma, Dry Eye Disease, and Chronic Conjunctivitis: Nationwide Cohort Study in Taiwan Yu-Kai Lin* Yu-Kai Lin Kuei-Zuo Lai Chih-Da Wu Hou-Wei Chu Chin-Kuo Chang

Long-term exposure to ambient air pollution has been associated with acute and chronic health disorders. Our eyes, the organs directly exposed to ambient air pollutants, attract special research interest regarding their susceptibility and vulnerability. Glaucoma is the second leading cause of blindness globally, right after cataracts, revealing a significant public health challenge. Additionally, ocular surface diseases, mainly referring to dry eye disease and chronic conjunctivitis, rarely cause blindness but still significantly impact sufferers' daily lives. Previous studies explored the association between these three eye conditions and air pollution. However, the findings were inconsistent. There was a particular lack of research focusing on long-term exposures assessed with cohort study design.

The Taiwan Biobank collected data from Taiwanese-representative residents aged 20 years or older in community from 2008. We utilized data from participants at their initial enrollment between 2008 and 2020, linking to the National Health Insurance Research Database with coverage of outpatient/emergency claims and inpatient claims to determine disease diagnoses in ICD-9/-10 codes. Cumulative exposure to six major ambient air pollutants (i.e., PM2.5, PM10, NO2, SO2, CO, and O3) assessed by air pollution stations in Taiwan for a decade preceding their enrollment was estimated, standardized, and categorized into tertiles. Cox proportional hazards regression was used to examine the hazard ratios for disease risk associated with air pollution exposure in tertiles for univariable and multivariable analyses with adjustment for potential confounders.

After excluding ineligible cohort members, Cohort 1 (glaucoma as the outcome) included 130,784 individuals, among whom 1,525 developed glaucoma. Cohort 2 (dry eye disease as the outcome) included 124,590 individuals, with 3,767 cases of dry eye disease identified. Cohort 3 (chronic conjunctivitis as the outcome) consisted of 100,651 individuals, with 6,606 cases detected in follow-up. Multivariable analysis by Cox regression revealed that in Cohort 1, NO2 and CO were positively associated with glaucoma risk (aHR [95%CI]: 2nd tertile NO2=1.29 [1.14-1.47]; 3rd tertile NO2=1.51 [1.32-1.70]; 2nd tertile CO=1.29 [1.15-1.47]; 3rd tertile CO=1.62 [1.42-1.84]), while O3 was inversely associated (aHR [95%CI]: 2nd tertile O3=0.71 [0.62-0.79]; 3rd tertile=0.76 [0.67-0.86]). In Cohorts 2 and 3, all six pollutants showed significant positive associations with the risk of dry eye disease and chronic conjunctivitis after confounding control, with potential dose-response relationships observed for specific pollutants.

Our findings suggest that vehicle-related air pollutants may increase the risk of glaucoma, while ocular surface diseases of dry eye disease and chronic conjunctivitis are pervasively sensitive to major air pollution. These results highlight the need to further explore the etiology of specific pollutants that increase the risk of these diseases in future.

Environment/Climate Change

Do green spaces moderate the impact of extreme heat on daily walking behavior? A nationwide multilevel geospatial analysis in Japan Masamichi Hanazato* Yoko Matsuoka Hiroaki Yoshida Ichiro Kawachi SV Subramanian Yasuyuki Sawada Kazuki Matsumoto Katsunori Kondo

Aim

Physical activity levels, including daily steps counts, typically decline during extreme heat days, specifically among populations susceptible to heat stresses. However, it is less well understood whether built environment factors such as green spaces moderate the association between extreme heat and walking behavior.

Methods

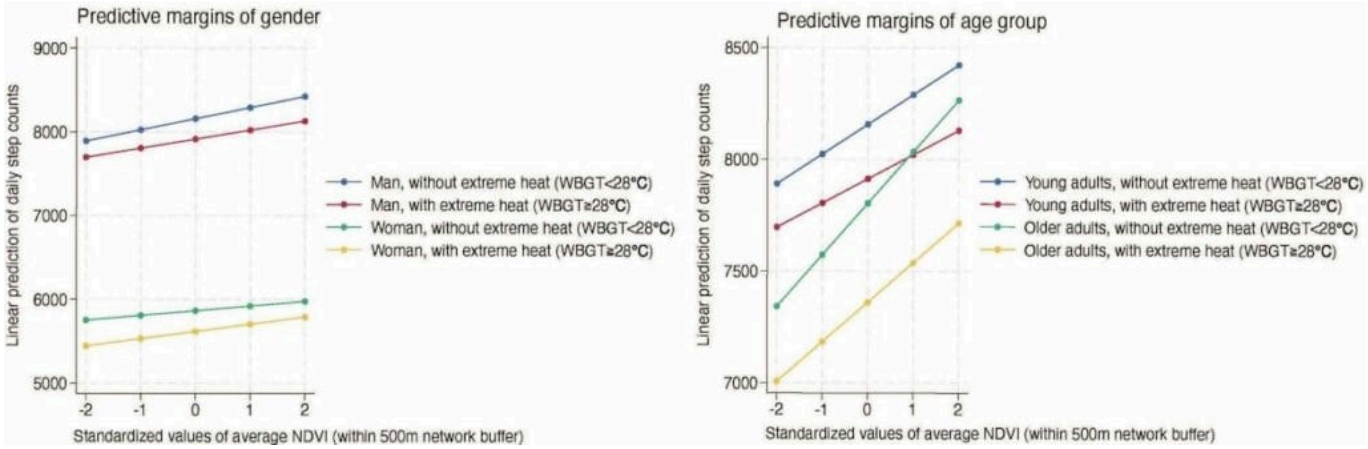
We utilized smartphone data from a national sample in Japan. Daily data were obtained from 16,690 users aged 18 years or higher, from April 26 to October 25, 2023. Socio-demographic information of the users were obtained from survey responses either in November or December of 2022. We linked individual data with daily data on Wet Bulb Globe Temperature as well as geospatial data on residential green spaces (Normalized Difference Vegetation Index within a 500m network buffer). Extreme heat stress was defined as days of 28 degree Celsius or higher. We conducted multilevel mixed-effect linear regression analyses with cross-level interaction terms for heat stress, green space, and socio-demographics (age, gender, or income).

Results

Overall, the median value of participants' average step counts during the period was 6143 (IQR: 4072 to 8731). Participants walked 244 fewer steps (95% CI: -274 to -214) on days with extreme heat compared to normal days. Additionally, regarding the two-way interaction term, older adults walked 199 steps less (-248 to -150) than younger adults on a day with extreme heat. According to the three-way interaction term, each 1-standard-deviation increase in residential green spaces was associated with 55 more steps (22 to 88) for women than men on a day with extreme heat. No clear association was observed for the low-income group.

Conclusion

Residential green spaces may buffer the adverse impacts of heat stress on walking, specifically for women.


Predictive margins of gender
Linear prediction of daily step counts
9000
8000
7000
6000
5000
-2
-1
0
1
2
Standardized values of average NDVI (within 500m network buffer)
Man, without extreme heat (WBGT<28°C)
Man, with extreme heat (WBGT≥28°C)
Woman, without extreme heat (WBGT<28°C)
Woman, with extreme heat (WBGT≥28°C)
Predictive margins of age group
Linear prediction of daily step counts
8500
8000
7500
7000
-2
-1
0
1
2
Standardized values of average NDVI (within 500m network buffer)
Young adults, without extreme heat (WBGT<28°C)
Young adults, with extreme heat (WBGT≥28°C)
Older adults, without extreme heat (WBGT<28°C)
Older adults, with extreme heat (WBGT≥28°C)

Environment/Climate Change

Residential Proximity to Oil and Gas Development and Prevalence of Postpartum Depression in a North American Preconception Cohort Study Kaylin Anne Vrkljan* Kaylin Vrkljan Amelia K. Wesselink Erin J. Campbell Martha R. Koenig Dmitrii Krivorotko Jordan R. Kuiper Nicole C. Deziel Jonathan J. Buonocore Yael L. Nillni Lauren A. Wise Mary D. Willis

Background: As oil and gas production continues to expand, a growing body of literature shows that communities residing near oil and gas development (OGD) have worse mental health outcomes than those living far from OGD. Postpartum depression (PPD) affects ~15% of birthing people and may be influenced by environmental exposures. To date, no studies have examined the relation between OGD and PPD.

Methods: We used data collected between 2017 and 2024 from U.S. participants in Pregnancy Study Online (PRESTO), an internet-based prospective preconception cohort study. At 6 months postpartum, participants who reported a birth were invited to complete a questionnaire, which includes a validated scale for symptoms of PPD (Edinburgh Postnatal Depression Scale, EPDS) and self-reported physician diagnosis of PPD. We calculated the distance between a participant's geocoded address at the time of the postpartum questionnaire and the nearest active OGD site. We examined the relation between residential proximity to an active OGD site and prevalence of PPD (EPDS >13 for primary models). We estimated prevalence ratios (PRs) and 95% CIs using log-binomial models, adjusting for maternal age, geographic region, year, and season.

Results: Among 1,021 participants, the prevalence of PPD was 11.6% by the EPDS and 20.5% when physician-diagnosed cases were added. Residence within 5 km of an active OGD site was associated with a higher prevalence of PPD (PR=1.3, 95% CI: 0.9, 2.0) compared with residences 20-50 km away. This association attenuated among participants who resided at further distances (e.g., 5-10 km [PR=1.1, 95% CI: 0.7, 1.9], 10-15 km [PR=0.9, 95% CI: 0.5, 1.5], 15-20 km [PR=0.7, 95% CI: 0.3, 1.5]). The association was weaker when we considered clinically-diagnosed PPD in conjunction with the EPDS (PR=1.1, 95% CI: 0.8, 1.5).

Conclusion: Preliminary results suggest that living within 5 km of an active OGD site may be associated with slightly higher prevalence of PPD.

Environment/Climate Change

Extreme Heat and Preterm Birth Risk: Insights from Chilean Birth Data (1991-2020) Estela Blanco* Estela Blanco José Daniel Conejeros Álvaro González-Reyes Paola Rubilar Pablo Sarricolea

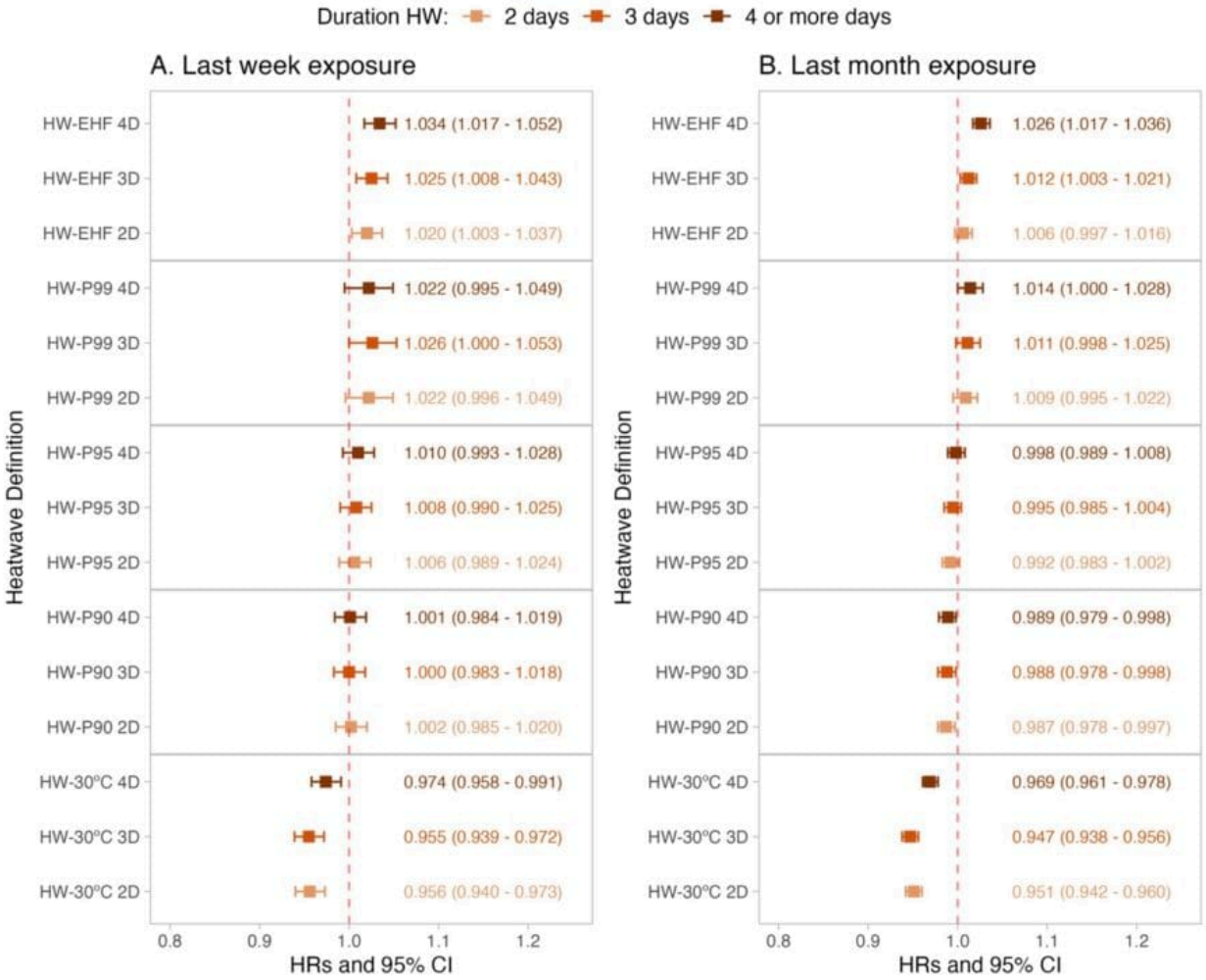
BACKGROUND: The relationship between extreme heat and preterm birth has been the focus of recent reviews and meta-analyses. Reports similarly conclude that exposure to high temperature during pregnancy may trigger a preterm birth. However, no studies addressing the relationship between extreme heat and preterm birth have been conducted in South America.

METHODS: We conducted a population-based cohort using information from birth records (1991-2020) and limited analysis to births in spring/summer (November to March; n= 969,842). Minimum and maximum daily temperatures were obtained from a gridded product CR2Met v2.5, that integrates re-analyzed data from ERA5, MODIS images, and in situ meteorological observations for the 33 urban municipalities of Santiago. Temperature percentiles and excess heat factor (EHF) were calculated for each municipality using historical data. EHF considers high historical temperatures (>95th percentile) and acclimatization in the previous 30 days. We calculated 15 metrics of heatwaves: 2, 3, and 4 consecutive days of temperatures >= 30 degrees Celsius, >=90th, 95th, and 99th percentile, and EHF for each municipality and assigned exposure (Yes or No) in the week and month prior to delivery. Cox proportional hazard models adjusted for maternal and paternal characteristics (age, education, occupation), newborn sex, vulnerability index for municipality, and year of last menstrual cycle.

RESULTS: Preterm birth occurred in 6% of births. There was spatial variability in extreme temperatures for the municipalities: 90th, 95th and 99th percentile ranged from 19 to 32, 20 to 33, and 21 to 34 ºC, respectively. Exposure to most heat wave metrics (2, 3, and 4 days at >=90th, 95th, and 99th percentile), did not relate to increased risk of preterm birth (Figure 1). Exposure to EHF for 2, 3, 4 days in the final week of pregnany was associated with 1.02 (95%CI 1.00-1.03), 1.02 (95%CI 1.00-1.04), and 1.03 (95%CI 1.01-1.05), respectively. Exposure to temperatures >= 30 degrees Celsius were associated with HRs <1 (Figure 1). Results were similar for exposure during the month prior to delivery.

CONCLUSIONS: We found evidence of increased risk of preterm birth, but only when evaluating exposure using EHF, a metric that considers acclimatization. Results from the Chilean population highlight the importance of evaluating and understanding regional impacts of climate change on child health.

Figure 1. Associations between extreme heat episodes and preterm birth in Santiago, Summer 1992 – 2020.



Abbreviations: HW heatwave. Cox proportional risk hazard model. Models were adjusted for newborn sex, maternal and paternal age, maternal and paternal education, maternal and paternal occupation, fixed effects with birth year, vulnerability of the municipality. We estimated hazard ratios (HR) and 95% confidence intervals (CI) for preterm birth and exposure to extreme heat during the last week and last month of gestation. Panel (A) N = 969,842 and Panel (B) N = 837,401. The summer period corresponds to the warm months of the Southern Hemisphere: November and December of the current year, combined with January, February, and March of the following year.

Environment/Climate Change

Exposure to extreme temperatures during pregnancy and birth weight: evidence from Chile (2011 – 2020) Estela Blanco* Estela Blanco José Daniel Conejeros Paulo Guiñez María Isabel Matute Paola Rubilar Raquel Jimenez Pamela Smith

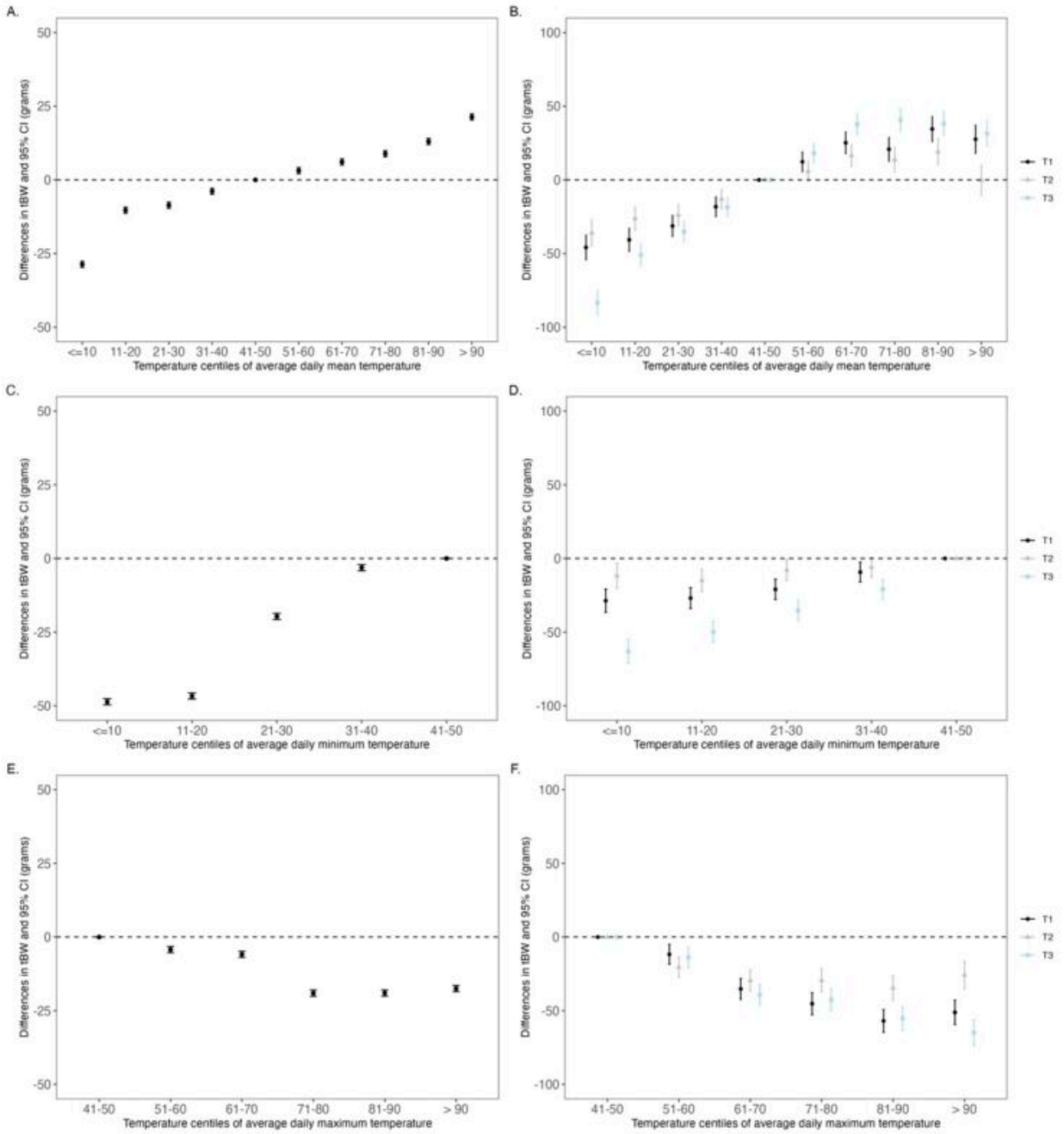
Background: Exposure to extreme temperatures during pregnancy can have adverse effects on birth weight, however, there is little evidence from Latin America.

Methods: We used birth records in 2011-2020. Mean, minimum, and maximum daily temperatures were obtained from meteorological stations in 26 municipalities representing different climatic zones of Chile. Temperature percentiles were calculated for each climatic zone and assigned for the entire pregnancy, trimester, and gestational week, using the 50th percentile for comparison. General additive models and distributed lag nonlinear models (DLNM) adjusted for month and year of last menstrual cycle and maternal and paternal: age, education, and employment.

Results: Exposure to cold mean temperatures (≤10th percentile) in the total pregnancy period and each trimester was associated with a lower mean birth weight (-28.7 gram for the total period, -45.9, -36.1, and -83.4 g for trimester 1, 2, and 3, respectively), whereas exposure to warm mean temperatures was associated with higher birth weight (21.3 g for >90th percentile). For extreme temperatures, exposure to both cold (≤10th percentile for minimum) and hot (>90th percentile for maximum) in the total pregnancy period related to lower birth weight: -48.7 g (95% CI -49.7; -47.6) and -17.48 g (95% CI -18.5; -16.4), respectively, with similar effects by trimester (Figure 1). In DLNM, consistent effects were observed later in pregnancy.

Conclusion: Lower birth weight was observed for exposure to cold temperatures and extreme heat. Exposure to warmer mean temperatures related to higher birthweight. Differing results from Chile highlight understanding regional impacts of climate change on child health.

Figure 1. Estimated differences in mean term birth weight (g) and 95% confidence intervals according to climate zone-specific centiles of average daily mean, minimum and maximum temperature relative to the reference category (41st–50th centile) among singleton term live births during the entire pregnancy (panel A, C, E) and by trimester (panel B, D, F) in the period 2011–2020.



Note: Models estimated using generalized additive model (GAM) with normal distribution and identity link function for tBW. Models were adjusted for: newborn sex, maternal and paternal age, maternal and paternal education, maternal and paternal occupation, year and month of last menstrual period splines (N= 330,118). tBW-term mean birthweight (mean birthweight among births>36 gestational age weeks).

Environment/Climate Change

Street-View Green Space Distribution across Racial/Ethnic, Neighborhood Socioeconomic Status and Individual Education Sub-groups in the Multi-Ethnic Study of Atherosclerosis

Tara Jenson* Tara Jenson Pi-I Debby Lin Peter James Perry Hystad Ana V. Diez-Roux Brent Coull Lilah Besser Esra Suel Jennifer Weuve Marcia Pescador Jimenez

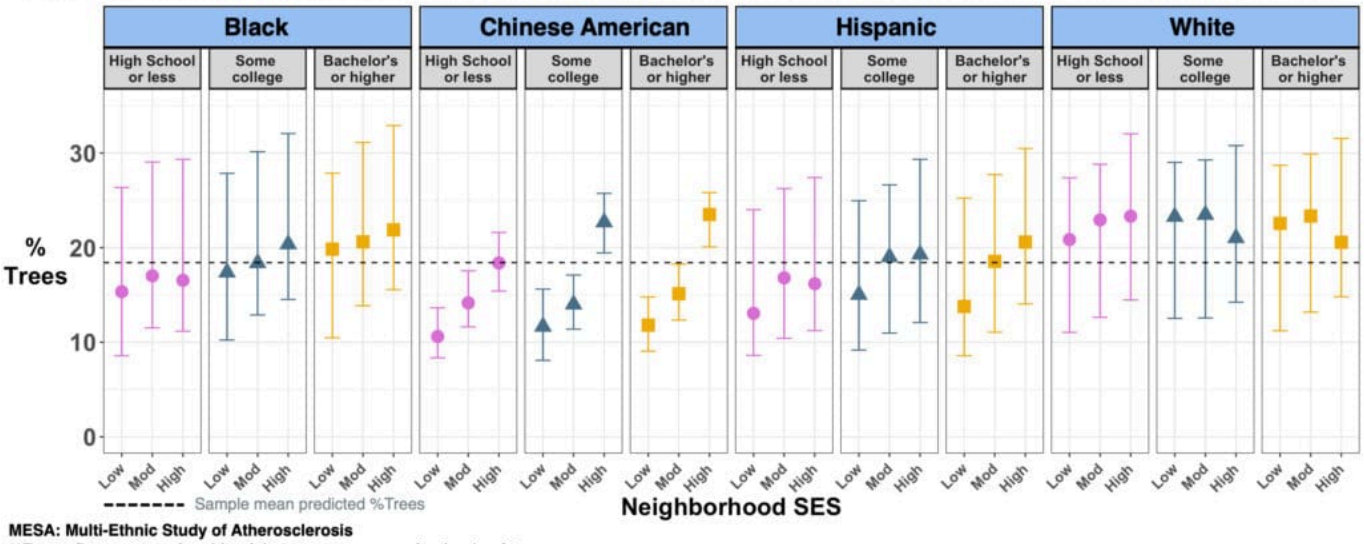
Background Green space exposure is associated with health benefits via physical activity opportunity and reducing air and noise pollution exposure. Black, Hispanic, and low-income communities are overall exposed to less green space. It is unclear if green space exposure disparities are more pronounced for combinations of race/ethnicity and socioeconomic subgroups.

Methods Applying deep learning to street-view images, we calculated tree percentage in residential green space (%Trees) for Multi-Ethnic Study of Atherosclerosis participants (N=5858; 2000-2002). We used Multilevel Analysis of Individual Heterogeneity and Discriminatory Accuracy to quantify %Trees disparities by clustering individuals into 36 intersecting strata of race/ethnicity (Black, Chinese American, Hispanic, White), education (high school, some college, bachelor’s degree), and neighborhood socioeconomic status (NSES; low, moderate, high). Models adjusted for age, sex, individual income, and study site.

Results Our overall sample (26% Black, 12% Chinese American, 22% Hispanic, and 40% White) had a mean %Trees of 19.0 (SD 8.8). The variance partition coefficient showed that %Trees differed across intersecting identity strata, accounting for 16% of total variance. In the random effects model (Figure 1), among Hispanic participants, %Trees was 13.1 for those with lowest education and NSES (95% CI 9.1, 23.8) versus 20.5 for those with highest education and NSES (95% CI 14.0, 30.4). Similar trends were found for Black and Chinese American participants. However, the lowest %Trees for Whites was observed for the highest NSES and education stratum (20.6, 95% CI 14.8, 31.5).

Conclusion Higher education and NSES strata were associated with higher tree percentage for non-White race/ethnicity groups, but this trend was reversed for Whites. Intersectional identities defined by educational attainment, NSES, and race/ethnicity contributed substantially to the observed variance in residential tree percentage.

Figure 1. Predicted street-view based %Trees across strata in random effects model. MESA 2000-2002, N=5858



MESA: Multi-Ethnic Study of Atherosclerosis
%Trees: Percentage of residential greenspace comprised only of trees
SES: socio-economic status

Environment/Climate Change

Wildfire smoke exposure and emergency department visits related to alcohol, overdose, and assault: A time-stratified case-crossover analysis Holly Elser* Holly Elser Yueqi Yan Mathew V. Kiang Joan A. Casey Sidra Goldman-Mellor

Background: Wildfires have become increasingly frequent and destructive in the United States due to anthropogenic climate change. While prior literature suggests climate change and the environment influence both physical and behavioral health, research that focuses on wildfire smoke exposure and externalizing behavioral health outcomes remains scarce.

Methods: We conducted a time-stratified case-crossover analysis to examine the association of wildfire smoke exposure with emergency department (ED) visits related to alcohol use disorder, overdose, and assault. Visits were identified using diagnostic codes in statewide ED visit data from the California Department of Health Care Access and Information from 2016–2020. Daily measures of fine particles <2.5mg/m3 in diameter (PM2.5) were available for all California zip codes. We implemented distributed lag nonlinear models to assess the association of lagged daily wildfire PM2.5 exposure over a weeklong period. Conditional Poisson models were used to estimate the percent change in rates of ED visits for each outcome.

Results: We identified 1,182,760 ED visits related to alcohol use disorder, 215,126 related to overdose, and 513,835 related to assault. An increase in the same-day concentration of wildfire PM2.5 from the median to the 95th percentile was not clearly associated with a change in the rates of ED visits related to alcohol use disorder (-0.3%, 95%CI: -0.7,0.2), although we observed increased rates 3 days later (0.5%, 95%CI: 0.3,0.8). Same-day wildfire PM2.5 exposure was associated with increased rates of ED visits related to drug overdose (0.7%, 95%CI: 0.0,1.3) and assault (0.4%, 95%CI: -0.1,0.9) **(Figure)**.

Conclusion: We found increased rates of acute ED visits for alcohol use disorder, overdose and assault associated with wildfire PM2.5 exposure. Additional research focused on identifying mechanisms that underlie these associations may yield insights into potential avenues for prevention.

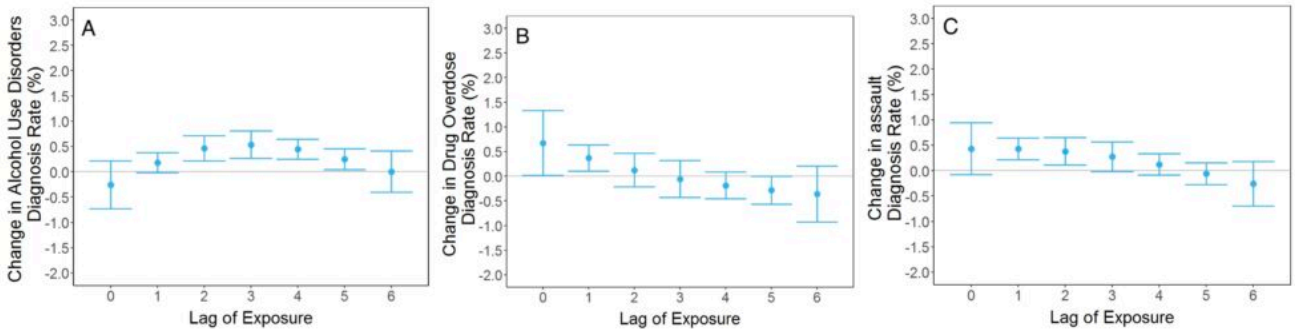


Figure. Association of wildfire PM2.5 exposure with ED visits for alcohol use disorder, overdose, and assault over the following 6 days in California, 2016–2020. We used distributed lag non-linear models to examine the association of wildfire PM2.5 exposure with ED visits related to alcohol use disorder **(Panel A),** drug overdose **(Panel B),** and assault **(Panel C)**. Poisson models were used to estimate the percent change in rates of ED visits associated with an increase in the concentration of wildfire $PM_{2.5}$ from the median to the 95^{th} percentile concentration for each outcome separately.

Environment/Climate Change

Association of Road Traffic Noise with the Risk of New-Onset Epilepsy Tresah Antaya* Tresah Antaya Britney Le Tor Oiamo Piotr Wilk Kathy N Speechley Jorge Burneo

Background

Environmental noise has been associated with the onset and exacerbation of other neurological disorders, but its relationship with new-onset epilepsy has been insufficiently explored. The study's objective was to assess whether long-term road traffic noise exposure is associated with the risk of new-onset epilepsy among adult residents of Toronto, Canada.

Methods

We conducted a nested case-control study using linked health administrative and environmental data. We included adult residents of Toronto as of January 1, 2010, with no history of seizures or epilepsy. Cases were those who developed epilepsy before December 31, 2016, and were each matched with up to five controls. We measured exposure to road traffic noise using three-year averages of the nighttime average (LAeq, 8 hr), daytime average (LAeq, 16 hr), and the 24-hour average (LAeq, 24 hr) road traffic noise levels at participants' postal code of residence. We estimated the associations of these three-year averages with the risk of new-onset epilepsy using conditional logistic regression models.

Results

We included 4,608 cases and 20,765 controls; 46.3% were female and the mean age was 48.3 (± 17.4). The median [interquartile range] three-year average noise levels were 54.4 [12.9] dB, 63.3 [11.3] dB, and 60.3 [11.8] dB for LAeq, 8 hr, LAeq, 16 hr, and LAeq, 24 hr, respectively. The odds ratios associated with a 10-dB increase in LAeq, 8 hr was 1.043 (95% CI: 0.994, 1.095), 0.999 (95% CI: 0.946, 1.054) for LAeq, 16 hr, and 1.031 (95% CI: 0.980, 1.086) for LAeq, 24 hr.

Conclusions

Despite our statistically non-significant findings, there may be an association between long-term exposure to road traffic noise, particularly at night, and the risk of new-onset epilepsy. Considering that little research has been published on the association of environmental noise with the risk of new-onset epilepsy, and given its biological plausibility, future research should continue to explore this potential association.

Environment/Climate Change

Longitudinal association between air pollution and suicide mortality among Canadian adults: An analysis of the 2006 CanCHEC cohort Brian Steele* Brian Steele Shelby Yamamoto Ambikaipakan Senthilselvan Roman Pabayo

Background. Long-term exposure to air pollution is associated with morbidity and mortality, including respiratory, cardiovascular, and oncologic outcomes. However, limited research has evaluated the association between long-term pollutant exposure and psychiatric outcomes. This study aimed to estimate the longitudinal association between air pollution exposure and deaths from suicide among Canadian adults in an administrative cohort.

Methods. Urban respondents in the 2006 Canadian Census Health and Environment Cohorts with residential mobility (postal code) data were followed from July 1 2006 to June 30 2017. Outcome data were obtained from the Canadian Vital Statistics – Death database. Individual- and area-level socioeconomic covariates were assigned at baseline using the 2006 Census. Particulate matter (PM2.5) and ozone obtained from the Canadian Urban Environmental Health Research Consortium were assigned at the postal code level and modeled as time-varying lagged exposures using restricted cubic splines. Analyses were conducted using extended Cox proportional hazard models with cluster-robust standard errors. Baseline hazards were stratified by age, sex, and income adequacy.

Results. Among the analytic sample of 1,588,340 Canadians, 104,450 deaths (6.6% of sample) were observed during follow-up, 2,790 of which were suicides (0.2%). In adjusted models, an IQR-range increase in PM2.5 exposure (2.73 µg/m3) was significantly associated with increased relative hazards of suicide (aHR: 1.27, 95% CI: 1.08 – 1.51). Coefficient plots show non-linear but positive associations between PM2.5 and suicide. Results were inconsistent for ozone.

Conclusion. Long-term PM2.5 exposure was associated with increased relative hazards of suicide mortality over time. Though limited by selection and information biases, these findings contribute some of the first evidence suggesting that suicide is one of the many conditions associated with long-term air pollution exposure.

Environment/Climate Change

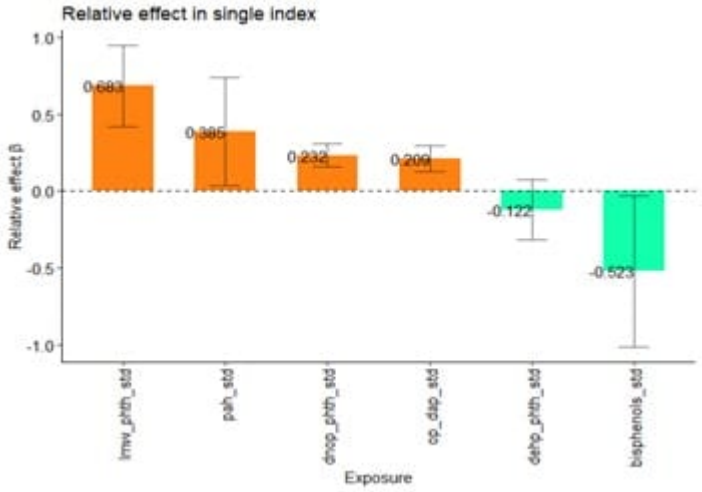
Exposure to endocrine disrupting chemicals and thyroid function in pregnancy: Data from a NYC birth cohort Akhgar Ghassabian* Akhgar Ghassabian Kristyn Pierce Yelena Afanasyeva Kim Nail Cajachagua Torres Kurunthachalam Kannan Mengling Liu Leonardo Trasande

Thyroid disruption during gestation is linked to adverse health outcomes in pregnant individuals and their offspring. We examined the extent to which exposure to commonly used plasticizers, pesticides, and other endocrine-disrupting chemicals contribute to thyroid disruption in pregnancy.

In 1053 pregnant participants of NYU Children's Health and Environment Study (2016-2021), we examined urinary concentrations of 2 bisphenols and 13 phthalate, 5 dialkylphosphate (DAP), and 8 polyaromatic hydrocarbons (PAH) metabolites at <18 weeks and 18-25 weeks of gestation. Measures were adjusted for urinary dilation and averaged across timepoints. Serum thyroid parameters were measured at <25 weeks. We examined independent and joint effects of exposure to chemical families on thyroid function using linear regression and partial-linear single-index models. Coefficients were reported as standard deviation change in the log10-transformed molar sums of chemical groups.

In single pollutant analyses, higher exposure to ∑bisphenols was associated with lower total thyroxine (β=-0.17, 95%CI: -0.33, -0.01). Higher exposure to di(2-ethylhexyl) phthalate (∑DEHP) and di-n-octyl phthalate (∑DnOP) were associated with lower free thyroxine (β for ∑DEHP=-0.02, 95%CI: -0.03, -0.01 and β for ∑DnOP =-0.02, 95%CI: -0.03, -0.001) and total thyroxine (β for ∑DEHP=-0.31, 95%CI: -0.47, -0.15 and β for ∑DnOP=-0.23, 95%CI: -0.39, -0.08). No association with thyrotropin was observed. In mixture analyses, there were indications for interaction between chemicals in association with thyroid parameters. We observed no joint effects of chemicals on free thyroxine. Chemicals had an inverse u-shape association with total thyroxine, with major contributions from low molecular weight phthalates, ∑PAH, and ∑DnOP.

These results show exposure to plasticizers may contribute to thyroid dysfunction in pregnancy, supporting the need for regulation of these chemicals.



Genetics

Identification of Dynamic Genetic influences on DNA methylation From Birth to Adulthood

Yueying Li* Yueying Li Josine Min Gibran Hemani James Staley Kate Tilling Tom Gaunt Venexia Walker Anna Grossbach Andrew Simpkin Rosa Mulder Claudio Cappadona

Background: DNA methylation (DNAm) is a key epigenetic mechanism underlying human trait diversity and exhibits time trajectories. While methylation quantitative trait locus (mQTL) studies have elucidated genetic factors associated with interindividual DNAm differences, it remains unclear whether genetic influences vary across developmental stages. This study aims to identify dynamic genetic associations with DNAm from birth to early adulthood (longitudinal mQTLs).

Methods: In the Avon Longitudinal Study of Parents and Children (ALSPAC) cohort, we used data from child participants with DNAm measurements available at ≥ 2 time points. Our analysis targeted 236,298 previously reported mQTL-CpG pairs from the Genetics of DNA methylation Consortium that were also associated in ALSPAC. Linear mixed models were used to evaluate interactions between mQTLs and age. The identified longitudinal mQTLs were tested for replication in the Generation R cohort and the Drakenstein Child Health Study.

Results: 2,210 longitudinal mQTLs (1.1% of tested mQTLs) associated with 2,329 CpG sites were identified, forming 2,393 mQTL-CpG pairs, of which 176 pairs involved long-range (trans) associations. The most pronounced changes in both mQTL-CpG associations and DNAm levels occurred between birth and age 7. The identified longitudinal mQTLs overlapped with 589 GWAS loci, where no single phenotype showed significant enrichment across the entire mQTL set. Compared to other CpGs, longitudinal mQTL CpGs were enriched in regulatory elements of gene expression across tissues and exhibited a greater proportion of variability attributable to genetic effects.

Conclusion: A minority of genetic variants are associated with DNAm in a dynamic manner, particularly during early developmental stages. Our findings provide insights into the discrepancies observed across mQTL studies in different age groups and underscore the need for research into biological mechanisms specific to childhood.

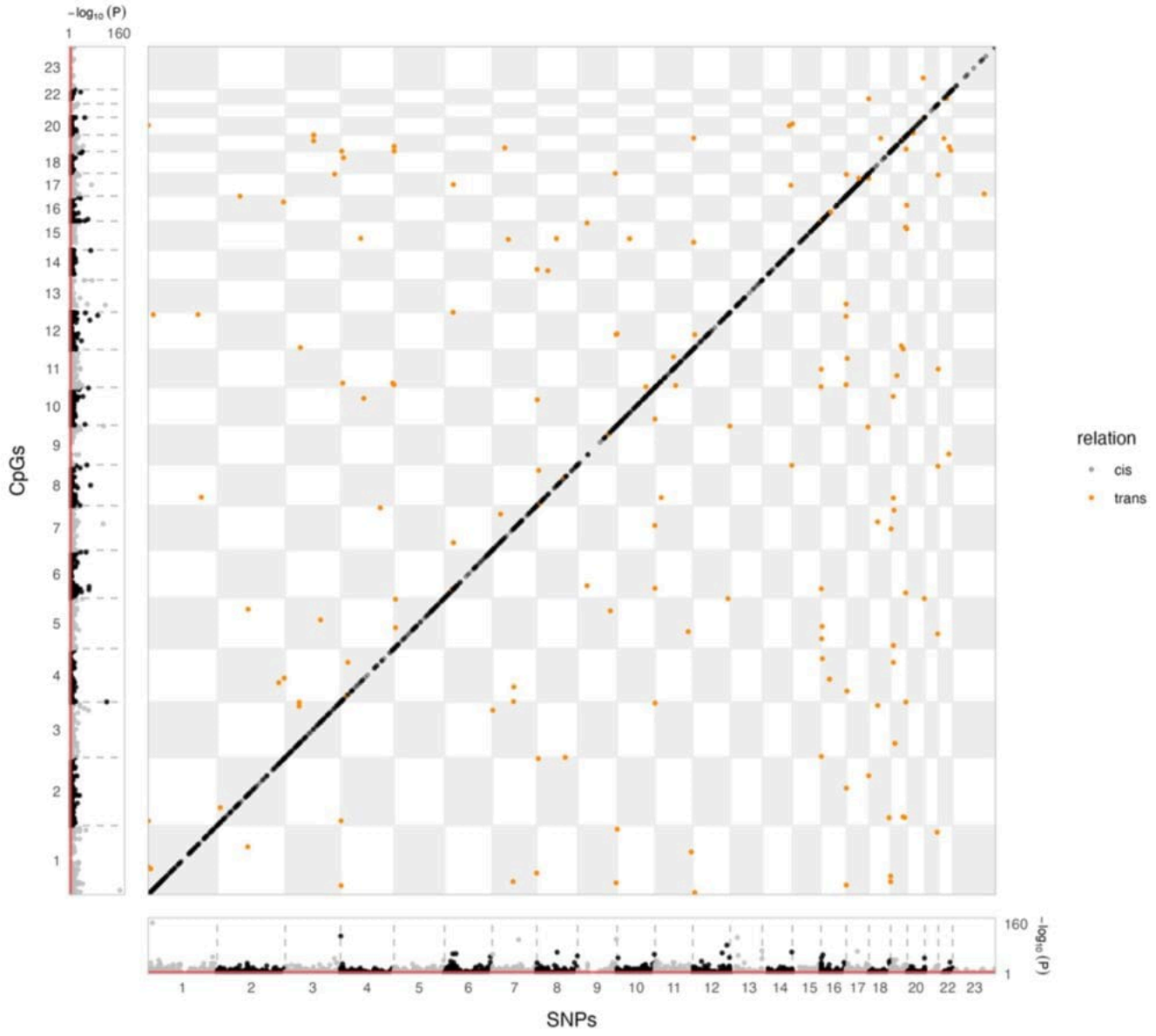


Figure. Chessboard plot of mQTL-CpG pairs with dynamic association

LATEBREAKER

Genetics

Adolescent body mass index and its association with DNA methylation: Findings from the Future of Families and Wellbeing Study Farah Ammous* Farah Ammous Jessica Faul Trey Smith Colter Mitchell

Background: DNA methylation (DNAm) is a key epigenetic mechanism influenced by environmental and lifestyle factors, including body mass index (BMI). Understanding the relationship between BMI at different life stages and DNAm is critical for understanding biological processes of obesity-related disease risk.

Methods: We analyzed data from the Future of Families and Child Wellbeing Study, examining salivary DNAm, measured at 850,000 CpGs using the EPIC array, and BMI at ages 9 and 15 (N =777 and 762, respectively). Analyses included (1) cross-sectional associations of BMI with DNAm at the same age and (2) longitudinal analysis of BMI at age 9 (BMI9) and change in BMI from ages 9 to 15 (ΔBMI15-9) with DNAm at age 15 (N= 760). Models were adjusted for sex, low birthweight, gestational age, and maternal factors (age, race/ethnicity, education, smoking, parity, BMI).

Results: Cross-sectional analyses identified two genome-wide significant loci (cg14120966, near ATP10B, P = 1.9 ×10-7 and cg17901584, near DHCR24, P = 1.4×10-7 at age 9 and P = 6.4×10-7 at age 15). Longitudinal analysis with DNAm at age 15 identified two CpGs (cg17265470, P = 3.6 ×10-7 and cg14120966, P = 2.2×10-8) associated with BMI9, and five CpGs suggestively associated with ΔBMI15-9 at P < 2.7×10-5 mapping to the WLS, S100A6, GDF7, RETREG1, and FAM3B genes. Some of these CpGs have been previously associated with BMI in adults. Enrichment analysis identified pathways associated with cholesterol metabolism, steroid biosynthetic processes, as well as regulation of natural killer cell differentiation.

Conclusions: Our study identified several BMI-associated DNAm sites in adolescence, some of which overlap with those linked to BMI in adults, suggesting a shared epigenetic signature across the lifespan. Pathway enrichment analyses point to metabolic and immune regulatory processes, providing insight into the biological mechanisms linking BMI to long-term health outcomes.

Genetics

Reverse Mendelian Randomization of Alzheimer's Disease Genetic Risk Score and Depression: Evidence from the Kaiser GERA Cohort Minhyuk Choi* Minhyuk Choi Scott Zimmerman Peter Buto Jingxuan Wang Willa Brenowitz Adina Zeki Al Hazzouri Katrina Kezios Maria Glymour Thomas Hoffmann

Background: Identifying prodromal changes associated with incipient Alzheimer's Disease (AD) is essential to guide prevention efforts and understand confounding in observational research. Depressive symptoms may serve as early manifestations of AD pathophysiology. However, empirical evidence regarding depression as a prodromal sign of AD is muddied because depression may also increase AD risk. Using genetic risk of AD in a reverse Mendelian Randomization design establishes temporal order. We estimated associations of AD genetic risk with incident major depressive disorders (MDD) across age strata. **Methods:** Genetic Epidemiology Research on Aging (GERA) cohort participants (N=69,571) who were dementia-free and aged 46+ at baseline were followed from 1997 or earliest Kaiser Permanente enrollment through 2020 for a first diagnosis of MDD. A z-scored AD genetic risk score (AD-GRS) was calculated using 83 single-nucleotide polymorphisms. Time-varying Cox proportional hazards models were used to estimate age-decade-stratified associations of AD-GRS with MDD. Individuals were censored at the diagnosis of MDD, end of enrollment, or dementia diagnosis (AD, vascular dementia, or non-specific dementia). Models were adjusted for race, 10 principal components of genetic ancestry, gender, smoking status, education, hospital visits and prescription counts. **Results:** In decade-stratified models, AD-GRS was associated with incident MDD among people ages 70-79 (HR = 1.051, 95% CI: 1.012–1.091, p = 0.01) and 80 or older (HR = 1.068, 95% CI: 1.012–1.127, p = 0.016) but not at earlier ages (Figure 1). **Conclusion:** AD genes may accelerate AD-related depressive symptoms starting in the age of 70s, but we found no evidence of reverse causation from AD to depression in middle aged adults.

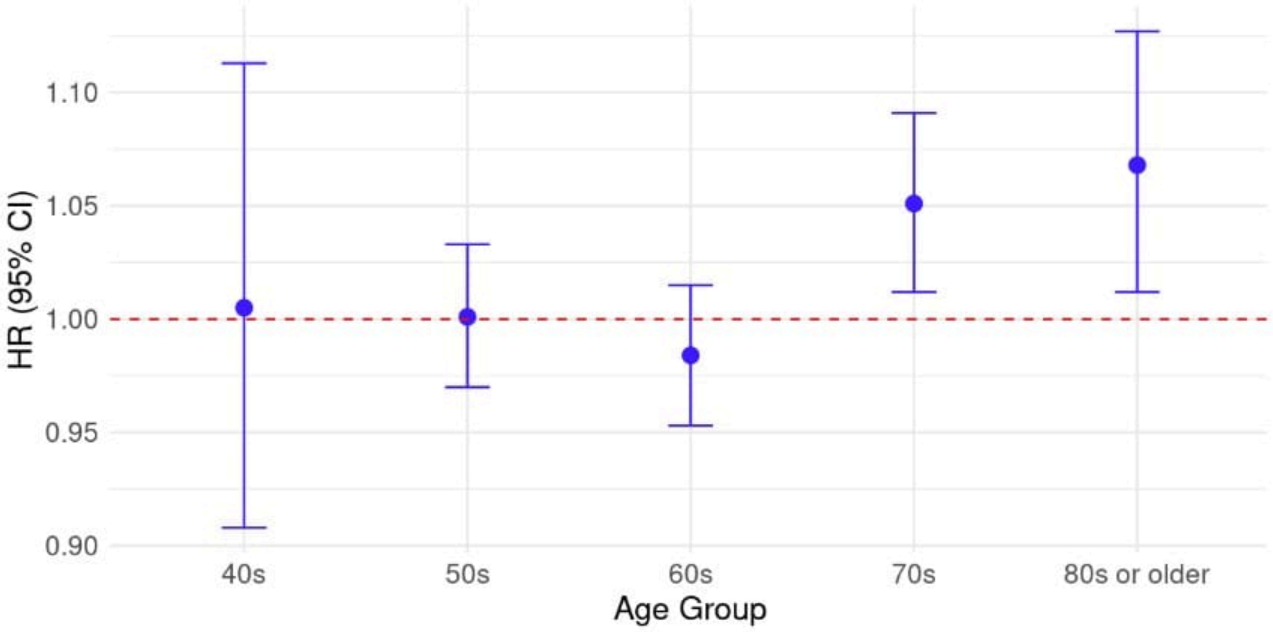


Figure 1: Association Between AD Genetic Risk Score and Major Depressive Disorder Stratified by Age Decades

Global Health

Effect of an integrated newborn care kit on neonatal and maternal health outcomes: A cluster randomized controlled trial in Gilgit-Baltistan, Pakistan Daniel Farrar* Daniel Farrar Lisa G. Pell Muhammad Yasin Falak Madhani Shariq Paracha Adria Rose Diego G. Bassani Imran Ahmed Muhammad Karim Nazia Jabeen Faisal Ali Masood Ali Khan Sajid B. Soofi Monica Taljaard Rachel F. Spitzer Sifat Wali Dr. Saleemuddin Sher Hafiz Khan Zulfiqar A. Bhutta Shaun K. Morris

Introduction: Pakistan experiences very high rates of neonatal mortality (NMR). Low-cost, community-based interventions are needed to prevent newborn deaths and related morbidities. We estimated the effect of an integrated newborn care kit (iNCK) on neonatal mortality, when delivered by Lady Health Workers (LHWs) to pregnant women.

Methods: We conducted a parallel-arm, pragmatic, open-label, cluster randomized controlled trial in Gilgit-Baltistan, Pakistan from March 2022–August 2024. Clusters were randomized to the iNCK or local standard of care (control) arm. Pregnant women were delivered the iNCK and/or standard of care by LHWs during the third trimester. The iNCK included a clean birth kit, 4% chlorhexidine gel, sunflower oil emollient, ThermoSpotTM temperature indicator sticker, fleece blanket, click-to-heat warmer, three 200 µg misoprostol tablets, and pictorial guide. The primary outcome was neonatal mortality, or death within 28 days after birth. Secondary outcomes include newborn omphalitis and maternal postpartum hemorrhage. The effect of the iNCK was assessed using generalized estimating equations and multivariable robust Poisson regression.

Results: 19352 pregnant women (8723 control, 10629 iNCK) and their 19237 live-born newborns (8682 control, 10555 iNCK) were enrolled. There were 174 newborn deaths, 88 in control clusters (NMR 10.1 per 1000 live births) and 86 in iNCK clusters (NMR 8.1 per 1000 live births). Neonatal mortality was not significantly different between arms (aRR 0.95, 95% CI 0.68–1.31; p=0.73) (Figure). Cumulative incidence of omphalitis was lower among newborns in iNCK clusters (aRR 0.20 vs. control, 95% CI 0.11–0.35, p<0.001). Among women delivering vaginally, postpartum hemorrhage was less common in iNCK than control clusters (aRR 0.43, 95% CI 0.20–0.90, p=0.03).

Discussion: The iNCK reduced morbidity among newborns and women in Pakistan. We will generate policy-relevant evidence for Pakistan and other settings with high NMRs.

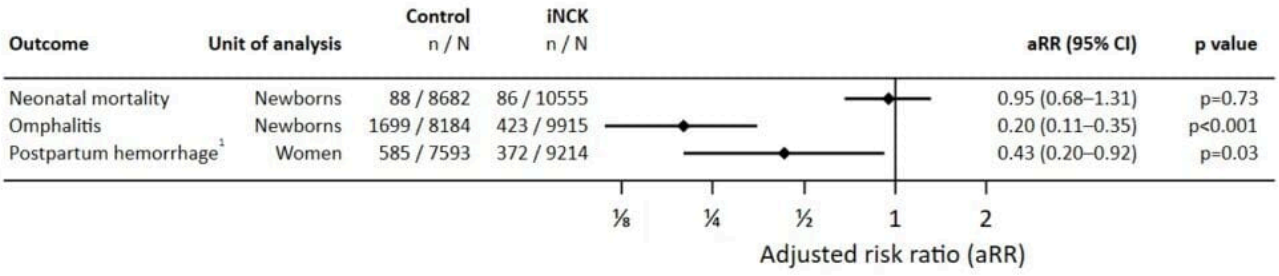


Figure. Effect of the iNCK on newborn mortality, newborn omphalitis, and maternal postpartum hemorrhage.

Analyses on the effect of the integrated newborn care kit (iNCK) vs. local standard of care (control) on newborn mortality, cumulative incidence of newborn omphalitis, and cumulative incidence of maternal postpartum hemorrhage (PPH) ([1]among women who delivered vaginally only). Associations were calculated using multivariable robust Poisson regression and generalized estimating equations. Analysis of neonatal mortality adjusted for newborn sex, number of antenatal care visits, study district, month of study (setting the month of study launch as zero), log cluster-specific baseline neonatal mortality rate, and cluster-specific baseline proportion of newborns delivered in health facilities. Analysis of omphalitis adjusted for newborn sex, number of antenatal care visits, and study district. Analysis of PPH adjusted for maternal age, parity, prior history of PPH, prior history of Caesarean section, study district, and log cluster-specific baseline proportion of women who experienced PPH. All covariates were defined a priori. "n / N" reflects the number of outcome events (n), over the number of participants with complete data (N).

LATEBREAKER

Global Health

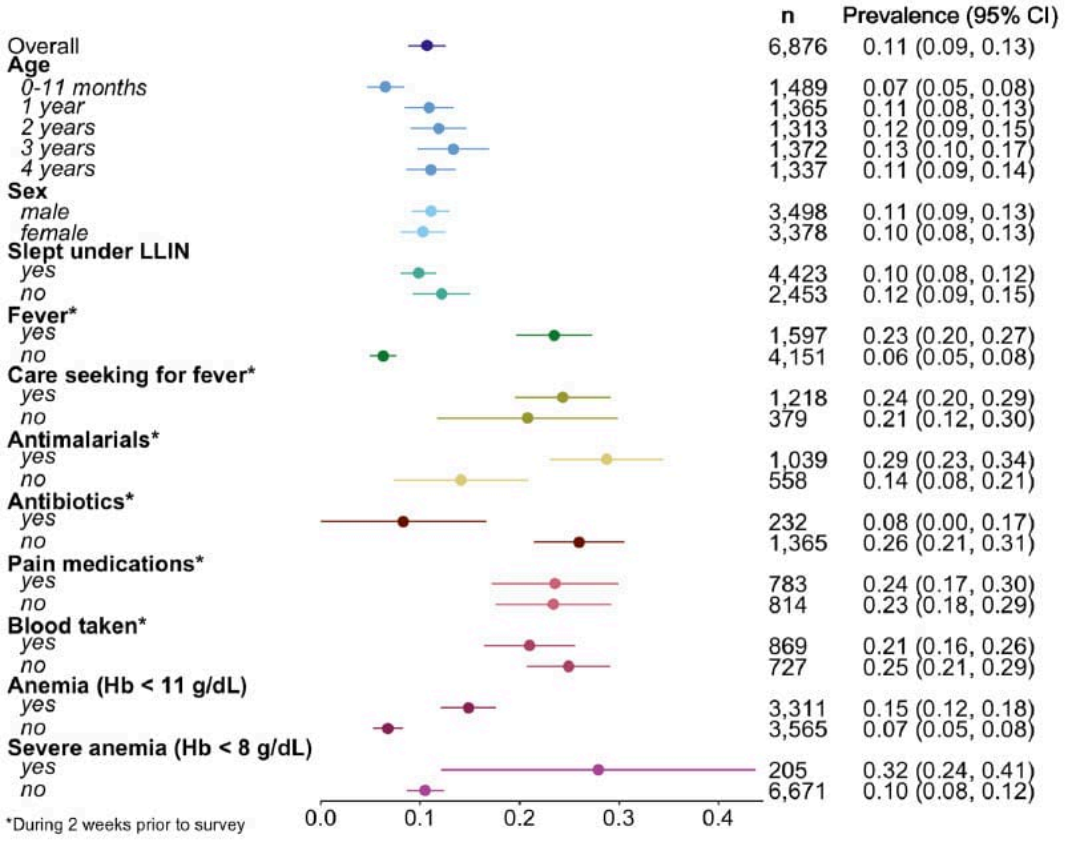
Prevalence of false-positive malaria rapid diagnostic tests among children under 5 in Uganda Caitlin A. Cassidy* Caitlin Cassidy Ross M. Boyce Emily J. Ciccone Emily W. Gower Bonnie E. Shook-Sa Jessie K. Edwards

Background: Malaria rapid diagnostic tests (mRDTs) are relatively simple, fast, and inexpensive tools that detect malarial antigens, typically histidine rich protein 2 (HRP2), in blood. HRP2 remains in the bloodstream and is detectable by mRDT even after treatment, leading to false-positive results. False-negative mRDTs are well-described, but less is known about the prevalence and consequences of false-positive results.

Methods: We analyzed cross-sectional data from the Malaria Indicator Survey in Uganda, conducted from December 2018 to January 2019. We included all children under 5 years of age with valid paired mRDT and light microscopy results. We define a false-positive result as mRDT(+)/microscopy(-). We estimated the prevalence of false-positive mRDTs among microscopy-negative children by applying two-stage survey weights. We constructed bivariate generalized linear models to estimate the prevalence difference (PD) of false-positive mRDTs for pre-specified covariates, including demographic and clinical characteristics.

Results: The weighted prevalence of false-positive mRDTs was 10.7% (849 of 6786) and was strongly correlated with malaria prevalence (r=0.90). Prevalence varied greatly by region, ranging from 1.4% in Kampala to 37.5% in West Nile. Prevalence was higher among children with recent fever (prevalence difference = 0.17 95% CI= (0.14, 0.21)), recent antimalarial use (0.15 (0.07, 0.22)), and comorbid anemia (0.08 (0.06, 0.10)) (figure). Prevalence was lower among those with recent antibiotic use (-0.18 (-0.23, -0.13)). Household factors, including urban residence, smaller household size, and electricity access were associated with lower false-positive mRDT prevalence.

Discussion: False-positive mRDTs are prevalent among children under 5 in Uganda and lead to overestimates of community level malaria prevalence. They may also contribute to unnecessary antimalarial use and consequently antimicrobial resistance. Increasing resistance by parasites to antimalarial drugs makes current treatments less effective and leaves children susceptible to complications from malaria. Future work should consider the impact of false-positive mRDTs on treatment algorithms and drug resistance.


n
Prevalence (95% CI)
Overall 6,876 0.11 (0.09, 0.13)
Age
0-11 months 1,489 0.07 (0.05, 0.08)
1 year 1,365 0.11 (0.08, 0.13)
2 years 1,313 0.12 (0.09, 0.15)
3 years 1,372 0.13 (0.10, 0.17)
4 years 1,337 0.11 (0.09, 0.14)
Sex
male 3,498 0.11 (0.09, 0.13)
female 3,378 0.10 (0.08, 0.13)
Slept under LLIN
yes 4,423 0.10 (0.08, 0.12)
no 2,453 0.12 (0.09, 0.15)
Fever*
yes 1,597 0.23 (0.20, 0.27)
no 4,151 0.06 (0.05, 0.08)
Care seeking for fever*
yes 1,218 0.24 (0.20, 0.29)
no 379 0.21 (0.12, 0.30)
Antimalarials*
yes 1,039 0.29 (0.23, 0.34)
no 558 0.14 (0.08, 0.21)
Antibiotics*
yes 232 0.08 (0.00, 0.17)
no 1,365 0.26 (0.21, 0.31)
Pain medications*
yes 783 0.24 (0.17, 0.30)
no 814 0.23 (0.18, 0.29)
Blood taken*
yes 869 0.21 (0.16, 0.26)
no 727 0.25 (0.21, 0.29)
Anemia (Hb < 11 g/dL)
yes 3,311 0.15 (0.12, 0.18)
no 3,565 0.07 (0.05, 0.08)
Severe anemia (Hb < 8 g/dL)
yes 205 0.32 (0.24, 0.41)
no 6,671 0.10 (0.08, 0.12)
0.0
0.1
0.2
0.3
0.4
*During 2 weeks prior to survey

Global Health

The children who go uncounted: Quantifying the surgical disease burden of gastrointestinal congenital anomalies in low-, middle-, and high-income countries Kelsey R. Landrum* Kelsey R. Landrum Emily R. Smith Henry E. Rice Pamela Espinoza Brian W. Pence Jessie K. Edwards Mark G. Shrime Naomi J. Wright

Background

The birth prevalence of congenital gastrointestinal (GI) anomalies and outcomes in affected children remain poorly defined in most countries, and the number of children with untreated GI anomalies has not been adequately estimated at regional or global levels. Our aim is to estimate the global and regional birth prevalence of six major GI anomalies, the proportion of GI anomaly cases globally and regionally that receive and do not receive treatment, and the proportion of GI anomaly cases globally and regionally that survive and do not survive given their treatment status.

Methods

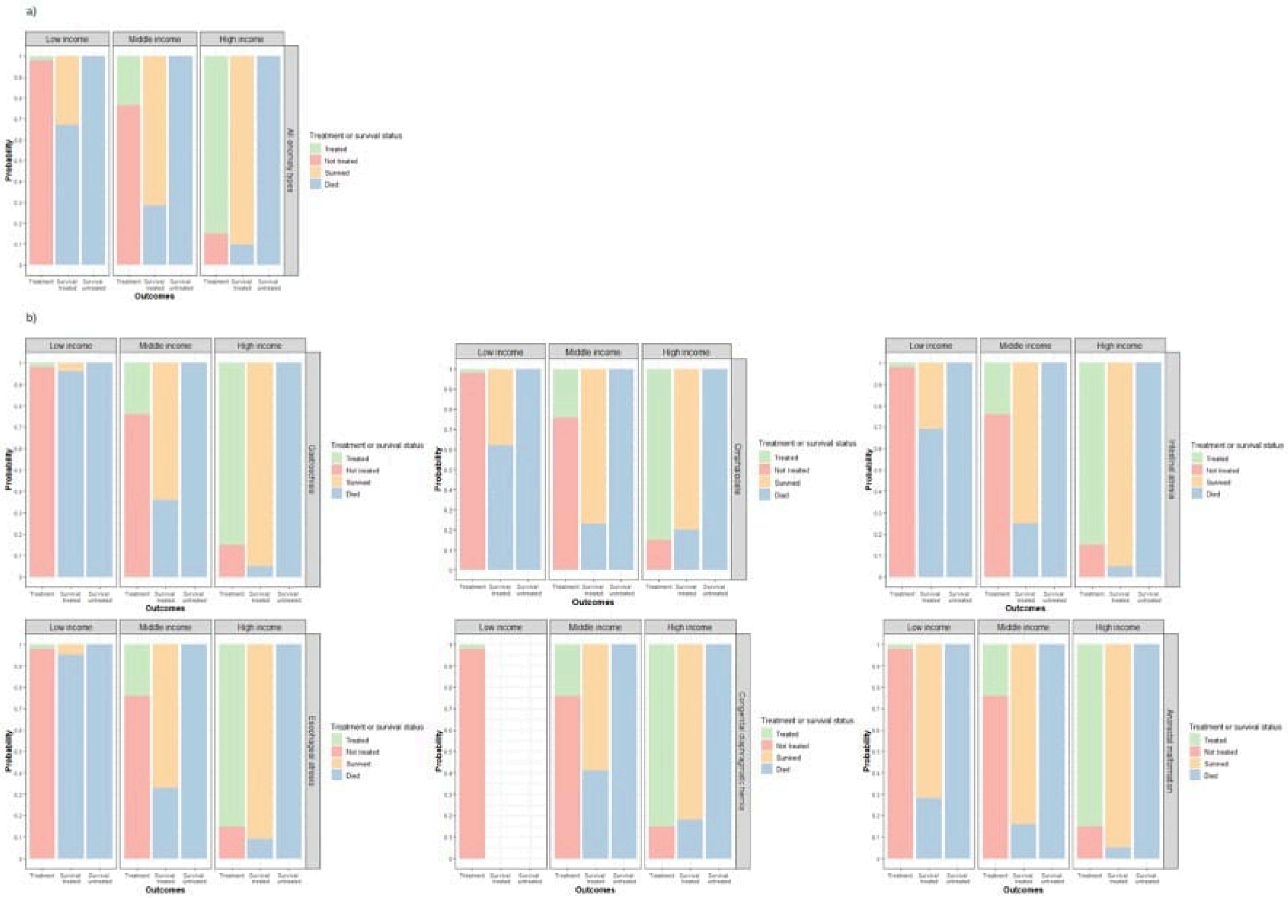
For congenital GI anomalies, we combined multiple data sources and a series of Monte Carlo simulation probability models to estimate 1) the birth prevalence of GI anomalies, 2) the proportion of children who are untreated, and 3) the proportion of children dying within 30 days of life or treatment initiation in 204 countries and territories in 2018 .

Findings

GI anomaly prevalence ranged from 1.30 to 4.22 children per 10,000 births depending on country income and anomaly type, resulting in 251,095 cases worldwide in 2018. We predicted the majority of children in low-income countries (LICs; 98%) and middle-income countries (MICs; 76%) and a smaller proportion of children in high-income countries (HICs; 15%) did not receive surgical treatment for GI anomalies globally in 2018 (n=186,131). Mortality among those treated was higher in LICs and MICs compared to HICs (as high as 96% in LICs, 41% in MICs, and 20% in HICs).

Interpretation

The burden of untreated disease and mortality from congenital GI anomalies is disproportionately high in LMICs compared to HICs. Access to surgical care and outcomes after receiving such care varied dramatically by country income level. This study provides a contemporary benchmark for birth prevalence, unmet need, and survival outcomes of children with major GI anomalies globally.


a)
Low income
Middle income
High income
All anomaly types
Treatment or survival status
Treated
Not treated
Survived
Died
Probability
Outcomes
b)
Gastroschisis
Omphalocele
Intestinal atresia
Oesophageal atresia
Congenital diaphragmatic hernia
Anorectal malformation

Global Health

Evaluating the Impact of Telemedicine Mobile Units on Health Outcomes, Healthcare System Resilience, and Disaster Response in Flood-Affected Areas: A Case Study of Sehat Kahani Hamna Khuld* Hamna Khuld

This study explores the implementation of telemedicine services through mobile units in the context of flood emergencies, examining their impact on health outcomes, mortality rates, and healthcare system resilience in disaster-affected areas. Sehat Kahani, a healthcare initiative, introduced a two-tier telehealth model involving physical camps, mobile units, and a telehealth app. Semi-structured interviews with key stakeholders, including Sehat Kahani staff, healthcare providers, beneficiaries, funders, and top-level management, gather insights. The findings highlight the importance of comprehensive assessments, budget analysis, collaboration with government agencies, and partnerships with corporate entities. Accessibility concerns in telehealth services were addressed through Sehat Kahani's multi-tiered model, which combines mobile clinics with a user-friendly telehealth app. Security, privacy, and confidentiality were prioritized, adhering to data protection regulations such as HIPAA. Effective training programs for healthcare professionals focused on empathy, rapport building, and technical proficiency. Sehat Kahani's scalability measures and preparedness for increased patient volume ensured efficient telehealth service delivery during disasters. The case study concludes that Sehat Kahani's comprehensive approach, covering resource analysis, accessibility, security, scalability, training, evaluation, collaboration, and sustainability, successfully integrates telehealth into disaster relief efforts. This model is poised to influence future telehealth initiatives in disaster response scenarios.

Keywords: Telemedicine services, disaster relief, mobile unit, developing nations, resource analysis, flood emergencies.

Global Health

Trends in incidence of trigeminal neuralgia with inflammatory bowel disease in Taiwan: a 14-year long term descriptive study Ting-Fu Huang* Ting-Fu Huang Fu-Huang Lin Chien-An Sun Yu-Ching Chou

Trends in incidence of trigeminal neuralgia with inflammatory bowel disease in Taiwan: a 14-year long term descriptive study

Ting-Fu Huang1, Fu-Huang Lin1, Chien-An Sun2, Yu-Ching Chou1*

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Background: Both inflammatory bowel disease (IBD) and trigeminal neuralgia (TN) are rare diseases that significantly impact patients' quality of life. Previous studies suggest that extraintestinal manifestations associated with IBD may explain the relationship between these two diseases, although evidence remains limited. This descriptive study examined the incidence of TN with IBD in a large-scale, population-based cohort in Taiwan.

Methods: From 2000 to 2013, about 66,489 new cases with IBD were identified in Taiwan's National Health Insurance Research Database (NHIRD). Chi-square test was used for evaluating incidence rates in different sex, age groups and periods. For long term trends, we assessed the change in the incidence rates over 14 years by linear trend analysis.

Results: The incidence of TN among IBD patients increased from 4.50 per 10,000 person-years in 2000 to 70.73 per 10,000 person-years in 2013, with an average incidence of 51.12 per 10,000 person-years. The incidence rate was 35.90 among men and 64.87 among women per 10,000 person-years. When stratifying patients into five age groups, the incidence of TN per 10,000 person-years was as follows: 5.34 (ages 20–30), 6.08 (ages 30–40), 9.77 (ages 40–50), 9.81 (ages 50–60), and 14.41 (ages ≥ 60). As age increases, patients with IBD tend to have a higher incidence of TN.

Conclusion: Over the 14-year study period, the incidence of TN significantly impacted the quality of life of patients. Our findings, based on big data analysis, indicate a steady rise in TN incidence among IBD patients. Thus, the study to indicate a positive correlation between IBD and TN is needed.

Global Health

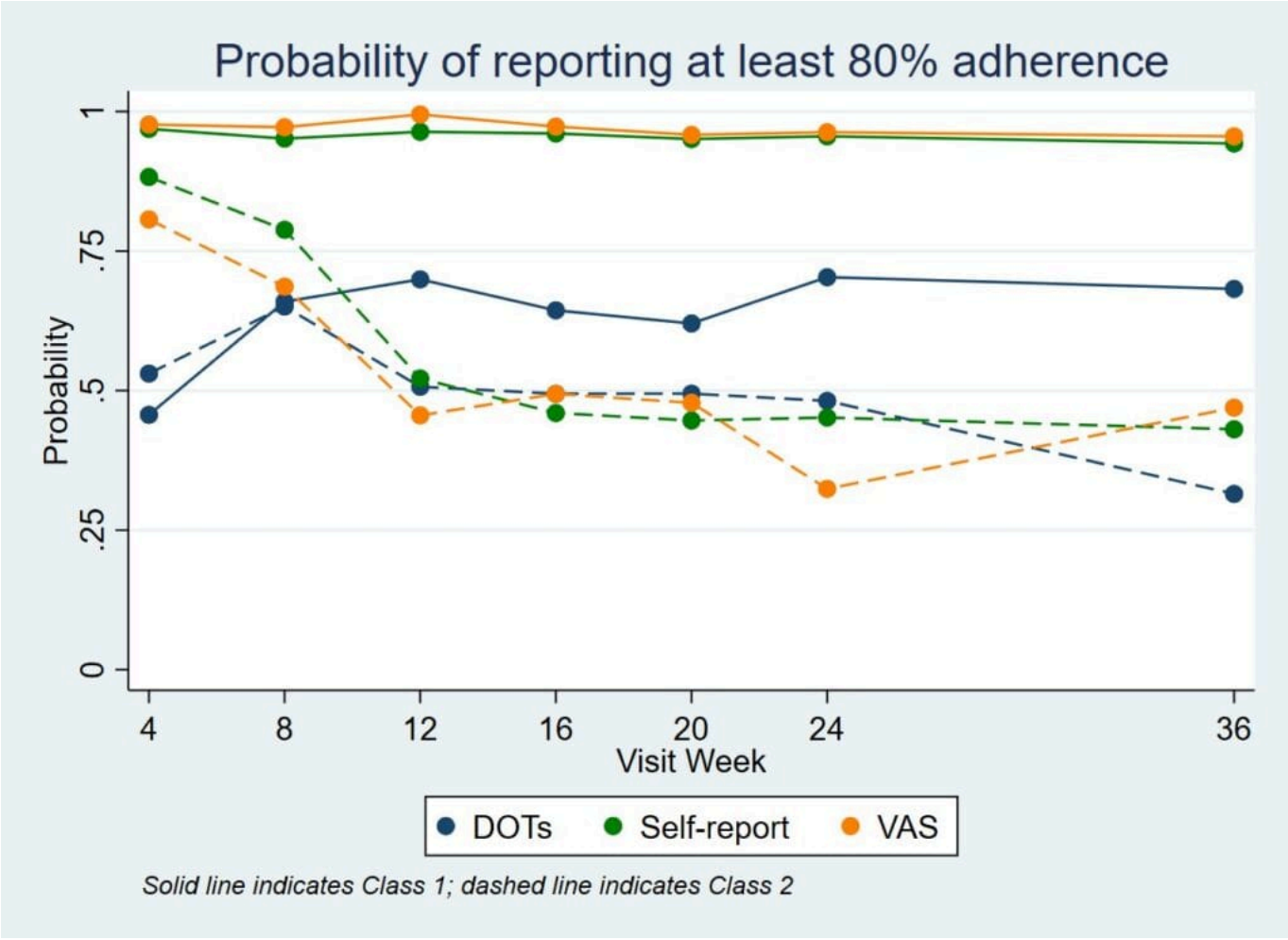
Adherence to multidrug resistant-tuberculosis treatment in a prospective study of people on treatment: a latent class analysis Sarah Brumfield* Sarah Brumfield Pawandeep Kaur Sonali Sarkar Valeria C Rolla Ashavaid Tester Padmapriyadarsini Chandrasekaran Amrose Pradeep Sanjay Gaikwad Afranio Kritski Fernanda CQ Mello Marina Figueiredo Camilla Rodrigues Timothy Sterling C Robert Horsburgh

Multidrug resistant-tuberculosis (MDR-TB) is a threat to TB elimination; successful treatment is important to interrupt transmission. However, treatment adherence by MDR-TB patients is difficult due to high toxicity, limited medication availability, and stigma associated with accessing treatment. Poor adherence can lead to adverse outcomes, including prolonged disease, recurrence, and death. To identify potential causal effects of predictors on treatment outcomes, accurate and complete measurement of adherence is important when studying MDR-TB.

We measured treatment adherence in the Predictors of Resistance Emergence Evaluation in MDR-TB patients on treatment (PREEMPT) study, a prospective cohort of people on treatment for MDR-TB. Adherence was collected using: 1) a self-reported questionnaire, 2) a visual analog scale (VAS), and 3) review of directly observed therapy (DOT) records. Follow-up visits took place every four weeks from baseline until week 24, and another visit took place at week 36. Due to the COVID-19 pandemic, VAS and especially DOT were difficult to collect in 2020-2021. For each of the three measures, we calculated binary variables indicating whether the participant reported taking at least 80% of their medications in the prior 30 days. These were used to conduct a latent class analysis assuming 2 underlying classes of adherence.

We enrolled 328 participants at 5 sites in India and 3 sites in Brazil between January 2019-December 2023. These participants completed 2,199 follow-up visits. Of these, 198 (9%) visits were missing self-reported adherence, 403 (18%) were missing VAS, and 957 (44%) were missing DOT information. Our latent class analysis predicted that 79% of participants were in class 1 (‘adherers’) and 21% were in class 2 (‘non-adherers’).

Using a latent class analysis, we were able to summarize participants’ adherence into a single variable that can be used in subsequent analyses.


Probability of reporting at least 80% adherence
Probability
0
.25
.5
.75
1
4
8
12
16
20
24
36
Visit Week
DOTs
Self-report
VAS
Solid line indicates Class 1; dashed line indicates Class 2

Global Health

The effect of alcohol consumption on periodontal disease among Indigenous Australian adults Xiangqun Ju* Xiangqun Ju Gloria Mejia Joanne Hedges Sneha Sethi Hawazin Elani Lisa M Jamieson

Objective: Drinking alcohol adversely impacts periodontal tissues, potentially leading to periodontitis, a condition that not only affects oral health but is also linked to systemic issues such as cardiovascular disease and diabetes. The study aimed to estimate the effect of alcohol consumption on periodontal disease while controlling for the mediating effect of smoking among Indigenous Australia adults.

Methods: Data were obtained from a longitudinal sample of Indigenous Australian (n=1011) adults aged 18+ years, conducted in 2018-19 and following in 2019-2020. The outcome variable was self-reported periodontitis which was dichotomized into 'No/mild' or 'Moderate/severe'. The exposure was alcohol consumption (daily, weekly/monthly, or never) and the mediator was smoke status (current, former or never smoker). Other confounders and risk factors included age, sex, residential location, education level, household income, self-rated general health and last dental visit status. A marginal structural model with stabilized inverse-probability weights was used to estimate the direct effect of alcohol consumption on periodontitis. Risk ratio (RR) and 95% confidence interval (CI) was calculated.

Results: A total 763 Indigenous Australian adults who completed a questionnaire at baseline and 12 months follow-up were included. The prevalence of periodontitis was 46.3%. After correcting periodontitis misclassification, the estimate effect of daily alcohol consumption was approximately 70% increased periodontitis (RR=1.67, 95% CI: 1.02-3.04) than those who consumed alcohol on a weekly or monthly basis, or not at all. Current smokers had nearly 1.5 times (RR= 1.43, 95%CI: 1.02-2.02) higher risk of periodontitis than those who had used or never smoked.

Conclusion: Alcohol consumption has a direct effect on periodontitis independent of smoking and other factors when estimated using marginal structural modelling. Smoking is also considered as a risk factor in periodontitis.

Health Disparities

Sexual orientation differences in female sexual dysfunction in a large cohort of nurses in older adulthood Tabor Hoatson* Tabor Hoatson Julia Bond Colleen Reynolds Julia Marcus Brittany Charlton

Background: Female sexual dysfunction (FSD) can profoundly inhibit quality of life, but little is known about disparities across sexual orientation groups.

Aim: We assessed sexual orientation-related disparities in FSD in a large cohort of female nurses in older adulthood.

Methods: This analysis included female nurses (n=84,790) from the Nurses' Health Study II, aged 48–69 years at the time of sexual function ascertainment in 2013. Sexual activity and FSD were measured using the Female Sexual Function Index-6 (FSFI-6). In 2017, sexual orientation identity, sexual attractions, and sexual contact were assessed. In statistical analyses, we generated prevalence ratios (PR) and 95% confidence intervals (CI) with log-binomial and multinomial models and additionally assessed effect modification by menopausal status.

Outcomes: We examined differences in past-month sexual activity, FSD, and individual FSFI-6 domains (e.g., arousal, lubrication) across sexual orientation subgroups.

Results: Compared with completely heterosexual participants, bisexual (PR:0.89, 95%CI:0.81–0.97) and lesbian (PR:0.76, 95%CI:0.72–0.82) participants had a lower prevalence of sexual activity. The point prevalence of FSD was also lower among bisexual (PR:0.81, 95%CI 0.65–1.01) and lesbian (PR:0.87, 95%CI:0.74–1.01) participants. However, the prevalence of low sexual satisfaction was greater in multiple sexual minority subgroups. Across all sexual orientation groups, menopause was associated with an increased prevalence of FSD. There was no statistical evidence of effect modification by menopause status.

Clinical Implications: Overall, sexual minority individuals were less satisfied with their sexual lives than completely heterosexual individuals; resources to support clinicians in culturally competent discussions of sexual satisfaction with sexual minority patients are needed.

Conclusion: To improve sexual function outcomes, further investigation is needed to identify what drives sexual activity and satisfaction among female sexual minority individuals in older adulthood, as well as identify protective factors against FSD for people of all sexual orientations.

Health Disparities

Intersectional demographic trends in infective endocarditis among 18-64 year olds in 2012-2021 Tamara Rushovich* Tamara Rushovich Alina Schnake-Mahl Ana V. Diez-Roux Neal Goldstein

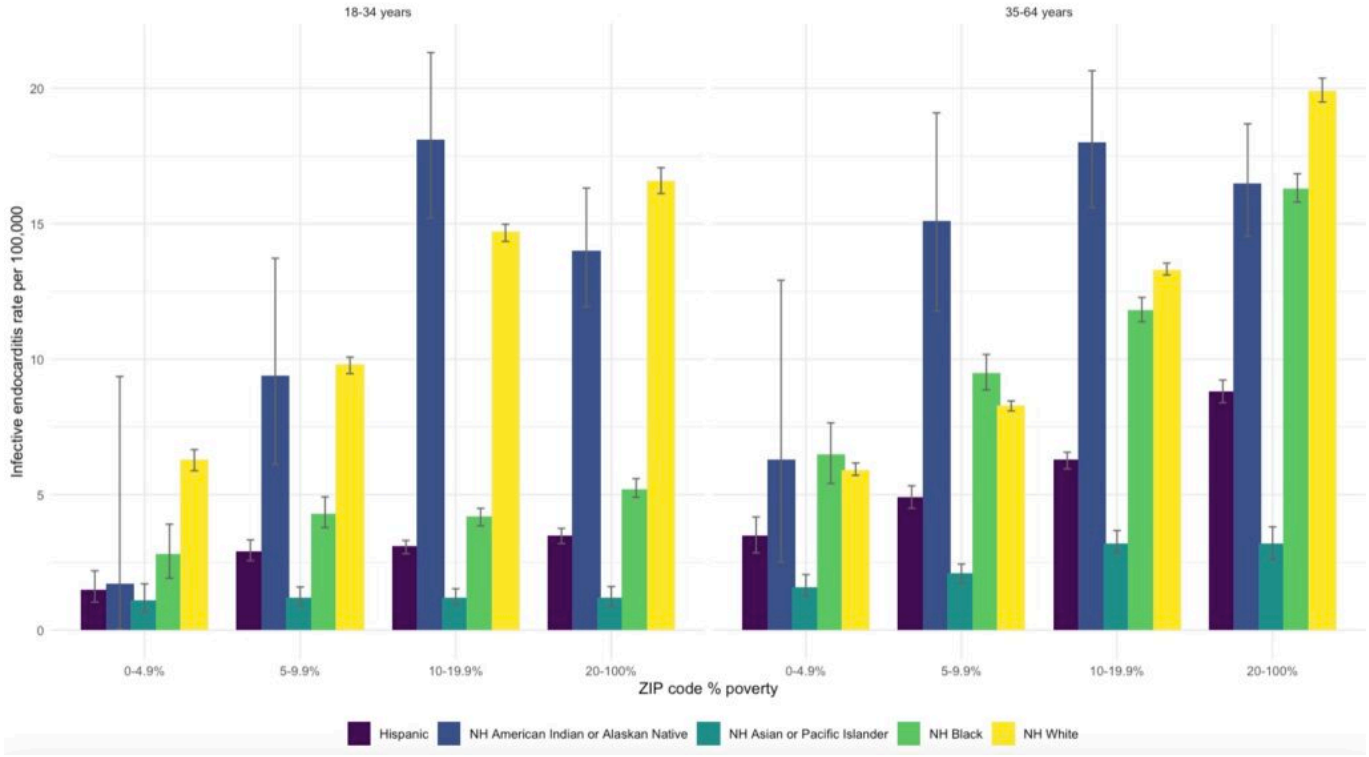
Background: The estimated number of people who use injection drugs in the US has more than quadrupled since 2010. Infective endocarditis (IE), a serious infection of the heart which can be caused by bacteria introduced during injection drug use, is a growing concern. Existing descriptive epidemiology of IE shows disparities by singular demographic groups, however disparities may differ by intersectional demographic groups, and over time.

Methods: Using data from AHRQ's State Inpatient Database and the American Community Survey, we calculated rates of IE hospitalization for 18-64 year olds, from 2012-2021, in 13 US states, by age, sex, racialized group, and ZIP code area poverty.

Results: IE rates per 100k people increased from 8.0 in 2012 to 11.9 in 2018 and decreased to 8.7 in 2021. From 2012-2021, the rates among 35-64 year olds were higher than those among 18-34 year olds. IE rates were highest among American Indian or Alaskan Native people (AMIAN)(15.6) followed by non-Hispanic (NH) White (11.9), NH Black (9.6), Hispanic (5.1) and Asian and Pacific Islander (2.0). Rates were higher among men than women (11.4 and 8.5) and highest in ZIP codes with the highest poverty levels (13.0).

Among those 18-34 years, women had higher rates than men (10.1 vs 7.7), but among those 35-46 years men had higher rates than women (13.7 vs 7.6). Among those 35-46 years, in the lowest poverty zip codes, Black rates were similar to White rates, but among the same age group in higher poverty zip codes, White rates were higher than Black rates. Among those 18-34 years, AMIAN and White rates were highest among all racialized groups in all poverty level ZCTAs.

Conclusion: Investigating disparities using multiple demographic categories revealed distinct vulnerable groups: AMIAN individuals, younger women, Black individuals in low poverty ZIP codes and White individuals in high poverty ZIP codes. Findings can help tailor interventions and guide resource allocation.


18-34 years
35-64 years
Infective endocarditis rate per 100,000
20
15
10
5
0
0-4.9%
5-9.9%
10-19.9%
20-100%
ZIP code % poverty
Hispanic
NH American Indian or Alaskan Native
NH Asian or Pacific Islander
NH Black
NH White

Health Disparities

Selection of Socioeconomic Status when Predicting the Likelihood of Lung Cancer Screening Brian Hixon* Brian Hixon Nikki M. Carroll Kris Wain Mahesh Maiyani Stacey A. Honda Robert T. Greenlee Christine Neslund-Dudas Roger Y. Kim Katharine A Rendle Anil Vachani Debra P Ritzwoller

Given persistent inequities in lung cancer mortality, there is key need to understand how different Social Determinants of Health (SDOH) impacts Lung Cancer Screening (LCS) in routine practice Understanding elements of SDoH that can better discern potential disparities for future interventions and research is important. This retrospective study compared the association of five geospatially mapped SDoH indices to predict an LCS-eligible individual completing an LCS scan within five diverse healthcare systems between January 1, 2014, through December 31, 2019. We used aggregate measures, univariable/ multivariable log-binomial regression, fit statistics, correlation matrices and mapping to assess census tract-based SDoH measures by census tract. Data for 52,296 LCS-eligible individuals were included in this study. All indices were highly correlated at >= 0.73 and showed similar likelihood of receipt of LCS using univariable and multivariable models. All indices demonstrated that higher relative SDoH was associated with receipt of LCS. Based on fit statistics in multivariable models the Social Vulnerability Index (SVI) had the best fit. Receipt of LCS was positively associated with higher levels of socioeconomic status among all indices but the level of that association varied. Understanding the construction of and interpretation of each index is essential in estimating the impact of SDoH on research findings.

Health Disparities

The association of the 2021 Child Tax Credit Expansion with Child Health and Development: Evidence from a Longitudinal Study Guangyi Wang* Guangyi Wang Daniel Collin Deborah Karasek Rita Hamad

The 2021 temporary expansion of the Child Tax Credit (CTC) alleviated material hardship among disadvantaged families during the COVID-19 pandemic, significantly reducing child poverty. While many studies have examined the impact of the expansion on health-related outcomes such as food insecurity and parental psychological well-being, few have linked it to child outcomes. This study investigates the association between the 2021 CTC expansion and child health and development outcomes, including self-rated health, the Strengths and Difficulties Questionnaire (SDQ), and food security. Using data from the 2020-2021 waves of the Child Development Supplement (CDS) of the Panel Study of Income Dynamics (PSID), we estimate within-person changes in outcomes for children who participated in both waves (n = 1,028). The CTC eligibility amounts before and after the expansion were calculated based on detailed benefit rules. The 2021 interview period spans November 2021 to June 2022, covering three distinct phases: 1) advanced CTC monthly payments (November–December 2021), 2) expired monthly payments (January–April 2022), and 3) distribution of remaining lump sum CTC (May–June 2022). We stratified the analysis by these periods to capture potential disparate impacts. Additionally, we examined whether the association differed by family income and race/ethnicity. The CTC expansion was associated with a reduction (i.e., improvement) in SDQ scores during the monthly payment period. However, after the CTC expansion expired, children from low-income families had worse self-rated health and higher SDQ scores compared to those from higher-income families. Differences by race/ethnicity were also observed. These findings inform ongoing state and federal poverty policymaking and contribute to theoretical knowledge on income and child health.

Health Disparities

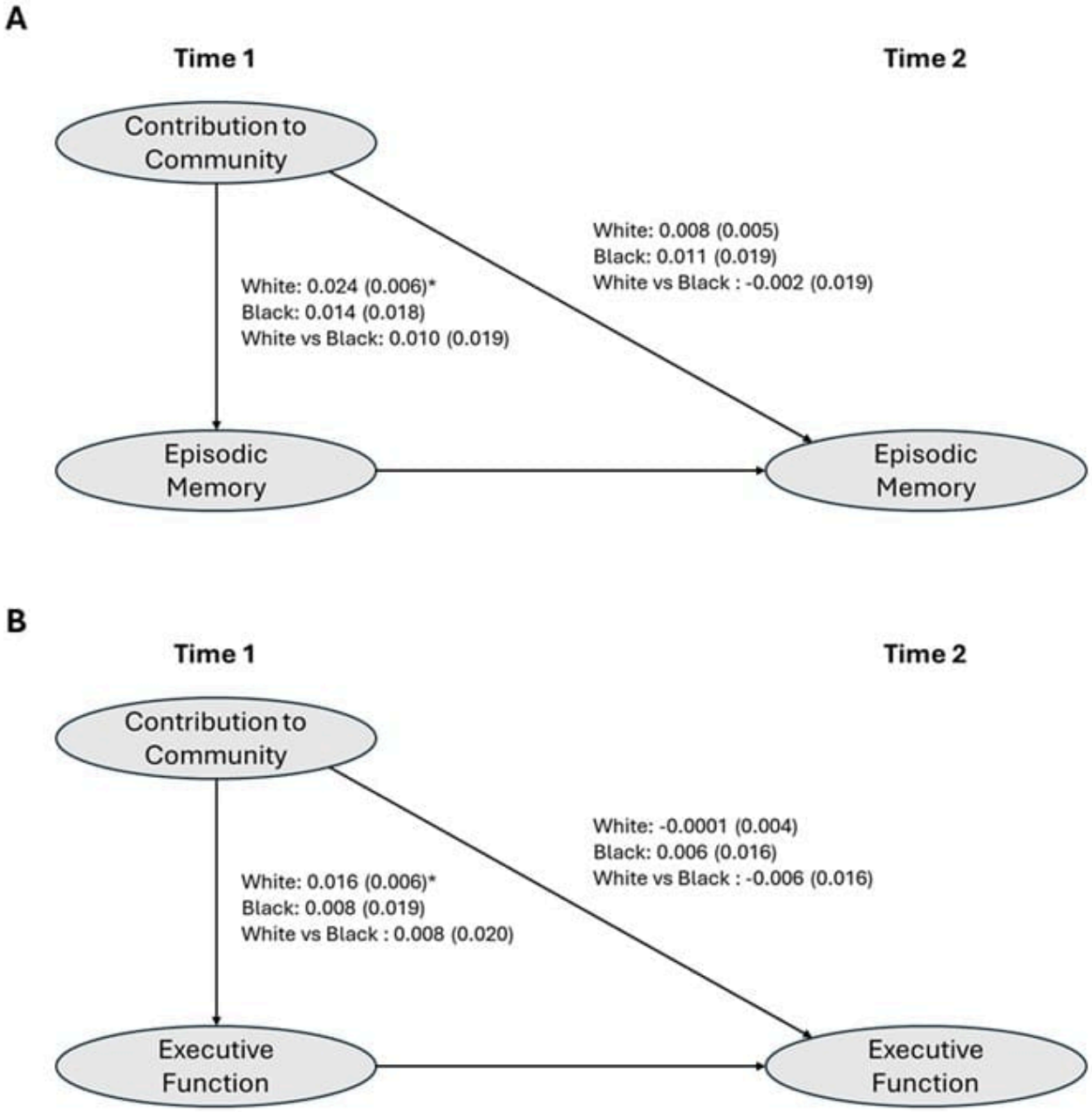
Long Term Effects of Community Involvement on Cognitive Function and Racial Disparities: Findings from the MIDUS Study Yu-Hua Fu* Yu-Hua Fu Josué Almansa Yun-Yi Pan Ruijia Chen Ester Villalonga-Olives

Introduction: Racial disparities in cognitive function between Black and White populations are well-documented, but the role of community involvement in mitigating these disparities remains unclear. This study examines the impact of community involvement on cognitive decline over a 10-year period and investigates potential racial disparities.

Methods: Data were drawn from the Midlife in the United States (MIDUS) study, including the core and Milwaukee samples. The analysis included 1844 White and 196 Black participants followed across two waves: 2004 (wave 1, baseline) and 2013 (wave 2, follow-up). Community involvement was measured with self-reported contributions to community, while cognitive function was measured using standardized scores for episodic memory and executive function. Two path analysis models were fitted to examine the effects of community involvement on cognitive decline (changes in episodic memory and executive function) and to assess race as a moderator, while adjusting for age, sex, education, income, and chronic conditions.

Results: Black participants had lower episodic memory and executive function scores but higher community contributions at baseline compared to White participants. Among White participants, higher community contributions were associated with better episodic memory (β = .024 [95% CI .01~.04)) and executive function (β = .016 [95% CI .01~.03]) at baseline. However, these associations were not observed in Black participants (episodic memory: β = .014 [95% CI -.02~.05]); (executive function: β = .008 [95% CI -.03~.05]). Lower cognitive function scores persisted at wave 2, and baseline community contributions did not predict changes in cognitive scores between waves. No moderating effect of race was observed.

Conclusion: The lack of a moderating effect of race suggests that promoting community involvement alone in Black communities may not address cognitive disparities. Further research is needed to explore other unmeasured factors.



The figure illustrates the structure of the pathway analysis (A: episodic memory; B: executive function), including estimated parameters (standard deviations) for White participants, Black participants, and the comparison between White and Black participants (White vs Black). An asterisk (*) denotes statistical significance at an alpha level of 0.05.

Health Disparities

The Long-Term Impact of Racial and Ethnic School Composition on Latinos' Late-Life Cognition Sirena Gutierrez* Sirena Gutierrez Paola Gilsanz Jacqueline M. Torres

Background: The educational experiences of older Latinx individuals, shaped by a history of segregation (e.g., designated "Mexican schools" with inequitable funding, unfair language assessments), may contribute to racial and ethnic disparities in dementia in the United States. The racial and ethnic composition of schools may serve as proxy for the resources available and the overall environment, influencing factors like sense of belonging and experiences of discrimination. However, data limitations have hindered research on this topic.

Methods: We used data from 314 Latinx participants of the Health and Retirement Study aged ≥ 50 years, born in the US or who migrated before the age of 6. Self-reported school racial/ethnic composition, collected in 2015-2019 was used to examine whether the number of years spent in schools with a majority White, Latinx, or Black students was associated with baseline memory function (score 0-20). Linear regression models were used, adjusting for sociodemographic variables, with sensitivity analyses additionally adjusting for educational attainment given that it may be a potential mediator.

Results: Attending a school with predominately Latinx students was not significantly associated with baseline memory function (b= -0.01 [-0.07,0.09]). Attending schools with predominately Black students was associated with lower baseline memory function (b= -0.26 [-0.52,0.00]). Conversely, attending schools with predominately White students was associated with higher baseline memory function (b= 0.09 [0.01,0.16]). After adjusting for educational attainment, results remained consistent.

Conclusion: Among older Latinx adults, the racial and ethnic composition of schools was associated with baseline memory function in qualitatively different ways. Further studies with larger samples are needed to confirm these findings and to better understand the mechanisms (e.g., inequitable distribution of school resources) driving these potential differences.

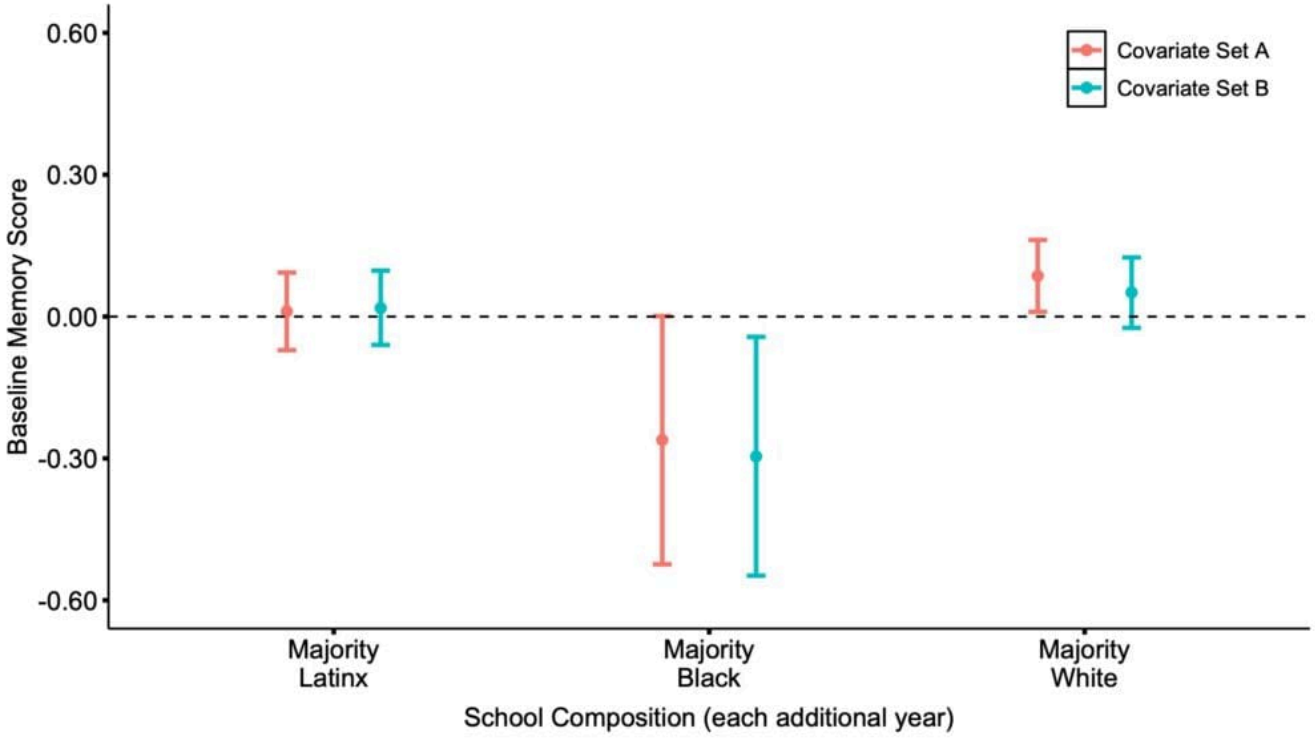


Fig 1. Associations between school racial and ethnic composition (in years) and baseline memory function. Note: Data drawn from the Health and Retirement Life History Surveys 2015-2019. N=314. Baseline memory function (0-20) composed of immediate and delayed verbal recall tasks from the participants' first HRS interview. Models 1-3 adjusted for covariate set A which included age, gender, birthplace (US South, US Non-South, non-US), birth cohort, and parental education. Models 4-6 adjusted for covariate set B which additionally included educational attainment.

Health Disparities

Examining the Association between Income Inequality and Physical Activity among Canadian Youth during the COVID-19 Pandemic Zack Perala* Zack Perala Valerie Carson Sentil Senthilselvan Roman Pabayo

Objectives Previous research has examined the association between income inequality and physical activity among youth; however, no studies have investigated the association longitudinally during the COVID-19 pandemic among Canadian youth. This study explored the association and mechanisms involved. Additionally, we determined whether associations were heterogeneous across gender.

Methods Longitudinal data from 9,423 students from Alberta, British Columbia, Quebec, and Ontario was obtained from the 2020/21, 2021/22, and 2022/23 survey waves of the Cannabis, Obesity, Mental health, Physical activity, Alcohol, Smoking, and Sedentary behaviour (COMPASS) study. A random intercept model was used to quantify the associations between census division-level income inequality (expressed as standardized Gini coefficients measured by after tax household income) and physical activity trajectories over time, adjusting for individual and school-level covariates.

Results Higher census-division level income inequality was associated with higher average physical activity levels in minutes per week for girls but not boys at baseline and during follow-up (Girls: ß = 8.126, 95% CI: 4.35, 11.90; p < 0.001; Boys: ß = 3.539, 95% CI: -0.0996, 7.177; p = 0.057). Furthermore, Income inequality was associated with higher odds of meeting the recommended physical activity levels of 60 minutes per day for boys and girls at baseline and during follow-up (Girls: OR = 1.412, 95% CI = 1.16, 1.727; P<0.01; Boys: OR =1.26, 95% CI = 1.02, 1.55; p = 0.03).

Conclusion Contrary to our hypothesis, areas of higher income inequality were associated with increased physical activity levels and proportion of meeting the recommended threshold of physical activity per day. Further research is needed to examine this complex association between income inequality and physical activity.

Health Disparities

When Education Fails to Protect: Severe Maternal Morbidity at the Intersection of Race/Ethnicity and Maternal Education Rashida S. Smith-Webb* Rashida S. Smith-Webb Martha M. Werler Samantha E. Parker Kelleher Collette N. Ncube

Background: Health disparities in severe maternal morbidity (SMM) across various dimensions of social inequality are well documented; however, limited research has explored how multiple axes of marginalization intersect to shape these disparities. Guided by intersectionality theory, we examined differences in SMM rates at the intersection of race/ethnicity and education.

Methods: We used the Massachusetts Pregnancy to Early Life Longitudinal Data System to identify nulliparous birthing people, aged 12-55 years, from 1998-2021. SMM during delivery hospitalizations was determined using the Centers for Disease Control and Prevention criteria. We used binomial regression models to estimate SMM rates and RD (95% CI) per 10,000 deliveries for six intersectional groups, defined by race/ethnicity (Black, Hispanic, White) and maternal education (no college degree, college degree or higher), adjusted for age, nativity, marital status, and delivery year.

Results: Rates of SMM were highest for Black birthing people with a college degree or higher (314) and lowest for their White counterparts (213). For White and Hispanic birthing people, higher levels of education were associated with lower rates of SMM. However, among Black birthing people, rates of SMM were similar for those with (314) and without a college degree (310). Compared to White birthing people with a college degree or higher, Black birthing people, regardless of education, had an excess of about 100 SMM cases: no college degree RD=102 (75, 128); at least a college degree RD=98 (83, 113). For Hispanic birthing people, RDs of 25 (4, 45) and 58 (46, 70) were observed for those with and without a college degree, respectively. Similar patterns emerged, albeit attenuated when examining SMM without blood transfusions.

Conclusion: Higher levels of education offer little protection against SMM for Black birthing people. Addressing structural racism and other socioeconomic drivers is critical to mitigating disparities in SMM.

Health Disparities

Using the Future of Families & Child Wellbeing Study to Test for Racial Disparities in Maternal Telomere Length Brittney Boakye* Brittney Boakye Rebecca Fix

Introduction: The weathering hypothesis postulates that socioeconomic disadvantage and chronic stress lead to accelerated biological aging, particularly in Black women. Telomere length can serve as an indicator of biological aging. This study examined the association between socioeconomic status, psychosocial factors, and telomere length among mothers. Methods: The Future of Families and Child Wellbeing Study (FFCWS) Dataset was used to explore the relationship between maternal race and telomere length with a sample size of 2,984 mothers. The primary outcome variable was log-transformed telomere length, reported in kilobases (kb). Predictor variables were race, age, sociodemographic variables (education, poverty level) and psychosocial variables (maternal stress, maternal depression, social support, child's mother and biological father relationship). Multivariable linear regression was used to estimate the association sociodemographic and psychosocial variables had with telomere length. Models were also stratified by race. All analyses were performed using SPSS version 29.0.2.0. Results & Discussion: Results depict a statistically significant association between race and telomere length, where Black mothers have significantly longer telomere lengths than White mothers (B=0.064, p-value=<0.001). Mothers who completed high school had significantly longer telomere lengths than those who did not complete high school (B=0.054, p-value=.036). Linear regression findings on sociodemographic associations with telomere length, including racial differences, were inconsistent with previous literature. Future research is needed to explore associations among Black women in a more nationally representative sample that considers resilience.

Health Disparities

Income inequality and risk for early age of initiation of alcohol use. A longitudinal examination of Canadian secondary school students Jason Were* Jason Were Karen A. Patte Scott T. Leatherdale Roman Pabayo

Background: Early initiation to alcohol is a known predictor of long-term usage of alcohol with severe impacts on health. Income inequality has been associated with underage drinking. However, less is known about its influence to early initiation of alcohol use. This study examined the association between income inequality and the early age of initiation to alcohol.

Methods: We used student cohort data (2017-2020) from the Cannabis, Obesity, Mental health, Physical activity, Alcohol, Smoking and Sedentary behavior project and census division (CD) data from the 2016 Canada census. Our sample was composed of 28,732 adolescents from 118 schools distributed in 39 CDs in 4 provinces in Canada (BC, AB, ON, QC). The outcome was defined as a nominal variable describing the age (in years) at which the student first drank alcohol that was more than a sip (never drunk, 8–12, 13-17, ≥18, and do not know). Income inequality (measured using the Gini index at the CD level) was grouped into tertiles (low, moderate, and high). Multilevel multinomial regression was used to examine the study objective.

Results: After adjusting for individual (age, gender, ethnicity, spending money, physical activity, smoking status, cannabis use, depression status and province) and CD (income and population size) covariates, the odds of early initiation to alcohol at 8–12 years old relative to those who have never consumed alcohol was higher for students attending schools in areas with moderate (OR=1.37; 95% CI=1.18–1.60), and high (OR=1.43; 95% CI=1.16–1.78) income inequality areas compared to areas with low income inequality. The association between income inequality and other age groups was not significant.

Conclusion: Our findings suggest that reducing income inequality may subsequently curb the initiation of alcohol consumption in the preadolescence stage. Public health should target alcohol prevention strategies among high school students in areas characterized with high-income inequality.

Health Disparities

Decomposition of influenza and pneumococcal vaccine uptake among immigrant and non-immigrant older adults in Canada: a cross-sectional analysis of data from the Canadian Longitudinal Study on Aging (CLSA) Ji Yoon Kim* Ji Yoon Kim Giorgia Sulis Alton Russell Seungmi Yang Jesse Papenburg Ananya Banerjee Patricia Li

Background: Immigrant older adults in Canada have lower uptake of influenza and pneumococcal vaccines than non-immigrant older adults. However, the contributions of sociodemographic, health-related, healthcare access, and environmental factors to these disparities remain understudied. Therefore, we decomposed vaccination disparities by immigrant status to assess the contributions of these factors to the disparities.

Methods: Using data from the Canadian Longitudinal Study on Aging, we analyzed self-reported influenza and pneumococcal vaccination among adults aged 65 years and older. Logistic regression models were used to estimate the odds of vaccination in immigrant and non-immigrant participants and the non-linear Oaxaca-Blinder decomposition method was used to assess the contributions of covariates to the disparities in vaccinations by immigrant status.

Results: For influenza vaccination, differences in covariate distributions (i.e., covariate effect) accounted for -50% of the disparity, suggesting that vaccination rates would be higher for immigrants compared to non-immigrants by half of the observed disparity if distribution of covariates were to be the same between immigrants and non-immigrants. Differences in covariate effects (i.e., coefficient effect) accounted for 150% of the disparity. For pneumococcal vaccination, differences in covariate distributions accounted for 37% of the disparity and the remaining 63% were attributed to coefficient effects. The relative contributions of specific covariates varied between the two vaccines.

Conclusions: Our findings suggest that equalizing covariate distributions could reverse disparities in influenza vaccination rates and reduce pneumococcal disparities by 37%. Future research should identify additional modifiable factors and develop vaccine-specific strategies to address disparities.

LATEBREAKER

Health Disparities

Age Differences in Superwoman Schema Endorsement Among Black Women Navigating Infertility Lasha Clarke* Lasha Clarke Izraelle McKinnon Isabel Morgan Oluyemi Farinu Maya Thirkill Bhuvaneshwari Muchandi McKenzi Thompson Natalie Hernandez-Green Karenne Fru Christy Erving

Background: Black women experience disproportionately high infertility rates and structural barriers to care, yet the psychosocial dimensions of infertility, particularly the Superwoman Schema (SWS), remain underexplored. SWS describes expectations for Black women to show strength, suppress emotions, and prioritize others over self, which may influence coping with infertility. While WWS has been linked to mental and physical health, our study is the first to examine SWS in the context of infertility and to assess age-related differences.

Methods: We analyzed data from 139 Black women (ages 25–45) in the Morehouse School of Medicine Fertility Equity Study, a mixed-methods study examining infertility experiences. SWS was measured using a validated 35-item scale. The primary exposure was age group (25–34 vs. 35–45), and the primary outcome was total SWS endorsement and subscale scores. Linear regression models estimated the association between age and SWS, adjusting for education, income, employment, marital status, and/or parental status in various models. We conducted sensitivity analyses excluding participants with imputed SWS data (n=3).

Results: Younger women (25–34) had significantly higher total SWS scores than older women (35–45) (β=8.18, p=0.017). The largest subscale differences were observed for obligation to show strength (β=1.73, p=0.009) and obligation to help others (β=2.99, p=0.034), with younger women scoring higher. Adjusting for SES slightly attenuated these associations, but all remained significant, suggesting SES does not fully explain age differences in SWS endorsement. Sensitivity analyses confirmed robustness to missing data.

Conclusion: Superwoman Schema is a salient psychosocial factor in infertility experiences, with younger Black women reporting higher endorsement. The findings suggest generational differences in coping with infertility and highlight the need for age-sensitive, culturally informed interventions in reproductive healthcare.

LATEBREAKER

Health Disparities

The Association Between Birth Region and Risk of Poor Cardiovascular Health: Findings from Oaxaca-Blinder Decomposition Analysis Shabir Sarwary* Shabir Sarwary Lynne Messer Sarah Andrea

Background. Cardiovascular (CV) disease (CVD) is the leading cause of death worldwide. For Middle Eastern/North African (MENA) countries, CVD is responsible for >30% of deaths. Our understanding of CVD burden for MENA individuals in the US is limited because they are often miscounted as white.

Methods. We explored the association between birth region (US, Mexico or Central/South America, Europe, MENA, Asia) and CV health (CVH) among 72,845 adults from the National Health Interview Survey (2014-2018). CVH was defined using a modified version of the American Heart Association Life's Simple 7 metric (range: 0-5). Participants received a 0 for not meeting or 1 for meeting recommendations for 5 CVH indicators (hypertension, dyslipidemia, diabetes, body mass index, smoking status), then dichotomized to poor (0-3, n=39,056) or ideal (4-5, n=33,933). Risk ratios (RR) and 95% CI were obtained from binomial regression. The contribution of sociodemographic (age, sex) and immigration variables (citizenship, health insurance, time in US) to CVH inequities was quantified using the non-linear extension of the Oaxaca-Blinder decomposition.

Results. Ideal CVH was higher among MENA immigrants compared to US-born White respondents (RR=1.40, 95% CI: 1.33, 1.48), and also observed for other immigrant groups. Differences in sociodemographic and immigration features between Europe-born and MENA-born explain 83% (coefficient: -0.12) of the total difference in CVH, suggesting that a larger proportion of MENA-born had characteristics associated with ideal CVH compared to Europe-born. A similar pattern was observed for Hispanic-, but not Asian-born.

Discussion. This national study suggests MENA immigrants have higher amounts of ideal CVH despite having less favorable CVH-associated sociodemographic and immigration-related features. While our findings may suggest a healthy immigrant effect among MENA-born US adults, further research is needed to corroborate our results and elucidate drivers.

Health Disparities

Disaggregating the Asian Racial Category on the Kidney Transplant Waiting List Jesse Howell* Jesse Howell Oscar K. Serrano Alejandro Diaz

Purpose: The Organ Procurement and Transplantation Network (OPTN) reports race/ethnicity in aggregate, which simplifies reporting but lacks granularity. This analysis evaluates the Asian, non-Hispanic (NH) category according to geographic subgroups to assess for geographic and ethnic disparities in this population.

Methods: We analyzed Asian, NH kidney registrations on the OPTN waiting list (WL) between 7/1/2022-6/30/2024 using race/ethnicity data from the Transplant Candidate Registration Form. We calculated dialysis time at listing by taking the difference between the dialysis start date and the WL registration date, and demographic factors using counts and percentages. We estimated one-year graft survival using Kaplan Meier for those transplanted between 7/1/2022-6/30/2023.

Results: There were 15,868 registrations in the WL cohort. The largest group was Asian: Not Specified/Unknown (n=4,302) followed by Filipino (n=3,518), and Asian Indian/Indian Sub-Continent (AIIS) (n=2,492). Most Asian, NH candidates were listed in OPTN Region 5 (42%), but only 23% of AIIS candidates were listed in this region compared to 67% of Filipino candidates. AIIS candidates were more likely to have a post-college graduate degree compared to the WL cohort (27% vs 14%), while the Vietnamese group was more likely to have a level of education of grade school or less (15% vs. 8.1%). The median dialysis time at listing for Asian, NH candidates was 164 days, ranging from 65 for the AIIS group to 235 for the Korean group. One-year graft survival estimates were not significantly different and ranged from .91 to .97.

Conclusion: There were differences in all factors evaluated, with the most impactful being OPTN Region, education, and dialysis time at listing. This may be indicative of varying access for certain Asian, NH candidates, though graft survival was similar. Where numbers allow, racial/ethnic groups should be disaggregated to evaluate for differences in access in diverse populations.

Table 1: Demographic Characteristics of the Asian, non-Hispanic Category										
Characteristic	Overall, N = 15,868	Asian Indian/Indian Sub-Continent, N = 2,492	Asian: Not Specified/Unknown, N = 4,302	Asian: Other, N = 1,976	Chinese, N = 1,465	Filipino, N = 3,518	Japanese, N = 350	Korean, N = 612	Multiple Categories, N = 288	Vietnamese, N = 865
Age at Listing										
<18	203 (1.3%)	52 (2.1%)	61 (1.4%)	43 (2.2%)	12 (0.8%)	17 (0.5%)	2 (0.6%)	6 (1.0%)	2 (0.7%)	8 (0.9%)
18-34	1,389 (8.8%)	216 (8.7%)	486 (11%)	238 (12%)	103 (7.0%)	196 (5.6%)	6 (1.7%)	31 (5.1%)	18 (6.3%)	95 (11%)
35-49	4,176 (26%)	614 (25%)	1,205 (28%)	562 (28%)	352 (24%)	926 (26%)	59 (17%)	138 (23%)	82 (28%)	238 (28%)
50-64	6,757 (43%)	1,089 (44%)	1,718 (40%)	762 (39%)	616 (42%)	1,626 (46%)	182 (52%)	266 (43%)	119 (41%)	379 (44%)
65+	3,343 (21%)	521 (21%)	832 (19%)	371 (19%)	382 (26%)	753 (21%)	101 (29%)	171 (28%)	67 (23%)	145 (17%)
Birth Sex										
Female	6,374 (40%)	791 (32%)	1,746 (41%)	848 (43%)	587 (40%)	1,572 (45%)	113 (32%)	226 (37%)	136 (47%)	355 (41%)
Male	9,494 (60%)	1,701 (68%)	2,556 (59%)	1,128 (57%)	878 (60%)	1,946 (55%)	237 (68%)	386 (63%)	152 (53%)	510 (59%)
OPTN Region										
1	559 (3.5%)	100 (4.0%)	188 (4.4%)	123 (6.2%)	52 (3.5%)	36 (1.0%)	1 (0.3%)	9 (1.5%)	4 (1.4%)	46 (5.3%)
2	1,721 (11%)	401 (16%)	600 (14%)	194 (9.8%)	93 (6.3%)	228 (6.5%)	5 (1.4%)	99 (16%)	34 (12%)	67 (7.7%)
3	874 (5.5%)	185 (7.4%)	322 (7.5%)	124 (6.3%)	37 (2.5%)	91 (2.6%)	7 (2.0%)	20 (3.3%)	27 (9.4%)	61 (7.1%)
4	1,016 (6.4%)	220 (8.8%)	460 (11%)	89 (4.5%)	42 (2.9%)	94 (2.7%)	5 (1.4%)	12 (2.0%)	12 (4.2%)	82 (9.5%)
5	6,659 (42%)	563 (23%)	1,167 (27%)	749 (38%)	687 (47%)	2,355 (67%)	204 (58%)	303 (50%)	152 (53%)	479 (55%)
6	887 (5.6%)	47 (1.9%)	181 (4.2%)	66 (3.3%)	64 (4.4%)	329 (9.4%)	100 (29%)	35 (5.7%)	20 (6.9%)	45 (5.2%)
7	1,118 (7.0%)	138 (5.5%)	525 (12%)	251 (13%)	36 (2.5%)	114 (3.2%)	5 (1.4%)	19 (3.1%)	10 (3.5%)	20 (2.3%)
8	430 (2.7%)	71 (2.8%)	209 (4.9%)	46 (2.3%)	17 (1.2%)	34 (1.0%)	10 (2.9%)	15 (2.5%)	3 (1.0%)	25 (2.9%)
9	1,638 (10%)	598 (24%)	173 (4.0%)	203 (10%)	406 (28%)	161 (4.6%)	4 (1.1%)	67 (11%)	15 (5.2%)	11 (1.3%)
10	372 (2.3%)	83 (3.3%)	182 (4.2%)	37 (1.9%)	10 (0.7%)	35 (1.0%)	6 (1.7%)	5 (0.8%)	7 (2.4%)	7 (0.8%)
11	594 (3.7%)	86 (3.5%)	295 (6.9%)	94 (4.8%)	21 (1.4%)	41 (1.2%)	3 (0.9%)	28 (4.6%)	4 (1.4%)	22 (2.5%)
Insurance Status										
Not Reported	18 (0.1%)	3 (0.1%)	6 (0.1%)	4 (0.2%)	0 (0%)	2 (<0.1%)	0 (0%)	1 (0.2%)	1 (0.3%)	1 (0.1%)
Private or Self	8,188 (52%)	1,342 (54%)	2,216 (52%)	876 (44%)	698 (48%)	2,027 (58%)	218 (62%)	271 (44%)	148 (51%)	392 (45%)
Public or Charity	7,662 (48%)	1,147 (46%)	2,080 (48%)	1,096 (55%)	767 (52%)	1,489 (42%)	132 (38%)	340 (56%)	139 (48%)	472 (55%)
Education										
Grade School or Less	1,282 (8.1%)	192 (7.7%)	346 (8.0%)	313 (16%)	202 (14%)	62 (1.8%)	0 (0%)	22 (3.6%)	15 (5.2%)	130 (15%)
High School or GED	3,807 (24%)	563 (23%)	1,042 (24%)	545 (28%)	376 (26%)	696 (20%)	66 (19%)	163 (27%)	67 (23%)	289 (33%)
Attended College/Technical School	3,412 (22%)	313 (13%)	957 (22%)	374 (19%)	205 (14%)	1,105 (31%)	103 (29%)	130 (21%)	69 (24%)	156 (18%)
Associate/Bachelor Degree	4,806 (30%)	703 (28%)	1,200 (28%)	474 (24%)	413 (28%)	1,386 (39%)	121 (35%)	211 (34%)	93 (32%)	205 (24%)
Post-College Graduate Degree	2,146 (14%)	667 (27%)	580 (13%)	203 (10%)	234 (16%)	224 (6.4%)	53 (15%)	78 (13%)	38 (13%)	69 (8.0%)
<5 Yrs Old	34 (0.2%)	10 (0.4%)	10 (0.2%)	4 (0.2%)	2 (0.1%)	6 (0.2%)	0 (0%)	0 (0%)	1 (0.3%)	1 (0.1%)
Unknown/Not Reported	381 (2.4%)	44 (1.8%)	167 (3.9%)	63 (3.2%)	33 (2.3%)	39 (1.1%)	7 (2.0%)	8 (1.3%)	5 (1.7%)	15 (1.7%)
Blood Type										
A	3,635 (23%)	519 (21%)	964 (22%)	421 (21%)	358 (24%)	788 (22%)	140 (40%)	201 (33%)	64 (22%)	180 (21%)
AB	898 (5.7%)	171 (6.9%)	246 (5.7%)	114 (5.8%)	78 (5.3%)	143 (4.1%)	29 (8.3%)	53 (8.7%)	21 (7.3%)	43 (5.0%)
B	4,673 (29%)	825 (33%)	1,276 (30%)	618 (31%)	391 (27%)	1,016 (29%)	72 (21%)	174 (28%)	81 (28%)	220 (25%)
O	6,658 (42%)	976 (39%)	1,813 (42%)	823 (42%)	638 (44%)	1,571 (45%)	109 (31%)	184 (30%)	122 (42%)	422 (49%)
Transplanted										
Transplanted	4,441 (28%)	702 (28%)	1,203 (28%)	563 (28%)	417 (28%)	922 (26%)	91 (26%)	212 (35%)	87 (30%)	244 (28%)
Not Transplanted	11,427 (72%)	1,790 (72%)	3,099 (72%)	1,413 (72%)	1,048 (72%)	2,596 (74%)	259 (74%)	400 (65%)	201 (70%)	621 (72%)
Dialysis Time at Listing	164 (0, 559)	65 (0, 448)	165 (0, 537)	192 (0, 610)	87 (0, 486)	215 (0, 626)	114 (0, 479)	235 (0, 632)	211 (0, 682)	230 (0, 582)

[1] n (%); Median (IQR)

Health Disparities

Using a Counterfactual Framework to Understand the Underlying Causes of Black-White Racial Disparities in Breast Cancer Mortality in the US Maret Maliniak* Maret Maliniak Jeffrey M. Switchenko Leah Moubadder Rebecca Nash Lindsay J. Collin Lauren E. McCullough

Background: Black women have the highest breast cancer (BC) mortality rate of any race group in the US. The disparity is often attributed to a higher prevalence of poor prognostic factors, such as estrogen receptor (ER)−negative tumors. However, racial disparities in BC survival are worse for patients with ER−positive tumors. Determining whether the BC mortality disparity is driven by the higher prevalence of poor prognostic factors or worse post-diagnosis survival can guide needed interventions.

Methods: Incident case counts and survival data for non-Hispanic Black (NHB) and non-Hispanic White (NHW) patients diagnosed with invasive BC between 31 to 84 years old during 2010 to 2019 were obtained from the US Surveillance, Epidemiology, and End Results (SEER)-17 cancer registries. We calculated age-standardized incidence-based mortality (IBM) rates for both NHB and NHW women in 2019 using patient data and the 2019 population-at-risk data from SEER. We used a counterfactual framework to estimate the Black-White ratios of IBM (IBMBW) assuming equal distributions of ER status or equal hazard rates of BC death (overall and by ER status) among NHB and NHW women.

Results: We included 50,922 NHB and 305,642 NHW BC cases in our analysis. Compared with NHW patients, NHB patients were more likely to have ER−negative tumors (28% vs. 15%). The estimated IBM rate per 100,000 for NHB women was 41.4 compared with 24.8 for NHW women (IBMBW = 1.67). When assuming equal distributions of ER status, IBMBW decreased from 1.67 to 1.43. When assuming equal hazard rates among NHB and NHW patients, regardless of ER status, IBMBW decreased from 1.67 to 0.87.

Conclusion: Our preliminary results suggest the racial disparity in BC mortality can be eliminated when survival rates, but not subtype distribution, are matched among NHB and NHW patients, underscoring the importance of post-diagnosis survival for mitigating racial disparities.

Health Disparities

Understanding Colorectal Cancer Disparities in the Mississippi Delta: The Role of Screening and Social Determinants of Health Sudheer Koutha* Sudheer Koutha

Title

“Understanding Colorectal Cancer Disparities in the Mississippi Delta: The Role of Screening and Social Determinants of Health”

Background

Colorectal cancer (CRC) is the second leading cause of cancer-related deaths in the United States. Mississippi leads the nation in CRC mortality, with an age-adjusted rate of 17.6 per 100,000 population (2018–2022). The Mississippi Delta, a region marked by high rates of chronic disease and significant socioeconomic challenges, bears a disproportionate burden of CRC. This study examines disparities in CRC outcomes and screening rates in the Delta, with a focus on understanding the interplay of risk factors and social determinants of health.

Methods

A cross-sectional analysis was conducted using data from the Mississippi Cancer Registry, Behavioral Risk Factor Surveillance System (BRFSS), and Social Vulnerability Index (SVI). CRC incidence, mortality, and screening rates were stratified by gender, race, and socioeconomic status. Modifiable risk factors, including obesity, smoking, physical inactivity, and suboptimal screening uptake, were assessed. Geospatial mapping was utilized to visualize the distribution of CRC outcomes, disparities, and screening gaps across the region.

Results

From 2018–2022, Mississippi’s CRC mortality rate (17.6 per 100,000) exceeded the national average (12.9 per 100,000) by 36%. Disparities were pronounced among Black males, who had a CRC mortality rate of 27.9 per 100,000—32% higher than the national rate for Black males (21.3 per 100,000). In the Delta region, Black males experienced a mortality rate of 37.0 per 100,000, 66% higher than their White counterparts (22.3 per 100,000). Screening rates were suboptimal, with only 59% of adults aged 45 and older meeting USPSTF recommendations in 2022. Delta counties consistently reported the lowest screening rates and highest mortality rates, exceeding the state average of 17.6 per 100,000.

Conclusions

Colorectal cancer disparities in the Mississippi Delta are driven by a confluence of modifiable risk factors, socioeconomic inequities, and limited access to preventive care. This study highlights the critical need for culturally tailored screening programs, enhanced healthcare access, and interventions addressing social determinants of health. Urgent, targeted efforts are essential to reduce CRC burden and improve health equity in this high-risk population.

Health Services/Policy

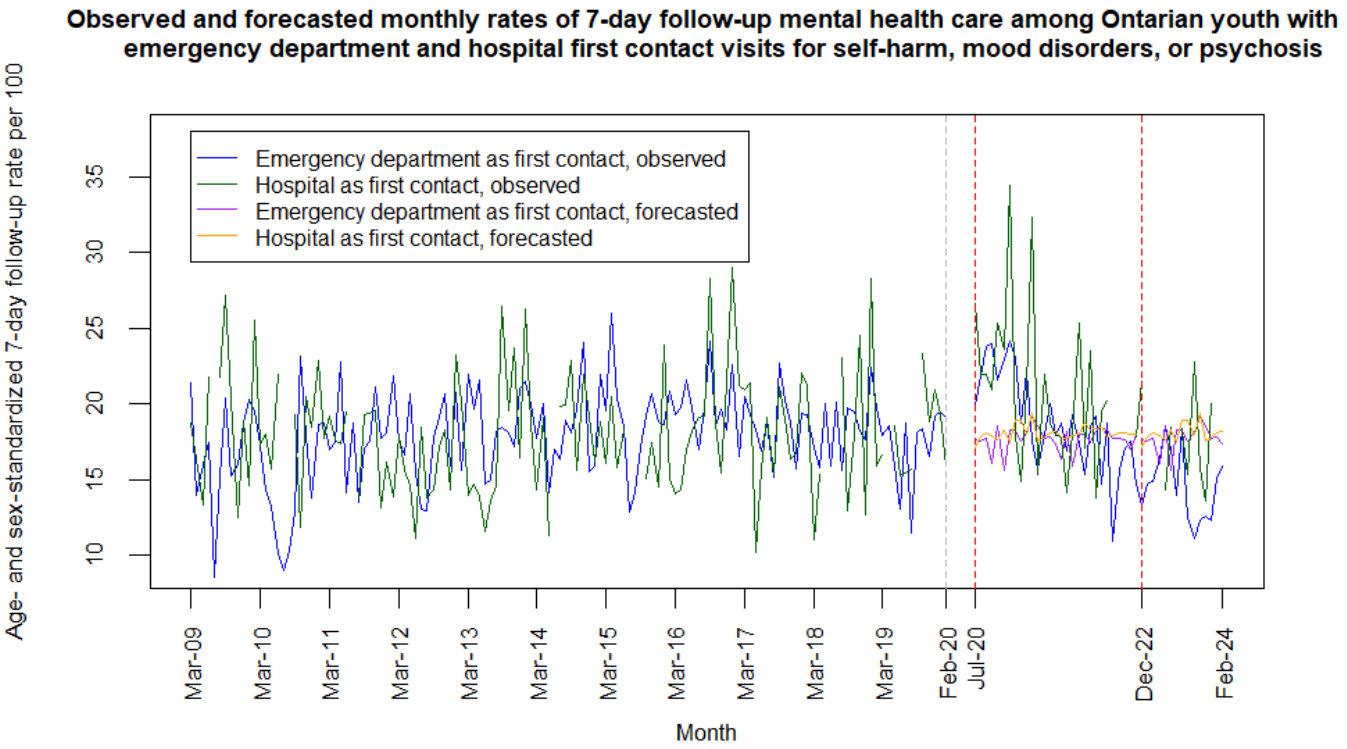
The association between the introduction of virtual care and follow-up mental health care among youth whose first mental health contact was through the emergency department or hospital Erica Wennberg* Erica Wennberg Aditi Patrikar Amreen Babujee Peter Austin Paul Kurdyak Kate Nelson Astrid Guttmann

Background: Timely follow-up care is crucial for youth whose first mental health contact is through an emergency department (ED) visit or hospital admission; virtual care could facilitate this. We examined the association between the introduction of virtual care in Ontario, Canada and rates of follow-up mental health care for these youth.

Methods: We conducted a population-based repeated cross-sectional study using linked health administrative databases. We identified youth (10-24 years old) with an ED or hospital first contact visit for self-harm, mood disorders, or psychosis between 1/Mar/2009 and 29/Feb/2024. Virtual care was introduced through temporary (Mar/2020-Nov/2022) and permanent billing codes (Dec/2022-present) (TBCs and PBCs). We used an ARIMA interrupted time series analysis to examine changes (vs pre-virtual care) in age- and sex-standardized monthly rates of 7-day mental health follow-up, with a March-June 2020 wash-out period.

Results: The study population included 40,598 youth with an ED (70.6%) and 16,886 with a hospital first contact visit. Pre-virtual care, the average standardized monthly rate of 7-day follow-up was 17.9 per 100 for youth with ED visits, and 18.1 per 100 for admitted youth. In the ED group, TBC introduction was associated with an immediate increase in 7-day follow-up (step change=5.3; 95% CI: 3.4 to 7.2), which then decayed (ramp change=-0.28; -0.38 to -0.17). In the admitted group, there was a similar immediate increase (step change = 6.6; 3.4 to 9.8) and subsequent decline (ramp change= -0.29; -0.49 to -0.10) in rates with TBC introduction. PBC introduction was not associated with significant changes in either group vs pre-virtual care.

Conclusion: For youth whose first mental health contact was through the ED or hospital, virtual care was not associated with changes in follow-up rates, excepting an initial increase in the first year of the COVID-19 pandemic. Further analyses will stratify by rurality and socioeconomic status.


Observed and forecasted monthly rates of 7-day follow-up mental health care among Ontarian youth with emergency department and hospital first contact visits for self-harm, mood disorders, or psychosis
Emergency department as first contact, observed
Hospital as first contact, observed
Emergency department as first contact, forecasted
Hospital as first contact, forecasted
Age- and sex-standardized 7-day follow-up rate per 100
10
15
20
25
30
35
Mar-09
Mar-10
Mar-11
Mar-12
Mar-13
Mar-14
Mar-15
Mar-16
Mar-17
Mar-18
Mar-19
Feb-20
Jul-20
Dec-22
Feb-24
Month

Health Services/Policy

Gender-Affirming Care Providers' Perspectives on the Question of Evidence: A Qualitative Study Laura Stamm* Laura Stamm Alaap Rag Ahona Shirin Inthava Muneath Maya Daniello

Objectives: Current policies on gender-affirming care (GAC) for transgender and gender-diverse (TGD) youth often exclude the perspectives of providers who specialize in GAC. This study aims to understand the perspectives of providers (MD, DO, PA, NP) treating TGD youth in politically and socially challenging environments, paying particular attention to how they view the role of evidence in their approach to GAC.

Methods: Forty-three semi-constructed interviews with providers of GAC were conducted by the study's principal investigator. The participants represent states with differing GAC legislation (shield law, legislative ban, no legislation), highlighting difficulties in practicing evidence-based care in areas with legislative bans. The interviews were analyzed thematically using qualitative coding. The following question is analyzed for this poster: Is there any evidence that would cause you to rethink your current position on GAC for minors? If yes, what?

Results: Of the 43 providers interviewers, 30 answered no to the question and 13 answered yes. For clinicians who answered no, the following themes emerged: evidence-based care, patient empowerment, and impact of delayed or denied care. For clinicians who answered yes, emerging themes included: open to future evidence, evidence-based care, and best practices. Regardless of their answer, providers emphasized the importance of evidence-based care to best treat TGD youth.

Conclusion: The study found that providers support necessary gender-affirming care for adolescent patients while also acknowledging the need for further research on best practices. These findings can help providers and legislators improve access to GAC for TGD youth and further the general scientific understanding of GAC.

Health Services/Policy

Validation of a health system-focused morbidity score for the Canadian population Emmalin Buajitti* Emmalin Buajitti Laura Rosella

Background. Multimorbidity is an important determinant of health care need and complexity, and presents a growing challenge for single-payer health care systems such as Canada's. Multimorbidity measurement in Canada has historically relied on equal- or mortality-based weighting of chronic conditions (e.g., Charlson index, number of chronic conditions). To better support health system planning and population health, we sought to create a health care utilization-driven morbidity score using multi-linked health administrative data.

Methods. Following the approach of the UK-based Cambridge Multimorbidity Score, we identified 23 common chronic conditions using outpatient and inpatient records for all Ontario residents since April 1992. For those alive in April 2022 (n=15,303,282), we identified 3 health system-relevant outcomes (number of primary care visits, unplanned hospitalization, and death) between April 2022 and March 2023. We used logistic regression and Poisson models to estimate outcome-specific coefficients, which we pooled to create a general-outcome weight for each condition. We compared the accuracy of our score to the original CMS using c-statistics for mortality and hospitalization.

Results. The 3 chronic conditions with the highest general-outcome weights were dementia (weight=2.11), substance use problems (1.77), and congestive heart failure (1.44). The condition weights and rank order were substantively different in Canada compared to the original CMS. The morbidity score slightly outperformed the original CMS in the Ontario population, with c-statistics of 0.880 and 0.807 for 1-year risk of death and hospitalization, respectively (CMS = 0.876 and 0.784).

Conclusion. Health system-focused morbidity scores accurately predict risk of death and hospitalization in a Canadian population. Locally-derived scores can support appropriate, context-driven health system planning and population health management.

Health Services/Policy

Trends in adverse perinatal outcomes and associated hospitalisations and healthcare costs between birth and early childhood in Northern Territory, Australia: A two-decade population-based study Tsegaye Haile* Tsegaye Haile Gavin Pereira Richard Norman Gizachew A. Tessema

Background: Perinatal morbidity, including preterm birth (PTB), small-for-gestational-age (SGA), and low birthweight (LBW) continue to impact children's health and healthcare demands in Northern Australia. We investigated the incidence, hospitalisation and Emergency Department (ED) presentations of these outcomes, and its associated healthcare costs up to age five from a health system perspective.

Methods: We used a retrospective cohort data of births from July 1, 2000, to June 30, 2016, from the Perinatal Trends dataset linked to the Inpatient and ED activity datasets. and cost-weight data. We measured healthcare costs using direct medical and non-medical costs and examined the trends across years and over childhood. All costs were standardised to Australian dollars (AUD, as of June 2024). To identify the drivers of cost, we used a Generalized Additive Model with a gamma distribution and log link function.

Findings: A total of 31,183 births were linked to hospitalisation and 42,174 to ED presentation. We found 8·7% PTB, 12·8% SGA and 7·7% LBW children. The mean hospitalisation per child was 3.1, and ED presentations were 3.0 over the first five years, with an increasing trend over the last decade, while the length of hospital stays decreased. The median hospitalisation cost per preterm child was AUD7,758(IQR: AUD 5,212 to 11,601), and the ED presentation cost was AUD 775(IQR: AUD 590 to 1,016) in the first five years. For SGA, the median hospitalisation cost was AUD 6,139 (IQR: AUD 4,278 to 8,639) and ED cost was AUD 720 (IQR: AUD 552 to 948). We observed higher costs of hospitalisations and ED presentations in later cohorts, while individual costs decreased as the child aged. Remoteness, Indigenous status, extremely low gestational age and birthweight, and length of hospital stay were the main drivers of costs.

Interpretation: The burden of adverse perinatal outcomes is increasing in the Northern Territory, imposing higher healthcare utilisation and costs, particularly due to extended hospital stays. Vulnerable populations, including Indigenous children and those in remote areas, incur higher healthcare costs than the average. Addressing this dual health and economic burden is crucial for cost savings and improving long-term well-being.

Health Services/Policy

Variations in Physician Age: A United States Urban–Rural Comparison Ryan Crowley* Ryan Crowley Jag Lally David M. Kline Amanda M. Bunting

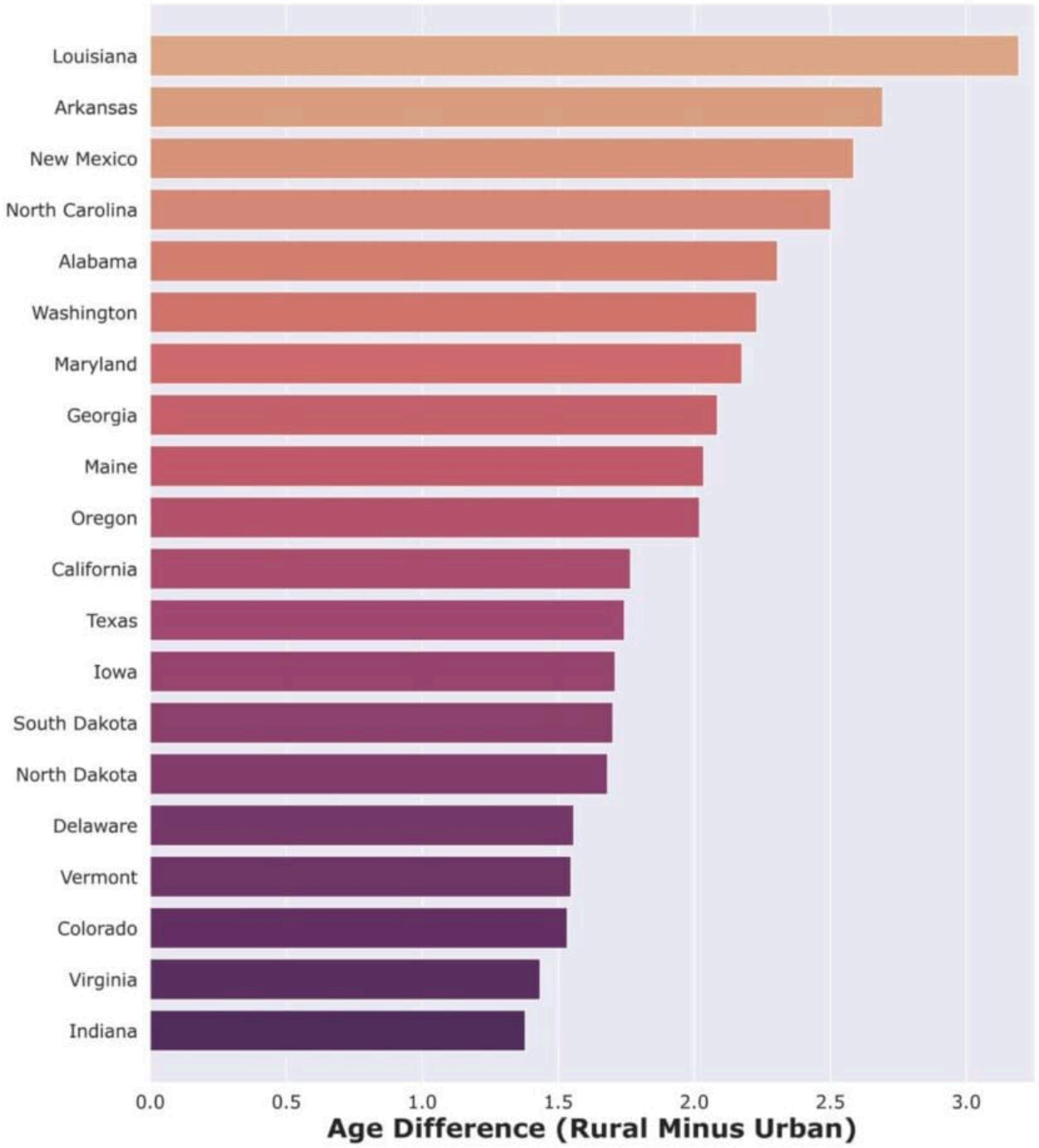
Background: Individuals in rural areas often suffer from a lack of adequate health care resources. The uneven distribution of physicians between urban and rural areas could exacerbate healthcare disparities, and these disparities could be worsened as physicians age and retire. We aimed to assess whether there are regional differences in the mean age of physician providers in urban versus rural areas.

Methods: We linked the Center for Medicare and Medicaid Services' Medicare Data on Provider Practice and Specialty (MD-PPAS) dataset with the November 2024 CMS Doctors and Clinicians national downloadable file using the National Provider Identifier (NPI). We used Rural-Urban Continuum Codes (RUCCs) as the metric of rurality with urban areas defined as RUCC codes 1-3 and rural areas defined as RUCC codes 4-9. We then identified the 20 states with the largest, statistically significant discrepancies in mean physician ages between urban and rural areas. We assessed differences in the mean age of physician providers in urban versus rural areas for states using a two-sample t-test for significance.

Results: Our linked cohort comprised 576,588 physicians. The average age across the US in urban areas was 52.5 years, and the average age in rural areas was 53.4 years (p-value <.00001). The states with the greatest difference in age between urban and rural areas with older providers in rural areas are Louisiana (3.2 years), Arkansas (2.7 years), and New Mexico (2.6 years). Only two states (New Jersey and New York) had statistically significant differences in age between urban and rural areas with older physicians in urban areas.

Conclusion: Physicians in rural areas are older than physicians in more urban areas, with certain states demonstrating especially large age disparities. These findings have important policy implications as aging of the rural physician workforce could exacerbate urban-rural health access disparities.

Figure: Top 20 States with the Largest Statistically Significant Difference in Mean Physician Age between Rural and Urban Areas



Health Services/Policy

Quantifying the primary care workforce in the U.S: A validation study with and without an imperfectly measured referent standard Nicole Rafalko* Nicole Rafalko Scott Siegel Paul Yerkes Jan Eberth Igor Burstyn Neal Goldstein

Purpose: To validate the ability of a commonly used data source, the National Provider Identifier (NPI), to identify primary care physicians, physician assistants (PAs), and nurse practitioners (NPs).

Methods: Validation studies were conducted calculating the sensitivity, specificity, and associated 95% confidence intervals for physicians, PAs, and NPs. For physicians, Medicare claims data was used as an imperfectly measured referent standard. For PAs and NPs, we used a simulation-based method to estimate sensitivity, specificity, and associated 95% credible intervals that assumes the NPI and Medicare claims are equally error-prone.

Results: Using the Medicare claims as the referent standard for physicians yielded a sensitivity and specificity of 0.9 (95% CI: 0.8, 1.0) and 0.8 (95% CI: 0.7, 0.8), respectively. Using the simulation-based method yielded a sensitivity and specificity of 0.6 (95% CI: 0.1, 1.0) and 0.5 (95% CI: 0.1, 1.0), respectively for physician assistants and 0.6 (95% CI: 0.1, 1.0) and 0.6 (95% CI: 0.1, 1.0), respectively for nurse practitioners.

Conclusions: Our validation results varied by provider role, with the highest accuracy observed for physicians further highlighting the challenges in quantifying PAs and NPs. Failure to consider potential misclassification in the NPI may result in biased health services research.

LATEBREAKER

HIV / STI

Development and Evaluation of an AI-Based Chatbot for HIV Pre-Exposure Prophylaxis Promotion Among Men Who Have Sex With Men Jun Tao* Jun Tao Ellie Pavlick Amaris Grondin Josue D. Bustamante Harrison Martin Hannah Parent Natalie Fenn Alexi Amonte Mofan Gu Jack Rusely Philip A. Chan

Background: Despite the effectiveness of HIV pre-exposure prophylaxis (PrEP), uptake remains low. Motivational interviewing promotes PrEP use but is resource-intensive, limiting scalability. Advances in large language models offer a scalable approach to delivering MI-based counseling. This study describes the development and evaluation of CHIA (Chatbot for HIV Prevention and Action), an AI-driven chatbot designed to conduct MI-informed counseling, deliver tailored HIV/PrEP education, and promote PrEP uptake among men who have sex with men. **Methods:** CHIA was developed using the AutoGen agentic framework, integrating three agents: the PrEP Counselor Agent for MI-based interactions, the Retrieve Agent for accessing validated HIV/PrEP information, and the Teachable Agent for retaining user-specific details to ensure continuity. CHIA operates on a fine-tuned ChatGPT-4o model trained on diverse MI transcripts. Its knowledge base, updated monthly with expert-validated content in English and Spanish, is optimized through fine-tuning and prompt engineering. Deployed in a secure AWS cloud environment with authentication, CHIA was evaluated using structured response- and conversation-level metrics. Evaluation scores will be passed into a reinforcement learning framework to improve CHIA's performance over time. **Results:** Preliminary assessments indicate CHIA effectively integrates MI skills, including open-ended questioning and reflective listening, while minimizing biased or misleading responses. CHIA consistently recalled and applied user-specific information across sessions. However, improvements are needed in human-like conversational style to enhance engagement and in the graphical interface to improve usability. **Conclusions:** CHIA represents a scalable, AI-driven approach to MI-based PrEP counseling. Future work will enhance human-like conversation, personalization, and multilingual support. These findings inform best practices for AI-driven public health interventions.

LATEBREAKER

HIV / STI

Understanding the prospective relationship between psychosocial factors and initiation of HIV pre-exposure prophylaxis (PrEP) among transgender women who are indicated for use

Roxana Rezai* Roxana Rezai Elizabeth A. Yonko Eun Kwak Jackie W. Hughto Bianca Robinson Katie B. Biello Matthew J. Mimiaga

Background: Transgender women (TGW) are the group at highest risk for HIV in the US, yet they remain underrepresented in studies on pre-exposure prophylaxis (PrEP). Antiretroviral PrEP is a highly effective at preventing HIV acquisition, but factors related to PrEP uptake, including social perceptions and satisfaction with one's gender identity and expression, among this population are complex. This study prospectively examined these factors and their association with PrEP initiation among TGW.

Methods: Data are from a randomized controlled trial of a behavioral intervention to increase PrEP update among adult TGW who are vulnerable to HIV. From 2022-2024, 99 TGW were enrolled. Bivariate and multivariable logistic regression was used to model the prospective relationship between gender affirmation (scale: 1-5, low to high gender affirmation), collective self-esteem (scale 1-7, low to high self-esteem), and PrEP subjective norms (scale: 0-24, low to high perception of how important others think they should behave) and our outcome, PrEP initiation within 1-month after enrollment; our final model adjusted for covariates and study arm.

Results: About 32% of the sample identified as a racial/ethnic minority, 15% were uninsured, and had a mean age of 30 years (SD=7.7); all participants were indicated for PrEP using the CDC's guidelines. Thirty four percent (n=33) initiated PrEP within 2-months.

In an adjusted multivariable model, gender affirmation (aOR=2.45, 95% CI: 1.06-5.67), collective self-esteem (aOR=2.34, 95% CI: 1.15-4.79), and PrEP subjective norms (aOR=1.23, 95% CI: 1.04-1.45) were all associated with an increased odds of PrEP initiation within 2-months.

Conclusion: Findings highlight the importance of social perceptions and satisfaction with one's gender identity and expression among TGW who initiate PrEP. Future research should assess the utility of an intervention that addresses these mechanisms as a method for enhancing PrEP initiation among TGW.

HIV / STI

Menstrual and menopausal health concerns of Women with HIV (WWH) in the United States: an exploratory study Deepthi S. Varma* Deepthi Varma Rebekah Kertz Kendall Robinson Kayla McNeely Liana Hone Robert Cook

Introduction: Women with HIV (WWH) face severe menstrual issues and earlier menopausal symptoms due to factors including HIV, STIs, stress, substance use, and reproductive health conditions.

Methods: Twenty-three WWH in Florida participated in 60-minute Zoom interviews, conducted using an IRB-approved semi-structured guide. Interviews were recorded, transcribed, quality-checked, and analyzed with Atlas.ti™. Two independent coders systematically coded the transcripts. In weekly team meetings they reconciled discrepancies and finalize codes collaboratively. In a second coding cycle, similar codes were grouped into broader themes, with subthemes identified to capture insights.

Results: Eleven women were aged 38-57, six were 18-37, and six were 57 or older. Nine were single, four married, two widowed, five divorced, and three living with a partner. Three women were diagnosed with HIV within the past five years, three within the last decade, and the rest over 10 years ago. Fourteen women reported current substance use, and all but one had a primary care provider. Key menstrual concerns included irregular cycles and flow, pain and treatment, premenstrual symptoms, fear of transmission during menstruation, ART/substance use impacts, and provider discussions. Menopause-related concerns included onset, symptoms (e.g., hot flashes, night sweats, irregular bleeding), and treatment.

Discussion: This study highlights the multifaceted menstrual and menopausal health challenges faced by WWH, emphasizing the urgent need for age-specific, culturally sensitive, and holistic care strategies that address menstrual irregularities, menopausal symptoms, and the interplay of ART, substance use, and stigma. Findings are crucial for optimizing symptom management, enhancing well-being, and improving provider-patient communication.

HIV / STI

Impact of Dolutegravir vs Efavirenz on Weight and Blood Pressure Among New Initiates in Johannesburg, South Africa: A 24-Month Study Amy Zheng* Amy Zheng Alana T. Brennan Eleanor J. Murray Jacob Bor Matthew P. Fox Willem DF Venter Mhairi Maskew

In 2019, South Africa's antiretroviral therapy (ART) treatment guidelines replaced efavirenz (EFV) with dolutegravir (DTG) in first-line ART. Some studies have shown associations with increased weight and blood pressure (BP) with DTG compared to EFV. We evaluated changes in weight, body mass index (BMI), diastolic and systolic BP from baseline to 12- and baseline to 24-months in people ART naïve initiating DTG to those initiating EFV.

We conducted a prospective cohort study of 13,507 adults from the Themba Lethu Clinical Cohort in Johannesburg who newly initiated onto DTG or EFV from January 2010-December 2021. Characteristics for those who initiated DTG or EFV were balanced using inverse probability weighting (IPW) based on directed acyclic graphs. IPW for missing data and retention were also generated. Linear regression models were used to evaluate outcomes.

Among 13,507 participants, 1,878 (14%) initiated a DTG-based regimen and 11,629 (86%) initiated an EFV-based regimen. At 12-months, those who initiated a DTG-based regimen had a higher mean change in weight (2.1 kilograms (kg); 95% Confidence Interval (CI): -4.2,8.4), BMI (0.8 kg/m2; 95% CI: -1.6,3.1), and systolic BP (2.8 mmHg; 95% CI: 0.9,4.8) compared to those initiating EFV-based regimens. Diastolic BP essentially remained unchanged (-0.4 mmHg; 95% CI: -1.8,1.0) among those who initiated DTG compared to those who initiated EFV. We observed similar trends at 24-months (Table 1).

Our estimates suggest weight steadily increases over the first 24 months of DTG treatment; the greatest change in systolic BP occurs in the first 12 months, followed by a plateau. While DTG is associated with greater weight gain and increased systolic BP compared to EFV, EFV's weight-suppressing effects may influence these results. Future studies should clarify whether these differences are driven by DTG or EFV's effects, as this will be important for guiding treatment decisions and managing long-term health risks for patients.

Table 1. Comparing DTG to EFV mean changes in weight, BMI, systolic and diastolic BP from initiation of treatment to 12- and 24-months

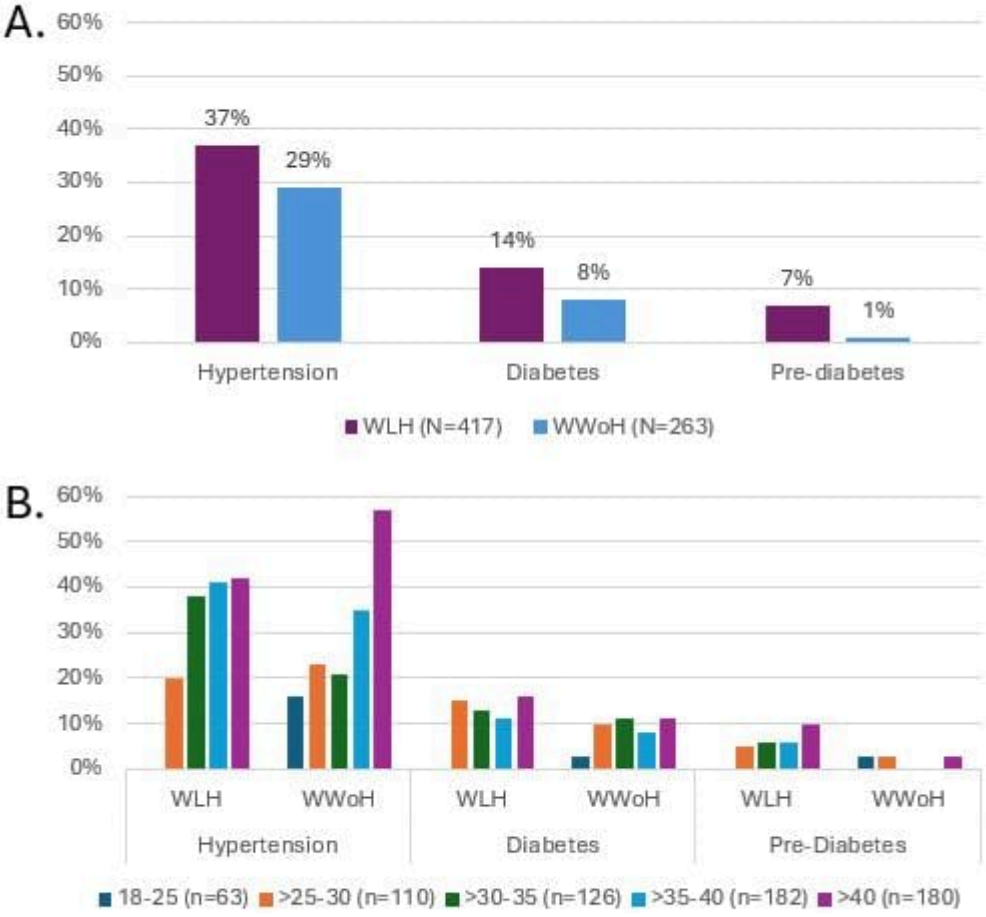
	Dolutegravir			Efavirenz			0-12 Month Change	0-24 Month Change
	Baseline Mean (SD)	*12-Month Mean (SD)*	*24-Month Mean (SD)*	*Baseline Mean (SD)*	*12-Month Mean (SD)*	*24-Month Mean (SD)*		
Weight	65.3 (16.1)	72.6 (17.1)	77.2 (48.4)	64.3 (14.3)	68.9 (15.0)	70.8 (15.8)	2.1 (-4.2, 8.4)	5.2 (5.0, 5.5)
BMI	24.4 (6.2)	27.1 (6.5)	28.8 (15.9)	23.8 (5.8)	25.5 (6.9)	26.2 (6.5)	0.8 (-1.6, 3.1)	1.4 (0.9, 1.9)
Diastolic BP	80.9 (13.8)	82.0 (12.2)	82.2 (11.8)	78.3 (13.6)	78.3 (12.9)	79.1 (12.9)	-0.4 (-1.8, 1.0)	-4.3 (-6.1, -2.5)
Systolic BP	126.5 (28.3)	131.2 (16.3)	132.3 (14.6)	125.1 (19.4)	126.5 (18.3)	128.8 (18.0)	2.8 (0.9, 4.8)	2.6 (0.1, 5.0)

HIV / STI

HIV Status and Cardiometabolic Comorbidities among Reproductive Aged Women in the STAR Cohort Danielle J. Carson* Angela Bengtson Danielle J. Carson Lauren F. Collins Christina C. Mehta Seble G. Kassaye Aadia Rana Daniel Westreich Elizabeth F. Topper Maria L. Alcaide Anandi N. Sheth

Women living with HIV (WLH) are at greater risk of cardiometabolic comorbidities than women living without HIV (WWoH) and may experience these conditions at younger ages. However, little is known about the burden of cardiometabolic comorbidities in WLH of reproductive age. Using data from the Study of Treatment and Reproductive Outcomes in Women (STAR) cohort, including WLW and WWoH across 6 sites in the Southeast United States, we assessed the prevalence of cardiometabolic comorbidities at enrollment, evaluated associations between HIV status using multivariable log binomial models, and explored effect modification by age. Cardiometabolic comorbidities were evaluated at cohort enrollment and included: 1) hypertension (systolic blood pressure (BP) ≥140 or diastolic BP ≥90 (international standard) or anti-hypertensive medication); 2) type 2 diabetes (anti-diabetic medication or HgbA1c ≥6.5% and fasting blood glucose (FBG) ≥126 mg/dL); 3) pre-diabetes (HgbA1c 5.7-6.4% and FBG 100-125 mg/dL). Among 680 women (417 WLH, 263 WWoH) at enrollment, the median age was 37 (IQR 30,41), median BMI was 32 kg/m2 (IQR 26, 42), and 75% identified as non-Hispanic Black race. Compared to WWoH in unadjusted analyses, WLH had a higher prevalence of hypertension (37% vs 29%), diabetes (14% vs 8%) and pre-diabetes (7% vs 1%) (Figure 1A) and had a higher prevalence of these comorbidities at younger ages (Figure 1B). After adjustment for age, obesity status, education, and ever smoking, HIV was not associated with prevalent hypertension (PR 0.85 95% CI 0.64, 1.13) or diabetes (PR 1.33 95% CI 0.70, 2.54) but was associated with prevalent pre-diabetes (PR 4.11 95% CI 1.20, 14.03), although precision was limited. In this diverse cohort of reproductive-aged WLH and WWoH, the burden of cardiometabolic comorbidities was high. Longitudinal follow-up is needed to determine how HIV status affects the incidence and age at onset of cardiometabolic comorbidities in reproductive-aged women.

Figure 1. Cardiometabolic comorbidities at enrollment into the STAR cohort among N=680 reproductive aged women living with HIV (WLH) and women without HIV (WWoH) A) overall B) stratified by age group.



Hypertension defined as systolic blood pressure (BP) ≥140 or diastolic BP ≥90 or anti-hypertensive medication. Type 2 diabetes defined as anti-diabetic medication or HgbA1c ≥6.5% and fasting blood glucose (FBG) ≥126 mg/dL). Pre-diabetes defined as HgbA1c 5.7-6.4% and FBG 100-125 mg/dL.

HIV / STI

Lost But Not Forgotten—An Analysis of Factors Associated with Loss to Follow-Up in a Randomized Controlled Trial Kara Herrera* Kara Herrera Mark S. Dworkin

Background: Ethnic minorities and youth are priority populations for HIV-related health interventions but are more likely to be lost to follow-up (LTFU) in randomized controlled trials (RCTs). Given RCTs provide the highest level of evidence to establish causal associations in clinical research and attrition can undermine study finding validity, understanding LTFU is essential. Therefore, we determined factors associated with LTFU among young Black men who have sex with men (BMSM).

Methods: We recruited young (18-34 years) HIV-positive BMSM throughout the United States for an RCT of an iteratively developed avatar mobile app intervention designed to promote antiretroviral adherence vs. an avatar app attention control focused on food safety. Enrollment coincided with COVID-19 stay-at-home orders. Participants were randomized in a 1:1 ratio to the intervention or attention control app and followed for 6-months. Logistic regression using backward model selection were employed to determine factors associated with LTFU.

Results: One-quarter (26.5%) of 253 young BMSM were LTFU at the 6-month follow-up. For each point increase in the Multidimensional Scale of Perceived Social Support, the prevalence of LTFU was 0.86 times as likely (PR: 0.86; 95% CI: 0.76-0.97). Additionally, those randomized to the attention control arm had over two-fold increased prevalence of LTFU compared to those randomized to the intervention (PR: 2.48; 95% CI:1.06-5.79).

Discussion: This is the first analysis investigating factors associated with LTFU in an RCT among HIV-positive BMSM. High LTFU was observed and was associated with randomization to the control arm and lower self-perceived social support. Future studies of young BMSM should consider developing an attention control as engaging as the intervention to minimize LTFU. Additionally, determining the prevalence of lower self-perceived social support during RCT approach development might be considered to obtain accurate sample size estimates.

HIV / STI

National HIV Testing Trends Among U.S. Adults, 2018-2023 Deesha Patel* Deesha Patel Weston O. Williams Carolyn Wright

HIV testing allows persons to become aware of their HIV status and to seek subsequent care. HIV screening is recommended for the general population, and more frequent HIV testing is recommended for groups at higher risk for HIV acquisition.

2018-2023 data from the Behavioral Risk Factor Surveillance System were analyzed to calculate percentages of ever tested for HIV and tested for HIV in past 12 months, overall and by age, sex, and race/ethnicity. A test for linear trends was conducted using logistic models, accounting for complex survey weights. To provide a meaningful description for linear trends, estimated annual percentage changes (EAPC) were calculated from model estimates. Sensitivity analysis was conducted to assess trends adjusting for the COVID-19 pandemic (i.e., years 2020 and 2021).

Overall, ever tested for HIV decreased from 40.2% in 2018 to 38.9% in 2023 (EAPC -1.6%, $p<.0001$). Decreases were observed for majority of subgroups, with the largest declines observed among persons aged 18-24 and 25-34 years (EAPC -3.8% for both) and Black/African American persons (EAPC -3.1%) (all $p<.0001$). Increases were observed among persons aged 45-64 years (EAPC +0.6%, $p=.013$) and ≥65 years (EAPC +1.9%, $p<.0001$). Overall, tested for HIV in the past 12 months decreased from 11.8% in 2018 to 11.3% in 2023 (EAPC -3.2%, $p<.0001$). Decreases were observed for most subgroups, with the largest declines observed among persons aged 18-24 (EAPC -6.6%) and 25-34 years (EAPC -4.7%) and Black/African American (EAPC -6.1%) (all $p<.0001$). No meaningful differences in estimates were found between primary and sensitivity analyses.

From 2018-2023, percentages of ever tested and tested in past 12 months generally declined for U.S. adults, including in groups that are at greater risk for HIV acquisition. HIV screening can be strengthened by expanding opt-out screening in healthcare settings and promoting HIV testing through non-traditional settings (e.g., self-test kits, mobile outreach).

Infectious Disease

Under-reporting of SARS-CoV-2 Infections in 27 Countries, 2020–2022. Kate Devlin* Mustapha Mustapha Kanae Togo Hannah R Volkman Jingyan Yang Alon Yehoshua Manuela Di Fusco John M McLaughlin Jennifer L Nguyen

Background

It is increasingly difficult to obtain reliable estimates of SARS-CoV-2 infections post-pandemic. In this study we quantified under-reporting of SARS-CoV-2 infections and assessed reporting trends across countries and by variant.

Methods

Using data from the Institute for Health Metrics and Evaluation (IHME) on reported and estimated total SARS-CoV-2 infections from February 2020– December 2022 in 27 countries, we calculated the under-reporting factor (UF), defined as the number of unreported infections per reported infection (regardless of symptom status).

Findings

In the 27 included countries, there were over 2.5 billion estimated infections but only 372.6 million reported infections, indicating over 2.2 billion unreported infections. UF varied considerably among countries, with overall median UF ranging from 1.1–27.5 unreported infections per reported infection during the pandemic. UF was highest during Omicron predominance (range of medians: 0.1–3.3, 0.3–14.6, and 2.1–187.7 during Alpha, Delta, and Omicron, respectively), particularly during BA.4/5 (range of medians: 2.5–244.3). UFs were generally lowest in European countries followed by North America, Middle East, East and Southeast Asia while South Africa and countries in South America generally had the highest UF.

Interpretation

SARS-CoV-2 infections are substantially under-reported globally. Under-reporting was highest during Omicron predominance, particularly during BA.4/5 predominance, and much lower during Alpha and Delta predominance. We found that the total number of SARS-CoV-2 infections during BA.4/5 predominance was 2.5–244.3 times higher than reported in the 27 included countries. Our findings for the BA.4/5 predominance period are likely relevant to the current post-pandemic setting given the absence of public health mandates and changes in testing behaviors during BA.4/5 predominance through present-day.

Funding

This study was sponsored by Pfizer.

Infectious Disease

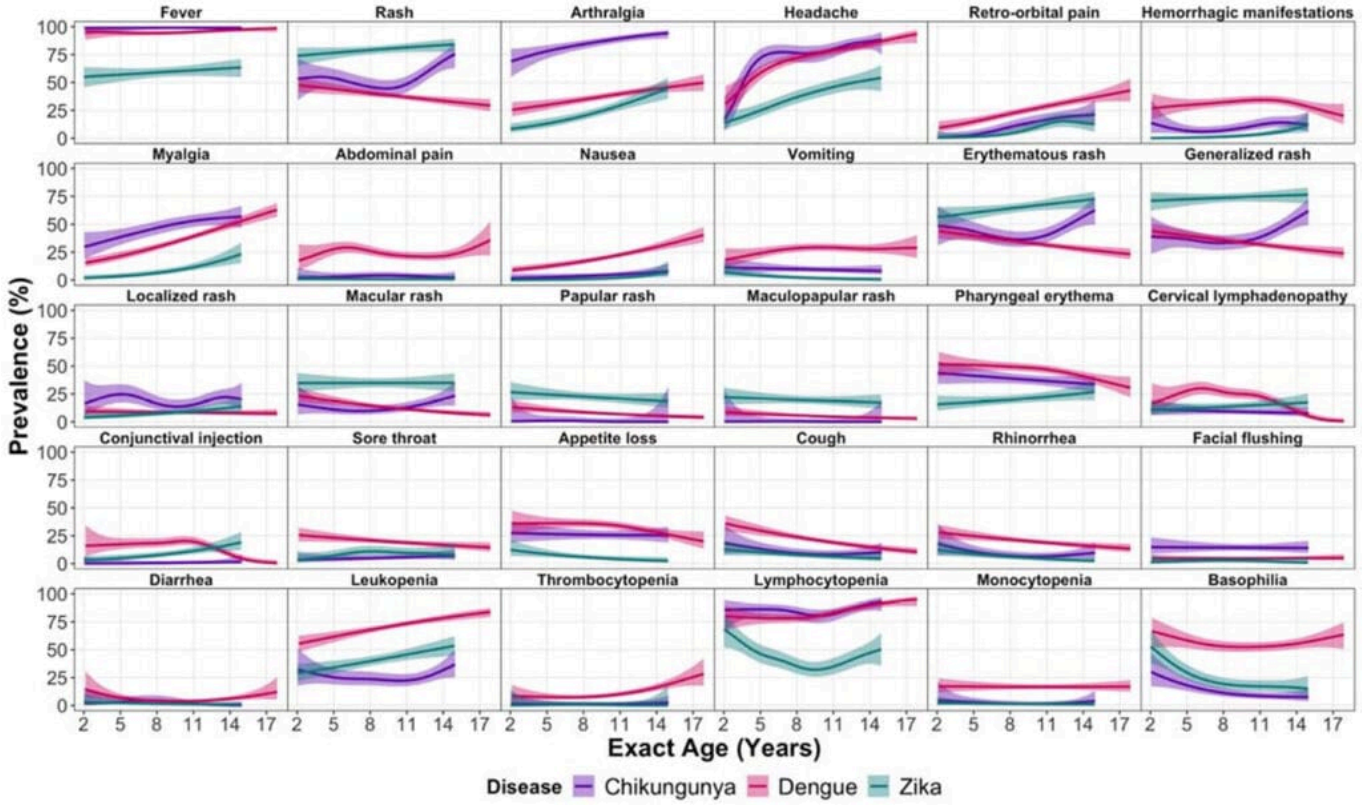
A comparative analysis of dengue, chikungunya, and Zika manifestations in a pediatric cohort over 18 years Fausto Andres Bustos Carrillo* Fausto Bustos Carrillo Eva Harris Sergio Ojeda Nery Sanchez Miguel Plazaola Damaris Collado Tatiana Miranda Saira Saborio Brenda Lopez Mercado Jairo Carey Monterrey Sonia Arguello Lora Campredon Zijin Chu Colin J. Carlson Aubree Gordon Angel Balmaseda Guillermina Kuan

Background Dengue, chikungunya, and Zika are mosquito-borne diseases of major human concern. Differential diagnosis is complicated in children and adolescents by their overlapping clinical features (signs, symptoms, and complete blood count results). Few studies have directly compared the three diseases. We assessed clinical features of cases aged 2-17 years experiencing these diseases.

Methods We characterized 1,405 dengue, 517 chikungunya, and 522 Zika pediatric cases occurring from January 2006 through December 2023 in a Nicaraguan cohort study. Clinical records and laboratory results across the first 10 days of illness were examined from a primary care health center. All cases were laboratory-confirmed. Data were analyzed with generalized additive models, generalized mixed models, and machine learning models.

Findings The prevalence of many clinical features exhibited by dengue, chikungunya, and Zika cases differed substantially overall, by age, and by day of illness. Dengue cases were differentiated most by abdominal pain, leukopenia, nausea/vomiting, and basophilia; chikungunya cases were differentiated most by arthralgia and the absence of leukopenia and papular rash; and Zika cases were differentiated most by rash and lack of fever and lymphocytopenia. Dengue and chikungunya cases exhibited similar temperature dynamics during acute illness, and their temperatures were higher than Zika cases. Sixty-two laboratory-confirmed afebrile dengue cases, which would not be captured by any widely used international case definition, presented very similarly to afebrile Zika cases, though some exhibited warning signs of disease severity. The presence of arthralgia, the presence of basophilia, and the absence of fever were the most important model-based predictors of chikungunya, dengue, and Zika, respectively.

Interpretations These findings substantially update our understanding of dengue, chikungunya, and Zika in children while identifying various clinical features that could improve differential diagnoses. The occurrence of afebrile dengue warrants reconsideration of current case definitions.


Fever
Rash
Arthralgia
Headache
Retro-orbital pain
Hemorrhagic manifestations
Myalgia
Abdominal pain
Nausea
Vomiting
Erythematous rash
Generalized rash
Localized rash
Macular rash
Papular rash
Maculopapular rash
Pharyngeal erythema
Cervical lymphadenopathy
Conjunctival injection
Sore throat
Appetite loss
Cough
Rhinorrhea
Facial flushing
Diarrhea
Leukopenia
Thrombocytopenia
Lymphocytopenia
Monocytopenia
Basophilia
Prevalence (%)
0
25
50
75
100
2
5
8
11
14
17
Exact Age (Years)
Disease
Chikungunya
Dengue
Zika

Infectious Disease

Double blind randomized controlled trial to evaluate the safety of Lactobacillus rhamnosus GG ATCC 53103 (LGG) vs. placebo in elderly subjects receiving standard-dose trivalent inactivated influenza vaccine Sam Gebeh* Sam Gebeh Sowmya Rao Patricia Hibberd

Background: Improving the immune response of elderly (≥65 years) to the influenza vaccine is a vital public health goal. We conducted a Phase 1 trial of a probiotic as a potential adjuvant, during the 2011-2012 flu season as required by the Food and Drug Administration. It was previously difficult to publish the safety and preliminary immunogenicity results from our small Phase I study, but given the current interest in the universal flu vaccine, our results may provide preliminary data for future studies of probiotics as potential vaccine immune adjuvants.

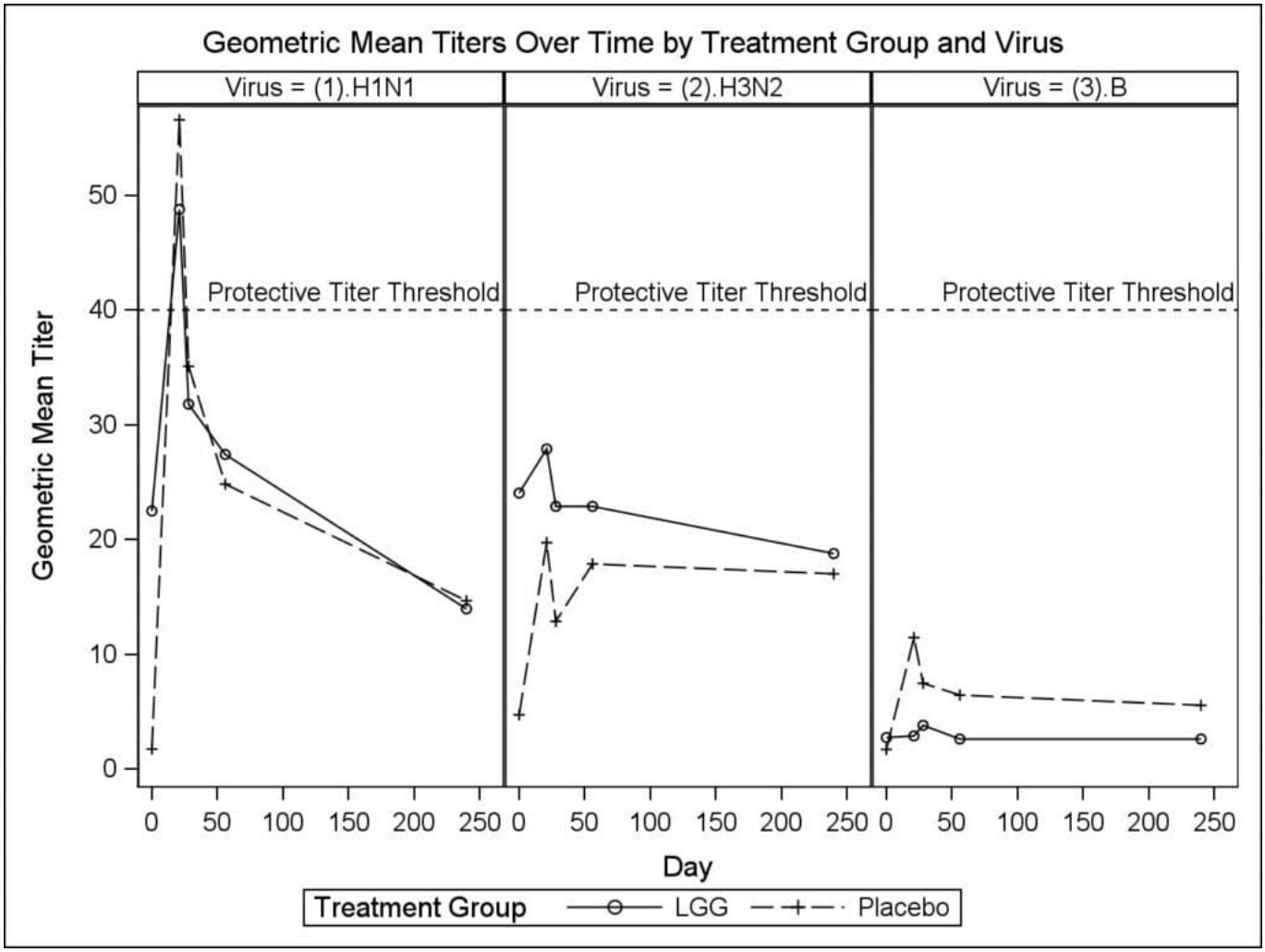
Objectives: (i) To assess the safety and tolerability of Lactobacillus rhamnosus GG (LGG) vs. placebo taken orally by elderly subjects for 28 days after standard-dose trivalent inactivated influenza vaccine (TIV); (ii) To measure anti-influenza systemic immune response (hemagglutinin inhibition (HAI) titers) from baseline to the end of the flu season.

Methods: Our double blinded randomized Phase I trial enrolled 28 elderly subjects who received TIV and were randomized to 1×1010 CFU LGG or placebo twice daily for 28 days. We assessed subjects for adverse events throughout the study and measured HAI titers (H1N1, H3N2, B) at baseline, day 21, 28, 56, and at the end of the flu season. We got summary statistics for adverse events. We used a 2-sample t-test to compare the change in log geometric mean titers from baseline to each time point and Fisher's exact test to compare proportions achieving protective titers (≥40) between groups.

Results: Of all subjects, 57% receiving LGG and 64% receiving placebo reported treatment related non-serious adverse events. We observed protective geometric mean titers only for H1N1. The change in the average log geometric mean H1N1 titers was 2.5 units lower at each time point, and for H2N3 and B, it was lower only at day 21 for LGG than placebo.

Conclusion: LGG was safe and well tolerated among elderly subjects, but didn't have an impact on HAI titers.

Trial registration: NCT01368029


Geometric Mean Titers Over Time by Treatment Group and Virus
Virus = (1).H1N1
Virus = (2).H3N2
Virus = (3).B
Protective Titer Threshold
Protective Titer Threshold
Protective Titer Threshold
Geometric Mean Titer
0
10
20
30
40
50
0 50 100 150 200 250
Day
Treatment Group
LGG
Placebo

Infectious Disease

Leveraging wastewater-based epidemiology to assess the prevalence, antibiogram and infection risks of Listeria monocytogenes in wastewater effluents in South Africa: A critical tool for public health surveillance Chidozie Declan Iwu* Chidozie Declan Iwu Anthony Okoh

Introduction: Wastewater-based epidemiology (WBE) is a valuable tool for monitoring public health risks, offering insights into the prevalence and antimicrobial resistance (AMR) of pathogens like Listeria monocytogenes in community settings. This study investigates the prevalence, AMR profiles, and infection risks of L. monocytogenes in the final effluents of three wastewater treatment plants in the Eastern Cape Province, South Africa.

Methods: Presumptive L. monocytogenes in wastewater effluents were detected using standard plate count methods, followed by the confirmation and screening for five virulence markers using polymerase chain reaction assays. Antibiotic susceptibility of confirmed isolates against 18 antibiotics was done using the disk diffusion method, and relevant resistance genes were screened via PCR. The potential risk of infection attributed to L. monocytogenes was assessed using the Quantitative Microbial Risk Assessment modelling. Monte Carlo simulation with 10,000 iterations was used to characterise the risk.

Results: The prevalence of L. monocytogenes in wastewater effluents was statistically significant ($P < 0.05$), ranging from log10 3.50 CFU/100 ml to log10 5.65 CFU/100 ml. Of 280 presumptive isolates, 20 (7.1%) were confirmed, with virulence genes detected at varying frequencies: inlA (95%), inlB (90%), actA (85%), hlyA (80%), and iap (75%). High phenotypic resistance was observed to tetracycline (80%), doxycycline (65%), cefotaxime (50%), penicillin (30%), and chloramphenicol (60%), with resistance genes detected as follows: tetA (60%), tetB (55%), tetC (50%), sulI (40%), sulII (35%), aadA (30%), aac(3)-IIa (25%), blaTEM (20%), blaCTX-M group 9 (15%), blaVEB (10%), and AmpC (10%). The average annual infection risk of 6.70×10^{-2} (range: 9.10×10^{-3} to 1.00) exceeded World Health Organisation standards for grey water.

Conclusion:
This study highlights the utility of WBE in detecting the prevalence, AMR, and infection risks of L. monocytogenes, emphasizing its value as a critical tool for public health surveillance and risk mitigation.

LATEBREAKER

Infectious Disease

A prospective, comparative cohort analysis of influenza antibody waning between regions with differing pandemic mitigations (Michigan vs Hong Kong) Jade Yangyupei Yang* Jade Yangyupei Yang Matthew Smith Faith Ho Rachel Truscon Sook San Wong Amy Callear Elie-Tino Godonou Nancy Hiu Lan Leung Arnold Monto Benjamin Cowling Emily Martin

Background: Reduced influenza transmission during COVID-19 mitigation has prompted concern about waning of population immunity to previously circulating strains. We evaluated this phenomenon by comparing longitudinal antibody data in two regions (Michigan (MI) and Hong Kong (HK)).

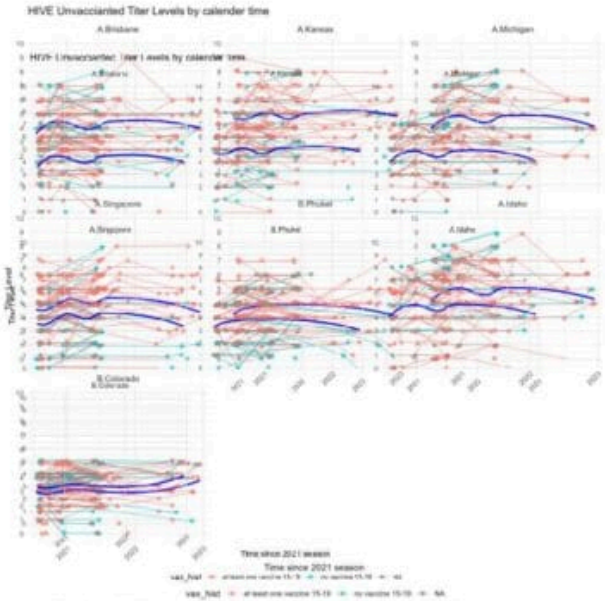
Methods: We analyzed participants who had neither influenza infection nor vaccine during 2020–2023 and provided at least two annual sera specimens from established longitudinal cohorts in MI, and in HK accounting historical vaccination. Sera were tested using hemagglutination inhibition assays against influenza strains included in vaccines. Antibody titers were log2-transformed, and geometric mean titers (GMT) with 95%CI were calculated by specimen collection period and region. Fold changes in GMT comparing the last and first sera for participants in study period were calculated.

Results: Among 57 participants (173 sera) in MI and 60 participants (259 sera) in HK cohort, **26%** and **93%,** respectively had not received historical influenza vaccine 2015–2019. The overall fold change in GMT ranged 1.2–2.6 (B/Phuket–A/Kansas;95%CI:0.5-3.3;1.1-6.1) in MI, 0.7–1.0 (B/Phuket–A/Kansas;95%CI:0.4-1.3;0.8-1.2) in HK. The GMT of the first sera collected in the 2020-21 season ranged 12.3–123.4 (A/Brisbane–A/Kansas;95%CI:8.7–17.0;84.1–181.1) in MI, 6.3–40.9 (A/Kansas–B/Phuket;95%CI:5.4–7.3;27.8–60.2) in HK (Fig). The GMT of the last sera collected in the 2022-23 season ranged 10.8–320.0 (A/Brisbane–A/Kansas;95%CI:8.0–14.6;152.8–670.1) in MI, 6.2–30.0 (A/Kansas–B/Phuket;95%CI:5.5–7.0;20.4–43.9) in HK.

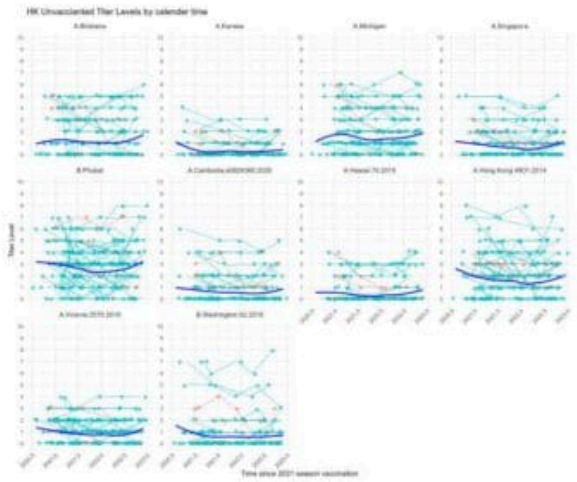
Conclusion: Minimal immunological waning was observed in both Hong Kong and Michigan. In some cases, GMT increased in Michigan, potentially due to circulating strains and the seasonal 2022-23 influenza epidemic. These findings provide insights into post COVID-19 pandemic influenza immunity in different epidemiological settings.

Figure: Antigen specific hemagglutination inhibition titer overtime by cohort and flu vaccination history

a) HIVE cohort (Michigan US)



b) EPI-HK cohort (Hong Kong, SAR China)



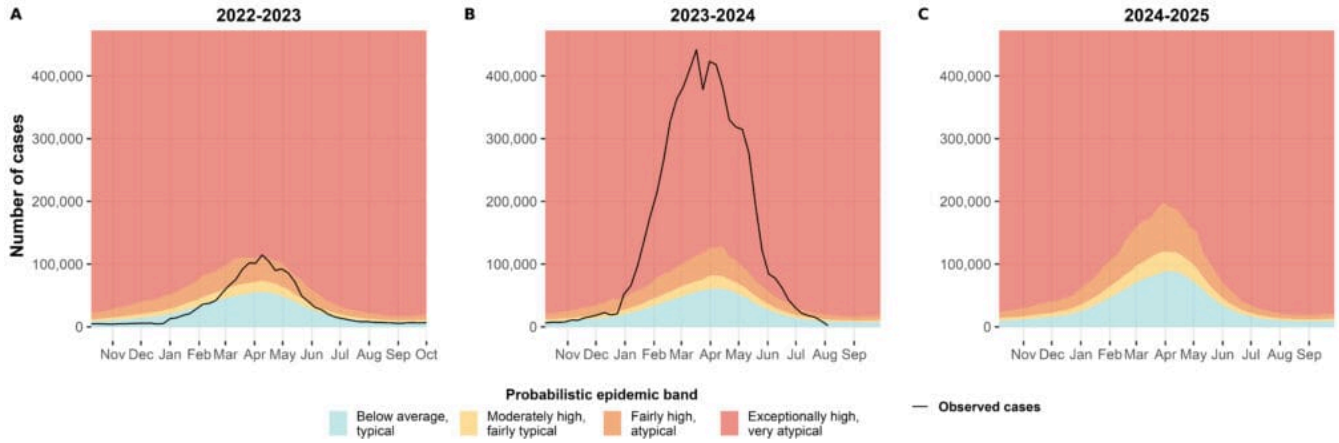
Infectious Disease

A Bayesian statistical model for forecasting probabilistic epidemic bands for dengue cases

Laís Picinini Freitas* Laís Picinini Freitas Danielle Andreza da Cruz Ferreira Raquel Martins Lana Ayrton Sena Gouveia Iasmim Ferreira de Almeida Marilia Sá Carvalho Flávio Codeço Coelho Oswaldo Gonçalves Cruz Cláudia Torres Codeço Leonardo Soares Bastos

Dengue is a vector-borne disease and a major public health concern in Brazil, with on average 1 million cases annually. Using dengue case counts from the national surveillance system (2015-2024), organized by the Dengue Forecast Sprint initiative by InfoDengue-Mosqlimate, we propose a Bayesian negative binomial mixed model to forecast the number of cases 52 weeks ahead for the 118 health districts of Brazil. Health district-varying random effects structured for the week and unstructured for the season year (from epidemiological week 41 to 40) are included. Predictions are obtained from approximating the posterior predictive per week and health district. Percentiles of the distribution of predicted cases are used to get four disjoint probabilistic bands (≤50%, (50%,75%], (75%,90%], and ≥90%) that we name considering the historical number of cases and past occurrence probability (below average, typical; moderately high, fairly typical; fairly high, atypical; exceptionally high, very atypical). We performed out-of-sample validation for 2022-2023 and 2023-2024 and forecasted 2024-2025. In the 2022-2023 and 2023-2024 seasons, the epidemic bands followed the observed cases' curve shape, with a sharp increase after January and a decline after the peak around April (Figure 1A and B). In 2022-2023, the observed cases curve fell within the "below average, typical" band in most weeks, increasing towards "moderately high, fairly typical" and "fairly high, atypical" bands until peaking. In 2023-2024, the observed number of cases was most of the time "exceptionally high, very atypical". This season had an unprecedented record of 6.6 million dengue cases. For the 2024-2025 season (Figure 1C), the bands' upper limits increased, influenced by the 2023-2024 data inclusion in the model. The probabilistic epidemic bands can be used for epidemic monitoring by comparing them prospectively with the observed cases curve to assess how an ongoing epidemic compares with past ones.

Figure 1. Estimated probabilistic epidemic bands of dengue cases for seasons (A) 2022-2023, B) 2023-2024, and C) 2024-2025, Brazil.



Infectious Disease

Does county tell the whole story? Assessing within-county heterogeneity in COVID-19 burden across levels of urbanicity and rurality. John T. Kubale* John Kubale Robert Melendez Andrew Hoover Paul Schulz Philippa Clarke Sonia T. Hegde Fan Bu Brady T. West Grace Noppert

Introduction: Within-county heterogeneity in infectious disease burden is well-documented in metropolitan areas (e.g., neighborhood hotspots during outbreaks). However, in micropolitan and rural areas, infectious disease burden is often assumed to be homogenous below the county level, and this may not be accurate. Assessing the level of within-county heterogeneity in infectious disease burden in non-metropolitan areas has key implications for forecasting and ensuring that appropriate policy measures are implemented.

Methods: Using census tract-level data for COVID-19 monthly case counts in Wisconsin and New Mexico (2020-2022), we fit two generalized additive mixed models with a generalized Poisson distribution. In model 1, a single random effect for county was included, while in model 2, an additional random effect for census tract was also included. Calendar month and number of cases in the prior month were included as predictors in all models using cubic splines. Using Rural Urban Commuting Area (RUCA) codes, communities were classified as metropolitan (RUCA 1-3), micropolitan (4-6), or rural (7-10), with models fit to each class. The importance of within-county heterogeneity in COVID-19 burden across levels of rurality was examined by comparing model 1 to model 2 using likelihood ratio tests.

Results: In Wisconsin, we observed significant within-county heterogeneity in disease burden within metropolitan areas ($p<0.0001$), but not in micropolitan or rural areas. In New Mexico, we observed significant within-county heterogeneity in both metropolitan and rural areas ($p<0.0001$), but not micropolitan areas.

Conclusions: Within-county heterogeneity does exist in non-metropolitan areas, but it is not consistent across states. Better understanding of the drivers of this heterogeneity is needed to recognize the importance of more spatially granular data for public health decision-making.

LATEBREAKER

Injuries/Violence

Determinants of child physical abuse in Guyana: Findings from the 2019 Guyana national survey. Gary Joseph* Gary Joseph Audrey Benn Cecil Boston Debra Lowe Karishma Jeeboo La-Toya Arthur-Tucker Lauristan Choy Lidon Lashley Gbenankpon M. Houvèssou Tammy Hopkinson Thomas B. Singh

Objective: To assess the prevalence and factors associated with physical abuse against children in Guyana.

Methods: This study utilized nationally representative data from the Multiple Indicator Cluster Survey conducted in Guyana in 2019. The percentage of children who endured physical abuse was the primary outcome studied. Logistic regression was used to assess the association between the exposure variables and the outcome. We calculated the slope index of inequality (SII) and the concentration index (CIX) to assess inequalities in child physical abuse.

Results: In Guyana, 53.1% and 4.4% of children endured moderate and severe physical abuse, respectively. Children aged 24 months or older (AOR: 2.29, 95% CI: 1.34–3.95), living in the Interior (AOR: 2.41, 95% CI: 1.21–4.87), in households headed by females (AOR: 2.32, 95% CI: 1.48–3.65), whose mothers ever consumed alcohol (AOR: 2.41, 95% CI: 1.54–3.79), or had positive attitudes toward child physical abuse (AOR: 4.37, 95% CI: 2.07–9.23) were at higher risk of experiencing moderate physical abuse. The risk of severe physical abuse increased among children whose mothers had positive attitudes towards child physical punishment and decreased according to the mother's level of education. Important disparities were observed between boys and girls according to maternal education and geographic regions.

Conclusion: Children in Guyana who endured moderate physical abuse exceed 50% of the country's child population. Guyana needs to enact legislation that prohibits the use of child physical abuse. Stringent enforcement is necessary to ensure Guyanese children do not continue to experience physical abuse.

Injuries/Violence

Neighborhood gun violence, psychosocial risks and perceived firearm access among youth in an emergency department setting Jungwon Min* Jungwon Min Vicky Tam Stephanie Mayne Polina Krass Joel Fein

Background: Youth firearm access is linked to psychosocial behaviors, violence and injury. Some youth without firearms at home perceive they could obtain one, indicating higher risk than those with securely stored firearms. We examined youth and neighborhood factors associated with perceived firearm access.
Methods: This cross-sectional study analyzed 23,334 Emergency Department (ED) visits by 14-18-year-olds completing Behavioral Health Screening (2013-2024) for firearm access and psychosocial risks. Neighborhood gun violence (shooting incidence rate per 1,000 residents) and Child Opportunity Index (COI) scores were linked to patients' census tracts. Patient and neighborhood characteristics were compared across groups: no firearm access, at-home access, and perceived access. Mixed-effects models and mediation analyses further examined the associations.
Results: Among 16,174 patients (63% non-Hispanic-Black, 65% Medicaid insured, 75% in very low COI neighborhoods with higher gun violence), perceived firearm access was associated with racial/ethnic minority status, reported fighting, retaliation, at-risk substance use, school bullying, intimate partner violence, lower COI and higher neighborhood gun violence. At-home firearm access was linked to non-Hispanic White status, non-Medicaid insurance, ED visits for mental health, higher COI, and lower gun violence (all $p < 0.001$). Among those without firearms at home, fighting (OR=3.6 [3.1-4.3]) and high neighborhood gun violence (OR=1.8 [1.5-2.3]) were positively associated with perceived access after adjusting for age and gender. Fighting behaviors mediated 32% of the total effect of neighborhood gun violence on perceived firearm access.
Conclusions: Youth fighting and high neighborhood gun violence were linked to perceived firearm access, highlighting the connection between violence exposure and firearm perceptions. ED-based screening for perceived firearm access may help intervene youth gun carriage and future violence.

Injuries/Violence

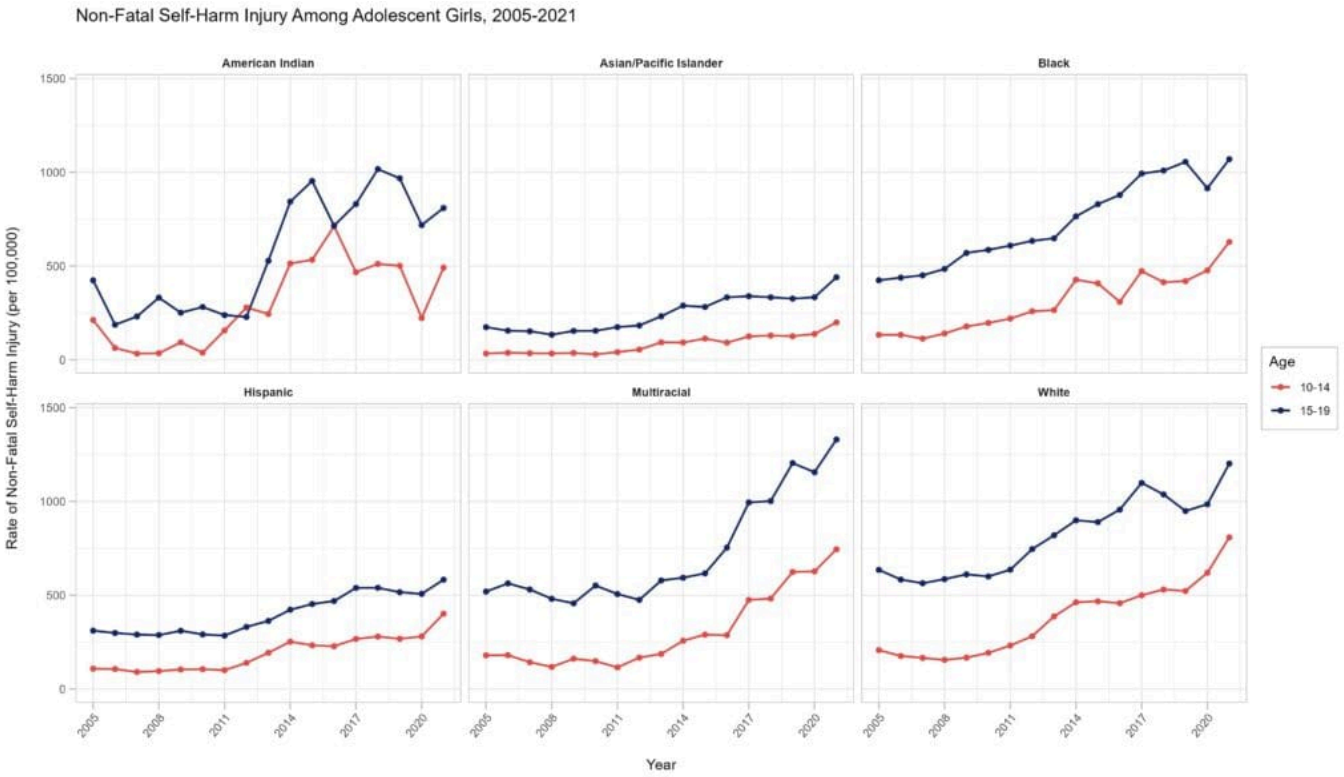
Trends in Non-Fatal Self-Harm Injury by Age, Sex, and Race and Ethnicity among Adolescents in California, 2005 to 2021 Emily F. Liu* Emily Liu Ellicott C. Matthay Kriszta Farkas Jennifer Ahern

Adolescent girls experience a higher burden of non-fatal self-harm and greater increases over time when compared to adolescent boys. Sex, age, and race and ethnicity are important dimensions of social identity and intersect to shape exposure to risk factors for self-harm. However, trends in self-harm within these subgroups have not been examined.

We analyzed statewide inpatient and emergency department hospital discharge data from California 2005-2021 among younger (aged 10-14 years) and older (aged 15-19 years) adolescents. Self-harm incidents were identified using diagnostic codes and rates were calculated per 100,000 person-years based on census data.

From 2005-2021, the self-harm rate among adolescents rose from 191.0 to 453.2 per 100,000 person-years, with larger increases among girls (281 to 729.7) than boys (105.2 to 187.10). In 2005, White girls aged 15-19 years experienced the highest self-harm rate at 635.1 per 100,000 person-years. After 2016, self-harm rates increased sharply among Multiracial adolescents. By 2021, the self-harm rate was still highest among older adolescent girls, but Multiracial girls now experienced the highest rate (1330.0), followed by White (1201.6) and Black girls (1069.7). American Indian, Hispanic, and Asian/Pacific Islander girls had lower self-harm rates of 809.5, 582.8, and 439.9 per 100,000 person-years, respectively. Among boys, high rates and substantial increases among Multiracial and American Indian youth were notable.

This study reveals striking differences in trends in adolescent self-harm across race and ethnicity groups. Further research is needed to examine whether these trends are driven by increasing exposure to self-harm risk factors and/or changes in how adolescents identify with race and ethnicity groupings. Caregivers, clinicians, and teachers should be aware of the alarming increases and racial and ethnic patterns in self-harm and play an active role in supporting adolescent mental health to reduce self-harm.


Non-Fatal Self-Harm Injury Among Adolescent Girls, 2005-2021
American Indian
Asian/Pacific Islander
Black
Hispanic
Multiracial
White
Rate of Non-Fatal Self-Harm Injury (per 100,000)
0
500
1000
1500
2005
2008
2011
2014
2017
2020
Year
Age
10-14
15-19

Injuries/Violence

Comparison of Interpersonal Violence and Homicide Rates Using FBI's Uniform Crime Report (UCR) Data, Hospital Injury Data and Vital Statistics Across California Cities, 2007-2017. Saron Goitom* Saron Goitom Shelley Jung Jennifer Ahern

Interpersonal violence, including fatal and nonfatal injuries, is a critical public health problem in the US. Yet, the longstanding surveillance system for violent crime in the US, FBI's Uniform Crime Reports (UCR), has limitations, including pervasive missingness, and unreliable estimates at smaller geographic levels. Leveraging hospital records and vital statistics may be an alternative source to identify interpersonal violence. In this study, we examined the agreement between violent crime as measured by FBI UCR versus hospital records and vital statistics in California.

We gathered violent crime data (murder, rape, aggravated assault, and robbery) from the FBI's UCR, nonfatal interpersonal injury data from hospital discharge records, and homicide data from vital statistics across California cities (incorporated places) for 2007-2017. For both crime (FBI) and health-based (hospital records and vital statistics) violence data, annual interpersonal violence and homicide rates were calculated as a count per 100,000 people for each city with complete data across the study period (418 cities with complete violent crime data; 79 cities with complete homicide data) and averaged across all cities for each year. We examined trends over time, and calculated spearman correlation coefficients to assess the level of agreement between the two measures. This analysis was replicated for the top 4 largest cities in California.

Across the study period, there was high correlation between crime and health-based interpersonal violence measures (R = 0.90), with less agreement between homicide measures (R = 0.60). However, for the top 4 largest cities, there was high correlation between the homicide measures [Los Angeles (R = 0.94), San Diego (R = 0.88), San Jose (0.78), San Francisco (R = 0.64)], while the correlation between the interpersonal violence measures for these same cities varied [Los Angeles (R = 0.76), San Diego (R = 0.80), San Jose (-0.28), San Francisco (R = 0.03)]. Further investigation into these differences is important to accurately measure interpersonal violence, and critical in determining where public health intervention and resources are needed most.

Injuries/Violence

Understanding Discordance of Self-Reported Child Abuse in the Health & Retirement Study

Sophie Selbe* Sophie Selbe Rachel Slimovitch Jeanine I. Nasser Michelle Flesaker Sarah E. Weber Virginia Cafferky Casey DeMarsico Anthony J. Rosellini Jaimie L. Gradus

Prior studies have assessed the validity of retrospective self-reporting of child abuse in research by examining individual characteristics and life events that may explain recall bias. Yet, none have evaluated potential predictors of reporting discordance in older adults. Data were from the Health and Retirement Study (HRS), a nationally representative longitudinal panel study that began in 1992 comprised of adults ages 50+ in the U.S. (n = 9,101). Child abuse was asked at two timepoints, 4 years apart, from 2006-2012, and was defined as any physical abuse by parents before age 18. Reporting discordance was defined as a changed response across timepoints. We evaluated possible predictors of reporting discordance at baseline including demographic, socioeconomic, physical and mental health, and other trauma-related factors. We further examined changes from 2006-2012 in socioeconomic, mental and physical health factors. We calculated crude RRs and 95% CIs to examine associations between potential predictors and child abuse reporting discordance. Two sets of analyses were conducted: one that examined participants who changed from yes to no (compared to concordant yes responses) and a second that examined participants who changed from no to yes (compared to concordant no responses). Among those who changed responses from no to yes, associations were found for depression (RR=2.3, 95% CI: 1.7, 3.0), improved depression between timepoints (RR=2.1, 95% CI: 1.4, 3.0), new psychological diagnosis (RR=2.5, 95% CI: 1.4, 4.3), family substance use problems (RR=2.6, 95% CI: 2.0, 3.5), and being a victim of a physical attack (RR=2.9, 95% CI: 2.0, 4.3). Among those who changed responses from yes to no, associations were found for Black/African American race (RR=1.6, 95% CI: 1.2, 2.1), Hispanic ethnicity (RR=1.4, 95% CI: 1.0, 2.0), and worse cognition between timepoints (RR=1.3, 95% CI: 1.0, 1.8). Results from machine learning random forests prediction models will also be presented.

Injuries/Violence

Nowcasting County-Level Homicide Rates Based on Newspaper Articles Amulya Akkapeddi* Amulya Akkapeddi Yingjie Ma Lina Zhou Janice Williams Dongsong Zhang Ahmed Arif Rajib Paul

Introduction: The lag in homicide incident reporting by the National Death Violent Reporting System (NVDRS) due to its reliance on extensive manual data extraction limits its utility for real-time public health interventions. In this case, can we predict current firearm homicide rates without experiencing delays associated with the NVDRS data availability? To answer this, the study explores the predictive capacity of newspaper articles as a proxy for nowcasting homicide rates at the county level in North Carolina (NC).

Methods: We first retrieved newspaper articles from 30+ NC open-source publications based on keywords like “gun”, “murder, and “shot” for the years 2017-2024, followed by spatiotemporal deduplication. We then aggregated articles from 2017-2021 at the county level and analyzed their correlation with the NVDRS data. Spatiotemporal analytics were finally applied to evaluate the feasibility and effectiveness of using newspaper data to forecast homicide rates.

Results: Our previous study using the NVDRS data from 2011-2021 showed that there was an increase in statewide homicide by 65%. The county-level Social Vulnerability Index (SVI) showed a positive association with homicide rates, with an incidence risk ratio (IRR) of 5.15 (95% CrI: 4.5-5.91). 155 newspaper articles in 2019 reported firearm homicides, compared to 704 reported in NVDRS. A strong county-level correlation (Pearson’s r = 0.95) between the two data sources was observed, indicating that newspapers are robust predictors of NVDRS data. Moreover, urban counties (r= 0.97) showed higher alignment between NVDRS and newspaper-reported incidents, compared to rural counties (r=0.70), likely reflecting differences in media coverage intensity and reporting practices.

Conclusion: Newspaper data show strong potential for nowcasting firearm homicides, particularly in urban areas, with alignment to NVDRS. This approach can enhance public health responses by providing timely and actionable insights.

Injuries/Violence

Evaluation of domestic violence legislation to reduce intimate partner violence in India: a difference-in-differences analysis across 28 Indian states Robin Richardson* Robin Richardson Soohyeon Ko Eva Portillo Molina

In 2005, India enacted comprehensive legislation to confront household violence. In this analysis, we evaluate the impact of state-level implementation on women's intimate partner violence (IPV) across 28 Indian states. We used state-level implementation information, including amount of state budget earmarked for the legislation, the number of newly created, specialized police officer positions trained in domestic violence, and the number of community-based organizations providing services to victims of violence funded through the legislation. We linked state-level implementation data with individual-level IPV data collected in population-based, repeated cross-sectional surveys conducted before (2005/2006) and after adoption of legislation (2015/16). Presence of IPV was captured with 12 questions about specific physical, sexual, or emotional abuse acts (e.g., husband ever slapped you). We used a difference-in-differences study design to evaluate the impact of implementation on IPV using linear regression models that controlled for country, year, individual-level factors (e.g., educational attainment) and time-varying state-level factors (e.g., state-level literacy rate), and estimated variances that accounted for state-level clustering. Using these model results, we estimated marginal changes in IPV prevalence between states with low vs high implementation (25th vs 75th percentile) to derive Prevalence Differences (PD) in IPV. Among the 124,156 women included in the study, 24.8% reported experiencing IPV. In fully adjusted models, more funded service providers corresponded to reductions in IPV (PD = 1.6%, 95% CI: -2.4%, -0.9%). However, amount of state-level budget allocated to legislation (PD = 2.2%, 95% CI: -1.0%, 5.5%) and number of specialized police officer positions (PD = -1.0%, 95% CI: -2.6%, 0.6%) was not associated with changes in IPV. Our results demonstrate that degree of implementation, as well as implementation activities, impact policy effectiveness.

Mental Health

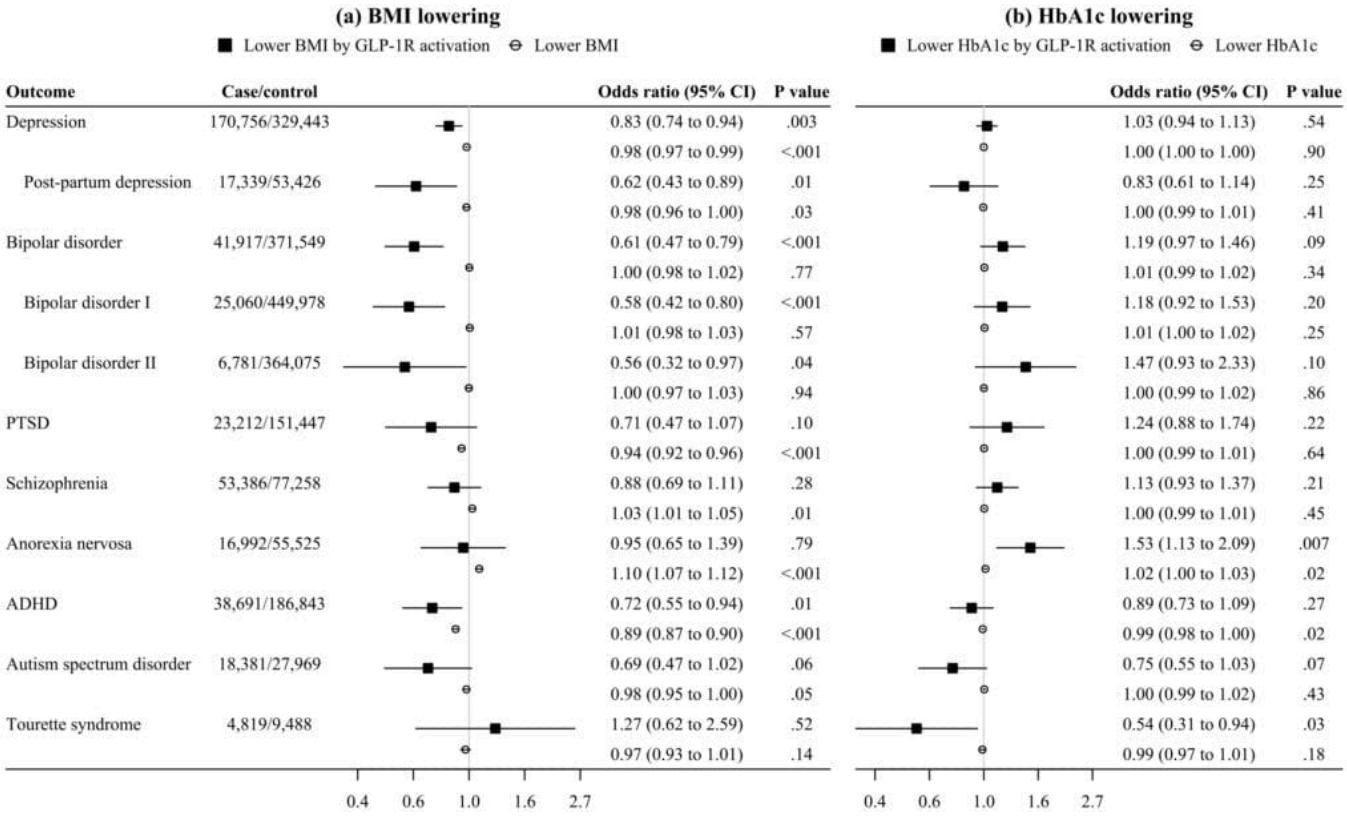
Glucagon-like peptide-1 receptor activation and mental health: a drug-target Mendelian randomization study Guoyi Yang* Guoyi Yang Stephen Burgess C Mary Schooling

Background: Concerns have been raised about the psychiatric safety of glucagon-like peptide-1 receptor (GLP-1R) agonists, but trial evidence suggests that they ameliorate depressive symptoms. We aimed to assess the associations of GLP-1R activation with mental health well-being and the risk of mental health disorders and substance use disorders.

Methods: We performed drug-target Mendelian randomization and colocalization analyses using the largest relevant publicly available genome-wide association studies in European ancestry individuals.

Results: After correcting for multiple comparisons, genetically predicted lower body mass index (BMI) via GLP-1R activation was associated with a better well-being spectrum (0.06 standard deviation [95% confidence interval 0.03-0.08]) and lower risk of depression (odds ratio 0.83 [0.74-0.94]) and bipolar disorder (odds ratio 0.61 [0.47-0.79]) per 1-kg/m2 decrease in BMI. There was also suggestive evidence that genetically predicted lower BMI via GLP-1R activation was associated with lower risk of post-partum depression, attention deficit hyperactivity disorder, and substance use disorders, and that genetically predicted lower glycated hemoglobin (HbA1c) via GLP-1R activation was associated with higher risk of anorexia nervosa but lower risk of Tourette syndrome. These associations were stronger than the associations for genetically predicted lower BMI and lower HbA1c based on genome-wide variants. The posterior probabilities of a shared causal variant affecting both BMI and the outcome at the GLP1R gene were 59.3% for the well-being spectrum, 3.8% for depression, and 45.9% for bipolar disorder.

Conclusions: GLP-1R activation was associated with better mental health well-being and lower risk of depression and bipolar disorder beyond that expected from the reduction in BMI and HbA1c.


(a) BMI lowering
Lower BMI by GLP-1R activation
Lower BMI
(b) HbA1c lowering
Lower HbA1c by GLP-1R activation
Lower HbA1c
Outcome
Case/control
Odds ratio (95% CI)
P value
Depression 170,756/329,443 0.83 (0.74 to 0.94) .003
0.98 (0.97 to 0.99) <.001
1.03 (0.94 to 1.13) .54
1.00 (1.00 to 1.00) .90
Post-partum depression 17,339/53,426 0.62 (0.43 to 0.89) .01
0.98 (0.96 to 1.00) .03
0.83 (0.61 to 1.14) .25
1.00 (0.99 to 1.01) .41
Bipolar disorder 41,917/371,549 0.61 (0.47 to 0.79) <.001
1.00 (0.98 to 1.02) .77
1.19 (0.97 to 1.46) .09
1.01 (0.99 to 1.02) .34
Bipolar disorder I 25,060/449,978 0.58 (0.42 to 0.80) <.001
1.01 (0.98 to 1.03) .57
1.18 (0.92 to 1.53) .20
1.01 (1.00 to 1.02) .25
Bipolar disorder II 6,781/364,075 0.56 (0.32 to 0.97) .04
1.00 (0.97 to 1.03) .94
1.47 (0.93 to 2.33) .10
1.00 (0.99 to 1.02) .86
PTSD 23,212/151,447 0.71 (0.47 to 1.07) .10
0.94 (0.92 to 0.96) <.001
1.24 (0.88 to 1.74) .22
1.00 (0.99 to 1.01) .64
Schizophrenia 53,386/77,258 0.88 (0.69 to 1.11) .28
1.03 (1.01 to 1.05) .01
1.13 (0.93 to 1.37) .21
1.00 (0.99 to 1.01) .45
Anorexia nervosa 16,992/55,525 0.95 (0.65 to 1.39) .79
1.10 (1.07 to 1.12) <.001
1.53 (1.13 to 2.09) .007
1.02 (1.00 to 1.03) .02
ADHD 38,691/186,843 0.72 (0.55 to 0.94) .01
0.89 (0.87 to 0.90) <.001
0.89 (0.73 to 1.09) .27
0.99 (0.98 to 1.00) .02
Autism spectrum disorder 18,381/27,969 0.69 (0.47 to 1.02) .06
0.98 (0.95 to 1.00) .05
0.75 (0.55 to 1.03) .07
1.00 (0.99 to 1.02) .43
Tourette syndrome 4,819/9,488 1.27 (0.62 to 2.59) .52
0.97 (0.93 to 1.01) .14
0.54 (0.31 to 0.94) .03
0.99 (0.97 to 1.01) .18
0.4
0.6
1.0
1.6
2.7
0.4
0.6
1.0
1.6
2.7

Mental Health

Exploring the relationship between mental wellbeing and identity affirmation among bisexual+ people G. Nic Rider* Nora Y. Sun Jennifer A. Vencill

Background: The dual continuum model posits that mental wellbeing and mental illness are distinct but related mental health dimensions, with mental wellbeing a better predictor of overall health. While studies suggest bisexual+ people (people with non-monosexual identities) experience higher rates of mental health concerns than lesbian/gay people, little is known about positive mental wellbeing among bi+ people.

Objective: To examine mental wellbeing (flourishing/moderate/languishing) among bi+ people, and identify culturally specific factors related to flourishing.

Methods: 446 bi+ adults took a survey with demographics, Mental Health Continuum-Short Form, Bisexual Identity Inventory (BII), and Bisexual Microaffirmation Scale (BMAFFS). We used multinomial logistic regression to test associations between mental wellbeing and age, race, gender, BII and BMAFFS subscales.

Results: Most participants reported moderate mental wellbeing (58.1%), whereas the remainder of the sample was split between flourishing (21.7%) or languishing (20.2%). Anticipated (OR: 0.73, 95% CI: 0.56, 0.95) and internalized binegativity (OR: 0.54, 95% CI: 0.3, 0.96) and all trans/nonbinary gender identities were associated with decreased odds of flourishing. Internalized bisexual illegitimacy (OR: 4.66, 95% CI: 1.98, 10.94), bisexual identity affirmation (OR: 1.81, 95% CI: 1.26, 2.6) and emotional support (OR: 1.11, 95% CI: 1.02, 1.21) were associated with increased odds of flourishing.

Discussion: A greater portion of bi+ adults in our sample are flourishing (21.8%) in comparison to general U.S. adults (17.2%). Bi+ people appear to flourish despite internal stressors (e.g., internalized bisexual illegitimacy), potentially due to stronger peer support and coping mechanisms developed due to identity-based marginalization. Strengths-based research incorporating nuanced psychosocial measures specific to bisexuality is critical to further understand the complexities of flourishing among bi+ people.

Table 1. Multinomial logistic regression model of association of experiences and attitudes towards bisexuality with flourishing and moderate mental wellbeing compared to languishing mental wellbeing.

	Flourishing			*Moderate*		
		95% CI			95% CI	
	OR	Lower	Upper	OR	Lower	Upper
Age	1.004	0.969	1.041	0.988	0.96	1.017
Gender identity (reference: cisgender man)						
Cisgender woman	0.508	0.181	1.423	1.137	0.467	2.771
Transgender man	**0.222***	0.054	0.919	0.329	0.1	1.08
Transgender woman	**0.183***	0.039	0.852	0.294	0.081	1.074
Non-binary	**0.225***	0.066	0.766	0.627	0.228	1.721
Other	**0.084*****	0.023	0.314	0.427	0.156	1.169
Race (reference: white)						
Black/African/African American	1.778	0.642	4.924	1.317	0.563	3.084
American Indian	3.526	0.597	20.844	2.117	0.421	10.656
Asian/Asian American	2.647	0.938	7.467	2.072	0.943	4.553
Multiracial	1.931	0.724	5.152	**2.398****	1.146	5.019
Other	1.115	0.217	5.729	1.258	0.368	4.303
Bisexual Identity Inventory						
Illegitimacy of bisexuality	**4.658*****	1.984	10.937	**2.826****	1.379	5.792
Anticipated binegativity	**0.728***	0.558	0.949	0.826	0.668	1.022
Internalized binegativity	**0.539***	0.304	0.957	0.798	0.564	1.13
Identity affirmation	**1.81****	1.26	2.601	1.16	0.881	1.528
Bisexual Microaffirmation Scale						
Acceptance	0.931	0.858	1.009	0.972	0.913	1.036
Social support	1.067	0.945	1.205	1.019	0.924	1.124
Recognition of bisexuality and biphobia	1.053	0.987	1.123	1.035	0.981	1.093
Emotional support	**1.11***	1.022	1.205	**1.075***	1.008	1.146

*p < .05, **p < .01, ***p < .001. All statistically significant (p < 0.05) OR are bolded.

Mental Health

Pre-Pregnancy Mental Disorders as Risk Factors for Poor Perinatal Health Outcomes: An Exploratory Analysis Jeanine I. Nasser* Jeanine Nasser Yasmin Barrientos Kofman Jennifer A. Sumner Jaimie L. Gradus Samantha E. Parker

In the U.S., over 33% of childbearing people develop mental health symptoms in pregnancy. While untreated maternal mental health disorders (e.g., depression, anxiety) adversely affect postpartum maternal and child health, the impact of pre-pregnancy psychiatric disorders on perinatal health is unclear. Examining a spectrum of these conditions offers a new opportunity to elucidate how mental health impacts perinatal outcomes.

Data were from a retrospective electronic medical record (EMR)-based cohort study of 3925 deliveries at a safety net hospital from 2016-18. Analytic variables were ascertained using documented International Classification of Diseases, 10th Revision (ICD-10) codes in the EMR before the study pregnancy. Psychiatric diagnoses included depressive, manic/bipolar, anxiety stress, and substance use disorders (SUD). Perinatal outcomes included pregnancy-related maternal disorders, labor/delivery complications, and puerperium-related complications. Log-binomial regression was used to calculate crude RRs and RRs adjusted for maternal age at delivery, race, insurance type, and parity.

Although documented SUD did not confer increased risk of any perinatal outcomes, this observation was inconsistent across other psychiatric disorders. Documented bipolar/manic disorders were associated with higher risk of puerperium-related complications (aRR=1.3, 95% CI=1.1-1.6). Similarly, documented stress disorders were linked to heightened risk of pregnancy-related maternal disorders (aRR=1.2, 95% CI = 1.0-1.3), as were depressive disorders (aRR=1.1, 95% CI=1.0-1.3). Documented anxiety disorders were also associated with higher risk of labor/delivery complications (aRR=1.2, 95% CI=1.0-1.3).

Our findings indicate pre-pregnancy psychiatric diagnoses are associated with elevated risk for poor perinatal outcomes, though these findings vary across psychiatric disorders. Clinical intervention pre-pregnancy may have salient implications in improving maternal and child health.

Mental Health

Dose-Dependent Risk of Psychosis in ADHD Patients Treated with Prescription Amphetamine Loreen Straub* Loreen Straub Jun Liu Joseph P. Skinner Lauren Moran

A recent cohort study reported an increased risk of psychosis in ADHD patients initiating amphetamine vs. methylphenidate. Subsequently, a case-control study suggested a dose-response association between prescription amphetamine and psychosis, but limitations included small samples and potential selection bias.

Using the Merative MarketScan Commercial Claims Database (2005-2022), we conducted a large cohort study based on a prevalent new user design to assess psychosis risk by amphetamine dose.

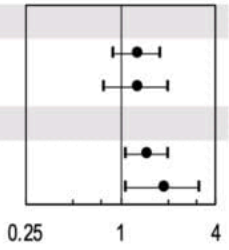
After initial restrictions, ADHD patients (ages 13-64) were categorized into 3 amphetamine exposure groups: high-dose (>30 daily dextroamphetamine equivalents), medium-dose (>15-≤30), and low-dose (≤15) users. Patients were 1:1 matched (high vs. medium; high vs. low) on prior exposure duration, year, and propensity score, accounting for a broad confounder range. Psychosis incidence was based on a validated algorithm. Follow-up continued until psychosis occurrence, death, disenrollment, exposure end or switch, 1 year, or study end. Cox proportional hazards models estimated hazard ratios (HR).

The cohort included 37,377 high-dose, 144,280 medium-dose, and 480,474 low-dose users; 32,927 patients remained in each group after matching. Before matching, the 1-year psychosis incidence per 1,000 patients was 2.68 (95% CI: 1.99-3.60; high dose), 2.20 (1.85-2.61; medium dose) and 1.89 (1.70-2.11; low dose), respectively, yielding crude HRs of 1.23 (0.87-1.73; high vs. medium) and 1.43 (1.05-1.96; high vs. low). Matched HRs were 1.23 (0.77-1.96) and 1.82 (1.06-3.11). Sensitivity analyses confirmed robustness across varying prescription gap periods and outcome definitions. Ongoing analyses include subgroup stratifications and replication in other datasets (e.g., nationwide Medicaid data).

Our findings suggest that caution should be exercised when prescribing high amphetamine doses, particularly given the uncertain clinical benefits. Regular screening for psychotic symptoms is recommended.

Figure. One-Year Incidence and Hazard Ratio of Psychosis Among A) High-Dose vs. Medium-Dose Prescription Amphetamine Users and B) High-Dose vs. Low-Dose Prescription Amphetamine Users, Before and After Matching, Using a Prevalent-New User Cohort Study Design.

Analysis	Exposure Group		Comparator Group		Hazard Ratio (95% CI)	Hazard Ratio (95% CI) Plot
	N Outcomes / N Total	1-Year Incidence per 1,000 (95% CI)	N Outcomes / N Total	1-Year Incidence per 1,000 (95% CI)		
A) High-Dose vs. Medium-Dose Users						
Crude	44 / 37,377	2.68 (1.99-3.60)	132 / 144,280	2.20 (1.85-2.61)	1.23 (0.87-1.73)	
Matched	40 / 32,927	2.79 (2.05-3.80)	32 / 32,927	2.27 (1.61-3.21)	1.23 (0.77-1.96)	
B) High-Dose vs. Low-Dose Users						
Crude	44 / 37,377	2.68 (1.99-3.60)	327 / 480,474	1.89 (1.70-2.11)	1.43 (1.05-1.96)	
Matched	40 / 32,927	2.79 (2.05-3.80)	20 / 32,927	1.54 (0.99-2.39)	1.82 (1.06-3.11)	



Mental Health

Depression screening using the Patient Health Questionnaire (PHQ)-9: Discrepancies between the sum score and diagnostic algorithm approach and the role of physical functioning in a nationally representative sample of U.S. adults Debbie Huang* Emily Goldmann Debbie Huang Rasmika Kumar Daniel Hagen Emily Goldmann

Background: The PHQ-9 is a validated instrument commonly used to screen for depressive symptoms. PHQ-9 scoring approaches include a dichotomized sum score (range 0-27) using a cut point of 10 and a diagnostic algorithm that reflects diagnostic criteria for major depressive episode in the Diagnostic and Statistical Manual of Mental Disorders (DSM)-5. Because several PHQ-9 items are somatic in nature, discordance in screening results using these scoring approaches may be related to physical functioning.

Methods: We used data from the 2021-2023 National Health and Nutrition Examination Survey (NHANES) for adult participants who had a positive screen for depression using the sum score approach (PHQ-9≥10) to compare those who did vs. those who did not also meet criteria for depression using the diagnostic algorithm approach (endorsed at least 5 of 9 PHQ-9 symptoms at least more than half of the days in the past two weeks, with at least one symptom being depressed mood or anhedonia). Logistic regression models examined the association between having a positive screen using the diagnostic algorithm approach and reporting at least one physical functioning limitation from the Short Set on Functioning (WG-SS), controlling for demographic variables.

Results: Among the 773 participants with PHQ-9≥10 (14% of 5,273 adult NHANES participants), 42% also screened positive using the diagnostic algorithm approach. Adjusting for age, gender, race/ethnicity, education, and marital status, physical functioning impairment was not associated with screening positive for depression using the diagnostic algorithm (adj. OR=1.1; 95% CI: 0.6,1.9).

Conclusion: Impairment in physical functioning did not explain differences between screening results using the sum score vs. the diagnostic algorithm approach among U.S. adults. Investigators should carefully consider the implications of using either approach. Further research on the comparative utility of PHQ-9 scoring approaches is warranted.

Mental Health

Unraveling the Impact of Early Adversity on Problem Gambling in Young Adults: Insights from the Add Health Study Krishna Vaddiparti* Krishna Vaddiparti Alyssa Falise Youngseo Cheon Catalina Lopez-Quintero

Aims: This study aimed to examine factors influencing problematic gambling, focusing on the impact of adverse childhood experiences like trauma, perpetration, and other negative adolescent events, to identify key contributors to its development in young adulthood.

Methods: Secondary data from the National Longitudinal Study of Adolescent Health was analyzed, including a total of 16,534 participants. Gambling behaviors were categorized as no gambling (n = 1,922), non-problematic gambling (n = 14,028), and problematic gambling (n = 584) based on self-reported responses. Individual-level factors examined included substance use, suicidal behavior, arrests for perpetration, trauma, adverse childhood experiences, and socioeconomic status. Chi-square analyses and logistic regression models were used to assess associations between these factors and gambling status.

Results: Individuals with problematic gambling (3.5%) exhibited significantly higher rates of adverse outcomes, including cigarette use ($p < 0.01$), alcohol consumption ($p < 0.01$), marijuana use ($p < 0.01$), parental incarceration ($p = 0.04$), witnessing violence ($p = 0.02$), and being arrested for perpetration before age 18 ($p < 0.01$), Male gender was strongly associated with problematic gambling (AOR = 4.5), as was substance use (e.g., cigarette use: AOR = 1.9). Although being arrested for perpetration before age 18 was significantly associated with problematic gambling in unadjusted models (OR = 2.4), the association was no longer statistically significant after adjustment. Similarly, while the number of traumas showed a weak trend toward an association with problematic gambling, it did not reach statistical significance.

Conclusions: Adverse childhood experiences, substance use, and male gender significantly increase the risk of problematic gambling in young adulthood. Early interventions addressing these factors are essential to prevent gambling-related harms.

Mental Health

Mental health and gestational weight gain: A comparison between Brazilian cohorts

Audêncio Victor* Audêncio Victor Perla Pizzi Argentato Liania A. Luzia Rinaldo Artes Patricia Helen Rondó

ABSTRACT

Introduction: The mental health of pregnant women is critical as it influences both maternal and neonatal outcomes. This study investigates the association between maternal mental health and gestational weight gain (GWG) in two Brazilian cohorts conducted in different periods.

Methods: The Jundiaí cohort (1997-2000) included 875 pregnant women, while the Araraquara cohort (2017-2024) evaluated mental health of 556 pregnant women from 2017 to 2019. Maternal mental health was assessed using the General Health Questionnaire (GHQ), the State-Trait Anxiety Inventory (STAI), and the Perceived Stress Scale (PSS) during the first, second, and third trimesters. GWG was categorized as adequate, insufficient, or excessive based on Institute of Medicine guidelines. Statistical analysis included bivariate tests (Kruskal-Wallis, chi-square, or Fisher's exact test) and multinomial ordinal logistic regression to evaluate associations.

Results: In the Jundiaí cohort, high stress levels in the first trimester were associated with lower odds of insufficient GWG (adjusted OR for second quartile: 0.36, 95% CI: 0.18-0.71). In the second trimester, high anxiety levels (TAI ≥ 40) were associated with higher odds of insufficient GWG (adjusted OR: 1.76, 95% CI: 1.12-2.76). In the third trimester, high stress levels (PSS fourth quartile) were associated with higher odds of insufficient GWG (adjusted OR: 1.72, 95% CI: 1.02-2.91). In the Araraquara cohort, no significant associations between mental health and GWG were found.

Conclusions: Our findings highlight the importance of incorporating psychosocial support in prenatal care to improve maternal and neonatal outcomes. Variations in socioeconomic and temporal contexts may influence the relationship between mental health and GWG. Future research should explore the underlying mechanisms and develop interventions tailored to different socioeconomic and temporal contexts.

Keywords: Maternal mental health, gestational weight gain, prenatal care, psychosocial support, Brazilian cohorts

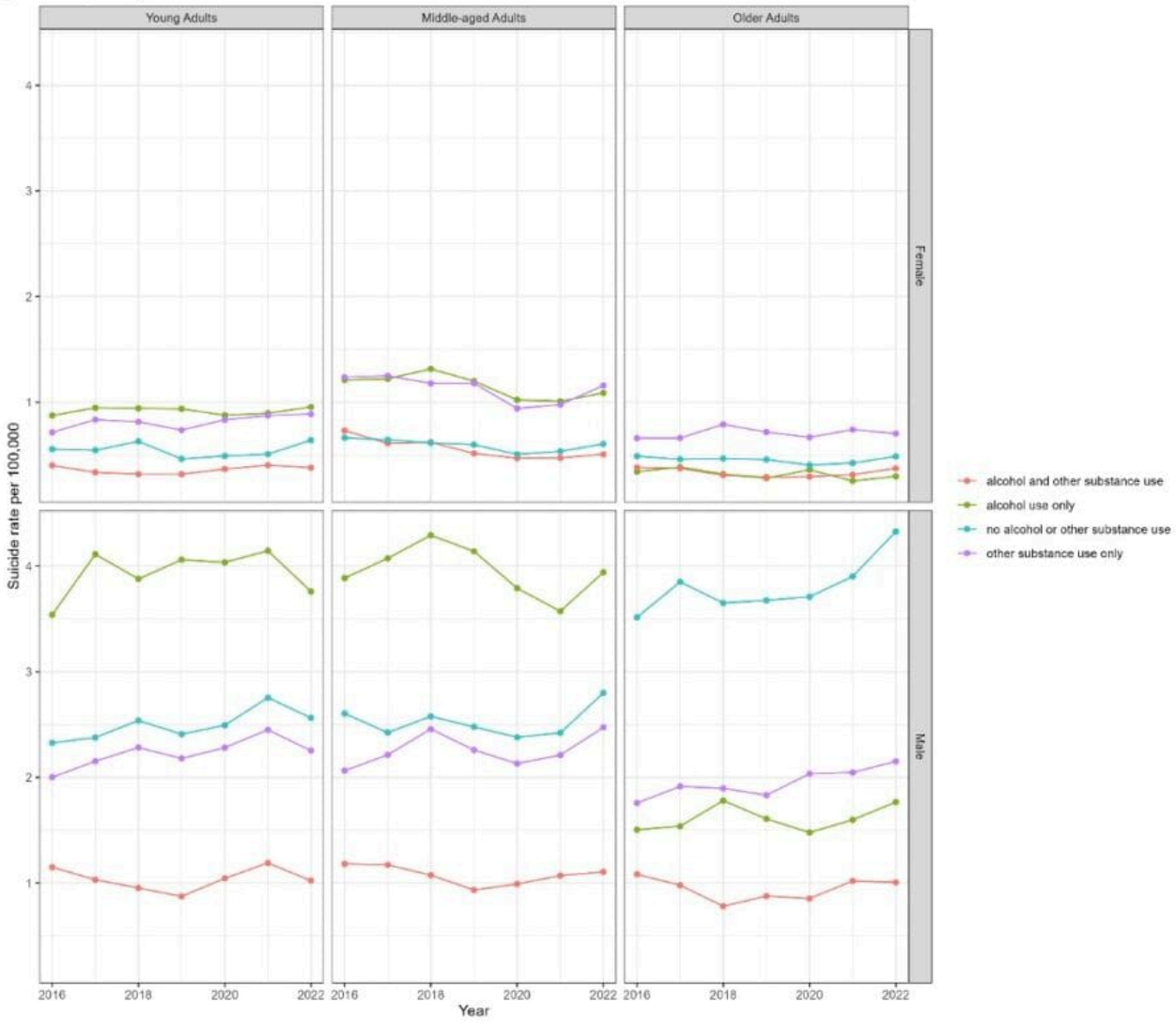
Mental Health

Trends in alcohol and other substance use preceding suicide death in the United States: age-specific temporal trends, 2016-2022 Katherine Keyes* Katherine Keyes Victoria Joseph Caroline Rutherford

Suicide death rates increased in the US over the past decade; identifying causes of these increases is critical to design intervention and prevention efforts. Concomitant to suicide deaths increases have been increases in alcohol and other substance use in the US population. Given that alcohol and other substance use are frequently proximal to suicide death, there is a potential role of population-level increases in use on suicide death. The present study analyzed time trends alcohol and other substance involved suicide death rates. We used data on 109,561 suicide deaths with toxicology and Blood Alcohol testing data from 32 states with consistent reporting for study years in the National Violent Death Registry, annually from 2016 through 2022. Alcohol involvement was determined by Blood Alcohol Concentration testing at the time of death, and substance involvement through toxicology. Population denominators drawn from the US census. For those deaths with alcohol and other substance testing data, Figure 1 shows the trend over time in alcohol-only, other-substance-only, alcohol-and-other-substance, and neither, by age and sex. Alcohol-only-associated suicide death remains high for young adult and middle-age adult men, with a death rate of approximately 4 per 100,000. There was no systematic trend over time in alcohol or substance involved suicide for any sex-age group, however, there was heterogeneity by state. Alcohol-associated suicide deaths rates significantly increased over the study period in Kansas; other-substance-associated suicide deaths increased in Arizona, Kansas, Massachusetts and Oregon; and alcohol-and-other-substance-associated suicide deaths increased in Colorado, and Oklahoma. Results underscore that alcohol use continues to be associated with high suicide rates among young and middle-aged men, and while trends over time are consistent nationally, certain states are evidencing increases which may call for targeted region-specific intervention.

Trends in alcohol and other substance use preceding suicide death in the United States: age-specific temporal trends, 2016-2022

Figure 1. Observed sex- and age group-specific suicide rate that were alcohol and substance use involved for which the decedent had a blood alcohol content ≥0.05 g/dl , alcohol/other substance use present among all suicide decedents (18+ years of age) in the National Violent Death Registry from 2016-2022 (N=112,828)

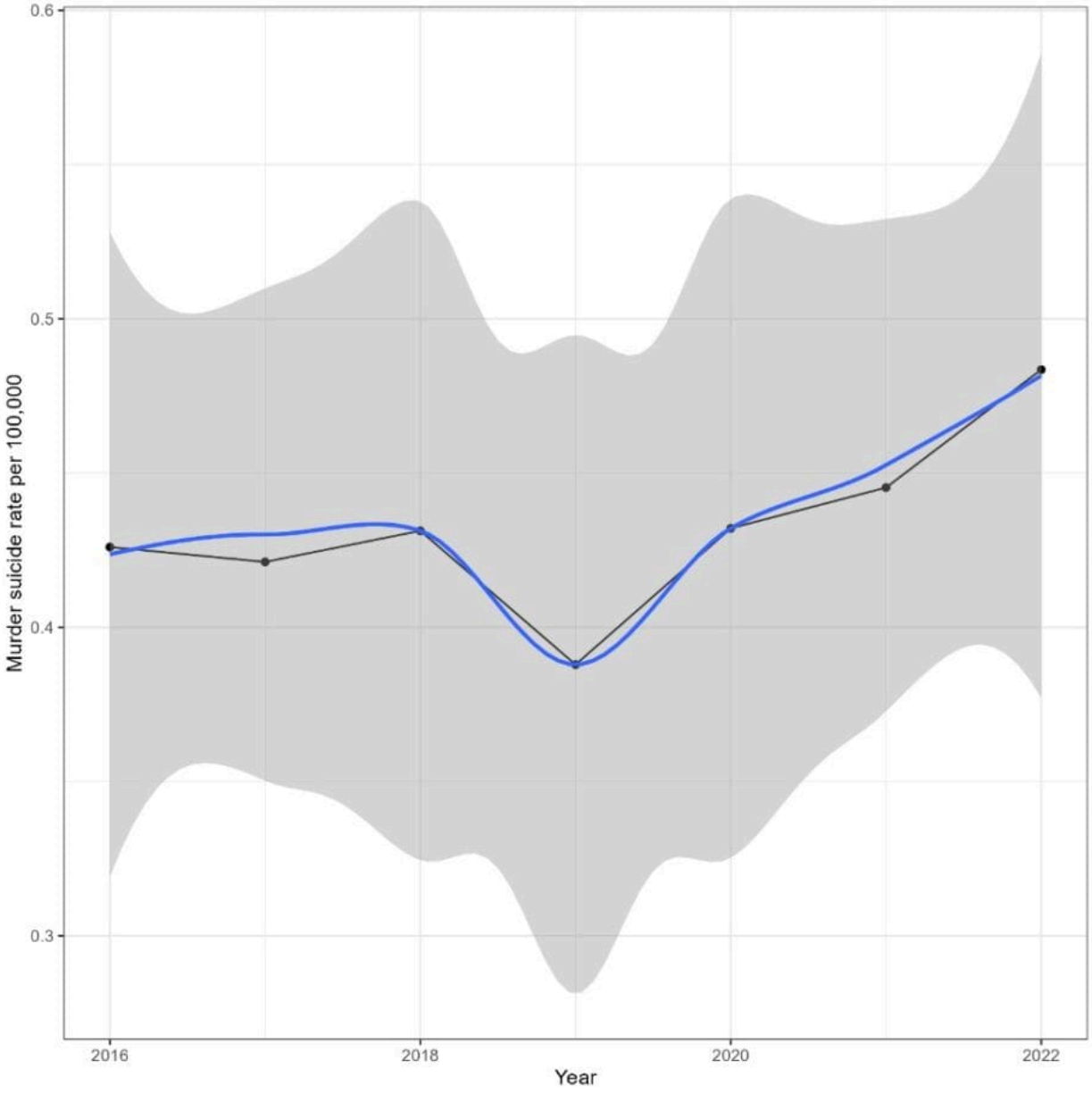


Mental Health

The epidemiology of murder-suicide in the United States, 2016-2022 Katherine Keyes*
Katherine Keyes Victoria Joseph Caroline Rutherford

Murder-suicide events occur when an individual commits one or more acts of homicide shortly before taking their own life. These events are often high profile, given the high level of violence involved, yet the epidemiology of murder-suicides, including trends over time and geographic concentration, has received limited research attention. The present study estimated murder-suicide rates and characteristics in 32 US states from 2016 through 2022. Overall, 5,964 deaths were involved in murder-suicide events during this time period (an average of 852 deaths per year), including 3,246 homicide decedents and 2,718 suicide decedents. The number of homicide decedents per incident ranged from 1 to 7, with 85.7% of events involving one homicide decedent, 10.6% involving 2, and 3.7% involving 3 or more. Among homicide decedents, 73.4% were men, and 43.4% were between 35-64 years of age. Among suicide decedents, 91.3% were men, and 54.3% were between 35-64 years of age. A total of 88.3% of homicides and 90.1% of suicides involved a firearm as the primary weapon in the death. Deaths between romantic partners were most frequent; 53.6% of homicide decedents were the spouse, ex- or current romantic partner of the perpetrator. Figure 1 shows the trend over time in the murder-suicide rate in the US; murder-suicides were lowest during the study period in 2019 (0.43 per 100,000) and have increased to 0.48 per 100,000 by 2022. By state, for those with data, murder-suicides are highest in Alaska (0.87 per 100,000), Arizona (0.70 per 100,000), Colorado (0.64 per 100,000) and Oklahoma (0.81 per 100,000). In summary, murder-suicides are increasing in the US, and particularly concentrated in romantic partnerships and predominately committed with firearms.

Figure 1. Murder suicide rate in the US per 100,000 (2016-2022)



Mental Health

Mixed methods assessment of mental health among adolescents at high risk for CKD of non-traditional origin in Central America Selene Vences Brown* Selene Vences Brown Damaris López-Pilarte Juan José Amador Velasquez Samantha Magaly Rosario Amador Sanchez Madeleine K Scammell Dan Brooks Jessica Leibler

Chronic kidney disease of non-traditional origin (CKDnt) is a leading cause of mortality in Central America. The disease is characterized by acute onset in early life and rapid progression, and the full etiology remains unknown. Although devastating to communities and families, research on the mental health burden of the CKDnt epidemic is scant. We assessed frequency of experiencing depressive symptoms within a prospective cohort study of adolescents in Nicaragua, a region highly affected by CKDnt (n=486), using the Patient Health Questionnaire (PHQ-2). We used open-ended questions to explore worry about CKDnt and its impact on life choices, including education and employment. Among participants, 14.8% (n=72) scored ≥3 on the PHQ-2, indicating high risk for depression. This finding is consistent with U.S. based estimates for Hispanic young adults. Most participants reported “always” worrying about kidney health of family and friends (n=298; 61.6%) while 28.9% (n=140) expressed concern that their daily activities harmed their kidneys. Nearly 20% (19.8%; n=96) indicated that the epidemic affected their employment decisions, while 9.6% (n=45) noted that the CKD epidemic disrupted their educational plans. Using a systematic inductive thematic qualitative analysis, we identified major themes around employment disruption, including: fear of developing CKDnt, inability to work due to disease, and avoiding jobs that may harm the kidneys. Minor themes included limiting physical exertion at jobs with heat exposure and concerns related to passing employer health screenings. Themes around educational decisions included concerns for career preparation, financial stability, and negative psychological and emotional impacts affecting their ability to concentrate on their studies. Our findings suggest that the CKDnt epidemic negatively affects life choices and opportunities for young people in affected regions, with implications for financial stability and mental health.

Mental Health

Psychosocial influencers of mental health and cognitive abilities in children of MAASTHI cohort in Urban India. Giridhara Rathnaiah Babu* Giridhara Rathnaiah Babu Siddhartha Mandal Shwetha Dixit Deepa R Debarati Mukherjee Prashanth NS Eunice Lobo, Suganya Rajendran, Amit Prakash, Smita Todkar, Astha Yadav, Jyothi Menon, Aditi Rao, Poornima Prabhakaran, Gauri Divan, Supriya Bhavnani, Prashant Thankachan, Sumathi Swaminathan

Introduction: Over 182 million children worldwide face risks that jeopardize their healthy development, with India accounting for the highest number (64.3 million) of children developing sub-optimally. The COINCIDE project aims to explore the combined effects of various psychosocial factors on children's cognition and mental health.

Methods: In 985 mother-child dyads within MAASTHI cohort, we assessed maternal mental health, maternal adversity, intimate partner violence (IPV), Family Care Indicator (FCI), Childhood Psychosocial Adversity Scale (CPAS) and the Child-Parent Relationship (CPRS). Children's mental health was assessed using the Strengths and Difficulties Questionnaire (SDQ). Cognitive performance, including fluid intelligence and non-verbal reasoning, was measured using Raven's Coloured Progressive Matrices (RCPM). Ridge regression was implemented to assess the joint effects using the R package ridge.

Results: In children with mean age of 5.35 years, FCI (β = 2.25) and high conflict relationship (β= 1.55) positively influenced cognitive performance. CPAS (β = 0.40) and IPV (β = 0.26) were positively associated with SDQ internalising behaviour, while a high closeness in relationship (β = -0.43) was negatively associated. CPAS (β = 0.52), and high conflict relationship (β = 0.99) showed significant positive associations with SDQ externalising behaviour while high closeness in the relationship (β = -0.37) and maternal depressive symptoms (β = -0.31) had a negative impact.

Conclusion: High-conflict relationships consistently predicted increased behavioural difficulties and lower cognitive performance. Conversely, high closeness in relationships mitigates internalizing and externalising behaviours, suggesting the protective role of a positive parent-child bond. IPV and CPAS significantly contributed to behavioural difficulties, underlining the importance of addressing domestic violence and social stressors in interventions aimed at improving child mental health.

Mental Health

Bullying victimization and mental health disorders in adolescents with and without autism

Kristi Bartholomay* Kristi Bartholomay Brady Holst Sarah Schmiege Lisa Wiggins Nuri Reyes Patrick Powell Elizabeth Wise Carolyn DiGuiseppi

Background Bullying victimization is associated with adverse mental health (MH) outcomes. Risks of bullying and MH disorders are higher in people on the autism spectrum and differ by sex.

Objectives We evaluated the association of bullying victimization with MH disorders in adolescents, and whether sex or autism modified the association.

Methods In a multi-site study, children aged 2-5 identified from health, education and vital records were classified into three groups after standardized evaluation: autism spectrum disorder (ASD), other developmental disorders (DD), and population comparison (POP). Caregivers completed follow-up health and development surveys on these individuals between ages 12 and 16. Log link binomial models estimated prevalence ratios of parent-reported current diagnoses of anxiety (ANX), depression (DEP) and self-injurious behavior (SIB) based on past-year bullying victimization. Interactions of bullying victimization with study group and birth sex, and potential confounders were assessed.

Results Of 287 ASD, 304 DD, and 287 POP adolescents, 62% were male and 67% non-Hispanic white; mean age=14.72 years. Prevalence of any ANX, DEP, or SIB differed significantly by study group: 53%, 34% and 24% in ASD, DD and POP groups, respectively ($p<0.001$). Adolescents bullied in the past year had higher prevalence of ANX (Prevalence Ratio (PR):1.97, 95%CI:1.59-2.42); DEP (PR:3.15, 95%CI:2.16-4.57); and SIB (PR:1.96, 95%CI:1.14-3.24). Interactions between study group or sex and bullying were not significant for any outcome ($p>0.05$). Neither sex nor maternal education confounded these relationships. Study group confounded the association with SIB (aPR: 1.40, 95%CI 0.83-2.30).

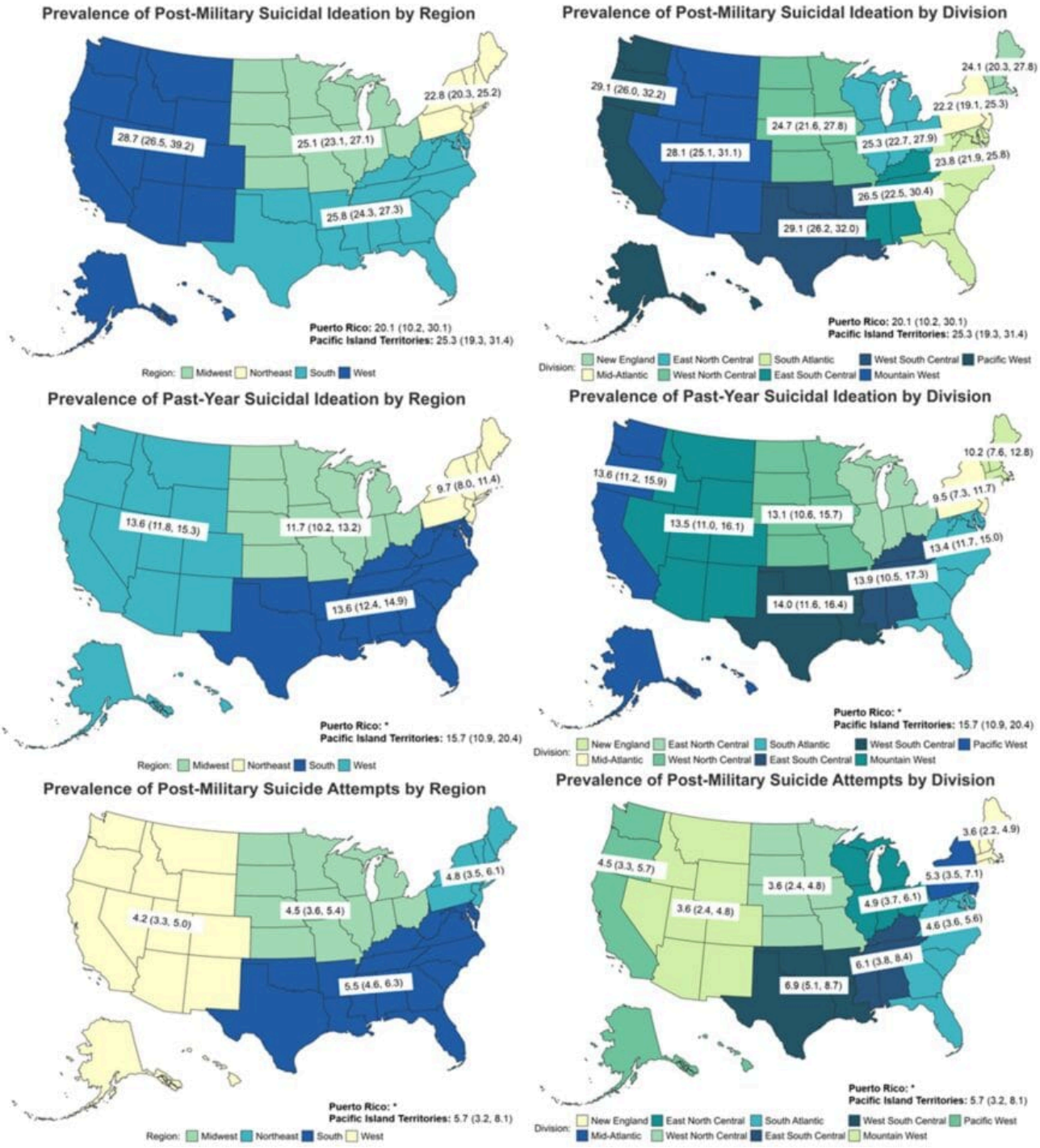
Conclusions These findings suggest that bullying victimization is associated with ANX and DEP independent of autism or sex and reiterate the importance of regular screening for MH disorders among autistic adolescents and those who are bullied, regardless of underlying development.

Mental Health

Geospatial Estimates of Suicidal Ideation and Suicide Attempt Prevalence in the U.S. Veteran Population (2022): The Importance of Disaggregation Julie Kittel* Julie Kittel Lindsey Monteith Ryan Holliday Alexandra Schneider Lisa Brenner Claire Hoffmire

Veteran suicide remains a major public health concern; rates increased from 2001 to 2022 and substantial geospatial variation exists. Surveillance of suicidal ideation (SI) and suicide attempts (SA) can provide insight to reduce suicide risk within communities. A population-based, cross-sectional survey of 17,946 Veterans residing in all 50 U.S. states, the District of Columbia, Puerto Rico, and U.S. Pacific Island (PI) Territories, was conducted in 2022 to assess SI and SA prevalence. Lifetime and post-military SI and SA and past-year SI prevalence, as well as proportions of SI methods were estimated by Census region, division, and state. Prevalence ratios were used to assess for post-military SI and SA differences by division. The West had the highest prevalence of lifetime (36.94%; 95%CI=34.65-39.23) and post-military SI (28.73%; 95%CI=26.51-30.96); for lifetime SI, prevalence was higher than all other regions except PI Territories and Puerto Rico. PI Territories had the highest prevalence of past-year SI (15.68%; 95%CI=10.91-20.44) and lifetime (9.86%; 95%CI=6.36-13.37) and post-military SA (5.67%; 95%CI=3.21-8.14). At the divisional level, the Pacific West had the highest prevalence of lifetime (36.99%; 95%CI=33.83-40.07) and post-military SI (29.12%; 95%CI=26.01-32.23) while West South Central had the highest prevalence of past-year SI (14.00%; 95%CI=11.59-16.40) and post-military SA (6.89%; 95%CI=5.07-8.70). The PI Territories remained highest for lifetime SA. After adjusting for covariates (age, race, gender, rurality, time since military separation), differences were not significant. Firearms were the most commonly considered method by Veterans in the Midwest, South, and West while motor vehicle collisions were most commonly considered in the Northeast and PI Territories. Further elucidation of differential factors and effective preventive efforts (e.g., lethal means safety) to address risk for Veterans across regions are paramount.

Figure 1. Maps of Prevalence Estimates of Post-Military and Past-Year Suicidal Ideation and Post-Military Suicide Attempt by Region, Division, and State



LATEBREAKER

Mental Health

The risk of anxiety and depressive disorder in the offspring of mothers with perinatal depressive disorders Biruk Shalmeno Tusa* Biruk shalmeno Tusa Rosa Alati Kim Betts Getinet Ayano Berihun Dachew

Abstract

Background: Maternal perinatal depression has been associated with an increased risk of anxiety and depression in offspring. However, existing studies often rely on self-reported measures, small sample sizes, and inadequate adjustment for confounders, while overlooking comorbid outcomes and the combined effects of maternal conditions.

Methods: This study analysed administrative health data from 223,068 mother-offspring pairs in New South Wales (NSW), Australia. Maternal perinatal depressive disorders and offspring anxiety and depressive disorders were identified using the International Classification of Diseases, Tenth Revision, Australian Modification (ICD-10 AM). A generalised linear model was applied to examine the association, and a propensity score matching (PSM) analysis was conducted to enhance comparability between groups.

Results: Offspring of mothers with perinatal depressive disorders had a 56% increased risk of depressive disorders (RR=1.56, 95% CI=1.05–2.29), though this association attenuated after PSM (RR=1.42, 95% CI=0.93–2.18). Maternal perinatal depressive disorders were associated with a higher risk of anxiety disorders (RR=2.10, 95% CI=1.78–2.48), which persisted after PSM (RR=1.90, 95% CI=1.59–2.28). Offspring of mothers with comorbid perinatal depressive and anxiety disorders had a 2.36-fold increased risk of depressive disorders (RR=2.36, 95% CI=1.21–4.63), a 2.56-fold increased risk of anxiety disorders (RR=2.56, 95% CI=1.89–3.48), and a 3.37-fold increased risk of comorbid depressive and anxiety disorders (RR=3.37, 95% CI=1.54–7.36). Maternal perinatal depressive disorders were also associated with a 94% increased risk of comorbid depressive and anxiety disorders in offspring (RR=1.94, 95% CI=1.20–3.16).

Conclusion: Our findings highlight the heightened risk of depressive and anxiety disorders in offspring of mothers with perinatal depressive disorders, with more pronounced associations observed when maternal depression coexists with anxiety. These results underscore the critical need for early detection and targeted interventions for maternal perinatal depressive and anxiety disorders to reduce the risk of adverse mental health outcomes in offspring.

LATEBREAKER

Mental Health

Risk Factors and Predication Models for Anorexia Nervosa Severity: A Comprehensive Population-based Study Across Two Countries Zi-Ping Zhang* Zi-Ping Zhang Janne Tidselbak Larsen Zeynep Yilmaz Loa Clausen Bjarni Jóhann Vilhjálmsson Liselotte Vogdrup Petersen

Background: Anorexia nervosa (AN), a life-threatening psychiatric disorder with high mortality and heterogeneous outcomes, remains poorly understood in terms of risk factors influencing illness severity. While genetic and environmental risk factors for AN onset are explored, their role in predicting severity is unclear. This study aims to identify pre-onset environmental risk factors and develop prediction models for AN severity.

Methods: Using Danish and Swedish national registers, severity are assessed for 14,000 individuals diagnosed with AN, via a Register-based Severity Index (continuous; categorized: severe/moderate/less-severe). We evaluate nine environmental domains: birth-related factors, pregnancy complications, adverse childhood experiences, early-life factors, pre-AN medical history, pre-AN psychiatric history, pre-AN prescription medications, family psychiatric history, and parental socioeconomic status (SES). Associations with severity are analyzed using univariate and multivaraite zero-inflated negative binomial (continuous) and multinomial logistic regression (categorical) models, adjusted for calendar year. Prediction models employing machine learning algorithms are trained on the Danish cohort (80% training, 20% testing) and externally validated on the Swedish cohort.

Preliminary Results: Initial analyses identified unexpected patterns: higher SES was associated with increased AN severity, while factors typically linked to social disadvantage—younger parental age (<20 years), paternal criminal history, and out-of-home care—appeared protective. Adverse perinatal (e.g., congenital malformations, placental disorders) and pre-AN medical conditions (e.g., metabolic disorders, gastrointestinal disease) trended toward positive severity associations, alongside family psychiatric history. Not all significant associations are detailed here; multivariable regression and prediction models' development are ongoing to disentangle these relationships.

Perspectives: This first multinational population-based study elucidates environmental predictors of AN severity. The prediction models, once validated, could enable early risk stratification and personalized interventions, advancing multifactorial clinical assessments.

LATEBREAKER

Mental Health

Stress disorders and risk of Human Papillomavirus-related cancers: a population-based cohort study in Denmark Sarah E. Weber* Sarah Weber Dóra Körmendiné Farkas Tina Bech Olesen Mette Nørgaard Jaimie L. Gradus

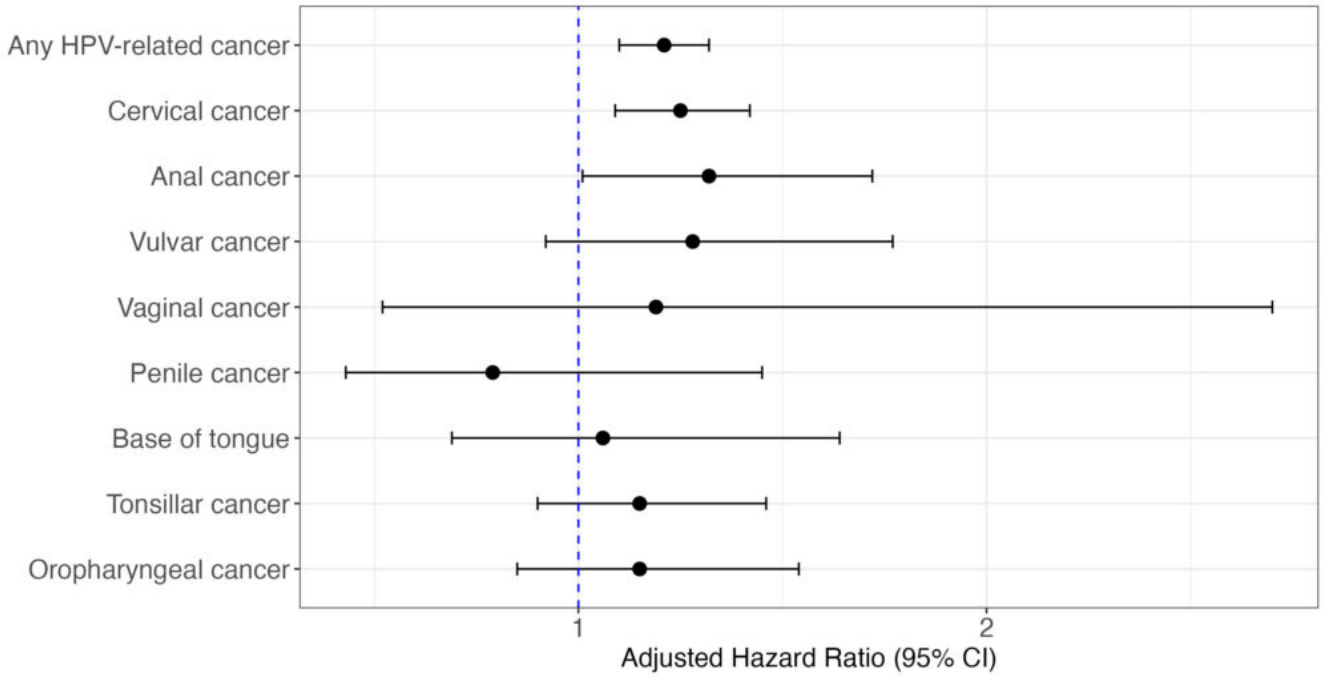
Stress disorders have been linked to immunosuppression, potentially reducing the ability to clear Human Papillomavirus (HPV) infections and increasing risk of HPV-related cancers. We investigated the association between stress disorders and HPV-related cancer risk in Denmark from 1995 to 2022.

We identified patients with stress disorder diagnoses (acute stress reaction, post-traumatic stress disorder, adjustment disorder, and other/unspecified reactions to severe stress) from population-based medical registries. Subsequent HPV-related cancers (cervical, anal, vulvar, vaginal, penile, base of tongue, tonsillar or oropharyngeal cancer) were identified using the Danish Cancer Registry. We followed patients from date of first stress disorder diagnosis until first cancer diagnosis, death, emigration or December 31, 2022, whichever came first. Using Cox proportional hazards regression, we computed the HR and 95% CI of any HPV-related cancer and specific cancer types in patients with stress disorders compared to an age and sex matched comparison cohort from the general population. We adjusted for potential confounders (i.e. cohabitation status, Charlson Comorbidity Index score, anxiety, depression and alcohol and drug dependency diagnoses).

We identified 242,830 patients with a diagnosis of any stress disorder (56.7% age 16-39 years; 59.8% female) with 755 cases of any HPV-related cancer observed over a median follow-up of 10.2 years. Of 1,199,400 patients in the comparison cohort, 2,820 were diagnosed with any HPV-related cancer. Patients with stress disorders were slightly more likely to develop any HPV-related cancer (adjusted HR=1.2, 95% CI: 1.1-1.3) and cervical cancer (adjusted HR=1.3, 95% CI: 1.1-1.4) compared to the comparison cohort (Figure 1).

Our results suggest that although risk of HPV-related cancer is low overall, risk of any HPV-related cancer, particularly cervical cancer, is slightly elevated in patients with stress-related disorder.

Figure 1. Risk of HPV-related cancers among individuals with any stress disorders compared to an age and sex matched comparison cohort, Denmark, 1995 – 2022



Hazard ratios adjusted for cohabitation status, level of comorbidity, anxiety, depression and alcohol and drug dependency diagnoses.

Mental Health

Evidence triangulation in suicide research: a systematic review of Mendelian randomization study Naohiro Yonemoto* Naohiro Yonemoto

Background: Suicide is a critical issue in public health, but it is multifactorial, and relatively rare in general populations, and risk factors need to be examined either in large observational data or in high-risk populations. In this study, we apply triangulation, a causal inference method in epidemiological studies that recently received considerable attention. Triangulation is a method to strengthen causal inference by integrating research results obtained from several different approaches. We performed a systematic review of Mendelian randomization for risk factors in suicide research.

Method: The literature search was conducted using MEDLINE, EMBASE, the Cochrane databases, and reference lists from previous related literature reviews. Preferred Reporting Items for STROBE-MR and the flow diagram were presented to reflect the search process. We summarized the characteristics of these eligible studies and synthesized their data for triangulation by risk factors.

Results: 59 studies were identified from the search. Risk factors such as psychiatric disease, smoking, alcohol, overweight, chronic pain, vitamins, and drugs, were investigated. While a study showed results that supported an association in some cases, the synthesis by triangulation showed that the causal relationship was unclear and questionable.

Conclusion: The triangulation approach would be a powerful tool for identifying risk factors in suicide research.

Mental Health

Associations Between Economic Hardships and Mental Health Outcomes in Idaho, BRFSS 2022-2023 Kailey Belcher* Kailey Belcher Deborah Taye Machell Town J'Neka S. Claxton Guixiang Zhao

Introduction

Economic stability is a key social determinant of health that influences mental health. Idaho's Division of Public Health has prioritized mental health, making it important to examine the associations between economic stability and mental health outcomes among adults.

Methods

We analyzed data from Idaho's 2022-2023 Behavioral Risk Factor Surveillance System, which included core questions and an optional module for social determinants and health equity, totaling to 12,528 adult participants, aged ≥ 18 years. Weighted prevalences of economic hardship variables (e.g., lost or reduced hours of employment, housing insecurity, experiencing threat to shut off utility services, receiving food stamps or SNAP, and food insecurity) and mental health related variables (e.g., mental stress and frequent mental distress) were estimated by demographic characteristics. Using log-linear regression analyses with robust variance estimator, the adjusted prevalence ratios were used to assess the associations between economic hardships and mental health related variables, adjusting for demographic characteristics.

Results

Prevalence estimates of economic hardship variables ranged from 5.8% (experiencing threat to shut off utility services) to 11.1% (food insecurity) and were generally higher among younger adults and those with less than a high school education. Prevalence estimates of mental stress and frequent mental distress were 14.6% and 14.2% respectively, highest among adults aged 18-34 years, women, those with less than a high school education, those with a household income <$25,000, and unmarried individuals. After adjusting for demographics, individuals reporting economic hardships had 2.1 to 4.0 times higher prevalence of mental stress and 1.7 to 2.6 times higher prevalence of frequent mental distress compared to those without hardships.

Conclusion

Addressing and providing support to those experiencing economic hardships may help improve mental well-being in Idaho.

Methods/Statistics

Sensitivity analysis to estimate bias-corrected validity measures in outcome validation studies under the “all possible cases” assumption in routinely-collected health databases

Norihiro Suzuki* Norihiro Suzuki Masataka Taguri Koichiro Shiba Masao Iwagami Takuhiro Yamaguchi

In studies using routinely-collected health databases (e.g., administrative claims databases), it is common to identify the subject’s outcome status by an algorithm (e.g., diagnosis code with a drug prescription). The validity of such an algorithm is assessed with measures such as sensitivity (Se), specificity (Sp), positive predictive value (PPV), and negative predictive value (NPV), based on the result of a validation study comparing the algorithm’s outcome classification with that of a gold standard. Due to time and financial constraints, researchers often use a subset of the study population in the database for validation, particularly for rare outcomes, with a sampling method under the “all possible cases” (APC) assumption—where all true cases (the denominator when calculating sensitivity) in the study population are included in the selected subset. This assumption is violated when unsampled true cases exist, which could lead to overestimated validity measures of the algorithm. However, no study has quantitatively assessed how the extent of unsampled true cases might bias the estimated measures. This study first derives formulas for the bias in each measure when the APC assumption is violated. Using these formulas, we propose a sensitivity analysis method to quantify the bias and compute bias-corrected estimates. We also propose an additional sampling approach in validation studies to obtain point and interval estimates of the bias parameters that can be used in the proposed sensitivity analysis. We illustrate that PPV can always be estimated without bias even when the assumption is violated, while the violation leads to overestimated Se, Sp, and NPV. Our applied examples using real-world data demonstrated that Se would be substantially biased as unsampled true cases increased, while Sp and NPV were relatively robust to the violation (See Figure).

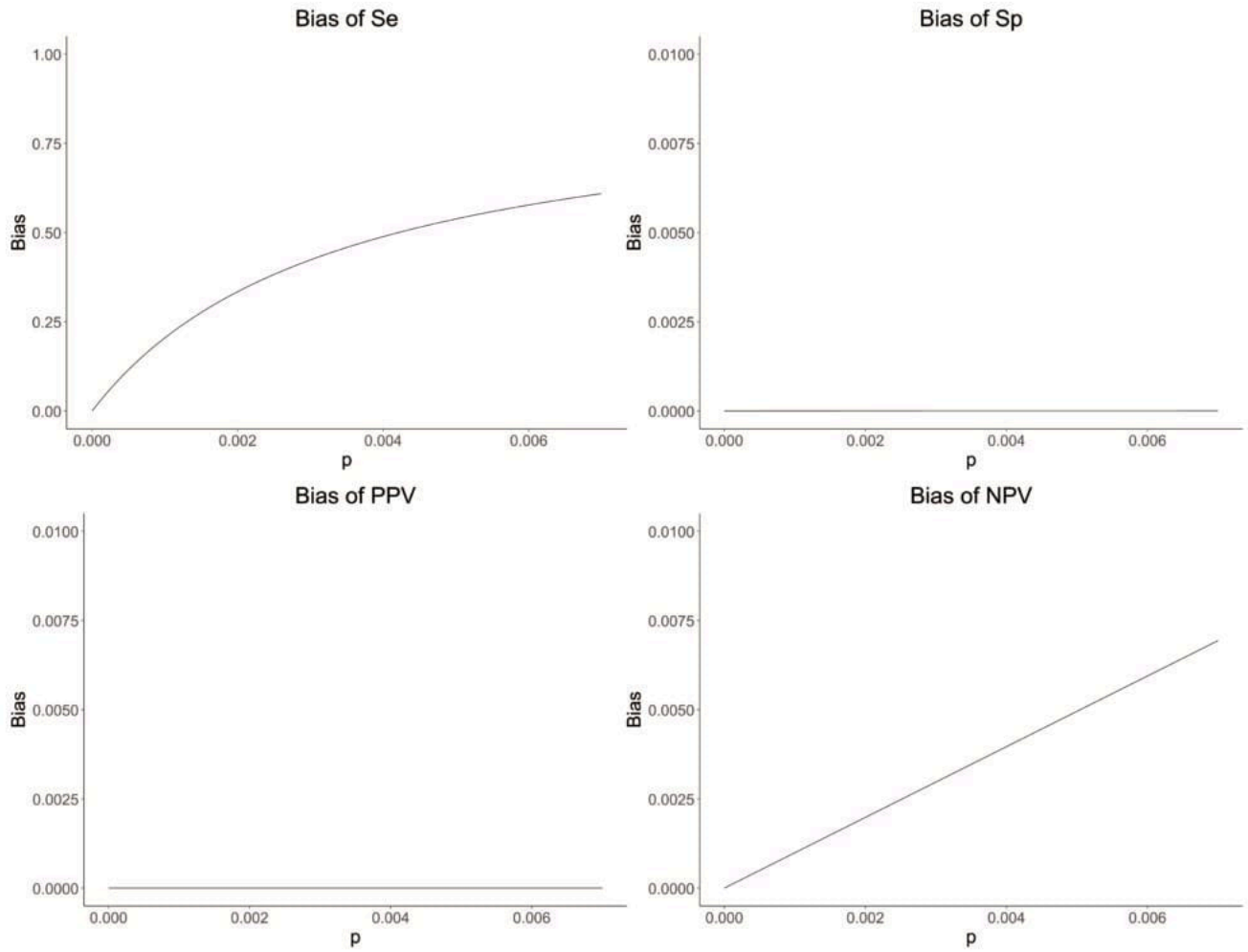


FIGURE. Biases of Se, Sp, PPV, and NPV for the 6th algorithm to identify multiple sclerosis in Widdifield et al. (2015) when the sensitivity parameter p is varied between [0, 0.007]. p is the proportion of unsampled true cases in the unsampled eligible population in the database.

Methods/Statistics

Within-person pooling of biospecimens, a solution to highly variable expensive biomarkers: practical or idealistic? Yajnaseni Chakraborti* Yajnaseni Chakraborti Enrique F. Schisterman Sunni L. Mumford Aijun Ye Stefanie N. Hinkle

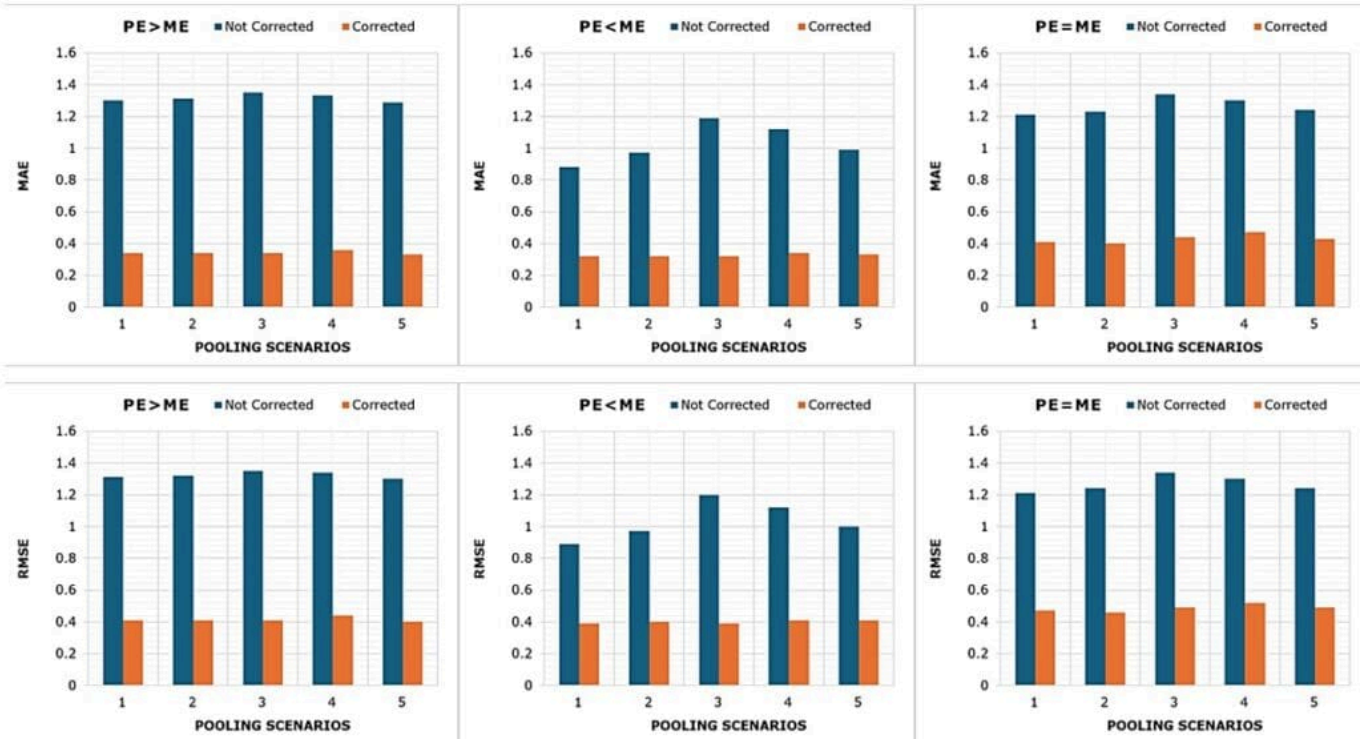
Background: Biomarkers are crucial for measuring exposure in environmental and nutritional sciences but can be costly. Pooling biospecimens across individuals is cost-effective but leads to biased exposure effect estimates (β) when target biomarkers have high temporal variability. A novel study design combined with a regression calibration approach is needed to address this issue, as repeated within-person samples for the whole study cohort are not always feasible.

Methods: We propose a hybrid pooled-unpooled study design, where biomarkers are repeatedly measured in a small subset of the cohort, while in the rest, biomarkers are measured from biospecimens that are pooled together before assay. To address any remaining measurement error (ME) and resulting pooling error (PE) from this pooling design, a correction factor was derived to obtain the bias-corrected estimate of the exposure effect (βc), along with the bias-corrected 95% CI. A simulation study (1000 runs, n=1088 with 10 repeated samples) was conducted with varying pooling sizes, and three variability scenarios: 1) PE > ME, 2) PE < ME, and 3) PE = ME. We assessed the robustness of the design by comparing the Mean Absolute Error (MAE) and Root Mean Square Error (RMSE) for uncorrected and bias-corrected estimates of β for a binary outcome, as well as the coverage of the 95% CIs.

Results: The MAE and RMSE for βc's were lower compared to uncorrected β's, across all scenarios of biomarker variability. Bias from not calibrating was more severe when PE > ME and PE = ME, compared to when PE < ME (Figure). Coverage of the 95% CIs were acceptable.

Conclusion: The approach of hybrid within-person biospecimen pooling, and bias correction through regression calibration, provides a robust and cost-effective solution for measuring highly variable, expensive biomarkers in research areas where exposure misclassification is a concern (e.g., to study the effect of exposure to environmental toxicant(s) on likelihood of live birth).

Figure: Distribution of Bias in the Simulation Study (Not Corrected vs. Corrected for biomarker variability)



Methods/Statistics

Choosing the link function for time-to-pregnancy analysis: An example based on assessing folate supplementation in PRESTO Vaishnavi Venkat* Vaishnavi Venkat Lauren A. Wise Kenneth J. Rothman Clarice R. Weinberg

Background: Three approaches to generalized linear model (GLM) analysis of time-to-pregnancy (TTP) data have been proposed, based on choice of the "link" function that connects the per-cycle probability of conception (fecundability) with a linear combination of predictors. We compared the performance of the logit, log, and inverse link functions for data from the PRESTO cohort, with use of folate supplements as the exposure.

Methods: We analyzed data from 15,847 participants who answered the question about folate supplements. Three GLMs were fitted to model the association between folate supplement use and fecundability. Models were adjusted for age, education, income, race, smoking status, and gravid status. Model fit was assessed using the Akaike Information Criterion (AIC), and the Hosmer-Lemeshow test.

Results: Without adjustment, folate supplement use was associated with increased fecundability across all link functions. After adjusting for confounders, the association remained positive in each analysis, but was attenuated. The logit-link model (equivalent to the Cox model for discrete time) yielded a fecundability odds ratio (FOR) of 1.31 (95% CI: (1.23,1.40)), the log-link model a fecundability ratio (FR) of 1.26 (95% CI: (1.18,1.33)), and the inverse-link model a population FR of 1.06 (95% CI: (1.02,1.10)). The logit and log-link models provided better fits than did the inverse-link model, as evidenced by lower AIC values (logit: 49961, log: 49967, inverse: 50153) and higher Hosmer-Lemeshow p-values (logit: 0.73, log: 0.39, inverse: 0.00), which are based on comparing the fitted to observed conception rates.

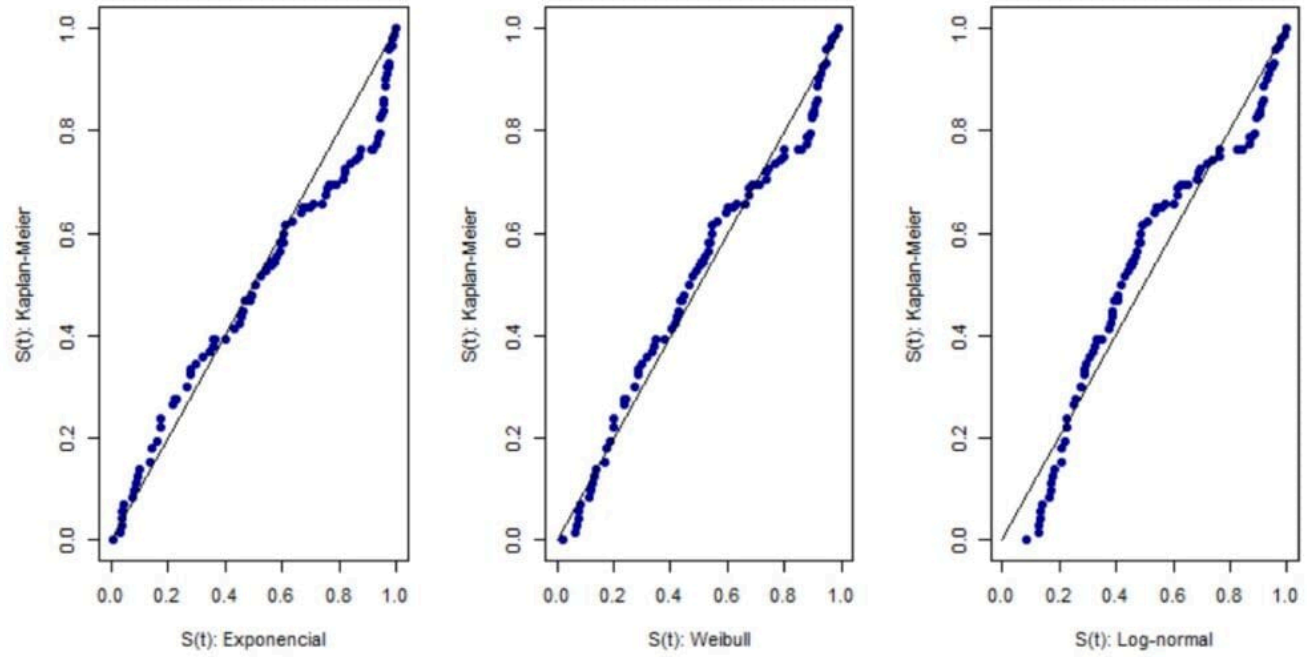
Conclusion: The logit-link and log-link models outperformed the inverse-link model for the PRESTO TTP data. These findings highlight the importance of careful selection of the link function in TTP analysis, based on comparing the fits and the predictive performances of the resulting models.

Methods/Statistics

Parametric Regression Model Using Weibull Distribution in Patients with Ovarian Carcinoma in the State of Paraíba Tiago Almeida de Oliveira* Tiago Almeida de Oliveira Vitoria Soares de Souza Débora de Sousa Cordeiro Cleanderson Romualdo Fidelis Roberta Moreira Wichmann Ana Patricia Bastos Peixoto Tiago Almeida de Oliveira

This study investigates the survival time of ovarian cancer patients in the state of Paraíba, considering factors such as age, race/ethnicity, diagnostic methods, and disease extent. The sample comprised 146 patients, 72% of whom died from cancer, while 28% were censored cases. The median age was 57.5 years, with women aged 50 and older at higher risk. The mean overall survival time, including failures and censored cases, was 516 days, with a median of 340 days, indicating short survival for many patients. Approximately 48.6% of patients were aged between 31 and 60 years, and 63.7% self-identified as Black or Brown, suggesting disparities in access to diagnosis and treatment. The most common tumor type was adenocarcinoma, with 93.8% of diagnoses made via histological examination. Kaplan-Meier survival curves indicated that younger and White women had better survival rates. Although statistical analysis showed no significant impact of age, race/ethnicity emerged as a relevant factor, with pronounced differences due to disparities in access to diagnosis and treatment among groups. Based on the Akaike Information Criterion (AIC), the Weibull model was identified as the most suitable parametric regression model. The presence of metastasis was the main factor contributing to a poorer prognosis, increasing the risk of death by approximately eightfold during treatment. Additionally, the lack of information on cancer extent further elevated the risk, likely due to late diagnoses or inadequate treatment. Interestingly, patients over 60 years of age showed a 16% reduction in failure risk, suggesting a more favorable response to treatment. These findings underscore the importance of early diagnosis and highlight the impact of socioeconomic and cultural factors on survival disparities in ovarian cancer in Paraíba.

Keywords: ovarian cancer; survival; risk factors; Health disparities.

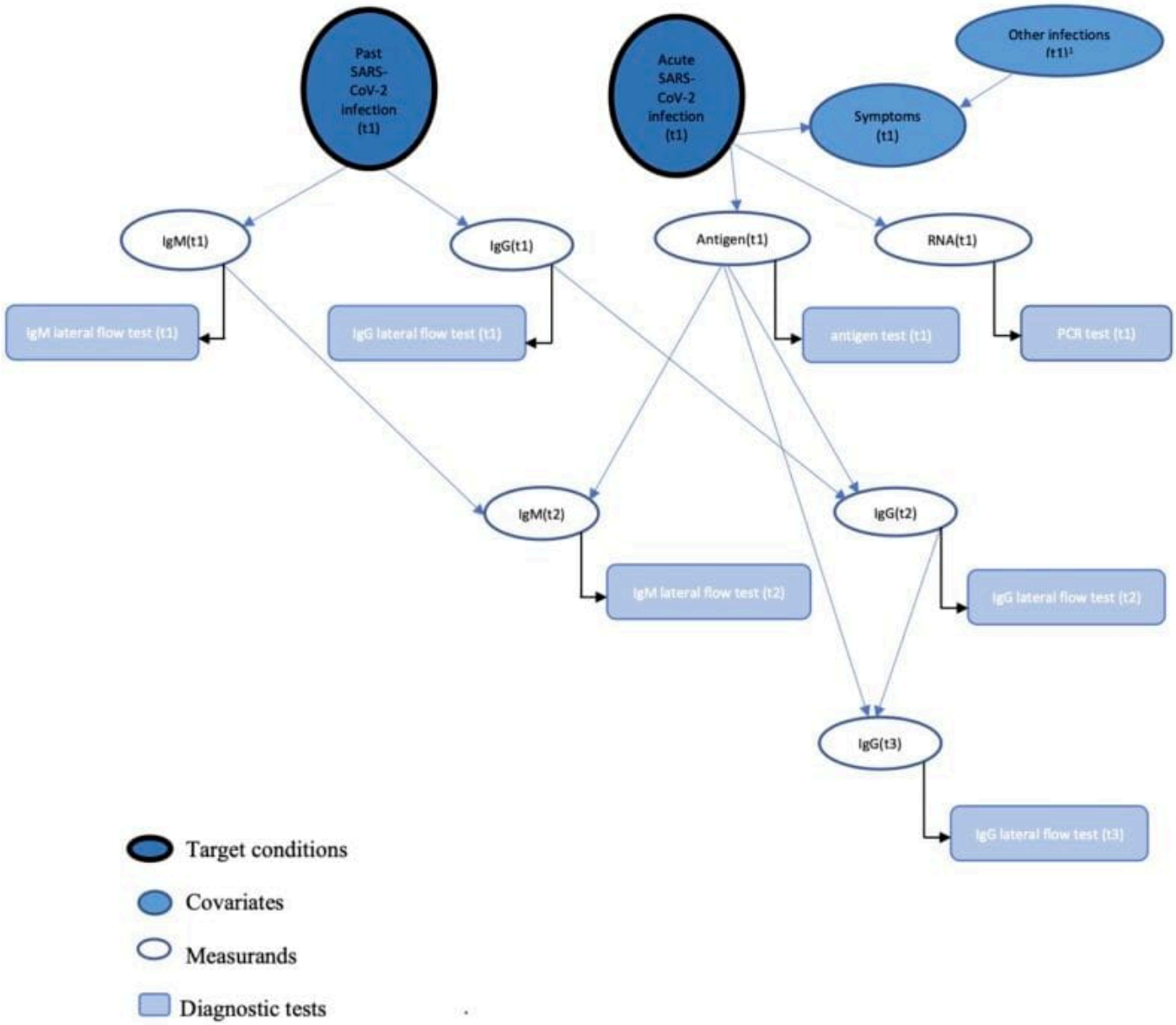


Methods/Statistics

Diagnostic accuracy of tests for SARS-CoV-2 acute infection: Distinguishing measurands from target conditions Joanna Merckx* Joanna Merckx Ian Schiller Yap Boum Patrick M Bossuyt Nandini Dendukuri

Test accuracy evaluation for SARS-CoV-2 infection is complicated by the lack of a perfect reference. Additionally, the available tests have different measurands further challenging performance estimation. The current literature reports that antibody test sensitivity varies according to time since symptom onset. Such reporting however conflates two separate parameters: the time-varying prevalence of antibodies (the measurand), and the time-invariant ability of the assay to measure antibodies. We improve the commonly used latent class model (LCM) via the decomposition of the diagnostic accuracy question into its elements: i) the tests under evaluation, ii) their measurands and iii) the target conditions. We use directed acyclic graphs (DAG) to visualize these elements. We use LC analysis (LCA) to model the relationships in the DAG and Bayesian inference to obtain estimates of accuracy of a PCR, antigen, and rapid IgM and IgG antibody test for the diagnosis of the target conditions acute and past SARS-CoV-2 infection and their prevalence. We introduce two random effects to capture the dependence between the measurands due to acute and past infection. We represent the results as posterior distribution medians with 95% credible intervals (CrI) and compare with a measurand naïve LC model. We apply our methods to a Cameroonian cohort of 1,194 adults tested at multiple-time points in the early pandemic. We estimated the prevalence of acute and past infection as 20% (95%CrI 17; 24) and 26% (95%CrI 20; 32), respectively. Sensitivity and specificity estimates are provided for all tests, measurands and their target conditions. We learned that by distinguishing target conditions and measurands and using a DAG to clarify their relations we were able to build a LCM with more insightful results on the performance of a range of COVID-19 tests. Similar models can enrich estimates of test accuracy and prevalence of infectious diseases specific target conditions in future studies.

FIGURE. - DAG representation of the diagnostic accuracy question, presenting the relationships between target conditions, measurands, tests and covariates.



[1]Other infections: not included in the modelling
t1: time at presentation, t2: 7 days after first presentation, t3: 14 days after first presentation.

The seven measurands by time and type are denoted as follows: RNA(t1), antigen(t1), IgM(t1), IgG(t1), IgM(t2), IgG(t2) and IgG(t3). The tests are denoted as PCR(t1), antigen test(t1), IgM test(t1), IgG test(t1), IgM test(t2), IgG test(t2) and IgG test(t3).

Methods/Statistics

MetaAnalysisOnline.com: a simplified solution for conducting meta-analysis Janos Tibor Fekete* Janos Tibor Fekete Balazs Gyorffy

Background. Meta-analysis is a robust quantitative research method widely employed in epidemiology and clinical medicine to systematically evaluate and synthesize existing studies, enabling comprehensive conclusions on specific topics. This study introduces a new bioinformatics tool designed to enhance visualization and analysis options for conducting meta-analyses.

Methods. A meta-analysis can utilize binary or continuous data as its basis for analysis. The primary statistical models, such as the random effect model and the fixed effect model, are delineated along with their corresponding statistical methodologies. Moreover, we incorporated graphical representations including forest plots, funnel plots, and Z-scope plots. While the forest plot effectively illustrates heterogeneity and pooled results, a funnel plot can uncover potential publication bias, and a Z-score plot demonstrates the robustness of the sample size used. In addition to traditional pairwise meta-analysis network meta-analysis (NMA) is also adapted.

Results. The outlined models and visualization options have been integrated into a new online web portal accessible without requiring registration. The web tool works on an Ubuntu server running Apache and enables researchers to conduct meta-analyses using results typically used in epidemiology and clinical trials including binary (total and event numbers), continuous (mean and standard deviation data), and time-to-event data (hazard rate and CI data). Results from commonly used spreadsheet applications such as Excel can be directly inputted into the system. The online tool makes use of the meta, metafor and netmeta packages in the R programming environment (R version 4.2.2) for statistical calculations and for drawing the plots. The Shiny interface is powered by shinyjs, shinydashboard, and rhandsontable R libraries. The portal generates a forest plot to summarize meta-analysis results, a funnel plot to visually detect potential bias, and a Z-score plot indicating the sufficiency of the cumulative sample number. The new bioinformatic tool is accessible at www.metaanalysisonline.com and does not necessitate any programming knowledge or the use of command lines.

Conclusion. MetaAnalysisOnline.com is a user-friendly and reproducible platform tailored for epidemiological research and clinical trials. It enables the swift integration and visualization of findings from multiple studies, bringing advanced meta-analytic techniques within reach for researchers without requiring programming skills.

Methods/Statistics

Using Probabilistic Bias Analysis to Adjust for Selection Bias in a Retrospective Case-Control Study Timothy L Lash* Huda Bashir Anke Hüls Richard F MacLehose Thomas P Ahern Lindsay J Collin Timothy L Lash

Retrospective case-control studies are susceptible to selection bias due to differential participation. Most studies present results from analyses on those who agreed to participate with acknowledgement of the potential for selection bias. To better understand the magnitude of bias and impact of bias adjustments, we conducted a simulation study using information about participants' exposure prevalence to inform non-participants' exposure prevalence and apply these in probabilistic bias analysis. Using a data-generating mechanism, we simulated 100,000 cohort studies, each with 40,000 subjects, true risk ratio of 2.00, exposure prevalence of 0.20, and baseline risk of 0.01. We then simulated 100,000 case-cohort studies within these cohort studies, sampling two controls per case. We evaluated three scenarios. First, we conducted studies with no selection bias. Second, selection bias was introduced by specifying that exposed cases were less likely to participate than unexposed cases (75 % vs 95%), and exposed controls were slightly more likely to participate than exposed cases (82%), but less likely than unexposed controls (88%). Third, participation rates for cases and controls were switched from the second scenario. In the first scenario with no selection bias, 95% of the 95% confidence intervals (CIs) covered the true odds ratio (OR), as expected. In the second scenario, with no bias adjustment, 77.7% of the CIs covered the true OR with a median estimate of 1.70 (1.29–2.23). In the third scenario, with no bias adjustment, 78% of the CIs covered the true OR with a median estimate of 2.36 (1.79–3.11). Four probability distributions (uniform, triangular, trapezoidal, and beta) for the exposure prevalence in non-participants, informed by participants, were used to obtain bias-adjusted estimates. The trapezoidal distribution provided the best coverage (scenario two: 94.7%, scenario three: 99.8%), and beta distributions provided the worst coverage (both scenarios: 77.3%).

Methods/Statistics

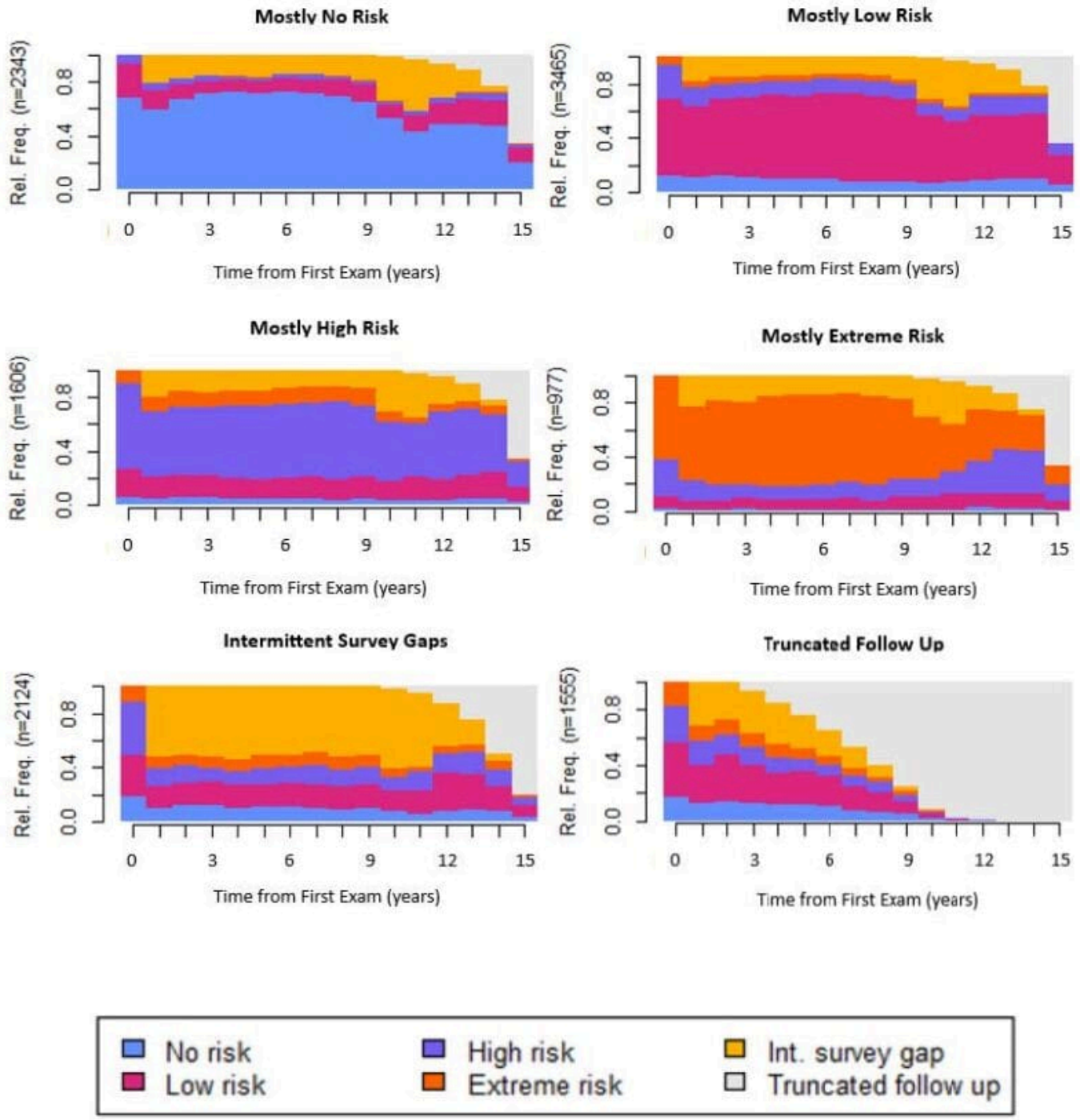
Evaluating the Longitudinal Utility of the Berlin Questionnaire for Obstructive Sleep Apnea Risk: A Sequence Analysis Approach Alexandra Mueller* Alexandra Mueller David Goldfarb David Appel Rachel Zeig-Owens David Prezant

Introduction: The Berlin Questionnaire (BQ), validated cross-sectionally and widely used, identifies Obstructive Sleep Apnea (OSA) risk. Its longitudinal performance remains unexamined. We used Sequence Analysis (SA) to evaluate temporal trajectories of BQ-identified OSA risk, assess clusters with similar trajectories, and characterize cluster differences.

Methods: Retrospectively, we studied Fire Department of the City of New York World Trade Center Program participants who completed BQ across multiple time points from 2009-2024 starting at first survey. At each exam, participants scored into 1 of 4 categories based on the number of positive BQ domains – snoring, fatigue, blood pressure/body mass index: no-risk (NR) (0/3), low-risk (LR) (1/3), high-risk (HR) (2/3), extreme-risk (ER) (3/3). SA identified longitudinal sequences of BQ risk classifications, clustering participants with similar trajectories. We calculated risk ratios using log-binomial regression and computed p-for-trend, adjusting for age at first BQ, race, sex, and smoking status.

Results: From 12,070 participants with 3+ BQ (mean=11), we identified 6 distinct clusters: mostly NR (19%), mostly LR (29%), mostly HR (13%), mostly ER (8%), intermittent survey gaps (18%), and truncated follow up (13%). Fig. 1 shows relative frequencies of each BQ-risk category over time per cluster. Over 80% consistently scored into their cluster's corresponding BQ-risk category >50% of surveys. Increasing risk severity cluster is associated with continuous positive airway pressure treatment authorization, notably with mostly HR and ER clusters differing significantly.

Conclusion: Most participants remained consistent in BQ-risk category over 15 years. While the BQ is only validated combining high- and extreme-risk, mostly HR and ER clusters differed, providing rationale for the use of 3 BQ risk categories in research settings. These findings suggest potential use of BQ risk as an OSA proxy in longitudinal studies.


Mostly No Risk
Rel. Freq. (n=2343)
0.0
0.4
0.8
0
3
6
9
12
15
Time from First Exam (years)
Mostly Low Risk
Rel. Freq. (n=3465)
0.0
0.4
0.8
0
3
6
9
12
15
Time from First Exam (years)
Mostly High Risk
Rel. Freq. (n=1606)
0.0
0.4
0.8
0
3
6
9
12
15
Time from First Exam (years)
Mostly Extreme Risk
Rel. Freq. (n=977)
0.0
0.4
0.8
0
3
6
9
12
15
Time from First Exam (years)
Intermittent Survey Gaps
Rel. Freq. (n=2124)
0.0
0.4
0.8
0
3
6
9
12
15
Time from First Exam (years)
Truncated Follow Up
Rel. Freq. (n=1555)
0.0
0.4
0.8
0
3
6
9
12
15
Time from First Exam (years)
No risk
Low risk
High risk
Extreme risk
Int. survey gap
Truncated follow up

Methods/Statistics

Impact of mortality on methods for handling missing data in longitudinal studies: an application to the study of frailty trajectories Anna* Anna Siefkas Rienna Russo Ariela Orkaby Yuan Ma A. Heather Eliassen Marian T. Hannan Jungwun Lee Sebastien Haneuse

Longitudinal studies are subject to missing data such as unit nonresponse, attrition, and item nonresponse. While inverse probability of censoring weights (IPCW) and multiple imputation (MI) are well-established, their appropriateness in longitudinal aging studies is not obvious due to often high mortality, which leads to truncated data that cannot logically be imputed.

We performed a simulation study to assess the impact of mortality on methods for handling missing data in longitudinal studies of frailty. We simulated two complete data sets, each including 3 baseline covariates (one continuous, two binary) and 10 binary frailty index (FI) items at 9 timepoints. In the first, all timepoints were observed for all participants (i.e. no mortality). In the second, we used the value of the FI to predict mortality and truncated some trajectories due to death. To each dataset, we also added unit nonresponse, attrition, and item nonresponse to FI items. Missingness was missing at random conditional on covariates and all other FI items. We compared the performance of methods commonly used in frailty research: complete case analysis, carry forward imputation, setting missing items to 0, prorating the FI denominator, and MI using generalized linear mixed effects models. Attrition was addressed with IPCW. In the data without mortality, FI trajectories were modeled with linear mixed effects models. In the data with mortality, models were partly conditional on death to avoid extrapolating trajectories past the point of mortality.

When mortality was absent, MI recovered model parameters with negligible bias. When mortality was present, all methods demonstrated bias, particularly for the intercept term; average FI was underestimated in imputed data with mortality.

Standard missing data methods should be used with caution in settings with high mortality. Novel methods are needed to address missing data in the presence of mortality, especially in complex settings of aging research.

Methods/Statistics

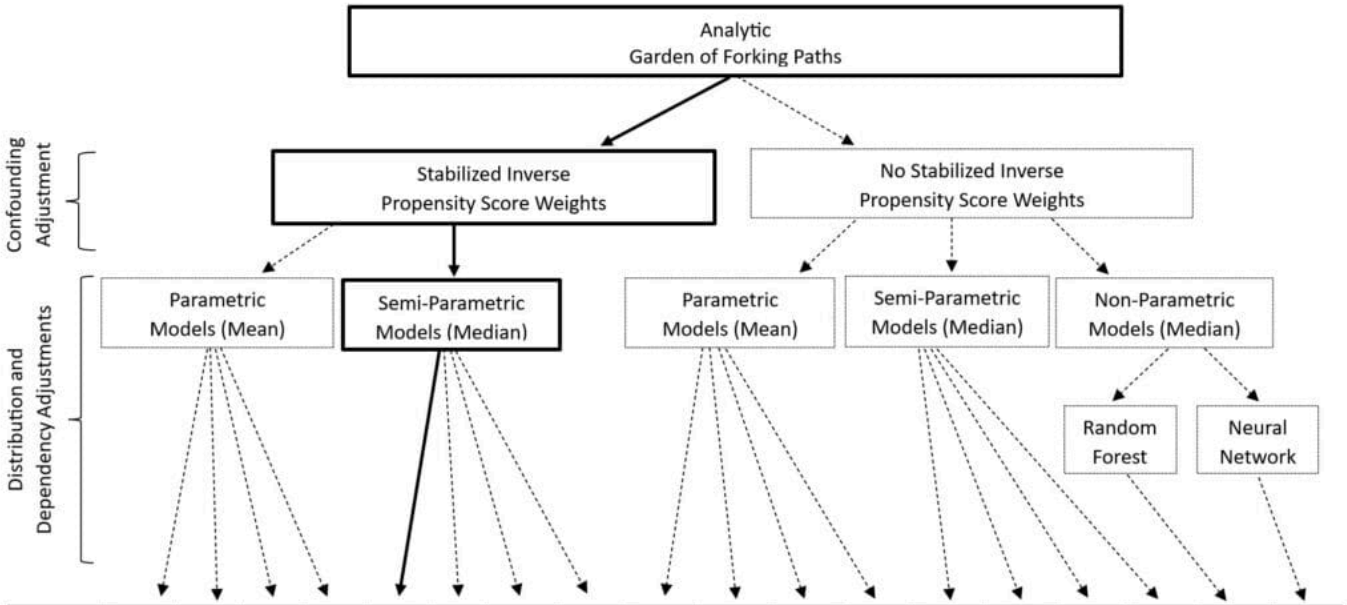
Multiverse sensitivity analysis: Examining robustness of multi-level quantile regression on sparse repeated measures Hayden L. Smith* Hayden Smith

Background: Studies have demonstrated infant positioning can influence physiologic states and neurologic development. Objective: to examine the sensitivity of multi-level quantile regression (MLQR) results versus varied approaches in assessing an intervention to improve infant positioning.

Methods: A pre-post study was conducted at a free-standing children's hospital in the United States. Study personnel collected patient positioning observations for a period before and after the implementation of the Infant Positioning Assessment Tool (IPAT) into standard practice by NICU nurses. Patients could have had repeated observations collected by study team members during their stay, creating patient level-clusters. The primary statistical model was a MLQR with stabilized inverse propensity score weights to balance covariates. A local analytic garden of forking paths was explored to examine the robustness of the primary results. Garden branches included distributional assumptions, data dependency assumptions, and controlling for possible confounders.

Results: The study included 158 infants with a median of 2 (IQR: 1, 3) repeated observations, represented by a total of 327 observations. One-hundred and sixty-nine observations were in the pre-intervention and 161 in the post-intervention periods. The MLQR model with weights revealed a 2.1 (95% CI: 1.6, 2.8) point median increase in observed positioning scores in the post-period. Figure presents the multiverse sensitivity analysis. Effects and precision estimates appeared robust across statistical methods (estimate range: 2.0-2.5 and confidence interval widths: 0.8-2.2).

Conclusions: Study revealed that within a nominal sized sample with limited repeated observations, results did not vary much by analytic method. Of note, there may have been limited confounding due to study design and a lack of consequential covariance between sparse repeated observations, possibly contributing to the insensitivity of analytic choice.



Model	MLM	FEr	FE	Drop	MLM	FEr	FE	Drop	MLM	FEr	FE	Drop	MLM	FEr	FE	Drop	FE	FE
Estimate	2.3	2.2	2.2	2.5	**2.1**	2.00	2.00	2.0	2.3	2.3	2.3	2.4	2.2	2.0	2.0	2.0	2.3	2.3
Lower CI	1.8	1.8	1.8	1.9	**1.6**	1.3	--	2.0	1.8	1.9	1.9	1.8	1.7	1.4	--	1.9	1.9	1.6
Upper CI	2.8	2.6	2.6	3.1	**2.6**	2.7	--	4.3	2.8	2.7	2.7	3.0	2.7	2.6	--	2.7	2.7	2.7

Figure. Analytic garden of forking paths for computing estimates of central tendency related to sparse repeated measures in an observational setting. Solid lines represent the primary analytic model used in the study, while dashed lines represent alternatives. Weighting attempted to balance potential confounders (i.e., direct admission, gestational age, and crib devices). Definitions: MLM = multi-level model; FEr = fixed effects with robust standard errors; FE = fixed effects; Drop = dropping non-initial observations and fitting a FE model; CI: confidence interval; --: model had a non-unique solution.

Methods/Statistics

Agreement between Two Methodologies in the Development of a Sexual Violence Risk Index Seema Nayak* Seema Nayak Noelle Horth Eileen Shields

Sexual violence is a significant social and public health problem. The New York State Department of Health developed a county-level sexual violence risk index (SVRI) to identify counties with high proportions of populations at risk for sexual violence. To validate identification of high-risk counties, we developed the index using two method and compared results. Comparing processes and results of the two methods provides insight and validation for future index development efforts.

Twelve individual, relationship and community-level risk factors for sexual violence victimization and perpetration were identified from literature and other online resources. County-level percentages and rates for risk factors were obtained from federal and state resources. In the first SVRI-calculation method, values for each risk factor were standardized by calculating their Z-scores for each county. Z-scores for each county were averaged across factors to create its composite SVRI score. The second SVRI-calculation method used a principal component analysis (PCA) where correlated risk factors were reduced to three components. Composite SVRI scores were calculated by aggregating component scores. In both methods, counties were categorized as low, low-medium, medium-high, and high-risk categories using quartiles of the composite SVRI distribution. County risk categories were compared using percentage agreement and Cohen’s Kappa coefficients to assess agreement between the methods.

With the Z-score methodology, 27% of the 62 counties were identified as high-risk including two in New York City (NYC) and 15 counties in Rest of the State (ROS). Using PCA, about 18% of counties were identified as high-risk including three in NYC and eight counties in the ROS region. Simple and weighted Kappa coefficients of 0.34 and 0.37 showed fair agreement between methods. About 47% of counties showed exact agreement, with highest agreement in the high-risk category. The Z-score method categorized 17 counties as high-risk and included 91% of the 11 counties identified as high-risk by PCA method.

The Z-score methodology was determined as more appropriate as it standardizes values allowing us to make comparisons between counties on the same scale and identify those with highest proportion of risk factors compared to the regional average.

LATEBREAKER

Methods/Statistics

Longitudinal effects of maternal depression on child's anxiety and depression in rural Pakistan: a marginal structural modelling approach Min Kyung Kim* Min Kyung Kim Paul N. Zivich Joanna Maselko

Introduction

Depression and anxiety are significant risks to child development, with maternal depression being an important predictor. But the complex longitudinal effects limit in identifying critical windows of maternal depression on child depression and anxiety.

Methods

We used marginal structural models to evaluate the longitudinal patterns of maternal depression – during pregnancy (third trimester), infancy (3 months, 6 months, and 1 year), early childhood (2, 3, and 4 years) and mid-childhood (6 and 7 years) – on 8-year-old children's depression and anxiety. In a cohort of mother-child dyads in rural Pakistan, we assessed maternal depression using the Patient Health Questionnaire (PHQ-9), and child depression and anxiety using the Revised Child Anxiety and Depression Scale (RCAD), and Spence Children's Anxiety Scale (SCAS), respectively.

Results

A total of 839 mother-child dyads were included in the analysis. Children exposed to high and sustained maternal depression during pregnancy, infancy, early childhood, and mid-childhood reported the highest average RCAD and SCAS scores at 4.83 (SD = 3.55) and 4.66 (SD = 3.19), respectively. Elevated PHQ-9 scores during infancy and early childhood led to an increased risk of depression among 8-year-old children (2.40, 95% CI = 0.21, 4.60), but the results were imprecise.

Discussion

We highlighted detrimental effects of maternal depression on child depression and anxiety during the child developmental periods. Interventions aimed at reducing maternal depression may offer benefits for both mothers and children's mental health.

LATEBREAKER

Methods/Statistics

A structural missing data investigation of economic hardship's effect on intimate partner violence perpetration by adolescent boys or young men in S. Africa during the COVID-19 pandemic C. Andrew Basham* C. Andrew Basham Rishav Singh Kalysha Closson Mags Beksinska Janan Dietrich Angela Kaida

Objective
We performed a structural missing data investigation (SMDI) of variables included in an analysis of economic hardship's effect on IPV perpetration among young men in S. Africa, during the COVID-19 pandemic.

Methods
Evidence for and against missing data generating mechanisms for each variable were evaluated as follows. Missing completely at random (MCAR) median (min, max) absolute standardized mean difference (ASMD) in other covariates between missing vs non-missing values <0.1, RF_AUC~0.5, p-Little and p-Hotelling both >0.05); missing at random (MAR) predictability of missing values using random forests multiple logistic regressions on other partially observed variables; missing not-at-random (MNAR): significant effect of missing value indicator variables on the outcome variable (IPV perpetration) after adjustment for the remaining covariates.

Results
The SMDI analytic sample included people with missing values for the outcome, exposure, covariates, and/or inclusion criterion (n=908) vs n=592 in complete case analysis. Median ASMDs ranged 0.226 (economic hardship) to 0.760 (number of children in household). Missingness prediction was unacceptable for sexual orientation, economic hardship, and alcohol use (AUC<0.60), acceptable (AUC=0.60-0.79) for IPV perpetration, excellent (AUC=0.80-0.89) for the number of children in household and number of seniors in household, and outstanding (AUC>0.89) for income, school/employed, and number of adults. Nonresponse to number of children in household had a strong adjusted positive association with IPV perpetration, as did sexual orientation's.

Conclusion
In a causal inference epidemiological study estimating the effect of incident economic hardship during COVID-19 on the odds of young S. African men perpetrating IPV we diagnosed the missing data generating mechanisms for the number of children in the household and sexual orientation to be MNAR. Outstanding predictability of other variables supports multiple imputation.

Covariate	ASMD (min/max)[1]	p Hotelling[1]	AUC[2]	beta univariate (95% CI)[2]	beta (95% CI)[3]
Income Category	0.750 (0.284, 1.704)	<.001	0.900	1.75 (95% CI 0.45, 3.05)	0.26 (95% CI -2.62, 2.84)
Sexual Orientation	0.377 (0.100, 0.890)	0.023	0.500	1.90 (95% CI 0.97, 2.85)	1.83 (95% CI 0.86, 2.81)
School/Employment Status	0.517 (0.278, 1.138)	<.001	0.900	1.04 (95% CI -0.30, 2.22)	-0.85 (95% CI -4.67, 1.68)
Economic Hardship	0.226 (0.016, 0.528)	0.758	0.500	0.49 (95% CI -0.39, 1.26)	0.50 (95% CI -0.40, 1.29)
Number of Children	0.760 (0.142, 1.907)	<.001	0.857	2.19 (95% CI 1.15, 3.31)	3.31 (95% CI 1.32, 6.32)
Number of Adults	NA (NaN, NaN)	<.001	1.000	1.97 (95% CI 0.63, 3.38)	14.78 (95% CI -53.40, NA)
Number of Seniors	0.424 (0.159, 0.854)	<.001	0.857	1.05 (95% CI -0.14, 2.10)	-16.02 (95% CI NA, 63.58)
HIV Status	NA (NaN, NaN)	0.761	0.500	NA (95% CI NA, NA)	NA (95% CI NA, NA)
Alcohol Use Frequency	0.421 (0.115, 1.409)	0.273	0.500	-13.87 (95% CI NA, 53.73)	-14.63 (95% CI NA, 96.48)
Perpetrated any IPV	0.407 (0.000, 1.704)	<.001	0.770	NA (95% CI NA, NA)	NA (95% CI NA, NA)

p little: <.001, Abbreviations: ASMD = Median absolute standardized mean difference across all covariates, AUC = Area under the curve, beta = beta coefficient, CI = Confidence interval, max = Maximum, min = Minimum

[1] Group 1 diagnostic: Differences in patient characteristics between patients with and without covariate

[2] Group 2 diagnostic: Ability to predict missingness

[3] Group 3 diagnostic: Assessment if missingness is associated with the outcome (univariate, adjusted)

Molecular

Utilizing DNA methylation chips to construct the epigenetic profiles among military staffs: a case-control study Yu-Shan Lin* Yu-Ching Chou Yen-Lin Li Chih-Yu Chou Jr-Tung Chou Yu-Shan Lin Chien-An Sun Yu-Ching Chou

Background: The physical health of military personnel directly impacts the fundamental combat effectiveness of the armed forces. Scientific evidence indicates that variations in genetic events and epigenetic events influence the health of military personnel. Epigenetics, defined as heritable changes in gene expression or cellular phenotypes without altering the DNA sequence, operates through mechanisms that are considered reversible. This project utilizes data from the Taiwan Biobank to compare the epigenetic profiles of military staffs with those of the general population, aiming to provide reference data for future applications in military selection medicine and personalized health management monitoring. **Methods:** This study utilized data from the Taiwan Biobank, selecting 67 participants from the “military staffs” category as the case group and performing 1:1 gender and age matching to select 67 controls in general population and create a total of 134 samples for epigenome-wide association studies (EWAS) analysis. Through EWAS analysis, loci with statistically significant differences between the case and control groups were identified, focusing on loci with p-values less than 10^{-20}. All statistical analyses were conducted using SAS version 9.4 and RStudio software. **Results:** The results showed no significant differences in gender and age distribution between the case group and the control group. Additionally, there were no significant differences between the two groups in health behaviors such as smoking, drinking, betel nut chewing, and exercise. The Manhattan plot identified five methylation loci (cg166430885, cg17268658, cg08979191, cg23753247, cg02067712) meeting the p-value threshold of 10^{-20}, located on chromosomes 1, 2, 4, 11, and 13. **Conclusion:** This study found significant differences in methylation profiles between military staffs and the general population in Taiwan. Five highly distinct methylation loci were identified, with gene functions potentially related to cancer suppression or progression, as well as influences on cardiac function, motor and neural functions, and mental states.

Neurology

Mixtures of key components of the external exposome in association with MRI biomarkers of brain structure: Multi-Ethnic Study of Atherosclerosis Cameron J. Reimer* Cameron Reimer Yorghos Tripodis Koichiro Shiba Peter James Kipruto Kirwa Susan R. Heckbert Jana Hirsch Lilah Besser Timothy M. Hughes Joel Kaufman M Maria Glymour Marcia Pescador Jimenez

Background: Environmental risk factor research in Alzheimer's disease and related dementias (ADRD) has primarily focused on individual environmental exposures. However, it remains unknown how combinations of components of the 'external exposome' (i.e., environmental mixtures) are associated with cognitive health.

Methods: In the Multi-Ethnic Study of Atherosclerosis (MESA), we evaluated the associations between a mixture of environmental exposures and Magnetic Resonance Imaging (MRI) biomarkers of brain structure for 1,156 participants (mean age: 74.2 years) using Weighted Quantile Sum regression, adjusted for individual sociodemographic factors and MESA field center. We examined exposures including: outdoor air pollutants, street view-derived greenspace, neighborhood amenities, walkability, population density, and neighborhood socioeconomic status, and assigned exposures as cumulative averages based on residential address beginning at baseline (2000-2002). MRI biomarkers (assessed 2017-2021) included total: gray matter volume (GMV), white matter hyperintensity (WMH) volume, and fractional anisotropy (WM-FA).

Results: The environmental mixture was negatively associated with WM-FA (-0.0036, 95% CI: [-0.0054, -0.0018]). The negative association with gray matter volume (mL) was not statistically significant (-2.24, 95% CI: [-4.63, 0.15]). Higher mixture values indicate greater levels of potentially harmful exposures (e.g., increased air pollution, decreased greenspace). The observed mixture effect was largely driven by exposure to fine particulate matter for models of WM-FA, and both walkability and nitrogen dioxide for models of GMV. The environmental mixture was not associated with WMH volume.

Conclusion: The environmental mixture was associated with lower total GMV and WM-FA, measures of macrostructural and microstructural integrity, respectively. These models indicate that specific exposures may present higher risks to particular aspects of brain health.

Neurology

Does seasonal influenza vaccination uptake increase after stroke? Evidence from a population-level administrative cohort Brian Steele* Brian Steele Michael D. Hill Jessalyn Holodinsky

Background. Observational evidence suggests that influenza vaccination may be associated with a reduction in stroke occurrence. This association is subject to treatment-selection bias; advancing age and the presence of stroke-related comorbidities are associated with both an increased risk for stroke and with an increased uptake of influenza vaccination. Using population-level data from Alberta, Canada, we estimated the effect of experiencing a stroke on the risk of receiving seasonal vaccination.

Methods. This study analyzed a cohort of linked administrative health records and registry data in a publicly funded healthcare system, covering the entire population of Alberta (n = 4.5 million) where seasonal influenza vaccinations are freely available to residents. Adults (aged 45-84) were eligible for inclusion and follow-up across 9 influenza seasons. For each season, individuals were 'at-risk' for vaccination between October and March and censored at first recorded seasonal vaccination, outmigration, or at season end. Cases were matched on demographic and medical comorbidity variables at each season using nearest neighbor matching without replacement. Marginal risk ratios were estimated with g-computation for the average treatment effect on the treated (ATT).

Results. The sample included 2.03 million adults (50.3% male) observed across one or more influenza season (2010-2011 to 2018-2019). Within the sample, 21,604 adults (1.1%) presented with a stroke event. Among cases, the risk of seasonal vaccination was 17% greater after experiencing a stroke (marginal RR: 1.17; 95% CI: 1.14 – 1.19).

Discussion. Our results suggest that seasonal influenza vaccination uptake increases following stroke. Sensitivity analyses are planned to examine incident cases alone and to evaluate alternative matching and weighting approaches. These findings will inform the design of studies evaluating vaccination for stroke-risk reduction and health promotion.

Neurology

Epidemiology of Balance and Dizziness Problems and Falls in Young Adults: National Longitudinal Study of Adolescent Health (Add Health) Chuan-Ming Li* Chuan-Ming Li Howard J. Hoffman Anne E. Hogan Gregory A. Flamme Jamie M. Bogle Helen S. Cohen

Background: Balance and dizziness problems (BDP) and falls are consequential across all ages.

Methods: Add Health is a longitudinal study of a nationally-representative, school-based cohort of more than 20,000 adolescents recruited from Grades 7–12 in 1994–1995. Waves I (n=20,745) and II (n=14,738) asked: “In the past 12 months, how often have you been dizzy?” Wave V asked participants, aged 32-42 in 2016-2018 (n=12,300), who had been in Waves I and II, additional questions on prior BDP history, symptoms and falls in the past 12 months. In Wave V most questions were answered via web-based or mailed questionnaires, but more detailed questions were asked via CAPI in subsample 2b (n=1,101). Multivariable logistic regression analyses were used to estimate odds ratios [OR, 95% confidence intervals (CI)] for associations between BDP and falls.

Results: BDP prevalence past 12 months was 39.1% at Wave I (mean age=15.6 years), 42.1% at Wave II (mean=16.2 years) and 30.6% at Wave V (mean=37.5 years). BDP symptoms that bothered most were: light-headedness (29%), vertigo (21%), and presyncope (15%). Falling prevalence was 26.2%. Wave V multivariable models included age, sex, race/ethnicity, head trauma, headache, and tinnitus. Significant associations with BDP were female sex (OR=2.1; 95% CI: 1.9-2.4), head trauma (OR=2.2; CI: 1.8-2.7), headaches (OR=2.8; CI: 2.5-3.8), and tinnitus (OR=3.2; CI: 2.6-3.8). After adjusting for age, sex, and race/ethnicity, BDP was significantly associated with increased risk of falls (OR=3.0; CI: 2.6-3.4). From Wave V, prior history of BDP was: 8.4% age <18; 10.8% age 18-24; 13.3% age 25-29; 16.3% age 30-34; and 18.3% age ≥35 years. BDP was associated with standing up (58%), headaches (42%), bending over (40%), quick head movement (31%), and tinnitus (25%).

Conclusion: BDP affects all ages and is associated with increased risk of falls. BDP risk factors and sequela should be evaluated in future Add Health waves as this U.S. cohort ages.

Neurology

Depressive symptoms and neuroimaging markers of brain aging in a racially diverse sample: a Bayesian analysis Tara E. Jenson* Tara Jenson Emma L. Gause Jingxuan Wang Sarah F. Ackley Jennifer Manly Evan Fletcher Paola Gilsanz Rachel Whitmer M. Maria Glymour Marcia Pescador Jimenez

Background: Depression has been associated with magnetic resonance imaging (MRI) measures of brain aging and atrophy in predominantly White groups, including smaller cerebral grey matter (GMV) and larger white matter hyperintensity (WMHV) volumes. It is unknown if similar associations are present, despite evidence of undertreatment of depression, in non-White groups.

Methods: A diverse sample (Asian (N=77), Black (N=290), Latino (N=90), and White (N=93)) from the Kaiser Healthy Aging and Diverse Life Experiences (age 65+) and the Study of Healthy Aging in African Americans (age 50+) based in northern California underwent MRI assessments between 2017-2022. Depressive symptoms (population average SD units) were measured at baseline using the NIH PROMIS toolbox. We used Bayesian linear regression with minimally informed priors to assess the association between depressive symptoms and log-transformed WMHV and GMV (cm3). We stratified analyses by race/ethnicity, adjusted for intracranial volume, age, gender, education, and time from baseline to MRI, and computed differences between stratum-specific estimates using a Bayesian iterative subtraction approach.

Results: Higher depressive symptoms were associated with larger log(WMHV) (0.21, 95% credible interval [CrI]: 0.004, 0.42) for Black participants; smaller GMV for Latino participants (-2.90, 95% CrI: -4.34, -1.50), and larger GMV for Asian participants (2.41, 95% CrI: 0.88, 3.95) (Table 1). Our Bayesian iterative subtraction approach showed that per 1SD higher depressive symptoms, Asian participants had 0.54 cm3 less log(WMHV) (-0.54, 95% CrI -0.96, -0.12) and 2.95 cm3 more GMV (2.95, 95% CrI 1.14, 4.69) than Black participants (ref. group). Latino participants had 2.39 cm3 less GMV per 1 SD higher depressive symptoms than Black participants (-2.39, 95% CrI -4.07, -0.70).

Conclusion: Contrasting with prior studies using mostly White samples, we demonstrated differences in the association of depressive symptoms with MRI measures of brain aging and atrophy across racial/ethnic groups, warranting further study. A Bayesian framework may be useful to investigate understudied populations with small sample sizes, but more study is needed to determine appropriate selection of priors for understudied populations on which the literature is sparse.

Table 1: Bayesian linear regression with informed priors of MRI measures associated with each standard deviation difference in depressive symptoms, stratified by race/ethnicity (KHANDLE and STAR Cohorts, California 2017-2022, N=550)

	Log(WMHV)	GMV (cm^3)
	β (95% CrI)	β (95% CrI)
Overall	0.06 (-0.06, 0.20)	-0.74 (-1.62, 0.15)
Asian	-0.33 (-0.70, 0.05)	**2.41 (0.88, 3.95)**
Black	**0.21 (0.004, 0.42)**	-0.52 (-1.49, 0.45)
Latino	0.18 (-0.18, 0.54)	**-2.90 (-4.34, -1.50)**
White	0.20 (-0.29, 0.70)	-0.53 (-2.47, 1.43)

Models adjusted for intracranial volume, sex, age at baseline, time from baseline to MRI scan, and college education.
MRI: magnetic resonance imaging
KHANDLE: Kaiser Healthy Aging and Diverse Life Experiences
STAR: Study of Healthy Aging in African Americans
Log(WMHV): log-transformed white matter hyperintensities volume
GMV: cerebral grey matter volume

Nutrition/Obesity

Long-term prescription opioid use is associated with poor diet quality in NHANES (2003-2018) John Mark* John Mark Elizabeth Charron Marianna S Wetherill Ellen C. Francis

Background: Long-term prescription (Rx) opioid therapy has been associated with obesity and poor micronutrient status. Our objective was to examine associations between short- and long-term Rx opioid use and diet quality in a nationally representative sample of U.S. adults.

Methods: We used data from 64,758 NHANES adults (2003-2018). Length of Rx opioid use was categorized as long-term (≥90 days; n=1,855), short-term (≥90 days; n= 941), and no use (n=61,962). Diet quality was measured using the Health Eating Index-2015 (HEI) derived from two 24-hour food recalls (0-100 points). We used multivariable linear models to estimate betas (95% confidence intervals [CIs]) with categorical length of Rx opioid use as the independent variable, accounting for the complex survey design and controlling for sex, age, race/ethnicity, education, marital status, smoking, insurance, and poverty-income ratio.

Results: The mean HEI for persons with short- and long-term Rx opioid use was 50.3 and 49.4, respectively compared to 51.07 for persons with no Rx opioid use. Compared to people with no Rx opioid use, those with long-term Rx opioid use had on average lower total HEI score (β = -1.71, 95% CI[-3.03,-0.40]), lower total vegetable score (β = -0.29, 95% CI[-0.40,-0.18]), lower bean and leafy green intake (β = -0.23, 95% CI[-0.37,-0.09]), lower protein intake β = -0.11, 95% CI[-0.21,-0.01]), lower moderation of added sugar (β = -0.60, 95% CI[-0.89,-0.30]), and increased moderation of sodium intake (β = 0.40, 95% CI[0.13,0.68]), while short term opioid use was not associated with significant difference in total or individual component HEI scores.

Conclusion: U.S. adults with long-term Rx opioid use reported poorer diet quality. Future studies should investigate the role of dietary factors on pain severity and management to identify non-pharmacologic intervention opportunities for people prescribed long-term opioid therapy.

Nutrition/Obesity

Endogenous Biomarkers in Adolescent Metabolic Syndrome: A Longitudinal Study on Incidence and Persistence Pei-Tung Lin* Pei-Tung Lin Pei-Wen Wu Yu-Ting Chin Sharon Tsai Wei-Ting Lin Chien-Hung Lee

Background: Insulin resistance-related pathophysiological mechanisms drive the excessive accumulation of cardiometabolic risk factors that trigger metabolic syndrome (MetS). This process is associated with endogenous biomarkers reflecting inflammatory responses and metabolic disturbances that contribute to the development and progression of MetS. This study aimed to investigate the roles of various endogenous biomarkers in the incidence and transition of adolescent MetS over a 2.3-year longitudinal follow-up period.

Methods: Participants were drawn from a community-based, randomly selected cohort of 1,075 adolescents conducted in southern Taiwan. We used two series of case-cohort samples—one sub-cohort for the incidence of MetS (n=357) and another for its persistence (n=374)—to evaluate the effects of endogenous biomarkers on the development of adolescent MetS. The biomarkers measured included high-sensitivity C-reactive protein (hs-CRP), interleukins, chemokines, tumor necrosis factor, as well as glucose, lipid, liver, and renal endogenous markers. We applied the Cox proportional hazards model and inverse probability weighting to assess the effects, adjusting for covariates.

Results: Higher baseline uric acid (UA) levels were associated with an increased hazard risk (HR) of incident MetS (adjusted HR=1.50 per 1 mg/dL increase). Adolescents with elevated total cholesterol and homeostasis model assessment-insulin resistance (HOMA-IR) had a higher HR for persistent MetS after 2.3 years. Additionally, serum hs-CRP levels significantly predicted both incident and persistent MetS and modified the HRs for UA on incident MetS and HOMA-IR on persistent MetS (p for interaction: 0.028 and 0.001, respectively). No mediation effects among the studied biomarkers were observed.

Conclusion: This study highlights the significant roles of endogenous biomarkers, particularly uric acid and hs-CRP, in the incidence and persistence of MetS among adolescents.

Nutrition/Obesity

Consumption of soy and other high protein foods and odds of adenomyosis: a case-control study Ling Guan* Ling Guan Kristen Upson Holly Harris

Adenomyosis, characterized by endometrial glands and stroma within the myometrium, can confer life-altering pelvic pain. The historic reliance on hysterectomy for diagnosis has limited the epidemiologic study of adenomyosis, including the investigation of dietary factors on disease risk. Using a novel case-control study design employing two control groups, we evaluated the association between soy and other high protein foods and adenomyosis. Among female enrollees aged 18-59 of a large, integrated healthcare system in western Washington State, we identified incident, pathology-confirmed adenomyosis cases diagnosed in 2001-2006 (n=386). Cases were compared to randomly-sampled age-matched enrollees with an intact uterus ("population controls", n=323) and hysterectomy controls (n=233). Participants completed an in-person interview and a food frequency questionnaire that included dietary intake of soy and high protein foods (red meat, poultry, eggs, dairy, and seafood) over the prior year. Adjusted odds ratios (ORs) and 95% CIs for the association between dietary factors and adenomyosis risk were estimated using logistic regression, comparing cases to each control group in separate analyses. In analyses using population controls, each serving per day of soy was associated with 66% lower odds of adenomyosis (OR=0.34, 95% CI: 0.08-1.50). Conversely, red meat intake (≥1 vs. <1 servings per day) was associated with a 2.25 higher odds of adenomyosis (95% CI: 1.05-4.83). No association was observed with egg, poultry, seafood, or dairy intake. We observed similar results in analyses using hysterectomy controls, except for the attenuated association with red meat intake (OR=1.21, 95% CI: 0.50-2.93). Our data suggest an altered odds of adenomyosis with soy and red meat intake. Given that estrogen and inflammation are central to adenomyosis pathogenesis, the observed associations with soy (a phytoestrogen) and red meat (linked with inflammation) warrant further investigation.

Nutrition/Obesity

Associations Between Food Insecurity and Patterns in Noticing and Using Calorie Information on Menus Among Gay and Bisexual Men Meg Salvia* Meg Salvia Heather Mattie Alvin Tran

Background:
Little is known about how experiencing food insecurity impacts noticing restaurant menus' calorie labels and subsequent use of this information. A better understanding of food insecurity as one component of social determinants of health is needed to facilitate policy-level and educational strategies to support improved nutrition status.

Objective:
The objective of this analysis was to evaluate patterns between food insecurity and noticing and using calorie information among sexual minority men. We also sought to understand potential differences across sexual minority subgroups.

Methods:
We analyzed cross-sectional data from 504 participants in the Men's Body Project, an online survey of participants who identify as gay or bisexual men. Specific questions assessed past-year food insecurity, whether participants noticed restaurant-menu calorie information, and if so, how they used this information to change their order. Multivariate logistic regression models evaluated associations between food insecurity and noticing calories and individual behavior changes in response to this information.

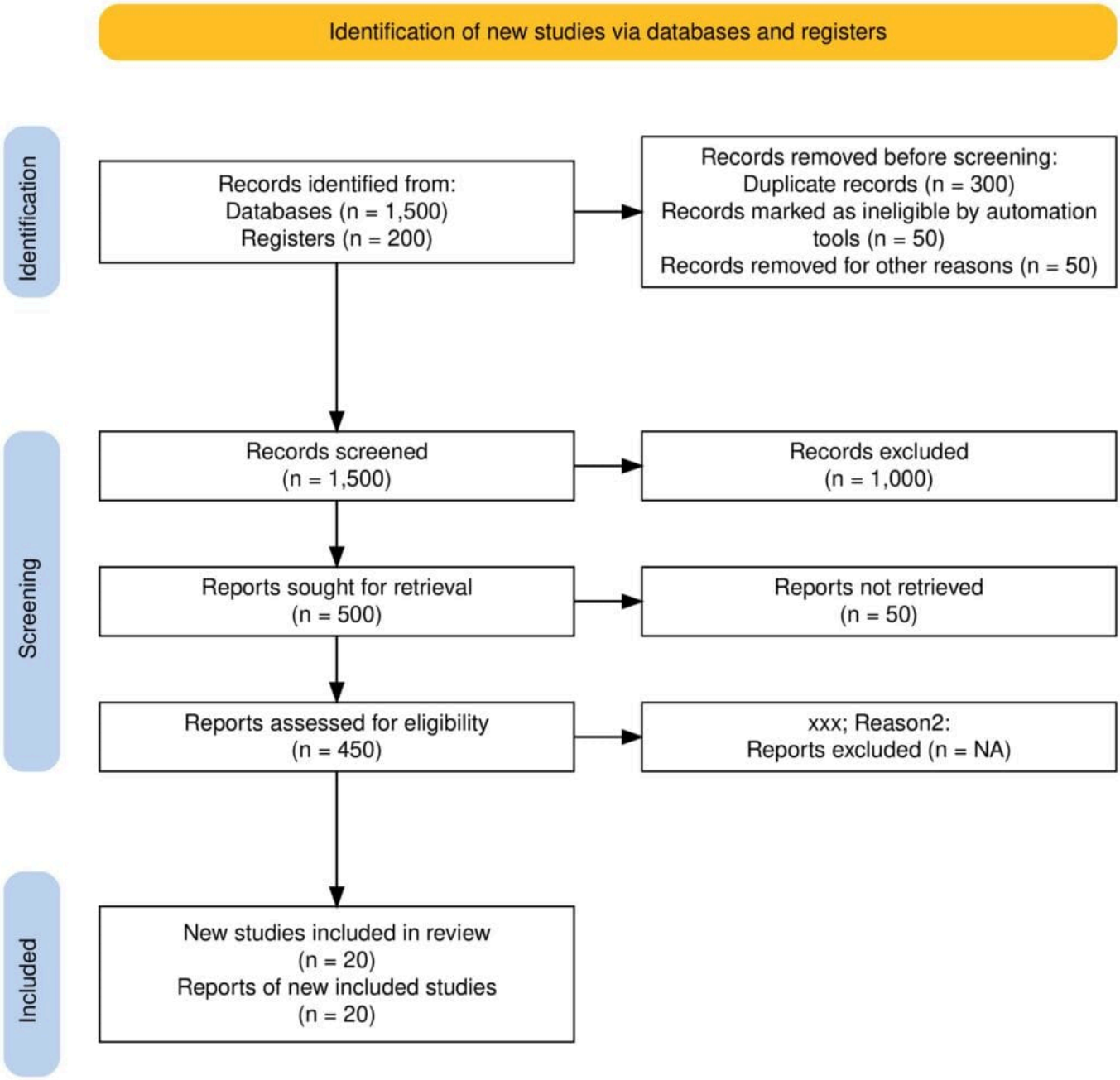
Results:
Over one-third of participants (35.9%) reported past-year food insecurity, and food insecurity was more prevalent among bisexual men. Over half of participants (55.0%) reported noticing calorie information. Among bisexual men, those who experienced food insecurity were more than twice as likely to report noticing calorie information (OR = 2.63, 95% CI: 1.32, 5.37), while the association for gay men was not significant. In analyses of individual behavior-change responses, gay men had higher odds of ordering smaller sizes (OR = 3.14, 95% CI: 1.26, 8.24), while bisexual men had increased odds of ordering more calories (OR = 3.28, 95% CI: 1.11, 10.11), ordering fewer items (OR = 2.48, 95% CI: 1.00, 6.29), and larger sizes (OR = 3.53, 95% CI: 1.32, 9.87).

Conclusions:
Observed patterns and associations were more pronounced for bisexual participants. Experiences with food insecurity may influence behavior changes in response to calorie information on menus.

Nutrition/Obesity

Effectiveness of interventions addressing the dual burden of malnutrition in mother–child pairs Muhammad Zia ul Haq* Muhammad Zia ul Haq Javeria Mansoor Zahid Ali Memon Zohra S Lassi

The dual burden of malnutrition (DBM)—coexisting undernutrition and overweight/obesity in mother–child pairs—requires integrated “double-duty” actions. We systematically reviewed interventions targeting DBM in mother–child dyads, focusing on effectiveness, feasibility, and acceptability.
Randomized controlled trials (RCTs) were included if they enrolled mother–child pairs with discordant nutritional status (e.g., overweight mother and undernourished child). We searched major databases (PubMed, Embase, Web of Science, Scopus), screened studies independently, and assessed risk of bias using RoB 2 (RCTs) and ROBINS-I. Primary outcomes were anthropometric measures; secondary outcomes included dietary diversity, micronutrient status, and program feasibility. Data were synthesized narratively due to heterogeneity in interventions and outcome reporting.
Five key trials met inclusion criteria. Two (including the MISAME-III sub-study in Burkina Faso) evaluated micronutrient-fortified balanced energy–protein (BEP) supplements during pregnancy, reporting significant increases in maternal and newborn fat-free mass indices (Argaw et al., 2023) without raising fat mass. The Indonesian NEO-MOM trial delivered nutrition education plus motivational interviewing to overweight mothers of stunted children; mixed factorial analyses indicated improved maternal dietary behaviors and modest child height-for-age improvements. Vietnam’s PRECONCEPT trial linked higher maternal preconception BMI with improved child size at 6–7 years, underscoring the importance of maternal weight optimization. Another study from Chile (CHiMINCs) integrated nutrition counseling and breastfeeding support to control gestational weight gain and promote healthy child growth.
Double-duty interventions integrating BEP supplementation, micronutrient fortification, and behavior-change education appear feasible and beneficial for DBM in diverse settings. While improvements in anthropometry and dietary outcomes are promising, future large-scale trials should incorporate cost-effectiveness and extended follow-up to sustain progress in mother–child DBM interventions.


Identification of new studies via databases and registers
Identification
Records identified from:
Databases (n = 1,500)
Registers (n = 200)
Records removed before screening:
Duplicate records (n = 300)
Records marked as ineligible by automation tools (n = 50)
Records removed for other reasons (n = 50)
Screening
Records screened
(n = 1,500)
Records excluded
(n = 1,000)
Reports sought for retrieval
(n = 500)
Reports not retrieved
(n = 50)
Reports assessed for eligibility
(n = 450)
xxx; Reason2:
Reports excluded (n = NA)
Included
New studies included in review
(n = 20)
Reports of new included studies
(n = 20)

Nutrition/Obesity

Validity and Reliability of a Diet Quality Screener in a Sample of Participants Enrolled in the Special Supplemental Nutrition Program for Women, Infants, and Children (WIC) Nour Hammad* Nour Hammad Meghan Zimmer Rebecca Mozaffarian Eric Rimm Erica Kenney

Objectives: This study aims to assess the validity and reliability of a brief parent-reported diet quality screener for young children.

Methods: We obtained data from 174 1-4 year-olds enrolled in a study of WIC. We conducted a cross-sectional evaluation of the psychometric properties of the 16-item rapid Prime Diet Quality Score screener for Kids (rPDQS-Kids), a brief food frequency questionnaire. We evaluated test-retest reliability and internal consistency. We also assessed criterion validity by comparing specific food categories from rPDQS-Kids with average intake from two 24-hr recalls measured via the Automated Self-Administered 24-Hour Dietary Assessment Tool (ASA24). We assessed construct validity by testing whether rPDQS-Kids scores were associated with food insecurity and parental education.

Results: The rPDQS-Kids showed moderate test-retest reliability (Intraclass Correlation Coefficient of 0.58 for total healthy component scores and 0.75 for total unhealthy component scores). Internal consistency reliability was also moderate, with Cronbach's α=0.61 and α=0.65 for the healthy and unhealthy component scores, respectively. Estimates of intake of healthy food categories from rPDQS-Kids were correlated with estimates from ASA24, with Spearman's r ranging from 0.31 for vegetables to 0.46 for fruits. However, rPDQS-Kids and ASA24 were inversely correlated for unhealthy components, ranging from -0.22 for refined grains to -0.65 for juice. Food insecurity and parental education were not significantly associated with total, healthy, and unhealthy component rPDQS-Kids scores.

Conclusions: The rPDQS-Kids shows potential as a low-burden tool for caregivers to proxy-report young children's intake. More research is needed to develop valid and reliable brief screeners of young children's diet quality.

Nutrition/Obesity

Perpetrators of sexual and physical abuse: Associations with disordered eating behaviors, intuitive eating, and orthorexic eating behaviors among college students Cynthia Yoon* Cynthia Yoon Craig

Background: During college, disordered and orthorexic eating behaviors peak, while intuitive eating becomes a challenge. Although abuse is related to disordered eating, the role of perpetrators on eating behaviors remain underexplored.

Purpose: To examine the associations of perpetrators of abuse and polyvictimization with disordered, intuitive, and orthorexic eating behaviors among college students.

Methods: Data were drawn from a cross-sectional study of college students (N=1,621 in 2022-2023). History of abuse, disordered eating (e.g., binge eating), intuitive eating (e.g., reliance on hunger and satiety cues), and orthorexic eating (e.g., obsessive focus on healthy eating) were self-reported. Modified Poisson regressions examined associations of perpetrators/polyvictimization with disordered/orthorexic eating adjusted for age, sex, race/ethnicity, education, and BMI; linear regressions examined associations between perpetrators/polyvictimization and intuitive eating.

Results: An adult family member as the perpetrator was associated with greater prevalence of disordered eating (PR=1.22-1.38), lower intuitive eating scores (β=-4.02, 95% CI=-6.88, -1.16), and greater orthorexic eating (PR=1.19, 95% CI=0.93-1.52). Similar patterns were observed with intimate partner as the perpetrator. Sibling as the perpetrator showed limited associations with disordered eating and no associations with intuitive or orthorexic eating. Polyvictimization were cumulatively associated with disordered eating, intuitive eating, and orthorexic eating, after adjustments.

Conclusion: Adult family members and intimate partners exert a stronger influence on college students' eating behaviors than siblings. Additionally, cumulative adverse experiences, regardless of perpetrator identity are associated with disordered and intuitive eating. Public health efforts should address the role of perpetrators and the cumulative effects of adverse experiences on college students' eating behaviors.

LATEBREAKER

Nutrition/Obesity

Adolescent Ultra-Processed Food Consumption Has Long-Lasting Effects on Cognition Through Mid-Adulthood: A Doubly Robust Causal Machine Learning Approach Yohannes Adama Melaku* Yohannes Adama Melaku Zumin Shi Danny Eckert Robert Adams

Background: Ultra-processed food (UPF) consumption has been linked to adverse health outcomes, yet its long-term cognitive effects remain underexplored. Adolescence is a critical period for brain development, and dietary habits established during this stage may influence cognitive trajectories into adulthood. This study employs a doubly robust causal machine learning approach to examine the impact of adolescent UPF consumption on cognitive function through mid-adulthood.

Objective: This study aimed to determine the causal effect of adolescent UPF consumption at age 16 on cognitive performance at ages 16, 24, 34, 42, and 46.

Methods: Data were obtained from the 1970 British Cohort Study (BCS1970), a nationally representative longitudinal dataset. Dietary intake at age 16 was assessed using a four-day 24-hour recall and categorised based on the NOVA classification of food processing. UPF consumption was classified into high and low intake groups (10th and 90th percentile, respectively). Cognitive function was assessed using standardised cognitive tests at multiple follow-up points. Targeted Maximum Likelihood Estimation (TMLE) with Super Learner was applied to estimate causal effects while adjusting for baseline sociodemographic, lifestyle, and health-related confounders. Sensitivity analyses using inverse probability weighting (IPW) and g-computation were conducted to validate findings.

Results: Among 4,150 participants (52.3% female, 47.7% male), high UPF consumption at age 16 was consistently associated with lower cognitive scores across all follow-up periods. The mean cognitive score difference between high and low UPF consumers was -0.15 SD (95% CI: -0.22, -0.08) at age 16, -0.18 SD (95% CI: -0.26, -0.10) at age 24, -0.21 SD (95% CI: -0.29, -0.13) at age 34, -0.24 SD (95% CI: -0.32, -0.16) at age 42, and -0.27 SD (95% CI: -0.35, -0.19) at age 46. These findings remained robust across multiple sensitivity analyses.

Conclusion: Higher UPF consumption in adolescence is associated with persistent cognitive decline through mid-adulthood. These findings highlight the need for early-life dietary interventions to support long-term cognitive health. Public health policies should prioritise reducing UPF consumption among adolescents to mitigate potential long-term neurocognitive risks.

LATEBREAKER

Nutrition/Obesity

Trans-ancestral analyses of obesity and socioeconomic status reveal significant associations with DNA methylation Hridya Rao Gardner* Lindsay Fernandez-Rhodes Scott Ratliff Jennifer Smith Junyu Chen Kari E. North Anne E. Justice Jessica D. Faul David R. Weir

The effects of socioeconomic status (SES) and DNA methylation on obesity have been robustly observed in different populations. Prior studies have identified evidence to support that methylation sites may mediate the effect of low SES on obesity. We sought to replicate recent socio-epigenomic findings in African Americans (AAs) using an independent trans-ancestral sample from up to 5,476 samples in the Genetic Epidemiology Network of Arteriopathy, the Intergenerational Blood Pressure and Health and Retirement Study and assess directional consistency of AA findings in Hispanic/Latinos and non-Hispanic Whites. We performed linear regression models of methylation sites ln of body mass index (BMI) and on highest educational attainment (in years), adjusting for cell proportions, smoking (current, former), alcohol (current), and first 5 genetic ancestry principal components and by race/ethnicity and sex. The trans-ancestral meta-analysis replicated associations at four of five previously described CpG sites ($p<0.01$). We observed array-wide significant sex-combined associations between lnBMI and cg05095590 and cg08972190 near *MAD1L1,* cg13708645 to the north shore of *KDM2B,* and with both lnBMI and education with cg18181703 to the north shore of *SOCS3*. Associations were directionally consistent across race/ethnic groups, and as seen previously the BMI association at cg18181703 was stronger in females (Figure 1, $p=0.002$). The trans-ancestral meat-analysis identified two additional *SOCS3* sites and three sites near *PCOLCE2, DENND2D,* and *SLC9A1* associated with both traits ($p<5\times10\text{-}8$), which we will further interrogate using mediation models and >10k adults from 5 race/ethnic groups. Our study replicates the presence of socioepigenomic loci for obesity in a diverse sample and lays the groundwork for further trans-ancestral exploration of the role of socioeconomic measures in the epigenetics of obesity.

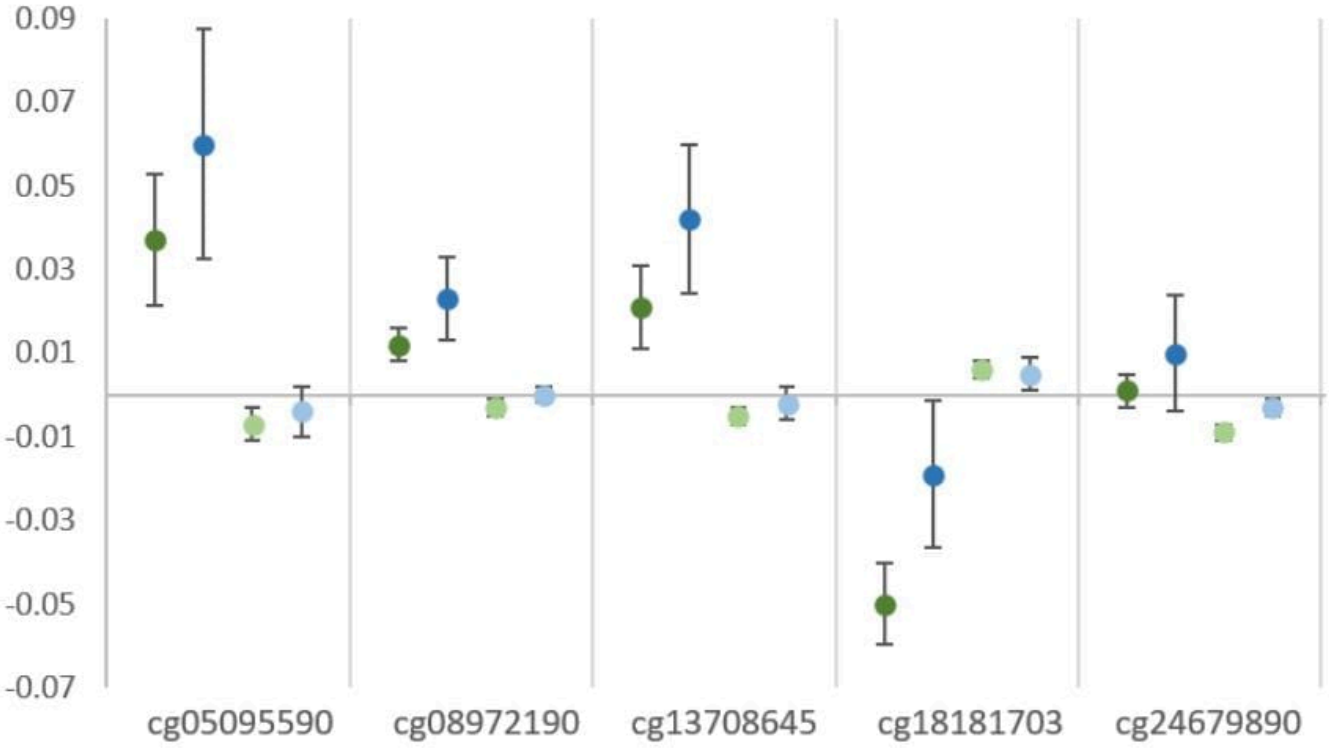


Figure 1. Sex-specific findings (female shown in green; male in blue) in a trans-ancestral sample, comprising African American, non-Hispanic White, Hispanic/Latino adults from three studies, and meta-analyzed to estimate effects (95% CI) among up to 4,240 adults with CpG information and natural log of body mass index (shown in dark symbols) and up to 5,476 adults with CpG information and education in years (shown in light symbols). Each of these CpG sites has been recently described as socio-epigenomic loci for obesity in African American adults, and cpg18181703 as having stronger effects in females and greater CpG mediation of SES-BMI effects than in males.

LATEBREAKER

Nutrition/Obesity

Demographic and behavioral correlates of coffee consumption Eduardo Ortiz-Panozo*
Eduardo Ortiz-Panozo Jorge E. Chavarro

Background: Coffee consumption is widespread and is often assumed to be a risk factor for various adverse health outcomes. We examined the association of demographic and high-risk lifestyle factors with coffee consumption.

Methods: This is a cross-sectional analysis of 28,686 female participants in the Nurses' Health Study 3; an ongoing, web-based cohort study of nurses and nursing students from the United States and Canada. Coffee intake was assessed with a validated food frequency questionnaire and behavioral and demographic correlates were collected in baseline and follow-up questionnaires. Logistic and multinomial logistic regression were used to quantify the association of demographic and behavioral factors with coffee consumption (yes/no) and the frequency of coffee consumption (never, less than once per day, once per day, and more than once per day).

Results: Only 29% of the 28,686 participants (median [IQR] age: 32 [27, 40] years) did not consume coffee, while 43% consumed coffee at least once daily. In multivariable models, consuming coffee at least once per day was associated with smoking (past, aOR: 1.88, 95% CI: 1.74-2.04; current, aOR: 2.09, 95% CI: 1.80-2.43), use of muscle building supplements (aOR: 1.47, 95% CI: 1.28-1.69), binge drinking (aOR: 1.35, 95% CI: 1.25-1.45), marijuana use (aOR: 1.38, 95% CI:1.27-1.49), and illicit drug use (aOR: 1.19, 95% CI: 1.07-1.32). These associations were stronger in multinomial logistic regression models comparing drinking coffee more than once per day to less than once per day, particularly for smoking (past, aRRR: 2.47, 95% CI: 2.25-2.72; current, aRRR: 3.54, 95% CI: 3.00-4.18) and binge drinking (aRRR: 1.56, 95% CI: 1.42-1.71).

Conclusions: Our findings suggest that coffee consumption and high-risk behavioral factors are related in a dose-response manner. Spurious associations between coffee intake and health outcomes may arise from lack of adequate accounting for demographic and behavioral factors associated with the behavior of drinking coffee.

Occupational

The risk of pancreatic cancer from occupational exposure to ethylene oxide Liz Best* Liz Best Tony Cappello Alex Riordan Hannah Mazzotta

We conducted a literature review and meta-analysis of studies that examined the risk of pancreatic cancer among persons occupationally exposed to ethylene oxide (EtO). Our literature search was performed in PubMed and identified 19 published papers that were considered in our meta-analysis. Pooled risk estimates were calculated using random effects models, stratifying by overall risk, duration of employment, and decade of publication. The overall meta-relative risk (meta-RR) for pancreatic cancer was 1.16 (95% CI 0.87-1.56). For duration of employment, we performed a meta-regression for every one year increase in employment, which demonstrated a flat slope/beta and lack of a statistically significant dose response (meta-regression beta = 0.13, 95% CI -0.07-0.334 or meta-RR = 1.14, 95% CI 0.93-1.40). Meta-RRs were elevated at a level of statistical significance for the earlier decades (1980s and 1990s) compared to the later decades (2000s and 2010s), reflective of study quality improvement over time. Based on this analysis, there is no evidence to suggest that occupational exposure to EtO is associated with an increased risk of pancreatic cancer.

Occupational

Chronic respiratory disease risk among Veterans of the United States military in the Long-term Impact of Fuel Exposure (LIFE) Study Nicholas A. Tilton* Nicholas Tilton Elizabeth R. Heitz Justin G. Bergeron Jennifer A. Rusiecki Gregory Wolff Aaron I. Schneiderman Edward A. Sheriff W. Scott Monks Terra D. Vincent-Hall

Military personnel frequently incur occupational exposure to jet fuels, which may have long-term health effects. While persistent immunotoxicity and short-term effects such as acute respiratory irritation are well-documented, the extent to which long-term occupational jet fuel exposure contributes to respiratory diseases such as asthma and chronic obstructive pulmonary disease (COPD) remain unclear. To address this question and assess other possible health effects, the Department of Veterans Affairs is conducting the LIFE Study, a retrospective cohort of more than 1.3 million US military Veterans who entered service in 1995 or later. The cohort includes all Veterans who worked in military occupations identified as involving probable jet fuel exposure and a random sample of non-exposed. The current analysis examined a subset of more than 800,000 Veterans with administrative records of healthcare encounters both during and after their service careers. Time spent working in fuel-exposed occupations was used as a proxy for duration of jet fuel exposure and was categorized into quintiles. Asthma and COPD cases were identified using ICD-9 and -10 diagnosis codes in the administrative encounters data. Cox proportional hazards models with time-varying exposure were used to estimate the effect of exposure duration on asthma and COPD risk. Models were adjusted for demographics, documented smoking and alcohol use, and military service characteristics (i.e., service branch, deployment, length of service, and rank). Results showed a small but significantly elevated risk of COPD in Veterans with approximately 3 to 6 years of exposure duration and of asthma with ≥7 years compared to those with no identified exposure. The LIFE Study may provide a model for cumulative assessment of military occupational exposures, and findings may inform policy changes around hazard control and Veterans' benefits. Future work will analyze other respiratory diseases and those of other body systems.

Occupational

Depression and anxiety disorders among Veterans following occupational jet fuel exposure: Preliminary findings from the Long-term Impact of Fuel Exposure (LIFE) Study Elizabeth R. Heitz* Elizabeth Heitz Nicholas A. Tilton Justin G. Bergeron Jennifer A. Rusiecki Gregory Wolff Aaron I. Schneiderman Edward A. Sheriff W. Scott Monks Terra D. Vincent-Hall

Occupational jet fuel exposure is common in military service members. Current evidence suggests a possible relationship between exposure to jet fuel and adverse effects on neurological function, cognition, and behavior. To better understand these and other possible health outcomes in Veterans, the Department of Veterans Affairs (VA) is conducting the LIFE Study. This retrospective cohort study utilizes administrative datasets from the Department of Defense (DoD) and VA to assess health outcomes in 1.3 million Veterans who entered service on or after January 1, 1995. Preliminary analyses were limited to Veterans with at least one documented healthcare encounter following their separation from service to ensure that longitudinal data were available for all subjects. Jet fuel exposure was classified based on military occupation codes, with total time spent in fuel-exposed occupations categorized into quintiles. Incident cases of anxiety and depressive disorders were identified using ICD-9 and -10 codes from DoD and VA health records. Cox proportional hazards models with time-varying exposure were used to estimate risk of anxiety and depression related to quintile of exposure. More than half of Veterans with anxiety or depression were diagnosed after separating from service. Initial results from regression models showed Veterans with approximately 3 to 6 years of occupational jet fuel exposure had the highest risk of anxiety and depression, compared to those with no fuel exposure. Associations were modest, but statistically significant, and consistent with results from past studies in other populations. LIFE Study analyses are ongoing. Its findings may have implications for both Veterans' healthcare and hazard control in the military.

Occupational

Mixtures Effect of Police Stressors on Psychological Health, a Machine Learning Approach
Ja Kook Gu* Ja Gu Erin McCanlies John Violanti Anna Mnatsakanova Samantha Services Penelope Allison Luenda E. Charles

Objective: Police officers often experience high stress levels due to occupational exposures that negatively impact their psychological health. This study utilized Bayesian Kernel Machine Regression (BKMR) to investigate the associations between multiple police stressors and psychological health.

Methods: Data were obtained from 315 officers (216 men) participating in the Buffalo Cardio-Metabolic Occupational Police Stress Study 2004–2009. Eight stressors were analyzed as predictors: night shifts, afternoon shifts, sleep quality, administrative stress, lack of support, physical threat, vital exhaustion (VE), and work exposures index. Psychological health score (PHS) as the outcome variable was measured as the sum of the scores from Beck Anxiety Inventory and Beck Depression Inventory. We examined the relationship between the stressors and PHS adjusted for covariates, stratified by sex. The contribution of individual stressor to the PHS was measured with the change in PHS for interquartile change in a stressor. Posterior inclusion probabilities (PIPs, range: 0-1) measure the relative importance of each stressor with higher values being more important.

Results: When all other stressors were fixed at 50th percentile, the strongest stressor(s) associated with PHS was VE (estimate=1.12; 95% credible interval=0.38-1.51) among women and VE (0.47; 0.14-0.80) and administrative stress (0.77; 0.51-1.04) among men. The stressors showing the highest importance in the associations were also supported by the PIPs: PIP=1.000 for VE among women; PIP=1.000 for both VE and administrative stress, followed by PIP=0.796 for sleep quality among men.

Conclusions: We identified VE and administrative stress as strong factors in the association between occupational stressors and PHS in male officers, while VE was the primary stressor for female officers. These findings highlight the benefits of analyzing combined occupational exposures to better understand officers' psychological health.

Perinatal & Pediatric

Comparison of the NICHD Fetal Growth Charts to Individualized Growth Assessment

Elizabeth Williams* Elizabeth Williams Maddy St. Ville Zhen Chen Jessica Gleason Dian He John Owen Roger Newman Edward Chien William Grobman Daniel Skupski Angela Ranzini Anthony Sciscione Jagteshwar Grewal Cuilin Zhang Fasil Tekola-Ayele Katherine Grantz

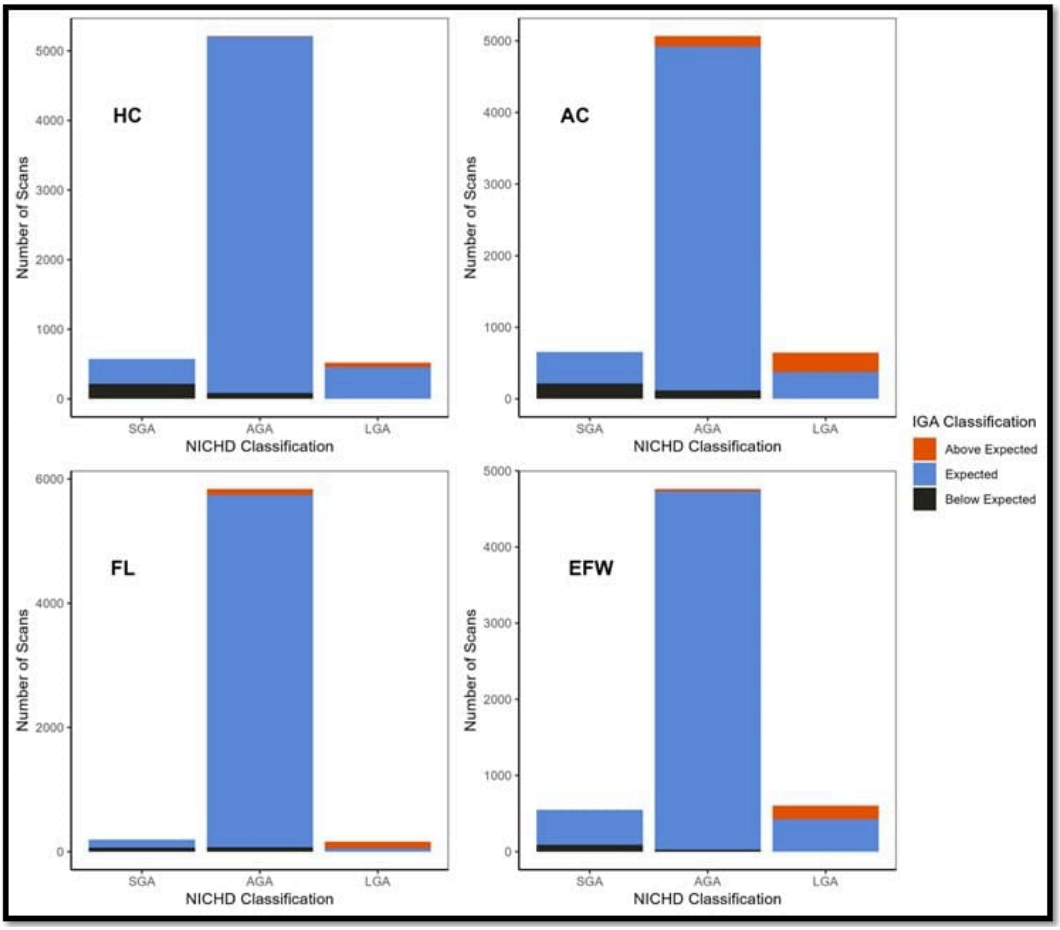
Abnormal fetal growth is associated with increased morbidity, yet no universal standard exists for identifying and classifying abnormal growth in practice. Specifically, distinguishing between pathologic fetal growth restriction (FGR) and benign constitutional smallness remains challenging. Individualized growth assessment (IGA) evaluates adequacy of fetal growth using each fetus as its own control and has been proposed as superior to standard population-based growth charts.

We compared these two methods using longitudinal ultrasound data in the NICHD Fetal Growth Studies-Singletons (N=2,447). For IGA, a set of 2nd trimester fetal measurements are used to fit a Rossavik growth model that predicts individual 3rd trimester (3T) growth potential within an expected range. We classified observed 3T fetal head circumference (HC), abdominal circumference (AC), femur length (FL), and estimated fetal weight (EFW) at each 3T visit as below, within, or above predicted ranges. We compared IGA classifications to small (SGA), appropriate (AGA), or large for gestational age (LGA) as <10th, 10-90th, or >90th percentile for GA, respectively, by NICHD charts by calculating percent concordance and performing Chi Square tests.

We found high concordance (94.9 to 98.9%) between IGA and the NICHD growth standard for fetuses classified as AGA according to the NICHD growth standard. However, IGA classified fewer fetuses at the extremes of growth compared to the NICHD growth standard (e.g., 2.0% and 3.4% were classified as EFW below and above expected by IGA, compared to 9.3% and 10.2% by NICHD, respectively; Figure).

If population-based SGA is a mix of benign and pathologically small fetuses, then it may be that those classified as below expected by IGA are pathologically small (2%), and those classified as SGA by the NICHD charts only as constitutionally small (7.3%). Future work is needed as better classification can improve resource utilization for at-risk pregnancies.

Figure. Number of scans classified by IGA within each NICHD classification group



Perinatal & Pediatric

Screening for Pediatric Safety Alerts Following Antipsychotic Treatment Initiation using a Tree-Based Scan Statistics Approach Loreen Straub* Loreen Straub Shirley V. Wang Kelly Fung Helen Mogun Massimiliano Russo Georg Hahn Krista F. Huybrechts

Antipsychotics (APs) are commonly prescribed to children. While pediatric studies have provided evidence on adverse events for widely used APs (i.e., aripiprazole, olanzapine, quetiapine, risperidone, ziprasidone), safety information on newer APs (i.e., asenapine, brexpiprazole, cariprazine, lurasidone, paliperidone) remains sparse.

Using tree-based scan statistics (TBSS) to screen a broad range of outcomes, we evaluated whether known associations for common APs could be identified, and whether previously unrecognized adverse effects associated with newer APs would be detected.

We identified children initiating APs (with quetiapine as the reference) within two large US health insurance databases 2000-2021. Leveraging the Multi-Level Clinical Classification tree which groups diagnosis codes into higher-level concepts, we scanned for incident outcomes within six months of AP initiation. Relative risks (RRs) were estimated with propensity score fine-stratification for confounding adjustment. A p-value threshold of <0.1 was used to define statistical alerts.

The number of exposed children ranged from 534 (cariprazine) to 664,967 (risperidone). Compared to quetiapine (N=286,192), multiple elevated risks, consistent with previous evidence, were identified for common APs, including endocrine, cardiovascular, hematologic, metabolic, neurologic and immunologic conditions. Among newer APs, no signals were detected for asenapine and brexpiprazole. For cariprazine, one alert for viral disease (RR=2.6) was found. Lurasidone was associated with metabolic, urinary, pituitary and platelet disorders (RR range 1.4-24.9), and paliperidone with extrapyramidal and pituitary disorders and allergies (RR range 1.8-18.0).

The detection of known associations supports TBSS' feasibility for pediatric drug safety surveillance. Continued monitoring of the newer drugs as more data accrue, in-depth assessment of clinical plausibility and replication in independent data sources remains essential.

Table. Statistical Alerts Identified (Based on a P-Value Threshold of <0.1) For Newer Antipsychotic Medications Using a Tree-Based Scan Statistics Approach.* The Cohort Included Children Initiating These Medications (Reference: Quetiapine Initiators) Within the Medicaid Analytic eXtract/Transformed Medicaid Statistical Information System Analytic Files (2000-2018) and the Merative MarketScan Commercial Claims Database (2003-2021).

Outcome	Events in Exposed (%)	Events in Referent (%) (Among N=286,192 Children)	Relative Risk	P-value
Asenapine (N=3,262 Children)				
<No signals detected>				
Brexpiprazole (N=780 Children)				
<No signals detected>				
Cariprazine (N=534 Children)				
Anxiety state, unspecified	27 (5.1)	5,429 (1.9)	2.66	0.0109
Contact with or exposure to other viral diseases	26 (4.9)	5,279 (1.8)	2.64	0.0176
Lurasidone (N=9,664 Children)				
Obesity unspecified	242 (2.5)	4,528 (1.6)	1.58	0.0001
Other bipolar disorder	150 (1.6)	2,306 (0.8)	1.93	0.0001
Obesity (higher-level category)	487 (5.0)	9,981 (3.5)	1.44	0.0001
Bipolar disorder (higher-level category)	1129 (11.7)	26,884 (9.4)	1.24	0.0001
Bipolar disorder, current episode depressed, mild	22 (0.2)	152 (0.1)	4.29	0.0002
Bipolar disorder, unspecified	379 (3.9)	8,459 (3.0)	1.33	0.0004
Nutritional, endocrine, or metabolic disorder (higher-level category)	810 (8.4)	20,132 (7.0)	1.19	0.002
Thrombocytopathy	<11	<11	22.63	0.004
Conjunctival edema	<11	<11	21.29	0.0058
Mood disorder, including bipolar disorder (higher-level category)	2076 (21.5)	55,917 (19.5)	1.1	0.037
Acute venous embolism/deep vein thrombosis of upper extremity	<11	<11	24.94	0.0374
Urethral stricture	<11	16 (0.0)	11.14	0.038
Pituitary disorder	<11	<11	23.79	0.0429
Disease of bladder or urethra (higher-level category)	27 (0.3)	321 (0.1)	2.49	0.0565
Neurogenic bladder	<11	28 (0.0)	7.44	0.092
Generalized anxiety disorder	278 (2.9)	6,423 (2.2)	1.28	0.1
Paliperidone (N=5,893 Children)				
Anterior pituitary hyperfunction	19 (0.3)	102 (0.0)	9.02	0.0001
Galactorrhea, not associated with childbirth	28 (0.5)	266 (0.1)	5.11	0.0001
Non-malignant breast condition (higher-level category)	75 (1.3)	1,575 (0.6)	2.31	0.0001
Hereditary and degenerative nervous system conditions (higher-level category)	72 (1.2)	1,629 (0.6)	2.15	0.0002
Acute dystonia due to drugs	32 (0.5)	491 (0.2)	3.17	0.0003
Symptoms in breast	11 (0.2)	87 (0.0)	6.15	0.0067
Dissociated deviation of eye movements	<11	14 (0.0)	18.01	0.0173
Allergy, unspecified	61 (1.0)	1,617 (0.6)	1.83	0.0313

Outcomes shown in black font indicate unclassified alerts pending further characterization. Outcomes shown in grey font refer to those related to on- or off-label indications.
Cell sizes less than 11 are suppressed according to the Centers for Medicare & Medicaid Services' [CMS] cell suppression policies.
"Higher-level category" refers to the grouping of individual diagnostic codes within the outcome tree, based on the Multi-Level Clinical Classification (MLCC).
* An unconditional Poisson tree-based scan statistic approach was used to calculate log likelihood ratios, relative risks, and p-values for each outcome node. The lowest level of the outcome tree consisted of individual International Classification of Diseases, 9th Revision (ICD-9) diagnostic codes (with ICD-10 codes being linked to their corresponding ICD-9 codes using the forward-backward mapping method developed by CMS) which were hierarchically grouped into higher-level clinically related concepts using the MLCC. Our threshold for identifying statistical alerts was a P-value <0.1 (in contrast to the traditionally used P-value threshold of 0.05) to reduce the risk of missing potential alerts. To reduce the risk of chance findings, we considered only outcome nodes with >3 exposed cases. Lastly, to reduce the risk of including pre-existing conditions, we did not test specific conditions if the same or clinically related conditions (diagnosis codes starting with the same 3 digits) were recorded within 15 months prior to treatment initiation. Nevertheless, as indicated in grey font in the table, some alerts presumably related to the indications (i.e., bipolar disorder [on the label] and anxiety [off-label]) were still detected.

Perinatal & Pediatric

How Childhood Neglect and Supportive Adults Enhance Academic Functioning through Transformational Development Takeo Fujiwara* Takeo Fujiwara

Background: While accounts of notable people facing early adversity followed by success in later life abound, epidemiological studies are lacking regarding whether specific types of adversity may contribute to positive outcomes, such as academic functioning, in particular circumstances.

Objective: To determine whether having experiences of neglect in early childhood and support from extrafamilial adults in early adolescence may enhance academic functioning in adolescence.

Methods: Prospective multi-site Longitudinal Studies on Child Abuse and Neglect (LONGSCAN) data were utilized to identify individuals who experienced neglect from birth to 6 years of age (based on Child Protective Services' records) and whether they had an extrafamilial supportive adult in their life at ages 12 and 14. Academic functioning at age 16 was based on Child Behavior Checklist Social Competency Items (CBCL SCI) School Scale. We analyzed the impact of childhood neglect (ages 0-6) and of having a supportive adult (ages 12-14) on academic functioning at age 16, using inverse probability weighting to control for site, sex, race, poverty level at age 6, as well as childhood physical, sexual, and psychological abuse, poverty level and at age 12.

Results: Early childhood neglect coupled with having an extrafamilial supportive adult in early adolescence was associated with better academic functioning at age 16 compared to academic functioning in children who had not experienced neglect and had a supportive adult (coefficient: 3.62, 95% confidence interval: 0.67 to 5.56). Total social competency was also better (coefficient: 2.62, 95% confidence interval: -0.13 to 5.37) in this group.

Conclusion: Neglect in early childhood and having an extrafamilial supportive adult may enhance later academic functioning. Suggesting transformational development, further epidemiological studies are needed to explore this phenomenon in greater depth.

Perinatal & Pediatric

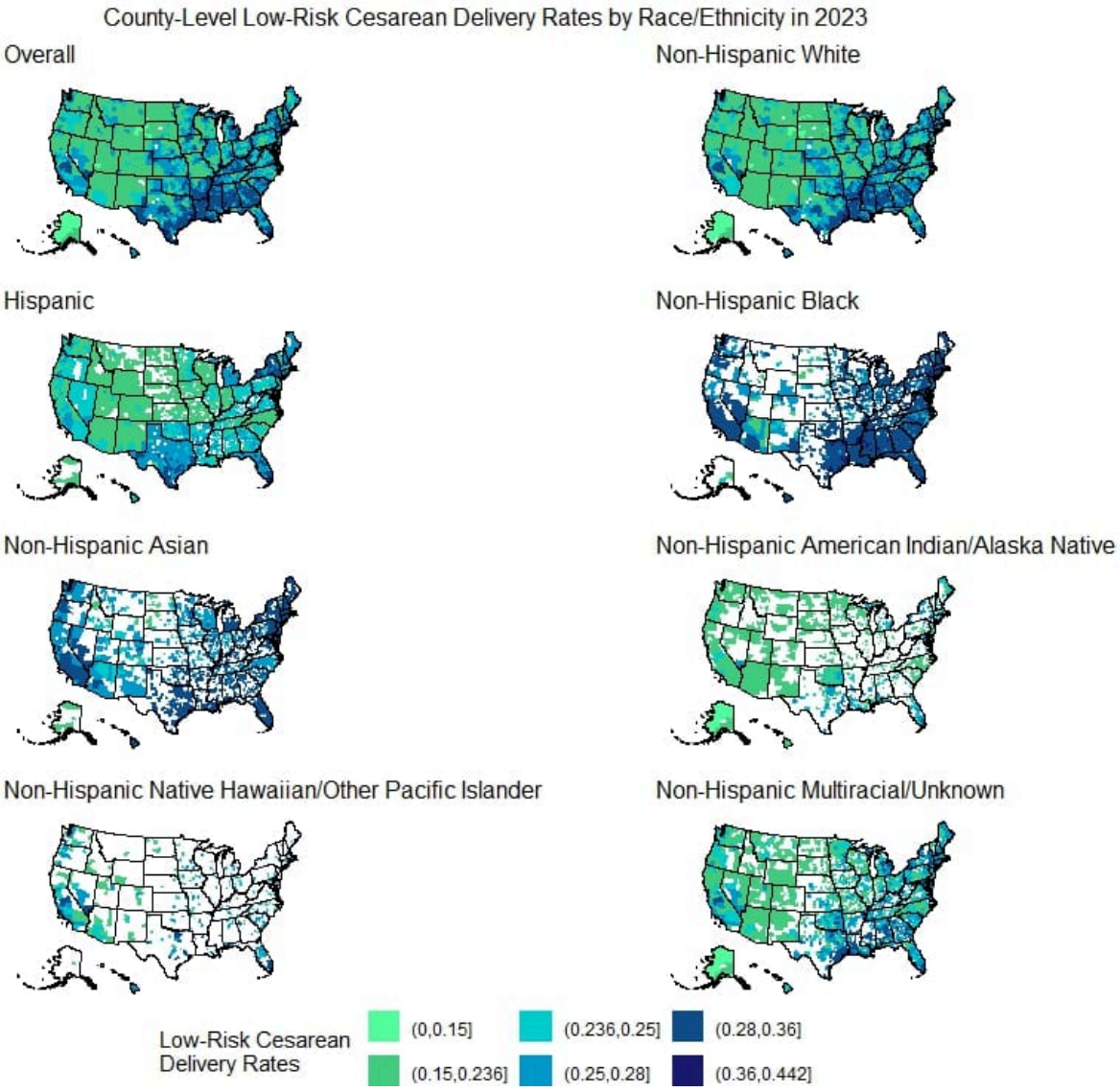
Low-Risk Cesarean Delivery Rates at the County Level: Progress toward Healthy People 2030 Objectives Lauren Rossen* Rachael Beer Michelle Osterman Lauren Rossen

Background: A Healthy People (HP) 2030 objective is to decrease cesarean deliveries among low-risk women with no prior births. Previous analyses have shown substantial geographic variability in low-risk cesarean delivery rates but have been limited to the state level. We estimate county-level rates to measure progress toward the HP2030 objective, assess geographic patterns in rates, and evaluate potential disparities by race/ethnicity.

Methods: Using 2023 US National Vital Statistics Natality data, we modeled county-level low-risk cesarean delivery rates with Bayesian hierarchical models that spatially smooth unstable estimates. We then determined the number of counties that met the HP2030 target rate of 23.6%, mapped county-level rates to assess geographic patterns, and generated county-level estimates by race/ethnicity to assess disparities.

Results: Of 3129 counties with at least one low-risk birth, 1016 (32.5%) achieved the HP2030 target low-risk cesarean delivery rate in 2023, and 471 (15.1%) had reduced rates since 2018. These results differed by race/ethnicity; among Non-Hispanic (NH) Black, NH Asian, NH Native Hawaiian/Other Pacific Islander (NHOPI), NH Multiracial/Unknown, NH White, Hispanic, and NH American Indian/Alaska Native (AIAN) groups, 1.9%, 2.5%, 25.5%, 37.1%, 37.3%, 40.4%, and 68.4% of counties with low-risk births met the HP2030 target, respectively. Geographically, counties in the West and Midwest tended to have lower rates that met the HP2030 goal, while counties in the South and Northeast tended to have higher rates. This pattern was also present among NH White, NH AIAN, NH NHOPI, NH Multiracial/Unknown, and Hispanic populations. Among NH Black and NH Asian populations, rates tended to be high across the US.

Conclusions: Overall, nearly one-third of counties achieved the HP2030 target in 2023. However, there were substantial disparities by race/ethnicity, with few counties meeting the HP2030 target for NH Black and NH Asian populations.


County-Level Low-Risk Cesarean Delivery Rates by Race/Ethnicity in 2023
Overall
Non-Hispanic White
Hispanic
Non-Hispanic Black
Non-Hispanic Asian
Non-Hispanic American Indian/Alaska Native
Non-Hispanic Native Hawaiian/Other Pacific Islander
Non-Hispanic Multiracial/Unknown
Low-Risk Cesarean Delivery Rates
(0,0.15]
(0.15,0.236]
(0.236,0.25]
(0.25,0.28]
(0.28,0.36]
(0.36,0.442]

Perinatal & Pediatric

Characteristics of US Emergency Department Visits Related to Ectopic Pregnancies, 2019–2020 Lindsay S. Womack-Martenson* Lindsay Womack Elizabeth Clark Sabrina Karim Lisa Ashley Busacker Angela Rohan

Background: Ectopic pregnancy is the leading cause of pregnancy-related death due to hemorrhage. Many are diagnosed in emergency departments (EDs) with more severe cases resulting in inpatient admission. This study aimed to estimate the number of ED visits related to ectopic pregnancies in 2019–2020, examine factors associated with inpatient admission from the ED, and analyze surgical treatment among admitted cases.

Methods: Using 2019–2020 HCUP Nationwide Emergency Department Sample (NEDS) data, we analyzed ED visits related to ectopic pregnancies among females aged 15–44 years, identified using ICD-10-CM, ICD-10-PCS, and CPT codes. Data in the NEDS can be weighted to provide national estimates; these weights were used in this analysis. Logistic regression models with predicted marginals were used to quantify the association between inpatient admission and patient, community, and hospital characteristics. Among inpatient admissions, surgical treatment was classified using ICD-10-PCS codes.

Results: Of 103,102 ED visits related to ectopic pregnancies, 15.5% resulted in inpatient admission. Admission rates were higher for patients aged ≥35 years (adjusted prevalence ratio [APR] 1.64; 95% CI, 1.15–2.35), Hispanic (APR 1.31; 95% CI, 1.09–1.58) or non-Hispanic American Indian/Alaska Native patients (APR 2.35; 95% CI, 1.06 –5.21), Medicaid/Medicare patients (APR 1.17, 95% CI, 1.01-1.35), those in the lowest income quartile (APR 1.46; 95% CI, 1.14-1.88), and patients at level III trauma centers (i.e., lowest level) (APR 1.93; 95% CI, 1.33-2.80). Among 15,964 admissions, 22.9% underwent open surgery, 45.2% had minimally invasive surgery, and 31.8% received non-surgical treatment.

Conclusions: There are differences in inpatient admissions among ED visits for ectopic pregnancies by age, race, ethnicity, socioeconomic status, and facility type. Higher admission rates at level III trauma centers may indicate differences in resource availability or patient characteristics.

Perinatal & Pediatric

Comorbidity patterns among pregnant individuals with migraine: A population-based latent class analysis in Ontario, Canada Melina Albanese* Melina Albanese Susan Bondy Christine Lay Manav Vyas Zhiyin Li Jun Guan Hilary Brown

Comorbidity is common with migraine. To inform healthcare services to prevent pregnancy complications and support maternal wellbeing, we identified comorbidity patterns in pregnant individuals with migraine. In a population-based cohort study of pregnancies conceived in 2007-2022 to individuals with migraine in Ontario, Canada, we used latent class analysis (LCA) to identify subgroups using 33 physical and psychiatric chronic conditions (CC). Classes were chosen based on statistical fit indices, parsimony, and clinical interpretability. We then compared the sociodemographic and reproductive health-related characteristics of the classes using standardized differences. Of 174,164 pregnant individuals with migraine, 67.2% had ≥1 CC. Most prevalent were mood/anxiety disorders (41.4%), low back pain (16.9%), obesity (12.1%), and asthma (10.6%). Three distinct subgroups best characterized comorbidity patterns. Class 1: 'Mood/anxiety disorder comorbidity' included 81.2% of the cohort, Class 2:'Mood/anxiety disorder and low back pain comorbidity' 8.3%, and Class 3: 'Other mental illness comorbidity' 10.6%. The 'Other mental illness comorbidity' group was younger, lived in lower income neighbourhoods, and had more long-term residents and nulliparous individuals than Class 1, while the 'Mood/anxiety disorder and low back pain comorbidity' group was older and had fewer nulliparous individuals than Class 1. Findings were similar in sensitivity analyses including only CC with ≥1% prevalence. In a LCA using only physical CC, we also identified three latent classes: 'Low back pain comorbidity' (4.3%), 'Obesity comorbidity' (2.8%), and 'No physical comorbidity' (92.9%). Identified patterns of comorbidity suggest subgroups who could benefit from preconception and perinatal supports for mental health and chronic pain. Screening for CC and coordinating primary, psychiatric, and obstetric care before or early in pregnancy may aid in early identification and management of migraine-related comorbidities.

Perinatal & Pediatric

Toddler diet quality: a factor associated with childhood growth? Xuanxuan Zhu* Edwina Yeung Xuanxuan Zhu Diane Putnick Priscilla Clayton Tzu-Chun Lin Edwina Yeung

Background. Childhood growth is crucial for long-term overall health and well-being. Diet quality is an essential component of nutritional status reflecting dietary patterns and nutrient intake. While research in adults has shown that higher diet quality is associated with a lower risk of obesity, its association with childhood growth has remained unclear. This study aims to evaluate the association between diet quality among toddlers and their growth in middle childhood.

Methods. Mothers from Upstate KIDS, a prospective cohort study, reported numbers of servings/day for specific foods fed to toddlers at 30 and 36 months of age such as dairy, fruit, vegetables, and meat. Accordingly, the Youth Healthy Eating Index (YHEI) was calculated to measure toddler diet quality (range 0-80) with higher scores indicating better diet quality. Children's height, weight, and waist circumference were reported up to three times when they were 7-9 years old, and corresponding height-for-age (HAZ), weight-for-age (WAZ), body mass index-for-age (BMIZ) z-scores and overweight status were calculated. Mixed effects models were used to estimate associations, adjusting for maternal age at delivery, race/ethnicity, education, private insurance, WIC participation, pre-pregnancy BMI, etc.

Results. Among 1,116 children (51.79% male, 86.74% non-Hispanic white), the mean YHEI score at 30/36 months of age was 44.578.54. A one-point increase in YHEI score would increase HAZ by 0.01 (adjusted =0.01, 95% CI: 0.0004, 0.02) and reduce waist circumference by 0.02 (adjusted =-0.02, 95% CI: -0.04, -0.002). YHEI scores were negatively associated with the risk of overweight (adjusted OR=0.96, 95% CI: 0.93, 0.99). YHEI scores were not associated with WAZ and BMIZ.

Conclusion. Higher toddler diet quality is associated with linear growth and reduced central adiposity and overweight in middle childhood. Interventions aimed at improving early diet quality are needed to promote healthy growth in childhood.

Perinatal & Pediatric

Placenta accreta spectrum conditions and associated outcomes by gestational age Sabrina Karim* Sabrina Karim Lindsay S. Womack-Martenson Elizabeth A. Clark Carla L. DeSisto Antoinette T. Nguyen Angela Rohan

Introduction: Abnormal placental adherence, including placenta accreta, placenta increta, and placenta percreta—collectively known as placenta accreta spectrum conditions (PAS) —can lead to life-threatening hemorrhage and other adverse outcomes. Despite increasing PAS incidence over time, little is known about its outcomes across multiple gestational ages. We examined national prevalence estimates of PAS overall and by gestational age at delivery, and the prevalence of adverse outcomes among deliveries with PAS across different gestational ages.

Method: This cross-sectional study used Healthcare Cost and Utilization Project National Inpatient Sample data (2016-2020). International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) codes were used to identify PAS and adverse maternal outcomes among delivery hospitalizations of patients aged 12-55 years for stillbirths and livebirths (weighted N= 17,865,109). We estimated the prevalence of PAS overall and by gestational age at delivery. For those with PAS, we estimated the prevalence of adverse maternal outcomes by gestational age at delivery.

Result: The prevalence of PAS among delivery hospitalizations was 0.12%, with the highest prevalence in deliveries at 28-31 weeks gestation (0.95%). Among deliveries with PAS, the prevalence of adverse outcomes varied by gestational age. Compared with deliveries ≥32 weeks, those at 24-27 and 28-31 weeks had higher prevalences of blood transfusion (36.0% at 24-27 weeks, 32.1% at 28-31 weeks vs 26.2% at ≥32 weeks), hysterectomy (59.9%, 69.4% vs 45.0%), DIC (12.8%, 9.6% vs 4.1%), shock (11.6%, 8.3% vs 4.2%), DIC with blood transfusion or shock (8.7%, 6.8% vs 2.7%), and placental abruption (8.1%, 9.6% vs 2.1%).

Conclusion: The higher prevalence of complications among deliveries with PAS at earlier gestational ages can inform screening practices and quality improvement initiatives for early identification and transfer of care, if necessary.

Perinatal & Pediatric

Exploring Patterns in Age at Menarche: The Effect of Are Deprivation Index Through a Lifecourse Perspective in the Bogalusa Heart Study Eunsun Gill* Eunsun Gill Katherine P. Theall Dohyeong Kim Soo Jung Kang Courtney J Thomas Jessica A Broach Lydia A. Bazzano Camilo Fernandez Emily W. Harville

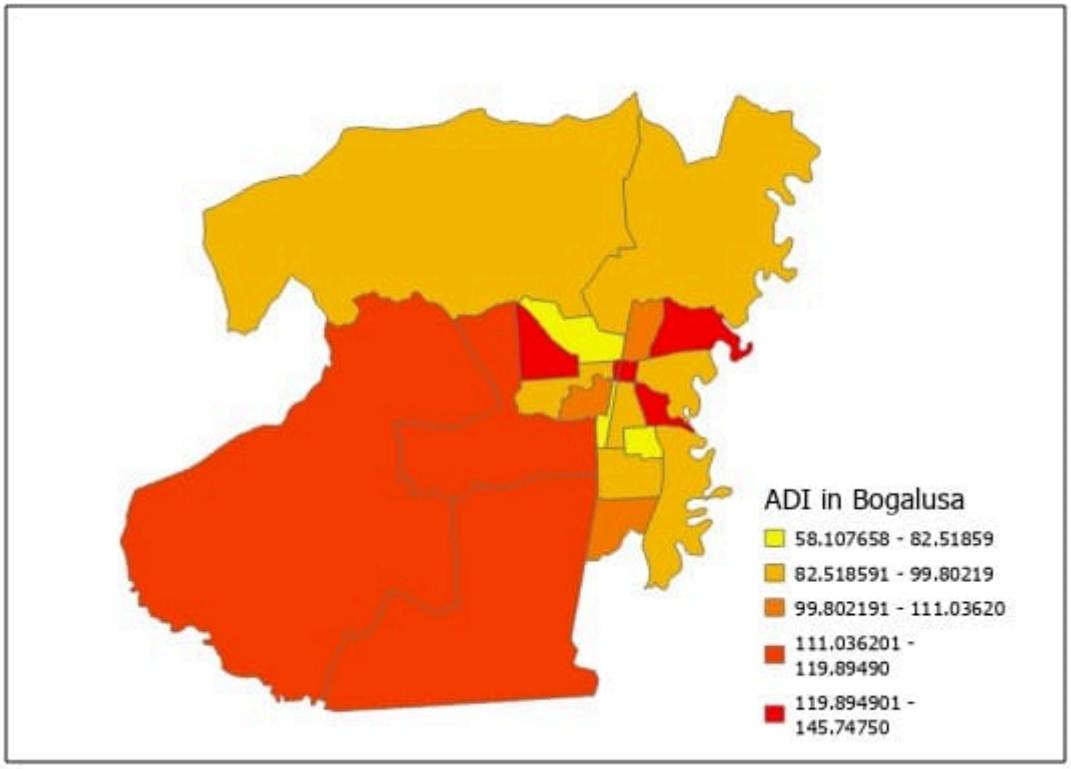
Introduction: Early and late menarche are related to adverse health outcomes. Area Deprivation Index (ADI), a measure of neighborhood socioeconomic conditions, may influence age at menarche (AAM), but its lifecourse evidence remains limited. We explored the influence of evolving ADI on AAM and moderating effect of obesity in the Bogalusa Heart Study (BHS).

Methods: A secondary longitudinal study (1974–2004) was conducted among 1,821 girls from the BHS, with up to six follow-up visits. ADI, based on 16 block-group census variables via factor analysis, was measured repeatedly and divided into quintiles (Q; Q1=least deprived; Q5=most). AAM was self-reported in year and month. Weibull accelerated failure time model analyzed the association between ADI and AAM, adjusting for race, exam year, maternal and paternal education, maternal smoking, systolic blood pressure, glucose, total cholesterol, and obesity with multiple imputation.

Results: Data from 1,821 girls (55.7% White; 44.3% Black; AAM: 7.1–16.8 years; median follow-up=4.2 years) showed a J-shaped association between ADI and AAM, with lower and higher deprivation linked to earlier menarche compared to the middle. Compared to girls in Q4, those in Q2 (Time ratio [TR]=0.97, 95% CI: 0.95–0.98), as well as those in Q1 and Q5 (TR=0.98; 95% CI: 0.97–0.99; TR=0.98; 95% CI: 0.96–1.00) exhibited earlier menarche, while the Q3 had a smaller effect (TR=0.99; 95% CI: 0.96–1.00, overall p=0.004). BMI modified the association, with significant effects among normal weight (Q2 vs. Q4: TR=0.97) and overweight (Q1 vs. Q4: TR=0.94), but not among obese (Q5 vs. Q4: TR=1.06; p for interaction: 0.045)

Conclusions: Both low and high neighborhood deprivation were associated with earlier menarche, a reproductive milestone linked to cardiometabolic and reproductive health risks. Environmental deprivation may shape long-term health trajectories via its influence on AAM.

Keywords: area deprivation index; menarche; neighborhood deprivation


ADI in Bogalusa
58.107658 - 82.51859
82.518591 - 99.80219
99.802191 - 111.03620
111.036201 - 119.89490
119.894901 - 145.74750

LATEBREAKER

Perinatal & Pediatric

Maternal Haplotypes in One-Carbon Metabolism and Risk of Congenital Heart Defects: Potential Therapeutic Implications Suman Maity* Suman Maity Mohammed S Orloff Horacio Gomez-Acevedo Nandini Mukhejee Lorenzo D Botto Richard H Finnell Meredith M Howley Andrew F Olshan Paul A Romitti Martha M Werler Wendy N Nembhard

Congenital heart defects (CHDs) represent the most prevalent category of birth defects impacting infant mortality. CHDs are often multifactorial, involving both genetic and environmental components. Recent research highlights the potential association of variants in the one-carbon (1-C) metabolism pathway with CHD outcome. This study focused on identifying maternal haplotypes within the 1-C metabolic pathway associated with increased risk of CHD-affected pregnancies. A case-control analysis was used based on the data from the National Birth Defects Prevention (1997-2011), with 917 cases, mothers with CHD-affected pregnancies, and 1,189 controls, mothers with unaffected pregnancies. We evaluated 921 single nucleotide variants (SNVs) across 62 genes within the 1-C metabolism pathway. Associations between maternal genetic variants and CHDs were assessed through allelic association and haplotype clustering utilizing moving window and optimized block-estimation algorithms in PLINK. Enrichment analyses (biological pathways and drug set enrichment) were performed to identify potential therapeutic targets. Fifteen SNVs exhibited significant associations with CHDs, notably within the MAT2A, GSTA1, and TRDMT1 genes. Among the 164 identified haplotypes, the TRDMT1 haplotype showed strong association ($P<0.01$). SNPs within this haplotype (rs2224532, n=903; rs3758415, n=916; rs4748363, n=905; and rs12266606, n=914) being localized near enhancer and promoter regions imply possible regulatory association. Drug-enrichment analyses elucidated the matching genetic activation profile of two therapeutic compounds—decitabine and azathioprine, with a link to methylation-related genes (DNMT3A, MGMT, and GSTA1). Our findings suggest maternal genetic variations, particularly within the 1-C metabolism and methylation pathways, might have a potential effect on CHD pathogenesis, and integrating genetic screening into prenatal care might result in better risk management of CHDs.

LATEBREAKER

Perinatal & Pediatric

Prenatal Care in a Pandemic: Interrupted Time Series Analysis of COVID-Era US Birth Outcomes Esther Priscilla Ebuehi* Esther Priscilla Ebuehi Liwei Chen

Background: Hypertensive disorders of pregnancy (HDP; chronic hypertension, gestational hypertension, preeclampsia, and/or eclampsia) are strong predictors of adverse birth outcomes (ABOs; preterm birth, low birthweight, and/or small for gestational age) that disproportionately impact women from racial and ethnic minority groups. Prenatal care utilization (PNCU) is declining nationally in the United States, and low PNCU can exacerbate racial disparities.

Methods: Data from the Pregnancy Risk Assessment Monitoring System (Phase 8: 2016-2022) (N=118,087) were applied to investigate whether (1) there is a racial disparity in the association between HDP and ABOs, (2) PNCU moderates the association between HDP and ABOs, and (3) racial disparities in ABOs are explained by PNCU for women with HDP. Weighted multivariable logistic regression models, including nested models, were used to estimate the adjusted odds ratio (aOR) and 95% confidence interval (CI) of ABOs. Interrupted time-series analyses will be used to examine these trends before and after the COVID-19 pandemic.

Results: HDP prevalence in the general sample was 20.1%, and was highest among Black (24.6%) and Native American women (21.0%). Compared to women with normotensive pregnancies, women with HDP had nearly twice the odds of having an ABO *(aOR = 1.64, CI = 1.56-1.73)*. Compared to White women with normotensive pregnancies, Black and Hispanic/Latine women with HDP had 29% and 26% higher odds, respectively, of experiencing an ABO *(Black aOR = 1.29, CI = 1.13-1.47; Hispanic/Latine aOR = 1.26, CI = 1.01-1.47)*. Among women with HDP, these racial disparities in ABO persisted, and adequate-plus PNCU did not mitigate the odds of ABO after sequentially adjusting for maternal race/ethnicity *(Black aOR = 1.45, CI = 1.29-1.64; Hispanic/Latine aOR = 1.22, CI = 1.06-1.41)*.

Conclusion: Racial disparities in adverse birth outcomes persisted, even among women with hypertensive pregnancies who utilized prenatal care the most. Findings from this study can be used to improve access to person-centered prenatal care.

**This abstract is being submitted during the latebreaker submission window because the presenting author was impacted by the LA wildfires during the general submission deadline, and we were encouraged by SER to submit during the latebreaker submission window. Thank you for your consideration.*

LATEBREAKER

Perinatal & Pediatric

Understanding the Burden of Adverse Pregnancy Outcomes in Canada: A Descriptive Analysis of Clinical, Social, and Environmental Determinants Sabrina Chiodo* Sabrina Chiodo Laura Rosella Sonia M. Grandi Jessica Gronsbell

Background: Adverse pregnancy outcomes, such as gestational diabetes, preeclampsia, and placental abruption, significantly impact maternal and fetal health. In Canada, national-level estimates of these outcomes and their clinical, social, and environmental factors are limited. This study aims to describe the prevalence of adverse pregnancy outcomes and their contributing factors using linked population health data.

Methods: This retrospective cohort study linked data from the Canadian Community Health Survey and the Discharge Abstract Database (2000–2017). Women aged 15-49 with a recorded delivery were included. Descriptive analyses were used to summarize individual and clinical characteristics of women (e.g., age, BMI), social determinants (e.g., income, immigration), and environmental exposures (e.g., air quality, greenspace). Unadjusted log-binomial models were used to describe relationships between these factors and adverse pregnancy outcomes.

Results: Among 13,000 women, 7% experienced an APO (gestational diabetes: 6%, preeclampsia: 1%, placental abruption: 1%). The risk of APOs was ~3 times higher in women aged 40-49 compared to those aged 25-29 (Risk Ratio [RR]=2.7, 95% Confidence Interval [CI]: 1.8–4.0). Immigrant women had a higher risk of APOs compared to Canadian-born women (RR=1.8, 95% CI: 1.5–2.2), as did visible minorities compared to non-visible minorities (RR=2.0, 95% CI: 1.7–2.5). Women in the lowest income quintile had higher risk than those in the highest (RR=1.7, 95% CI: 1.1–2.4). Poor self-reported health (RR=2.7, 95% CI: 1.8–4.0; vs. excellent) and severe obesity (RR=3.0, 95% CI: 2.0–4.5; vs. normal weight) were also found to be associated.

Conclusion: This study provides a contemporary overview of the burden of adverse pregnancy outcomes and its contributing factors, and highlights the need to address health inequities and develop targeted public health interventions. Forthcoming results will examine additional social and environmental factors.

LATEBREAKER

Perinatal & Pediatric

Lifecourse psychosocial stressors and excessive gestational weight gain among employed pregnant individuals Lizette Mendez* Lizette Mendez Jian Li Lu Zhang Amy Crockett Onyebuchi A Arah Liwei Chen

The impact of psychosocial stressors across the lifecourse on gestational weight gain (GWG) remains understudied. This study examined associations of adverse childhood experiences (ACEs) and maternal stressors (work and non-work-related) with excessive GWG among pregnant individuals in the United States. We analyzed data from a cohort of 1,068 pregnant individuals employed during pregnancy. The majority of participants (91.48%) were covered by Medicaid, and 65.92% were classified as overweight or obese at baseline. ACEs were measured at early pregnancy (<20 weeks gestation) and maternal stressors during late pregnancy (~30 weeks gestation) using validated questionnaires. Excessive GWG was categorized using the Institute of Medicine's guidelines, which categorize weight gain during pregnancy as excessive if it exceeds the recommended range based on pre-pregnancy Body Mass Index (BMI). Multivariable linear and logistic regression models were used to assess associations, adjusting for age, education, Medicaid status at delivery, marital status, race, employment status, tobacco use during pregnancy, pre-pregnancy BMI, parity, and care group. After controlling for confounders, excessive GWG was positively associated with physical abuse (OR=1.50; 95% CI: 1.08-2.07), emotional abuse (OR=1.41; 95% CI: 1.06-1.87) during childhood, and experiencing the hospitalization of someone close during pregnancy (OR=1.62; 95% CI: 1.13-2.33), but not any maternal work stressors. In conclusion, this study found that physical and emotional abuse during childhood and non-work-related maternal stressors were associated with increased risk of excessive GWG. Our findings underscore the need for further research into preventing excessive GWG arising from childhood and maternal stressors.

Perinatal & Pediatric

The association of maternal intellectual and developmental disabilities with severe maternal morbidity in California Catherine Psaras* Catherine Psaras Gretchen Bandoli Rita Ryu

Background. Intellectual and developmental disabilities (IDD) involve cognitive and adaptive deficits beginning before age 18–22. Fertility rates among people with IDD are rising, but they still face health disparities during pregnancy. This study examined the relationship between IDD subtypes and severe maternal morbidity (SMM) and identified factors mediating SMM in women with IDD. **Methods.** This population-based study analyzed linked California data (2007–2021), including birth, infant death, discharge, emergency department, and ambulatory surgery center records. Singleton births to women with preexisting IDD (autism spectrum disorder (ASD), cerebral palsy (CP), intellectual disabilities (ID), chromosomal abnormalities, and other IDD) were compared to those without IDD, with disabilities identified using diagnosis codes. SMM was defined as a composite of 21 diagnostic indicators from conception to 42 days postpartum. We estimated relative risks and the proportion of the total effect of IDD on SMM mediated by pre-pregnancy characteristics. **Results.** The data included 6,430,534 singleton pregnancies from 2007–2021. 4,713 pregnancies were among women with IDD (non-mutually exclusive subtypes: ASD: 458; CP: 1019; ID: 1817; chromosomal abnormalities: 1571; other IDD: 600). All IDD subtypes were associated with SMM (any IDD: 2.88 [95% CI: 2.52, 3.29]). The strongest mediators were anxiety or depression (10%; 95% CI: 3%–17%) and epilepsy (12%; 95% CI: 5%–19%). There was heterogeneity by IDD subtype in the total effect and mediation analyses (ASD 2.66 [1.68, 4.22]; ID 3.35 [2.63, 4.27]; CP 2.33 [1.69, 3.23]; chromosomal abnormalities 2.29 [1.77, 2.96]; other IDD 4.60 [3.43, 6.17]). **Discussion.** There was excess risk of SMM among women with IDD, some of which was mediated through pre-pregnancy characteristics such as epilepsy and mental health diagnoses. Quantifying excess risk and associated mediating pathways can inform intervention strategies.

Perinatal & Pediatric

Hypertensive disorders of pregnancy among women with intellectual disability: a population-based study Rita Ryu* Rita Ryu Catherine Psaras Gretchen

Background. Women with intellectual and development disabilities (IDD) face increased risk of adverse maternal outcomes. Among IDD subtypes, intellectual disability (ID) may confer unique risks, but these are poorly understood due to low prevalence. Thus, we investigated associations between women with ID and hypertensive disorders of pregnancy. **Methods**. This study used a cohort derived from linking 2007-2020 California birth and fetal death records with hospital discharge, emergency department, and ambulatory surgery data. From 6,099,797 singleton births, we created a 1:3 matched cohort of women with and without ID, exact matched on age, race/ethnicity, payer type, participation in a supplemental nutrition program, and maternal nativity. ID status and outcomes were identified from International Classification of Diseases codes at delivery. Generalized linear modeling was applied to estimate risk measures, and mediation analysis was used to calculate the proportion mediated by chronic comorbidities and lifestyle characteristics. **Results.** Among the matched cohort, women with ID (n=1,107) had higher risks of gestational hypertension (RR: 1.8, 95%CI: 1.5,2.2), preeclampsia (RR: 2.8: 2.2,3.5), and severe maternal morbidity (SMM) (RR: 3.4: 2.7,4.4), compared to women without ID (n=3,321). Gestational hypertension was partially mediated by anxiety (proportion mediated: 23%), epilepsy (10%), respiratory conditions (8%), and preexisting diabetes (8%). For preeclampsia, significant mediators were preexisting hypertension (25%), anxiety (14%), preexisting diabetes (11%), epilepsy (10%), and depression (8%), and strongest for SMM were epilepsy (18%), respiratory conditions (13%), and preexisting hypertension (11%). **Discussion.** Women with ID face elevated risks of hypertensive disorders of pregnancy, which are partially explained by chronic comorbidities. Future studies will conduct multiple mediation analyses to inform interventions aimed at improving maternal health.

Perinatal & Pediatric

Effectively targeting perinatal home visiting interventions: estimating heterogeneous treatment effects on infant hemoglobin, breastfeeding, and diet using sorted effects Siva Balakrishnan* Siva Balakrishnan Gary Darmstadt Yunwei Chen Sean Sylvia So Young Ryu Ann M Weber

Introduction

Heterogeneous treatment effects (HTE) are undertested in public health evaluations. We explored HTE of a stage-based home counseling intervention on exclusive breastfeeding (EBF), child hemoglobin and dietary diversity (DDS).

Methods

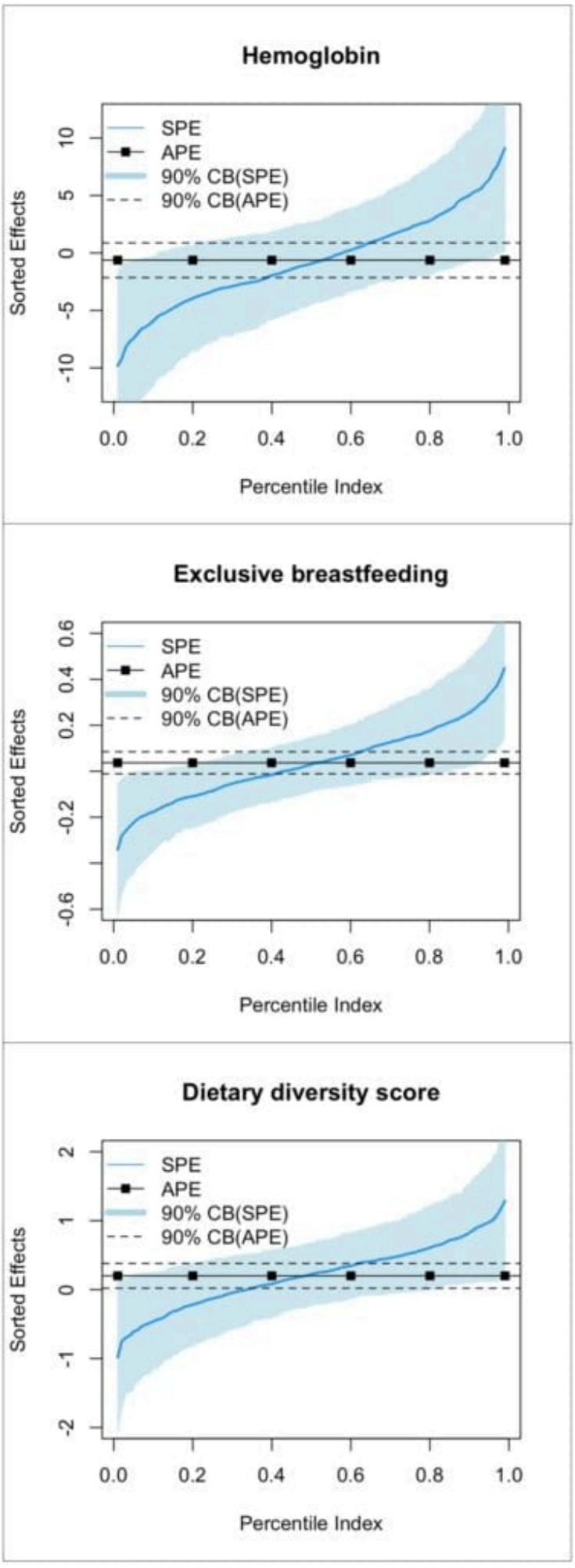
In a cluster randomized controlled trial, pregnant women and caregivers of infants <6 months of age were enrolled in intervention (n=486) or control (n=663) arms in rural Sichuan, China. Community health workers delivered educational modules tailored to participants' stage of development for 12 months. A novel sorted effects method was used to estimate HTE. Individual conditional average treatment effects (CATE) were modelled by regressing baseline characteristics, treatment, and interactions thereof on outcomes. Characteristics of the 20% most and 20% least affected families were compared using multiple t-tests and adjusted p-values to identify those associated with HTE.

Results

Evidence of HTE on outcomes was strong with significant individual CATE on EBF and DDS among the 20% most affected families (Fig 1). Mothers with higher baseline caregiving knowledge (score difference between top and bottom quintiles: 0.83 SD) or who gave birth vaginally (prevalence difference: 0.17) saw greatest increases in EBF. Mothers pregnant at baseline (prevalence difference = 0.45) or with less social support (score difference: -0.77 SD) saw the most benefits on hemoglobin. Mothers with lower caregiving knowledge (score difference: -0.59 SD) had greatest increases in DDS.

Discussion

The evidence supports the use of stage-based curricula and targeting mothers from pregnancy to obtain the greatest increases in child hemoglobin and EBF. To improve overall effects on EBF, breastfeeding modules may need to adjust content for first-time mothers and those with low caregiving knowledge. Partnering with hospital staff may improve EBF, particularly after c-section. Engaging family members to strengthen maternal social support may improve infant DDS.

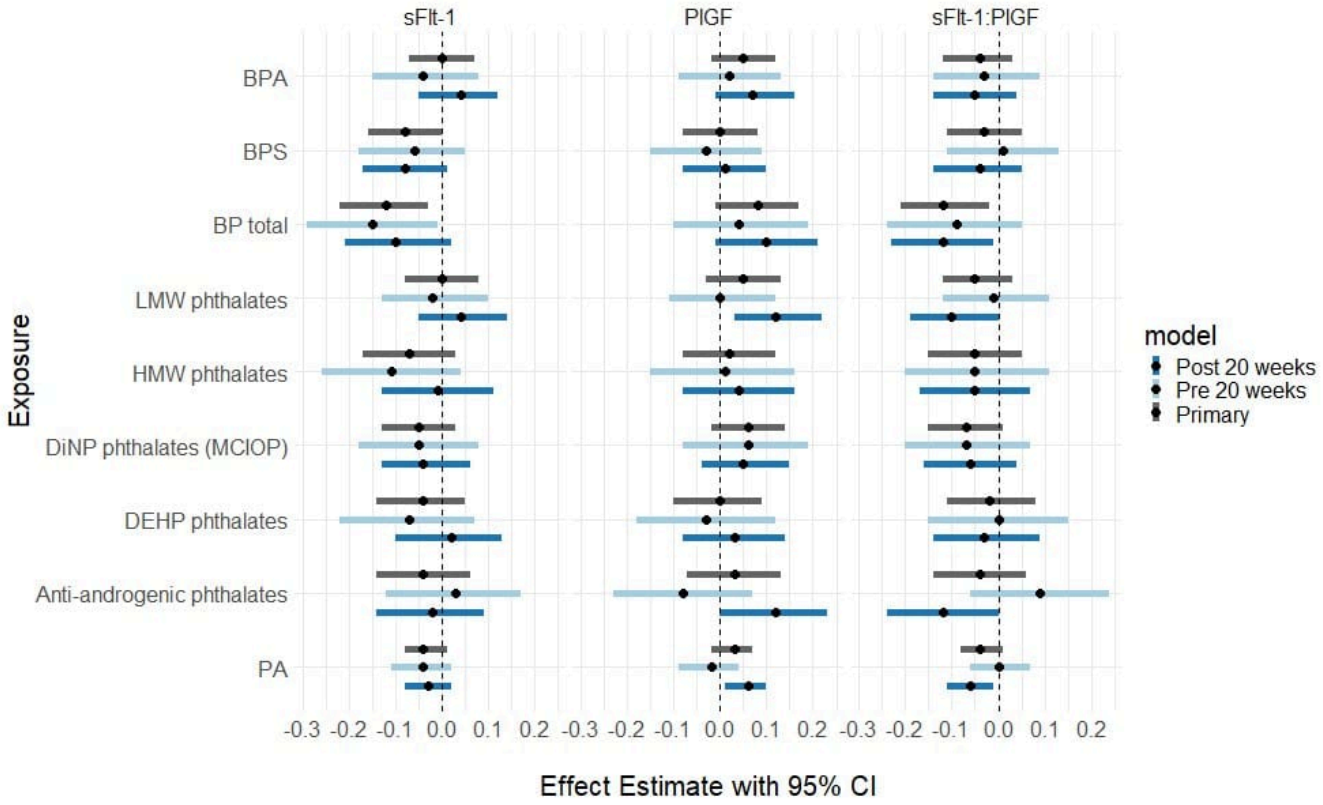

Hemoglobin
SPE
APE
90% CB(SPE)
90% CB(APE)
Sorted Effects
10
5
0
-5
-10
0.0
0.2
0.4
0.6
0.8
1.0
Percentile Index
Exclusive breastfeeding
SPE
APE
90% CB(SPE)
90% CB(APE)
Sorted Effects
0.6
0.4
0.2
-0.2
-0.6
0.0
0.2
0.4
0.6
0.8
1.0
Percentile Index
Dietary diversity score
SPE
APE
90% CB(SPE)
90% CB(APE)
Sorted Effects
2
1
0
-1
-2
0.0
0.2
0.4
0.6
0.8
1.0
Percentile Index

Perinatal & Pediatric

Placental angiogenic biomarkers in relation to prenatal bisphenol and phthalate exposure

Eleanor Medley* Eleanor Medley Emma Spring Mia Charifson Sarah Adelman Yelena Afanasyeva Eunsil Seok Kurunthachalam Kannan Shilpi Mehta-Lee Whitney Cowell Linda Kahn

Placental growth, including the creation and expansion of blood vessels, is regulated by the concentration gradients of numerous growth factors and hormones. The development of placental vasculature has implications for both fetal and maternal health, as the vessels deliver nutrition to the fetus and regulate maternal blood pressure. Placental growth factor (PlGF) is a vascular endothelial growth factor (VEGF) hormone that promotes vasculogenesis and angiogenesis in the placenta. Soluble fms-like tyrosine kinase-1 (sFlt-1) binds to and inhibits VEGFs, preventing angiogenesis. An elevated ratio of sFlt-1:PlGF in maternal serum is predictive of preeclampsia. Exposure to two classes of ubiquitous endocrine-disrupting chemicals, bisphenols and phthalates, has also been previously linked to preeclampsia development. We investigated the relation of urinary concentrations of bisphenols and phthalate metabolites, measured up to three times during pregnancy, with serum concentrations of sFlt-1, PlGF, and their ratio in the New York University Children's Health and the Environment Study. Linear mixed models with random intercepts were utilized to analyze up to three measurements of PlGF and sFlt-1, adjusted for gestational age at the time of serum collection. We found that the molar sum of bisphenols BPA and BPS was associated with lower sFlt-1 (-0.12, 95% CI: -0.22, -0.03), higher PlGF (0.08, 95% CI: -0.01, 0.17), and a lower sFlt-1:PlGF ratio (-0.12, 95% CI: -0.21, -0.02). No statistically significant associations were observed with six phthalate metabolite groups. The unexpected relationship between prenatal bisphenol exposure and lower sFlt-1:PlGF, possibly due to the estrogenicity of bisphenols, warrants further investigation. These results suggest that the effect of these endocrine-disrupting chemicals on placental health may be more complicated than what is currently understood through these biomarkers.



Perinatal & Pediatric

Trajectories of perinatal depressive symptoms in Black and Latina pregnant individuals

Sara Aghaee* Sara Aghaee Lyndsay A. Avalos Elaine Kurtovich Ai Kubo

Over 10% of pregnant individuals experience perinatal depression, with disproportionately high rates among Black and Latina individuals. The literature suggests that perinatal depression is better characterized as trajectories, yet studies on these populations are scarce. This study examines trajectories of perinatal depressive symptoms among Black and Latina individuals in an integrated healthcare delivery system, and their associations with clinical outcomes.

We determined trajectory groups using the Patient Health Questionnaire-9 (PHQ-9), a 9-item depression screener. Total scores range 0-27. Depression severity is characterized as little (0-4), mild (5-9), moderate (10-14), moderately severe (15-19), and severe (20-27). Scores of 10+ are associated with clinical levels of depression. Outcomes included preterm delivery (<37 weeks), low birth weight (<2500 grams), low APGAR scores (0-3, 4-6) and having a c-section. Data were extracted from the electronic health records and research databases.

We examined data from 10,562 pregnancies resulting in singleton live births among Black (22%) and Latina (78%) individuals starting June 2022. We identified 5 trajectory groups using SAS procedure TRAJ: low-stable (23%), mild-stable (45.9%), mild-increasing (13.1%), moderate-stable (13.1%), and moderate-increasing (4.9%). Individuals in the mild-stable (OR: 1.25, 95%CI: 1.04-1.51), mild-increasing (1.35, 1.05-1.172), moderate-stable (1.29, 1.01-1.66) and moderate-increasing (1.45, 1.04-2.01) groups had increased odds of experiencing preterm births compared to those in the low-stable group. Similar associations were found for low birth weight and APGAR scores.

Our findings suggest that having even subclinical levels of depression may be associated with birth outcomes, and that effect estimates vary by severity and trend. Serial depression screenings may be a cost-effective tool for reducing health disparities associated with perinatal depression.

Pharmacoepidemiology

Frankenstein Surveys in Pharmacoepidemiology: Fusing Multiple Surveys Together to Produce Generalizable Estimates from Rare Populations Karilynn Rockhill* Karilynn Rockhill Joshua C. Black Elizabeth Bemis

Surveys are a critical tool in pharmacoepidemiology for population assessment of use patterns and drug effects. Behavioral surveys often utilize online recruitment and are plagued by selection bias and may not be generalizable to other populations of interest. We propose a new model for connecting multiple surveys to optimize data availability, reduce error, enhance inference, and reduce cost. This is accomplished through intentional design elements and correcting for differential selection forces across samples, which can be expressed in a DAG (Figure). We demonstrate this approach using a behavioral surveys designed to measure psychedelic drug use; a rare behavior (<5%) in the general population making a tool to detect differences difficult.

The Approach – This approach requires intentional study design including a large, population-representative survey (‘anchor’, Z’) and then connects targeted, smaller surveys to it (Z’’). When fused, interpretable estimates are created (X and Y) that are otherwise not possible through one survey alone. The anchor collects data to generate estimates to its target population and measures all hypothesized selection forces for itself (S’) and the target survey (S’’). The targeted survey measures more in-depth content for a given topic; it must measure all selection forces and be powered to detect differences in its subpopulation. These two surveys can be fused together, using statistical transport weights, to make generalizable estimates on the focused topic to the to the target population.

The Data – Data from the targeted survey among adults using ≥1 psychedelic drug in the last year (n=2,306) and our nationally-representative drug use survey (n=28,679) will be shown. We explored 2,048 bias-correction models. For example, frequent mental distress was estimated at 41.9% in the sample alone, and 47.0% in the fused data, a 5.1% change. The average residual bias was reduced to 2.7% across demographics, 10.5% across health metrics, and 4.8% across other substance use. Comparison to independent external population estimates will be provided.

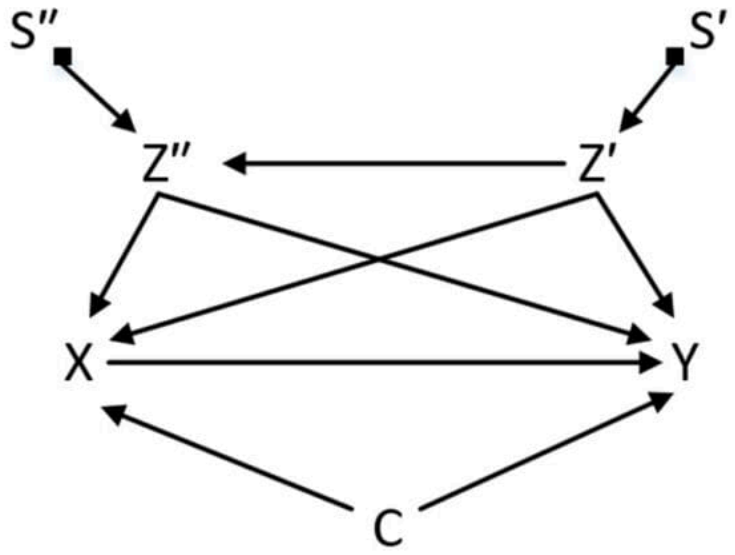


Figure: Targeted surveys (Z'') can be fused with large representative surveys (Z') by accounting for all differential selection forces (S'' and S') between the populations recruited to make generalizable estimates (X and Y).

LATEBREAKER

Pharmacoepidemiology

Medication use during pregnancy in Japan from 2005 to 2019: drug utilization study

Motohiko Adomi* Motohiko Adomi Takamasa Sakai Taku Obara Krista F. Huybrechts

Background: The prevalence of chronic conditions among pregnant individuals has been increasing over the past several decades, leading to growing medication use during pregnancy. Identifying commonly used medications and assessing their safety is crucial, yet only a few studies have examined these trends in Japan.

Objectives: To examine medication use during pregnancy among employment-based insured pregnant individuals and identify frequently used medications with limited safety evidence.

Methods: Using the administrative claims database from JMDC Inc. (2005-2019), we identified a cohort of pregnant individuals whose pregnancy ended in live birth. Medication use was defined as ≥1 dispensing during the first trimester of pregnancy. We identified the most frequently prescribed medication at the generic name level and examined yearly trends at the class level. For the top 30 most commonly prescribed medications, we assessed their teratogenic risk based on TERIS, categorizing the quantity of evidence as None to Fair, Fair to Good, or Good to Excellent.

Results: We identified 110,969 pregnancies. The ten most prescribed medications were acetaminophen (15.5%), metoclopramide (9.1%), chloramphenicol (3.7%), oxiconazole (3.2%), cefcapene (3.2%), salicylic acid (3.1%), loxoprofen (2.9%), clarithromycin (2.6%), cefditoren (2.1%), and metronidazole (1.8%). Utilization of analgesics, antiemetics, immunosuppressants, and thyroid-related medications increased over time, while psychotropics and antibiotics remained stable. Among the top 30 individual medications, 20 fell into the “None to Fair” category for evidence on teratogenicity.

Conclusions: This study highlights increasing trends in medication use in the first trimester of pregnancy in Japan, with analgesics, antibiotics, and antiemetics being commonly prescribed. Limited safety data exist for two-thirds of the most commonly used medications, underscoring the need for prompt safety evaluations.

Pharmacoepidemiology

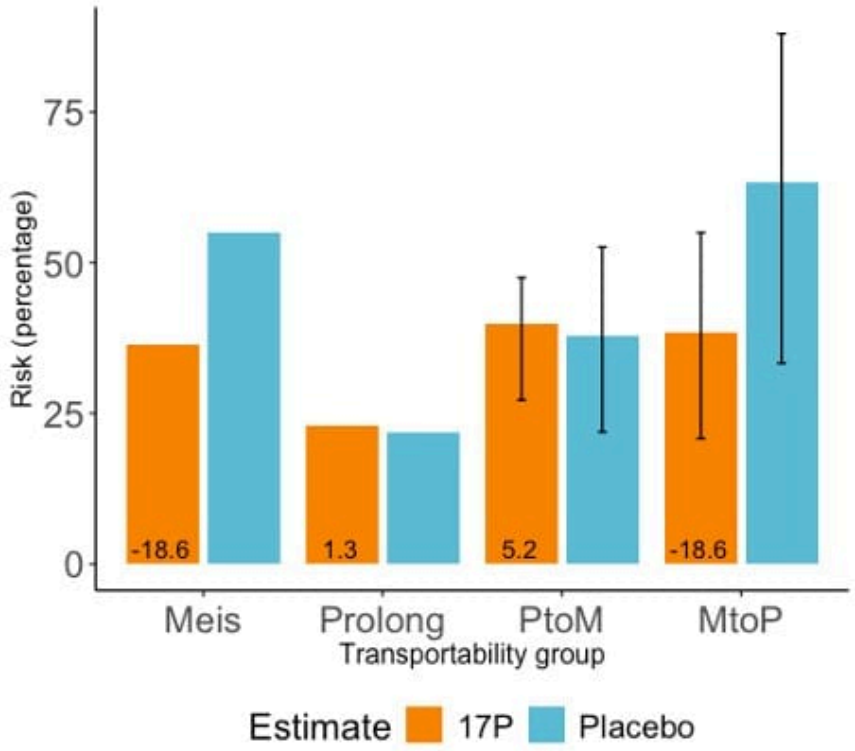
Reconciling conflicting results from trials of 17P and preterm birth Arti Virkud* Arti Virkud Eric Tchetgen Tchetgen Enrique F. Schisterman Beth Pineles Lisa Levine Stephen R. Cole Stefanie N. Hinkle Sunni Mumford Sean Blackwell Alan Peaceman Ellen Caniglia

The Meis et al. trial identified a clinically significant benefit of 17-alpha-hydroxyprogesterone caproate (17P) on reducing the risk of recurrent spontaneous preterm birth (SPTB). However, the confirmatory PROLONG trial identified no effect of 17P on SPTB. PROLONG had a different study population than Meis, despite efforts to recruit similar trial participants. Meis participants had a higher count of prior SPTBs, higher BMI, and were more likely to smoke during pregnancy. Approximately 59% of Meis participants identified as non-Hispanic Black, compared to fewer than 7% of PROLONG. We implemented state of the art machine learning techniques for transportability to investigate whether the conflicting results might be driven by measured differences.

We first estimated RDs for SPTB by treatment arm in both trials, adjusting for measured baseline variables. We then transported the risk of SPTB in each arm of Meis to estimate the causal RD in the PROLONG population and vice versa from PROLONG to the Meis population, using direct standardization via outcome regression, inverse odds weighting, and doubly robust estimators leveraging ensemble learning via SuperLearner and cross fitting. We additionally evaluated if the results changed among individuals enrolled in the US and those with only one prior SPTB. We obtained 95% CIs via nonparametric bootstrap.

Comparing 17P to placebo, the adjusted RD (95% CIs) was -16.4% (-26.7%, -6.9%) in Meis and 1.1% (-3.3%, 5.2%) in PROLONG. Comparing 17P to placebo, the doubly robust RD was -18.6% (-57.3%, 6.2%) when transporting Meis to PROLONG and 5.2% (-18.0%, 17.4%) when transporting PROLONG to Meis (Fig 1). These results were consistent across the other estimators and sensitivity analyses.

Existing methods for transportability approach did not reconcile the conflicting results between the two trials of 17P and SPTB. There may be several explanations for these results including unmeasured effect measure modification between the trials.



Meis represents original Meis 2003 study results (n=459, unadjusted); PROLONG represents original PROLONG 2020 study results (n= 1684, unadjusted); PtoM represents PROLONG transported to the Meis population; and MtoP represents Meis transported to the PROLONG population. The value at the bottom of the 17P bars represents the risk difference for spontaneous preterm birth prior to 37 weeks between 17P and Placebo

Pharmacoepidemiology

Temporal Treatment Patterns and Disparities By Race and Ethnicity in Management of Patients Diagnosed with Triple Negative Breast Cancer in United States: A Surveillance, Epidemiology, and End Results-Medicare Study Kehinde Adeyemi* Farzin Khosrow-Khavar Kehinde Adeyemi

Background: Chemotherapy is a mainstay treatment in management of triple negative breast cancer (TNBC). There are gaps in knowledge regarding how patients with TNBC are managed with different chemotherapy regimens in United States. Thus, the aim of this study was to examine temporal trends of first-line chemotherapy regimens among patients with TNBC in United States and to examine potential disparities by race and ethnicity.

Methods: Using Surveillance, Epidemiology, and End Results (SEER)-Medicare data sources, we identified patients ≥ 66 years with TNBC between 2010 and 2019 with follow-up to 2020. Poisson models were used to estimate annual standardized treatment initiation rates and 95% confidence intervals (CIs) for guideline recommended chemotherapy regimens within one year after TNBC diagnosis. Age-adjusted rate ratios (aRR) and 95% CIs were estimated to compare chemotherapy initiation rates by race and ethnicity.

Results: Among 11,496 patients with TNBC, 53.3% initiated chemotherapy. The median age was 74 years, 73.4% of patients were Non-Hispanic White (NHW), and 91.6% were diagnosed with locoregional TNBC. The most common first-line chemotherapy regimens were docetaxel with cyclophosphamide (TC; 33.7%) and doxorubicin with cyclophosphamide followed by paclitaxel (AC-P; 18.7%). The rate of initiation with AC-P increased between 2010-2020 while it remained constant for other chemotherapy regimens. Non-Hispanic Black (NHB) and Hispanic patients were less likely than NHW patients to initiate any chemotherapy (aRR: 0.89, 95% CI: 0.81-0.99 and aRR: 0.83, 95% CI: 0.72-0.95 respectively) including TC and AC-P.

Conclusion: In this study, we found a temporal increase in rate of first-line treatment with AC-P among patients with TNBC. NHB and Hispanic patients were less likely to initiate chemotherapy, including TC and AC-P, compared with NHW patients. Further research is needed to understand the determinants of disparities in TNBC chemotherapy by race and ethnicity.

Pharmacoepidemiology

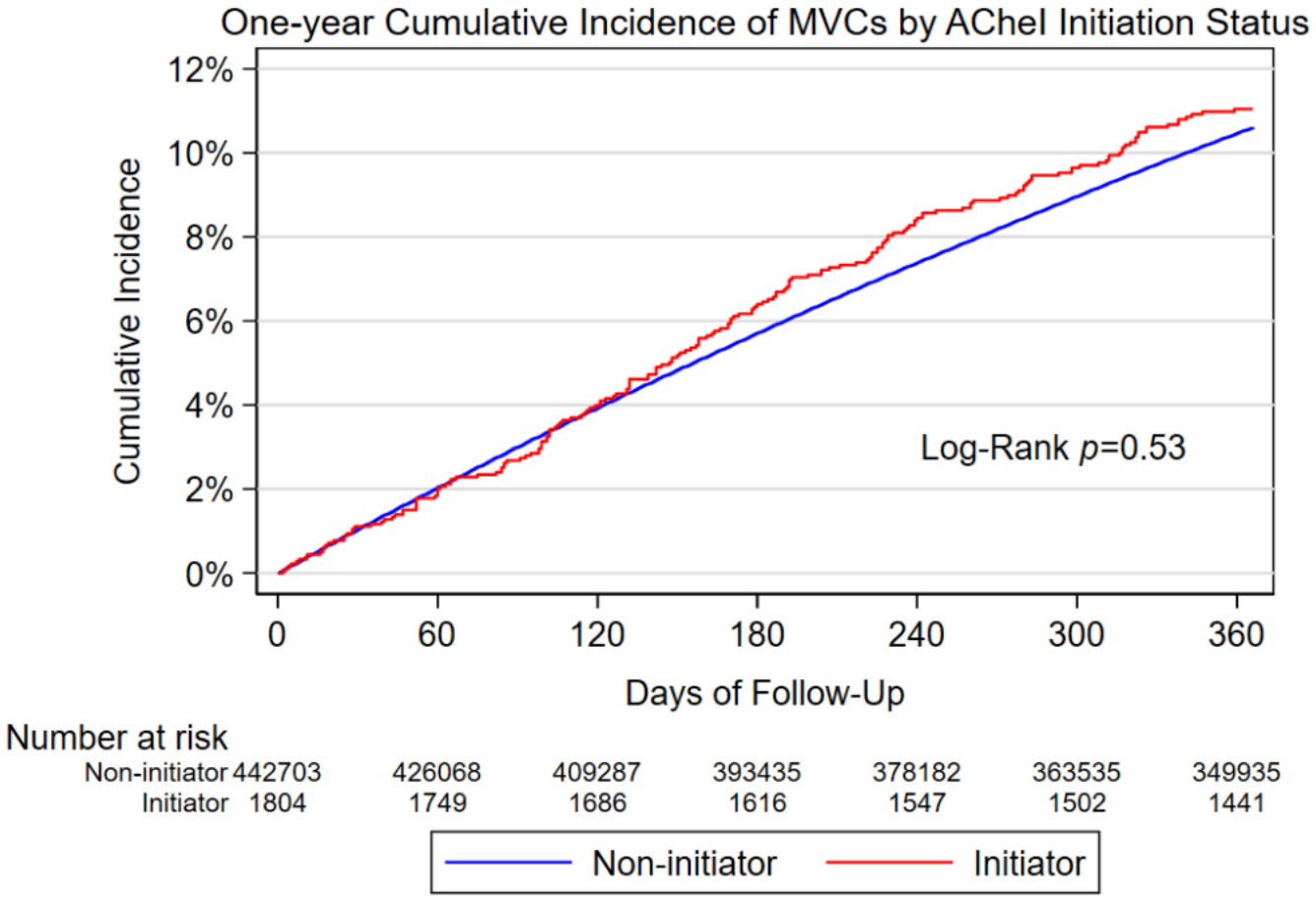
Motor Vehicle Crash Risk Among Adults With Alzheimer's Disease Following Acetylcholinesterase Inhibitor Initiation: A Target Trial Emulation Fiona Bhondoekhan* Fiona Bhondoekhan Andrew R. Zullo Brian R. Ott Melissa Pfeiffer Seth A. Margolis Marzan A. Khan Allison E. Curry Nina Joyce

Background: Acetylcholinesterase inhibitors (ACheIs) improve cognitive symptoms/delay progression in mild-to-moderate Alzheimer's disease (AD). Their impact on motor vehicle crashes (MVCs) has not been evaluated, despite AD causing attention, perception, and executive function deficits which threaten safe driving. We compared the one-year crash risk in adults with mild-to-moderate AD who initiated ACheIs vs. those who did not.

Methods: We defined a target trial using New Jersey drivers' licensing and police-reported crash data linked to Medicare claims and performed 470 sequential emulations, each starting on a consecutive calendar week from January 1, 2008-January 1, 2017 (unit of analysis: person in a trial). At the start of each week, we identified ACheIs initiators and non-initiators among adults aged ≥66 years with mild-to-moderate AD and an active driver's license. We included ACheIs (donepezil, galantamine, rivastigmine, or tacrine) initiated within seven days after a ≥97-day washout. Follow-up lasted one year or until MVC, death, or loss to follow-up, whichever occurred first. We computed one-year cumulative incidence of MVCs using Kaplan-Meier curves.

Results: We identified 444,507 person-trials, of which 1,804 (0.4%) initiated ACheIs. Initiators were more often Hispanic (6.5% vs. 5.2%) and female (54.9% vs. 52.1%) than non-initiators, and they had more preventive healthcare visits (≥3 visits: 19.6% vs. 18.8%). Non-initiators had higher comorbidity scores (mean [SD]: 4.6 [3.3] vs. 3.9 [3.0]) and more hospitalizations (49.2% vs. 36.0%). We observed 191 (10.6%) initiators and 44,376 (10.0%) non-initiators with an MVC (**Figure**). More non-initiators died (7.3% vs. 6.4%) and were lost to follow-up (6.4% vs. 5.3%).

Conclusion: Our findings suggest no significant differences in one-year crash risk by AChеI initiation status. Ongoing analyses will account for baseline covariate differences, censoring, and potential immortal time bias to refine our estimates of crash risk for adults with AD treated with AChеIs.


One-year Cumulative Incidence of MVCs by AChel Initiation Status
Cumulative Incidence
12%
10%
8%
6%
4%
2%
0%
0
60
120
180
240
300
360
Days of Follow-Up
Log-Rank p=0.53
Number at risk
Non-initiator 442703 426068 409287 393435 378182 363535 349935
Initiator 1804 1749 1686 1616 1547 1502 1441
Non-initiator
Initiator

Pharmacoepidemiology

The association between immune-modulating advanced treatments and endometriosis outcomes in a large US database Milena Gianfrancesco* Milena Gianfrancesco Emily Riseberg Madhav KC Xinli Hu Ken Dower Adina Lemeshow

Background. Although endometriosis is considered a hormonally-driven and treated chronic condition, it has a significant inflammatory and fibrotic mechanistic axis, and yet no inflammatory or fibrotic treatment currently exists. Indication expansion, or approval of alternative indication targets for existing approved treatments, is a valuable process to uncover underlying biology and promote rapid drug discovery. We evaluated whether existing immune-modulating advanced treatments (AT) were associated with outcomes in a large US database.

Methods. Women with an endometriosis diagnosis (Optum Electronic Medical Records 2007-2023), prescribed an AT <=1 year of diagnosis (AT Group) or not (No AT Group), were followed and censored at time of event, lost to follow-up, or at time of new AT initiation. Outcomes included hysterectomy, laparoscopy, and endometrial ablation. Cox proportional hazards models adjusted for type of inflammatory disease, smoking, malignancy, comorbidities, body mass index, and oral contraceptive and hormone therapy use.

Results. There were 1631 females in the AT Group and 6675 in the No AT Group; 14% and 13% had a procedure during follow-up, respectively. The most common therapies were anti-TNF (N=805; 49%), PDE4 inhibition (N=274; 17%), and B cell depletion (N=238; 15%). In adjusted analyses, the AT Group demonstrated higher incidence of laparoscopy (HR=2.36; 95%CI=1.74-3.20), but not hysterectomy (HR=1.46; 95%CI=0.96, 2.22) or endometrial ablation (HR=1.87; 95%CI=0.98, 3.56) compared with the No AT Group.

Conclusion. Women with endometriosis receiving AT did not demonstrate lower incidence rates of outcomes compared with those not receiving AT (overall and by specific AT). Results may be due to confounding of underlying disease-related factors or that anti-inflammatory strategies to treat endometriosis may require combinatorial approaches. This methodology may be useful for exploring indication expansion in inflammatory and other chronic diseases.

Pharmacoepidemiology

Assessing Reliability of an Electronic Gout Flare Assessment Protocol Applying GAFFO Criteria: The TRUST Trial Shravani Chitineni* Shravani Chitineni Daniel H. Solomon Hyon K. Choi Ana Fernandes Shreya Billa Kiara Tan Chio Yokose Michael J. Berry Misti L. Paudel

Background: The TRUST Trial is a multi-center randomized clinical trial comparing two gout management strategies: treat-to-target serum urate versus treat-to-avoid symptoms. This pilot study assessed whether electronic surveys could provide comparable accuracy to telephone surveys in reporting gout flares, while accommodating patient preference and reducing staff burden.

Objectives: To assess reliability of a two-step electronic self-reported gout flare assessment compared to a staff-conducted telephone questionnaire.

Methods: A convenience sample of TRUST trial participants completed biweekly electronic surveys via StudyTrax (ST), reporting gout flares, primary outcome, in the past two weeks (yes, maybe, or no). Upon completion, blinded staff conducted the gout flare survey at standard biweekly telephone visits. AT gout flare prevalence of 0.20, estimated 82 flare surveys and ≥ 17 flares are needed to detect Kappa lower confidence level of 0.75 at 0.15 precision. In R, agreement was assessed by extended Kappa statistic and intraclass correlation coefficient (ICC) with 95% CI. Then, GEE with family=binomial, link=logit and exchangeable correlation structure were used to model log odds of reporting a flare electronically using telephone responses as independent variable.

Results: Among 28 participants (mean age 60.5 years, SD 13; 93% male), 213 flare surveys were completed (108 electronic, 105 phone) with mean of 3.5 surveys per enrollee (Table 1). Total reported flares were 23 and 22 for electronic and phone surveys, respectively, with overall flare rate of 21%. Agreement between survey types was 96%, with extended Kappa statistic of 0.475 (95% CI: -0.16 to 0.55) and high expected agreement 91%. ICC = 0.88 (CI: 0.83–0.92) demonstrates strong concordance between survey types.

Conclusions: The pilot study shows strong agreement between electronic and telephone gout flare assessments, ICC = 0.88, supporting electronic surveys as an accurate, efficient alternative.

Table 1. Characteristics of the Patients

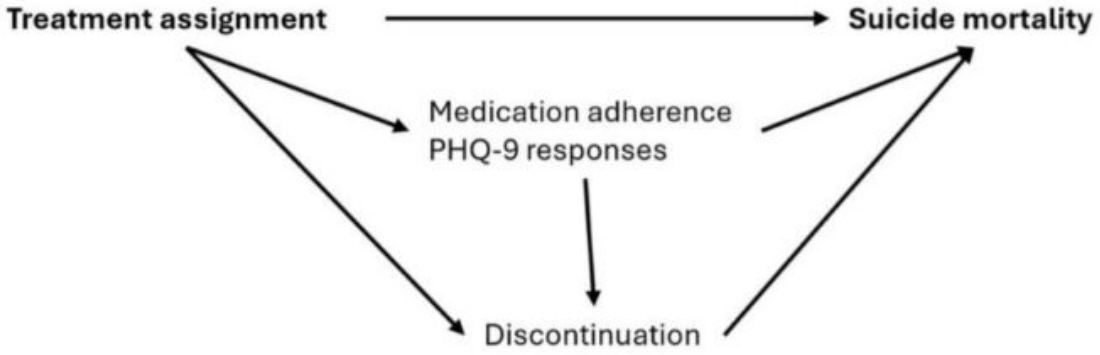
	Gout pilot participants (n = 28)	All TRUST Enrollees (n = 35)
Age, years, mean (SD)	60.5 (13)	61.7 (13)
Male, sex, n (%)	26 (93)	32 (91)
Hispanic ethnicity, n (%)	1 (4)	1 (3)
Race, n (%)		
Asian	3 (11)	4 (11)
Black or African American	4 (14)	5 (14)
Native Hawaiian or Other Pacific Islander	0	0
White	20 (71)	25 (71)
More than one race	0	0
Other	1 (4)	1 (3)
Tophi Assessment Present, n (%)	1 (4)	1 (3)
Baseline Serum Urate Level, mean (SD)	7.3 (0.9)	7.4 (0.9)
Number of Baseline Gout Flares, n (%)		
1	8 (28)	11 (31)
2	7 (25)	10 (29)
3	7 (25)	7 (20)
4	3 (11)	3 (9)
5+	3 (11)	4 (11)
Baseline Allopurinol Usage, n (%)	4 (14)	7 (11)

Philosophy of epidemiology

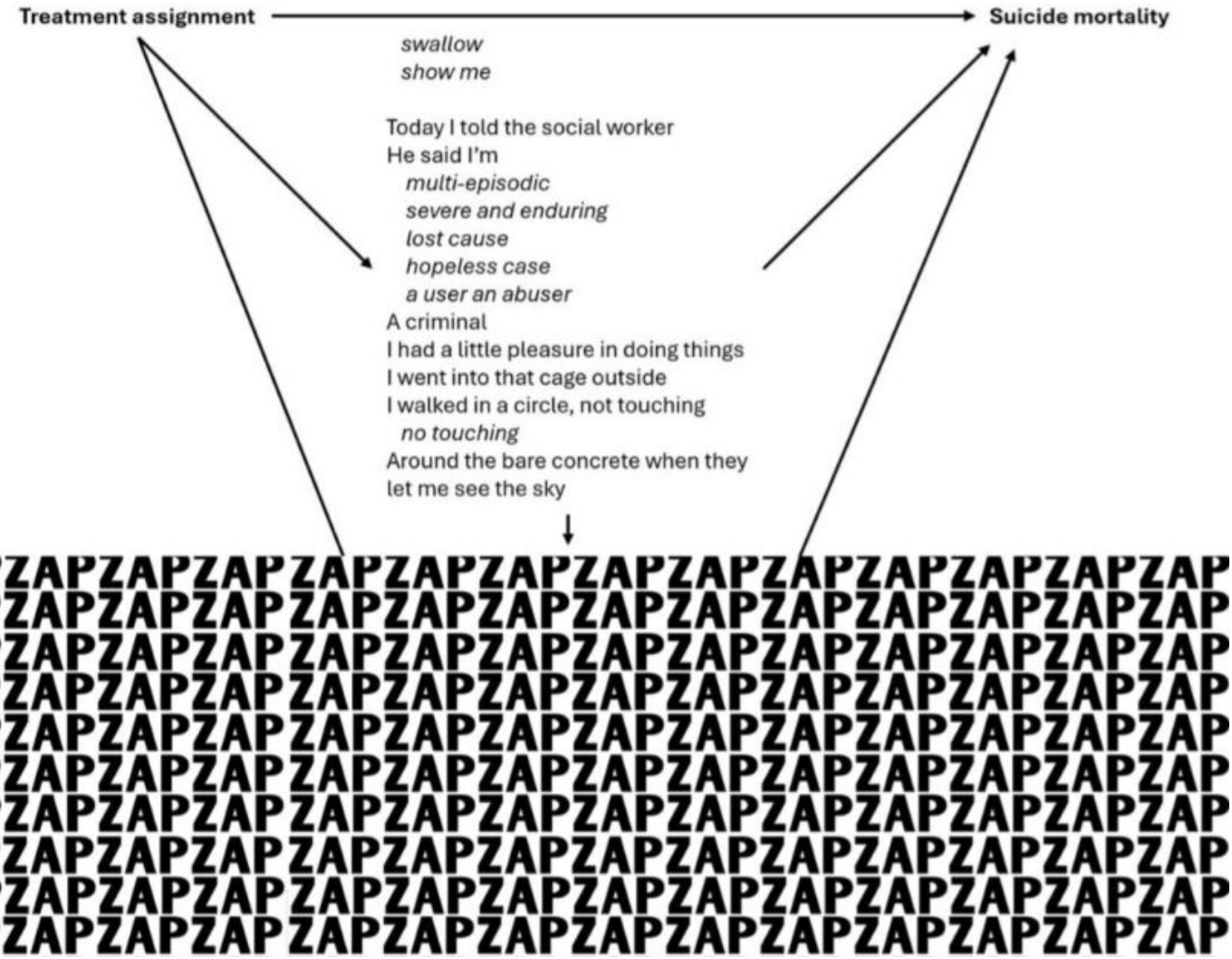
Look at this DAG and feel something: emotion in DAG-drawing in epidemiology research
Kate Vinita Fitch* Kate Vinita Fitch

By necessity, directed acylic graphs (DAGs) simplify the rich networks of factors that contribute to health and disease in human populations. In drawing them, epidemiologists accomplish several tasks: (1) coherently distilling the universe of causation surrounding our research questions, (2) identifying strategies to correct bias in our estimates, and (3) transparently communicating the assumptions we made to accomplish tasks (1) and (2) to our colleagues and peers. In closely reading how DAGs are discussed in core epidemiologic literature and considering the contrast between the emotionless and robotic nature of DAG-drawing and the human suffering which they depict, I argue that DAGs serve another purpose. This purpose is to help epidemiologists perform emotional distancing as part of our aspiration or instruction to achieve unfeeling objectivity. Then, in this work, I interrupt emotional distancing by transforming DAGs into works of art and poetry. The works included primarily consist of simplified DAGs centered around carceral epidemiology, which is my area of interest. I have added poetry and images to these DAGs in a format reminiscent of collage. Through these works, I comment on the emotional experience of DAG-drawing, wed the qualitative and the quantitative, and, above all, highlight the tragedy contained in the nodes of these DAGs in order to evoke emotion and feeling in a format where this response is typically suppressed.

Response/Discontinuation - Original



Response/Discontinuation - Transformed



Policing/Incarceration

Epidemiology of suicide in prisons in Japan Naohiro Yonemoto* Naohiro Yonemoto

Background: The problem of suicide in prison facilities such as prisons and jails, and after release, has been the topic of many research reports from Europe and the United States. It is internationally recognized as a high-risk population for suicide. However, there are few research reports from outside Europe and the United States. This study reports on the epidemiology of suicide in prisons in Japan.

Methods: Suicide rates (per 100,000) were calculated and examined for annual trends and summarized background of suicides. The number of suicides and the denominator, the number of persons institutionalized, was taken from the official statistics, National Criminal Statistics (1952-2022; 1990-2022 for males and females) in Japan.

Results: The annual trend results showed that for the period 1952-2020, the suicide rate varied considerably from year to year (min 5.5 – max 46.8) In the period 2010-2022, there were 184 suicides, with a minimum suicide rate of 5.9 and a maximum rate of 31.8. The background of the suicides was 89% male and 10% female. Age was 9% in their 20s, 26% in their 30s, 34% in their 40s, 12% in their 50s, 13% in their 60s, and 5% in their 70s, respectively. Sixty percent were prisoners and 37% were jailed.

Conclusion: The epidemiology of suicide in prisons in Japan was presented. Although persons in prisons are a special group and environment, and comparisons might be difficult, there were some years when the suicide rate was higher and some years when it was lower than that of the general population in Japan. Yearly trends were very different from those of the trend of total in Japan, and there was no association with Japan’s overall suicide rate. Because of the large number of males in prisons, there were more male suicides. Compared to Western studies, the suicide rate in Japan was not high.

Reproductive

Identification of preeclampsia subtypes via machine learning and associations with risk of perinatal and postpartum outcomes Hongyi Chen* Hongyi Chen Amanda L Ngo Lauren D Liao Yeyi Zhu

There has been increasing recognition of pre-eclampsia (PE) heterogeneity. We aimed to identify PE subtypes using routinely available clinical data via Uniform Manifold Approximation and Projection and Density-Based Spatial Clustering of Applications with Noise. We assessed associations of identified PE subtypes with risk of perinatal and postpartum outcomes via modified Poisson regression and Cox regression, adjusting for maternal age, race/ethnicity, parity, and pre-pregnancy body mass index. In a cohort study of 14,132 racially and ethnically diverse individuals with PE in Northern California in 2011-2021, we split the sample into one training (80% of 2011-2020) and two validation sets (1: 20% of 2011-2020; 2: 2021). In the training set, 4 clusters (C) were identified: C1 (68.3%), C2 (20.4%), C3 (8.7%), and C4 (2.6%). C1 (0.3%) and C2 (0.6%) had nearly no gestational diabetes mellitus (GDM), whereas all individuals in C3 and C4 had GDM. Compared to no gestational hypertension (GH) in C1 and C3, all individuals in C2 and C4 had GH. C1 (92.2%) and C3 (93.4%) were more likely to have late onset PE (≥ 34 gestational weeks), compared to C2 (88.3%) and C4 (89.9%). C3 and C4 were more likely to have pre-existing conditions (prediabetes, polycystic ovary syndrome, dyslipidemia and obesity), and to be older and multiparous, compared to C1 and C2. Compared to C1 as the mildest and most common subtype, C2 had higher risk of small for gestational age (RR 1.14; 95% CI: 1.04-1.25), C3 had higher risk of cesarean delivery (1.08; 1.00-1.16) and large for gestational age (1.49; 1.30-1.71), and C2, C3, and C4 had 1.23/1.11/1.36-fold higher risk of preterm birth, 1.14/1.11/1.23-fold higher risk of neonatal intensive care unit admission, and 1.60/1.26/1.62-fold higher risk of postpartum hypertension (all $P < 0.05$). Findings were similar in the two validation sets. Subtyping PE may inform personalized risk assessment and management to improve associated maternal and child outcomes.

Reproductive

Ruminant-specific and ruminant-predominant fatty acid levels in relation to infertility treatment outcomes Xi Zhang* Xi Zhang Russ Hauser Lidia Minguez-Alarcon Jorge Chavarro

We evaluated the relation between circulating levels of odd-chain fatty acids and ruminant-predominant trans fat isomers, known biomarkers of dairy food intake, and outcomes of infertility treatment with Assisted Reproductive Technology (ART). Couples enrolled in the EARTH Study between 2004 and 2019 provided pre-treatment blood samples. We measured serum levels of fatty acid known to be exclusively (13:0, 15:0, 17:0, 19:0 and 23:0) or predominantly (16:1n-7t, 14:1n-5t) of ruminant origin using gas chromatography in these samples. The study outcome was live birth per initiated treatment cycle. Logistic regression models using cluster-weighed generalized estimating equations to account for repeated treatment cycles were used to estimate the odds of live birth, after accounting for potential confounders. The analysis include 306 women who completed 537 ART cycles of which 191 ended in a live birth. Serum odd chain fatty acids and ruminant-predominant trans fatty acids were positively related to dairy intake and unrelated to red meat intake. There was no association between serum odd chain or ruminant predominant fatty acids with the probability of live birth following infertility treatment with ART. The multivariable adjusted OR (95% CI) of live birth for women in increasing quartiles of serum odd chain fatty acids was 1 (ref), 1.02 (0.60, 1.73), 0.83 (0.49, 1.40) and 0.75 (0.44, 1.29). The corresponding estimates for increasing quartiles of ruminant predominant trans fatty acid levels were 1 (ref), 0.71 (0.43, 1.18), 0.86 (0.52, 1.42) and 1.06 (0.65, 1.74). These findings are not consistent with a strong beneficial or deleterious effect of dairy food consumption on outcomes of infertility treatment with ART.

Enter number 1736

Reproductive

Expanding our methods for studying contraceptive preferences: Application of the multilevel analysis of individual heterogeneity and discriminatory accuracy (MAIHDA) approach to the statewide Surveys of Women Mikaela Smith* Mikaela Smith Payal Chakraborty Robert Hood Autumn Kirkendall

Introduction: Most research on contraceptive access focuses on use rather than preference. Given existing reproductive coercion and medical mistrust, an intersectional framework may better capture equity gaps between preference and use. We used a new quantitative method to examine how race/ethnicity, sexual orientation, and socioeconomic status (SES) inform the social patterning of preferred contraceptive use.

Methods: We used 2021–2023 data from 7 states from the state-representative Surveys of Women (N=12,947). We conducted an intersectional multilevel analysis of individual heterogeneity and discriminatory accuracy (MAIHDA). We nested participants within 32 social strata defined by race/ethnicity, sexual orientation, and SES. We fit two multilevel logistic models via Bayesian MCMC with noninformative priors: (1) an empty model with random intercepts for social strata (simple intersectional) and (2) a model adding fixed effects for social strata (intersectional interaction). We compared MAIHDA with a traditional logistic regression approach with interaction terms.

Results: Overall, 27% of respondents (N=3,385) were not using their preferred contraceptive method. Lesbian, gay, bisexual, and other sexually minoritized (LGB+) women, racial/ethnic minoritized women, and women with lower SES had lower odds of preferred method use. Additive effects explained 91% of the between-stratum variance in preferred method use while interaction effects explained 9%. Black LGB+ women without college degrees and with incomes under $100,000 had the lowest probability of preferred method use (51%), while White heterosexual women with college degrees and incomes over $100,000 had the highest (80%). ORs from MAIHDA and the traditional approach were similar.

Conclusion: Our findings reflect structural inequities in the healthcare system. Traditional models show how isolated identities predict preferred method use but are insufficient in capturing nuances in intersectional experiences.

Reproductive

Associations Between Maternal Injury and Adverse Maternal Outcomes Allison Musty* Allison Musty Elizabeth T. Jensen David Stamilio Asma M. Ahmed

Background

Maternal injury affects 6-8% of pregnancies and is associated with perinatal complications. Variation of associations by injury characteristic is underexplored. We estimated associations between maternal injury and adverse maternal outcomes.

Methods

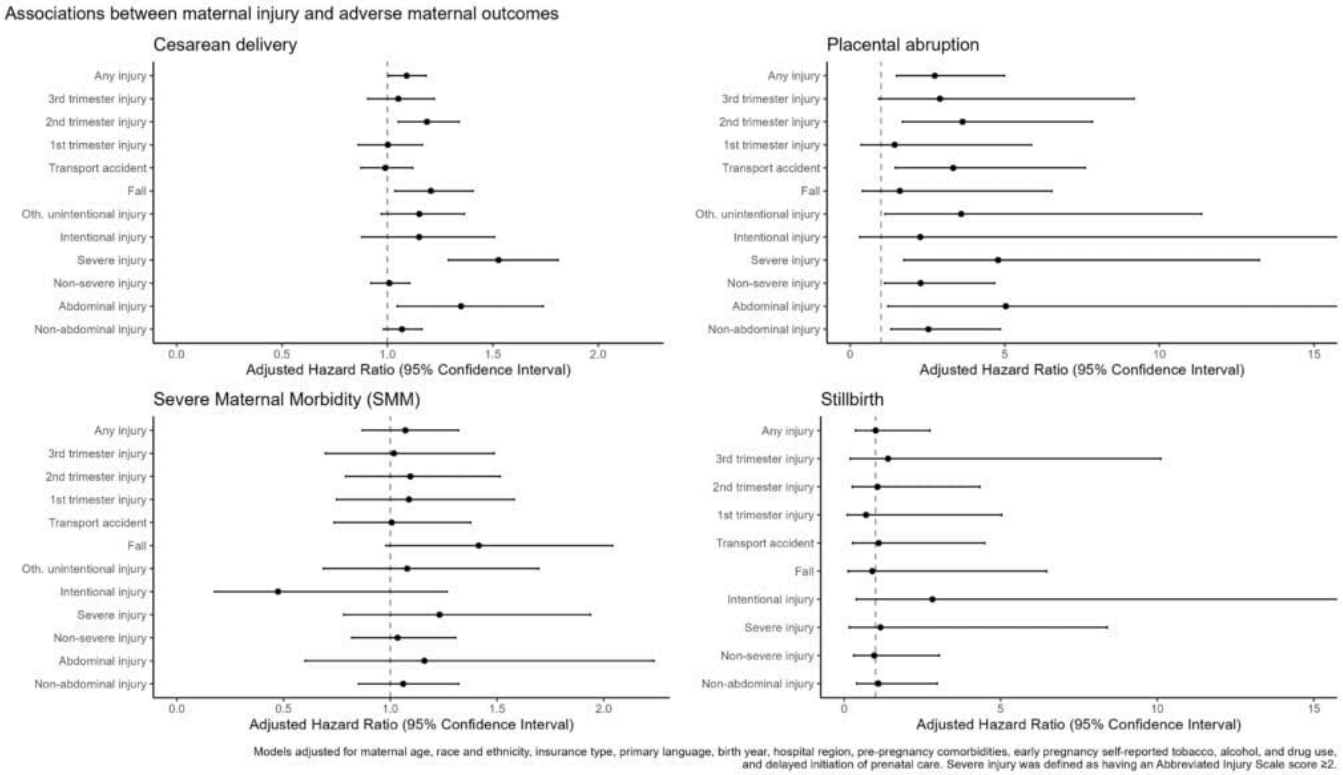
In a retrospective cohort study using electronic health record data at Atrium Health Wake Forest Baptist (2018-2024 births), we identified maternal injury using ICD-10-CM diagnosis codes. Injury was stratified by mechanism (transport accident, fall, other unintentional, intentional), trimester, location (abdominal, non-abdominal), and severity (severe: Abbreviated Injury Scale≥2). Time-varying Cox proportional hazards models estimated associations between injury and severe maternal morbidity (SMM), stillbirth, cesarean delivery, and placental abruption, identified using ICD-10-CM diagnosis and procedure codes. Follow up spanned 20 weeks gestation to outcome occurrence, delivery, or 43 days postpartum for SMM.

Results

Among 58897 deliveries, 3.1% had maternal injury. SMM, stillbirth, cesarean delivery, and placental abruption affected 4.6%, 0.2%, 35%, and 0.3%, respectively. The **Figure** shows associations between outcomes and maternal injury. Injury was associated with increased risk of cesarean delivery (hazard ratio [HR] 1.09, 95% CI 1.01-1.18), especially from falls (HR 1.21, CI 1.04-1.41), and placental abruption (HR 2.74, CI 1.50-4.99), especially from transport accidents (HR 3.33, CI 1.46-7.61). Second trimester, severe, and abdominal injury increased risk of these two outcomes (e.g., severe injury cesarean delivery risk: HR 1.53, CI 1.29-1.81 v. non-severe: HR 1.01, CI 0.92-1.11). Injury was not associated with SMM or stillbirth.

Conclusions

Maternal injury was associated with increased risk of cesarean delivery and placental abruption, particularly for second trimester, severe, and abdominal injury. These findings may inform post-injury clinical care, focusing on pregnancies most at risk for these outcomes.


Associations between maternal injury and adverse maternal outcomes
Cesarean delivery
Placental abruption
Severe Maternal Morbidity (SMM)
Stillbirth
Any injury
3rd trimester injury
2nd trimester injury
1st trimester injury
Transport accident
Fall
Oth. unintentional injury
Intentional injury
Severe injury
Non-severe injury
Abdominal injury
Non-abdominal injury
Adjusted Hazard Ratio (95% Confidence Interval)
Models adjusted for maternal age, race and ethnicity, insurance type, primary language, birth year, hospital region, pre-pregnancy comorbidities, early pregnancy self-reported tobacco, alcohol, and drug use, and delayed initiation of prenatal care. Severe injury was defined as having an Abbreviated Injury Scale score ≥2.

Reproductive

Clusters of sociodemographic and socioeconomic factors and preconception folic acid supplementation in the National Birth Defects Prevention Study, U.S. 2004-2011 Julie M. Petersen* Julie Petersen Eirini Nestoridi Rashida S. Smith-Webb Wendy Nembhard Jenil Patel Bailey Wallace Shannon Evans Suzan L. Carmichael Gary Shaw Martha Werler Mahsa Yazdy Anne Marie Darling the National Birth Defects Prevention Study

Background: Disparities in preconception folic acid (FA)-containing supplement use are well documented. However, limited research has examined the intersection of sociodemographic and socioeconomic factors to identify subgroups in greatest need of intervention.

Methods: Data were from US women who birthed liveborn, nonmalformed infants 2004-2011. Seven individual and 19 census tract variables were input in a hierarchical clustering model to define common patterns of sociodemographic and socioeconomic factors and determine whether they correspond with differences in any FA supplement use 1 month before pregnancy. Supplement use was not included in the algorithm.

Results: The algorithm identified 5 clusters (A n=502, B n=1448, C n=1294, D=738, E n=1351). The proportion of women supplementing with FA increased across Clusters A (13.6%), B (25.8%), C (33.2%), D (37.7%), and E (54.0%). As supplement use increased, some patterns emerged. For instance, the following maternal characteristics decreased: age <20 years, less than a high school education, and household income <$10,000; the proportion with census tract crowding index and income:poverty ratio <1 above the median also decreased. Cluster A had the highest proportion of Hispanic women, Clusters C and E were predominantly non-Hispanic White, and Clusters B and D had the most women identifying as non-Hispanic Black and residing in census tracts with a higher than median proportion of Black residents. Cluster A and C women resided in census tracts with higher than median proportions of manual workers. The proportion of women who intended the pregnancy was higher in Cluster E.

Conclusion: FA supplement use was consistently lower among clusters that tended to be younger, less educated, and have lower income. These data stress the correlations among social determinants of health and the need to understand barriers and develop interventions in socioeconomically deprived communities.

Table. The distribution of preconception folic acid supplementation and individual and census tract characteristics[1] across statistically-constructed subgroups (clusters A to E), National Birth Defects Prevention Study, US 1997-2011

	Cluster A N=502 %	Cluster B N=1448 %	Cluster C N=1294 %	Cluster D N=738 %	Cluster E N=1351 %
Individual Characteristics					
Folic acid supplementation (any, month before pregnancy)	13.6	25.8	33.2	37.7	54.0
Maternal age					
<20 years	15.1	12.0	8.9	5.2	2.4
20-34 years	76.3	75.6	82.2	79.1	70.0
35+ years	8.6	12.5	8.9	15.7	27.6
Maternal education					
<12 years	42.2	20.7	14.5	13.4	1.9
12 years	27.3	29.5	29.5	13.4	13.1
>12 years	30.1	49.7	56.0	73.0	85.0
Maternal race/ethnicity					
White non-Hispanic	17.7	36.5	80.5	50.4	83.6
Black non-Hispanic	2.2	34.0	4.0	19.0	2.9
Hispanic	73.5	19.6	9.6	19.5	4.4
Other	6.6	9.9	6.0	11.1	9.1
Income					
<$10,000	33.1	25.2	16.1	13.4	3.5
$10,000 to $50,000	50.4	47.0	53.8	33.2	24.4
>$50,000	10.8	22.9	26.7	51.5	70.9
Wanted to become pregnant	55.8	48.4	56.6	59.6	74.2
Census Tract Variables[2]					
Household median income	21.9	20.4	26.0	91.3	92.5
Households earning <$30,000	80.5	84.1	70.5	7.5	5.8
Income:poverty ratio < 1[3]	91.0	85.9	51.2	27.4	7.6
Public Assistance Income	96.0	68.2	57.1	22.5	21.7
Renter occupancy	64.3	70.2	30.2	39.6	21.0
Renters affordable housing	60.0	57.2	25.5	53.1	33.7
Affordable housing with mortgage[4]	93.2	66.5	22.2	52.2	42.0
Affordable housing without mortgage[5]	48.2	61.4	39.3	37.7	55.5
Home value ≥$300,000	58.8	39.7	15.3	70.1	80.1
Crowding index[6]	98.0	70.2	48.6	38.1	18.4
Female headed households with dependents	68.1	79.8	33.9	57.7	22.4
Males in management/ professional occupation	13.0	37.2	22.1	78.3	88.8
Manual occupation[7]	92.0	57.4	88.5	16.4	7.9
Self-employed ratio[8]	59.0	36.0	65.4	41.6	51.6
Unemployment	87.9	74.6	35.1	53.8	23.0
Low education	97.8	80.8	62.5	16.4	6.0
Black or African American	32.9	87.5	24.6	84.4	21.8
White	13.0	12.1	85.7	18.7	87.2

[1]Multiple imputation used to replace missing values.

[2]Table shows the proportion with a value that is greater than the median value for that census tract variable

[3]Percent of those with an income to poverty ratio < 1 among the total in sample

[4]Percent of owner-occupied housing units with a mortgage whose monthly owner costs as a percentage of household income is 30% or more

[5]Percent of owner-occupied housing units without a mortgage whose monthly owner costs as a percentage of household income is 30% or more

[6]Percent of owner-occupied house units with more than 1.01 occupants per room among the total occupied house units, dichotomized at the median

[7]Workers in nature, construction, or transportation, including farming, fishing, forestry, construction, extraction, maintenance, production, transportation, and material moving occupations.

[8]Percent of the employed civilian population age 16 years or older who reported being an unpaid family worker or self-employed (unincorporated). Unpaid family workers include people who worked without pay in a business or on a farm operated by a relative. Self-employed in own not incorporated business workers include people who worked for profit or fees in their own unincorporated business, profession, or trade, or who operated a farm.

LATEBREAKER

Reproductive

The role of women's empowerment in the uptake of maternal health services in LMICs: a propensity score-matched analysis. Daniel G. Belay* Daniel Gashaneh Belay Gizachew A. Tessema Jennifer Dunne Richard Norman Aditi Roy

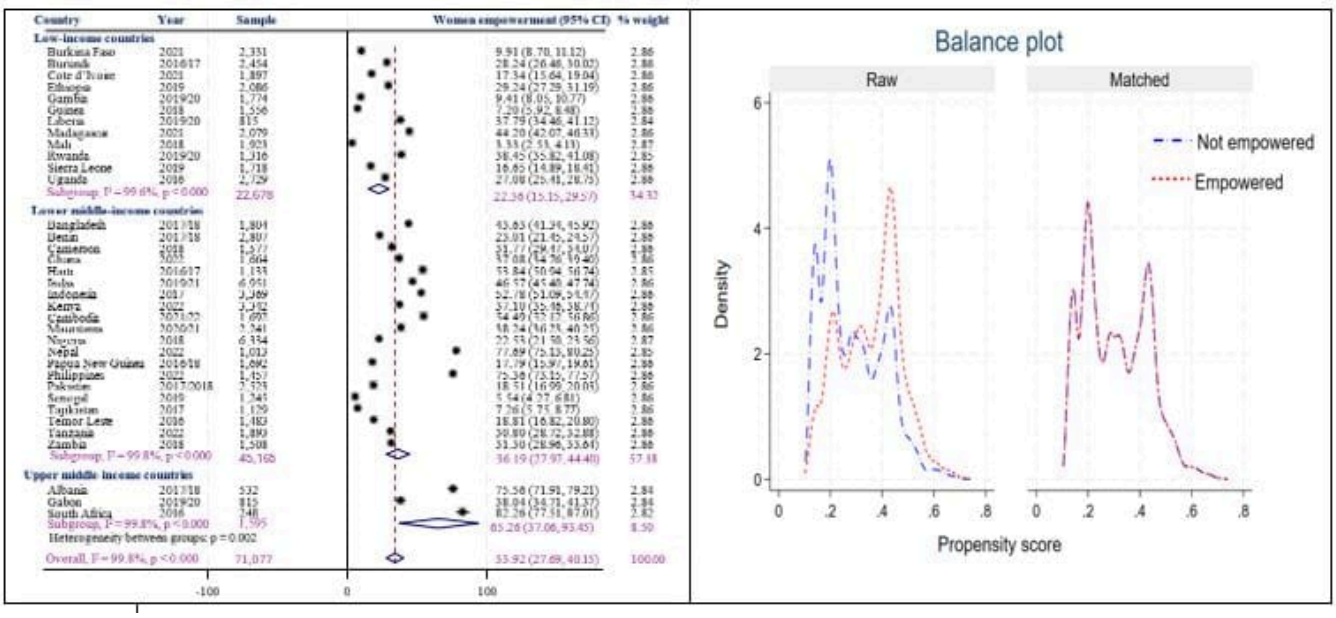
Abstract

Background: Women's empowerment directly influences the quality and timeliness of the maternal healthcare they receive. A lack of women's empowerment, particularly in low- and middle-income countries (LMICs), is likely to contribute to poor uptake of maternal health care. This study aims to evaluate the role of women's empowerment in maternal healthcare in LMICs.

Methods: We used the recent Demographic and Health Survey (DHS) data from 35 LMICs. A total of 71,077 married/partnered women were included. Women were categorised as empowered if they participated in all decision-making activities and were able to disagree that a husband is justified in hitting or beating his wife for any reason. A logit propensity score matching (PSM) analysis was used to estimate the effect of women's empowerment on maternal health services.

Result: In this study, only one-third (33.8%) of reproductive-age women in LMICs (95% CI: 27.7%, 40.8%) reported being empowered. Women's empowerment was associated with an 11.2 percentage point increase in having adequate ANC visits (average treatment effects on the treated (ATT) of 0.112, standard error (SE): 0.026), and an 8.0 percentage point increase in the likelihood of health facility childbirth (ATT=0.078, SE: 0.039). However, there was insufficient evidence for early PNC visits.

Conclusion: Empowering women has a positive association with the utilisation of adequate ANC visits and health facility childbirth in LMICs. These findings underscore the necessity for public health programs aimed at empowering women and enhancing their decision-making abilities to improve maternal health care uptake, such as health facility childbirth and ANC visits.



Respiratory

Differential Expression Analysis to Identify Molecular Signatures of Asthma and Chronic Obstructive Pulmonary Disease (COPD) and Asthma-COPD Overlap (ACO) among Smokers

Tianjiao Shen* Tianjiao Shen Mohammed S. Orloff

Background:

COPD and asthma often coexist as Asthma-COPD Overlap (ACO), a debated condition lacking clear classification. Patients with ACO experience more severe symptoms, frequent exacerbations, and reduced life quality than those with asthma or COPD alone. Diagnosis of ACO is challenging due to lack of biomarkers to differentiate ACO from asthma or COPD. Hence the need to have distinct identification and well-defined recommendations for ACO.

Methods:

We analyzed 536 whole-blood RNA sequencing data from the COPDGene Study (GSE97531). Participants were classified into asthma, COPD, ACO, and control groups based on FEV1/FVC and post-bronchodilator tests. Quality control and alignment were performed with FastQC and “Spliced Transcripts Alignment to a Reference (STAR) “. Differential expression analysis was conducted using edgeR and limma, identifying significant expressed genes (FDR < 0.05).

Results:

We identified 9 DEGs comparing in ACO vs. asthma, 28 in ACO vs. COPD, 871 in ACO vs. controls, 10 in asthma vs. controls, and 1490 in COPD vs. controls in DE analysis. Notable DEGs distinguishing ACO from asthma/COPD included **PAICSP6** (ACO vs. asthma, LogFC = -2.35, FDR = 0.027) and **GRHL3-AS1**(ACO vs. COPD, LogFC = 1.08, FDR = 0.047). A total of 442 were unique to ACO vs. controls with no significant changes in asthma- or COPD-only comparisons, suggesting their potential as ACO-specific biomarkers. **ADGRG7** was significantly differential expressed across multiple asthma-related comparisons (ACO vs. COPD, ACO vs. controls, and Asthma vs. controls), indicating a potential role in asthma-like features within ACO. Additionally, **IFI27** was a DEG associated with ACO, asthma, and COPD, suggesting involvement in common lung function mechanisms.

Conclusion:

Transcriptomic and molecular changes identified provide insight into ACO, distinguishing it from asthma and COPD and identifying potential biomarkers for improved disease characterization.

Respiratory

Evaluating climate drivers of influenza dynamics across tropical and temperate regions

Aleksandra Stamper* Aleksandra Stamper Rachel Baker

Influenza infections contribute significantly to global morbidity and mortality each year. Climate plays a critical role in shaping influenza outbreaks, with distinct patterns observed across regions. In temperate areas, influenza epidemics typically occur in the wintertime, while tropical regions exhibit more persistent influenza activity throughout the year with less defined outbreak peaks. Specific humidity, a measure of water vapor per volume of air, has been identified as a key climate driver of influenza dynamics in temperate regions, where lower levels of specific humidity are associated with higher transmission rates. In tropical regions, influenza transmission occurs in both cold, low-specific humidity and hot, high-specific humidity conditions.

Epidemiological compartmental models provide a valuable tool for investigating relationships between climate and influenza activity. However, existing models are often tailored to specific climatic regions, and no universally validated model currently exists to account for influenza dynamics across a wide range of weather conditions. Using an epidemiological model fit to historic climate and influenza data, we explore whether a common set of climate drivers can explain influenza dynamics across diverse climates.

We adapted the Susceptible-Infected-Recovered model, applying it to data from a northern hemisphere temperate location (Michigan, United States), a southern hemisphere temperate location (Paraná, Brazil), and a tropical location (Nicaragua). The model was fit to historic weekly influenza and climate data. By calculating the predicted reproduction number for various combinations of climate factors, we map the nonlinear relationship between specific humidity, temperature, and influenza transmission. The framework developed here offers insight into the feasibility of a universal influenza model, which could play a crucial role in assessing the potential impacts of climate change on future influenza outbreaks.

Science Communication & Media

Characterizing health journal policies' for communicating race, ethnicity, sex, and gender

Rae Anne Martinez* Rae Anne Martinez Michael Esposito Nafeesa Andrabi Noah Haber Lillian Norman Kene Orakwue Natalie Smith Shengeng Vang

Recent research has illuminated the lack of rigor regarding the use of social determinants in the health sciences. To address this deficit, a growing number of health journals have adopted policies with explicit instructions for communicating race, ethnicity, sex, and gender since 2021. However, the prevalence of these policies as well as their content and scope remain unexamined. We aim to systematically review and characterize journal editorial policies related to race, ethnicity, sex, and gender in three disciplines – Clinical Medicine, Epidemiology, and Public Health. We used Clarivate Analytics 2023 Journal Citation Reports to identify health journals by disciplinary classification from the Science Citation Index Expanded. Two independent samples were taken: (1) a random sample of 30% of all English language journals stratified by discipline (n=137) to provide insights into broader disciplinary-specific trends; (2) a non-random sample of 5-6 top, field-leading journals to provide insight into specific disciplinary leaders (n=16). Journals' publicly available websites and manuscript submission portals were reviewed for relevant policies and information regarding enforcement; all information was entered into a standardized REDCap form. For comparison, we also identified and reviewed AI, casual inference, and EQUATOR Network policies. Sample 1 data collection is underway; 33% has been collected (n=45). In sample 2, we find that 60% of top Clinical Medicine and Public Health journals have race and ethnicity policies, while top Epidemiology journals have none. In all disciplines, at least 40% of top journals have sex and gender editorial policies. Content analysis will be conducted to further interrogate the race, ethnicity, sex, and gender policies in both samples. Journal editorial policies may be key structural levelers to shift disciplinary practices surrounding social determinants, but their adoption may lag behind other policy types and vary by discipline.

Table. Policy characteristics of field-leading journals (Sample 2)

	Clinical Medicine (N= 5)		Epidemiology (N= 6)		Public Health (N= 5)	
	N	(%)	N	(%)	N	(%)
Editorial policies on						
Artificial intelligence	5	(100)	3	(50)	4	(80)
Casual language	3	(60)	2	(33)	0	(0)
EQUATOR Network*	5	(100)	4	(66)	5	(100)
Race and ethnicity	3	(60)	0	(0)	3	(60)
Sex and gender	2	(40)	3	(50)	4	(80)
Reference policies of						
ICMJE**	5	(100)	5	(83)	2	(40)
Counsel of Science Editors (CSE)	1	(20)	0	(0)	0	(0)
Committee of Publication Ethics (COPE)	3	(60)	1	(17)	3	(60)

(*) Journals with at least one EQUATOR Network policy. (**) ICMJE: International Committee of Medical Journal Editors. Clinical Medicine journals: *Annals Int Med*, *BMJ*, *JAMA*, *Lancet*, *NEJM*; Epidemiology journals: *Annals Epidemiol*, *Epidemiology*, *Euro J Epidemiol*, *J Clinical Epidemiol*, *J Epidemiol & Comm Health*; Public Health journals: *AJPH*, *Envir Health Persp*, *Health & Place*, *Lancet Public Health*, *Soc Sci & Medicine*.

Screening

Screening test for the potential prevention model based on natural history of disease in preventive medicine Noriko Miyake* Hideo Yamazaki Xiao Qing Hikaru Yamazaki

Introduction: One of the most effective preventive measures to prevent lifestyle-related diseases (LRDs) is an active health-oriented approach in primary prevention. Two application stages of the primary prevention should be addressed during the susceptibility phase of the natural history of disease. In practical activities of community health based on Health Promotion (HP) proposed by the World Health Organization (WHO), health-oriented practical efforts in the susceptibility phase are particularly effective. The present study proposes a potential prevention model as a new framework that contributes to active health in the susceptibility phase from a light of HP. As a basis for the proposal, a screening test that enables practical application of the potential prevention model will be discussed.

Methods: Based on the authors' previous findings, the potential prevention model is presented. In addition, the screening test was conducted to enable practical application of the model. The analyzed data for the screening test were obtained from questionnaire surveys of the elderly as linkage data. Then a principal component analysis (PCA) was applied to valid data.

Results: The semi-health index was calculated by applying PCA to identify the semi-health status, a lower level of health condition, in the susceptibility phase. Then the index score was calculated by the norm eigenvectors of the first principal component (PC1). Furthermore, a distribution of the elderly with the semi-health status was determined by using this score. As a result, the prevalence, sensitivity, specificity, positive predictive value, negative predictive value, and false positive rate showed 39.2%, 85.0%, 76.8%, 70.3%, 88.8% and 0.23, respectively.

Conclusions: The findings from this study made it possible to divide the susceptibility phase into the good health and semi-health phases. From the perspective of HP activities, it will be possible to take measures specifically for the semi-health phase.

Social

Education and Income trajectories of CARDIA Participants and their Association with Early Adulthood Identity-based Discrimination and Late Adulthood Cardiovascular Health

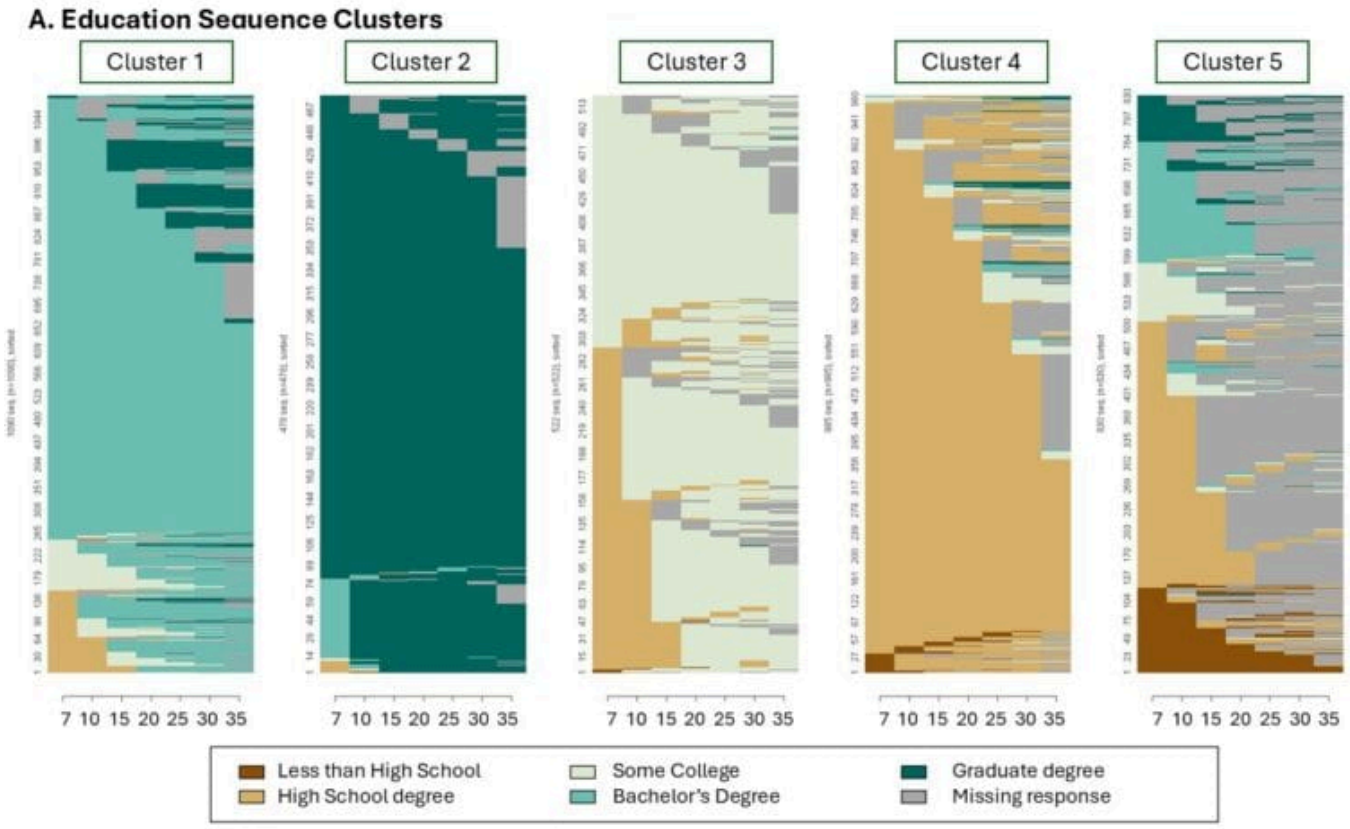
Adovich Rivera* Adovich Rivera B.R. Slone Grace V. Avila Stephanie Hernandez Gregory Phillips II Patrick Janulis Mercedes Carnethon Ankeet S. Bhatt James M. Shikany Cora E. Lewis Pamela Schreiner Lauren B. Beach

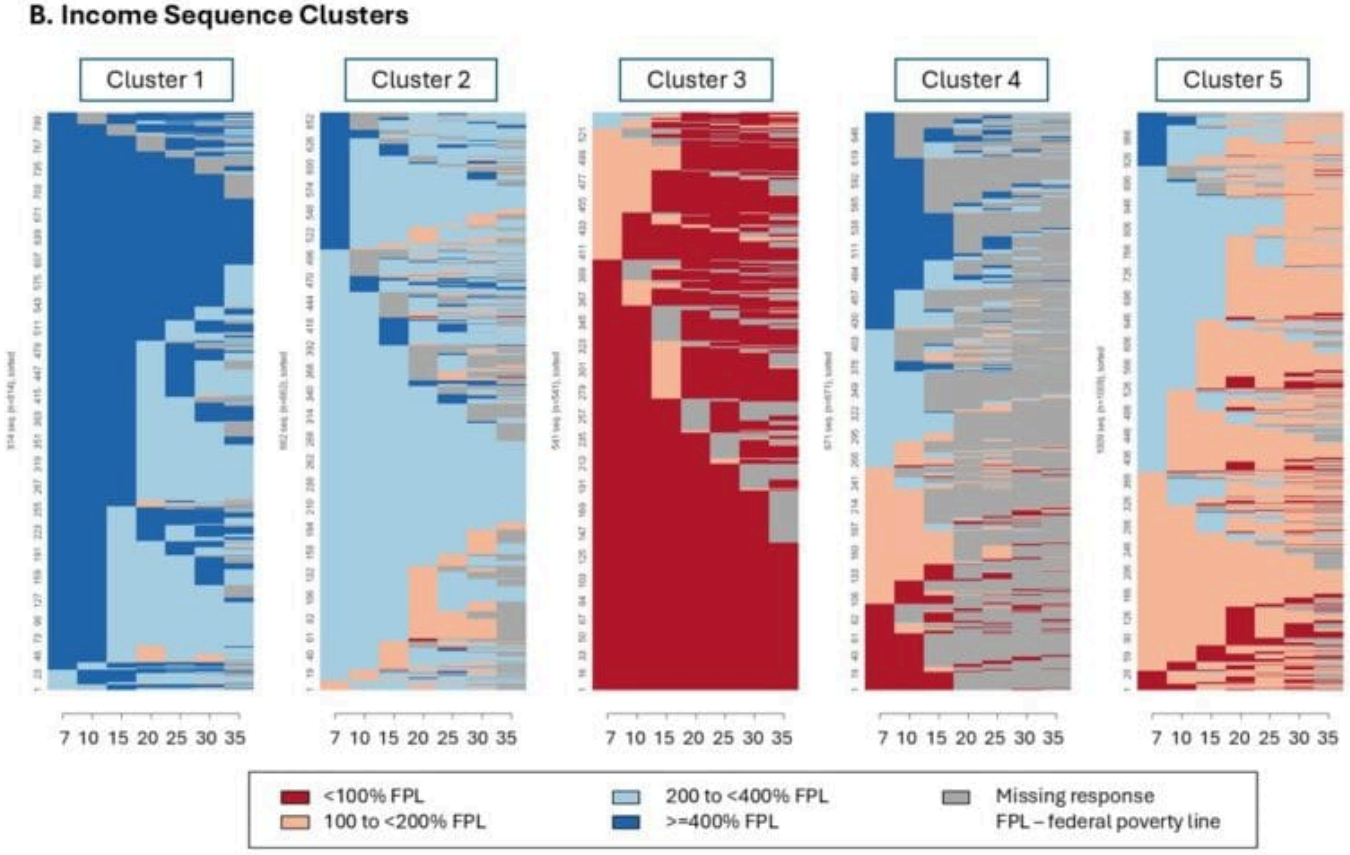
Cardiovascular health (CVH) as measured through attaining ideal behavior (e.g., not smoking) is associated with lower CV disease risk. While socioeconomic position (SEP) is a known driver of CVD risk, its role in CVH via a life course approach is less studied. Also, discrimination is theorized to adversely affect SEP, but more studies are needed. We investigated the interrelationships of experienced discrimination, income/education trajectories, and CVH using Coronary Artery Risk Development in Young Adults (CARDIA) cohort data.

We first identified Year (Y) 7-35 education and income trajectories using sequence and cluster analysis based on optimal matching for dissimilarities calculation and hierarchical agglomerative clustering. This approach uncovers heterogeneity in SEP trajectories which maybe hidden in methods focused on averages. We then assessed if the clusters differed by Life's Simple 7 (LS7) score, a CVH measure, in older adulthood (Y35) with linear models adjusted for race, sex, age, and CARDIA field center. Lastly, we assessed if cluster membership differed by race, sex, or sexual orientation discrimination in early adulthood (Y7) with multinomial models adjusted for the above covariates.

Our analysis (n=3905) identified 5 education and 5 income clusters based on the Calisnki-Harabasz index (Figure). We found that clusters with lower educational attainment (clusters 3 & 4) and low income (clusters 2 & 3) had significantly lower Y35 LS7 scores than cluster 1. Those reporting Y7 gender or race discrimination had a lower probability of being in education cluster 4. Gender discrimination was also associated with lower probability of being in income cluster 3. Sexual orientation discrimination was not associated with membership.

In sum, we uncovered heterogeneous SEP trajectories with different CVH scores in later life. Early adulthood discrimination was associated with SEP trajectories. Further work is recommended to uncover mechanisms of these associations.


A. Education Sequence Clusters
Cluster 1
Cluster 2
Cluster 3
Cluster 4
Cluster 5
7 10 15 20 25 30 35
Less than High School
High School degree
Some College
Bachelor's Degree
Graduate degree
Missing response


B. Income Sequence Clusters
Cluster 1
Cluster 2
Cluster 3
Cluster 4
Cluster 5
7 10 15 20 25 30 35
<100% FPL
100 to <200% FPL
200 to <400% FPL
>=400% FPL
Missing response
FPL – federal poverty line

Social

Associations between food instability and overall and mental well-being among US adults: Findings from the 2023 BRFSS Social Determinants and Health Equity module J'Neka Claxton* J'Neka Claxton Guixiang Zhao Machell Town

Background: Food stability is a critical public health issue that can adversely affect one's overall well-being and mental health. Understanding the role of a social support system is crucial as it may buffer the negative effects of food instability.

Method: Using data from the 2023 Behavioral Risk Factor Surveillance System Social Determinants and Health Equity module data, we examined the associations of food instability with self-rated fair/poor health and mental health outcomes including frequent mental distress (FMD) and stress and explored the role of social and emotional support in this relationship. Food instability was defined as receiving food stamps or responding Always/Usually/Sometimes to the question of food scarcity due to insufficient funds. Cox regression with a robust variance estimator was used to estimate prevalence ratios, adjusting for sociodemographic variables.

Results: Of the 293,981 respondents eligible for the study, 20% of the population experienced food instability. Prevalence estimates for health outcomes were higher among adults experiencing food instability than those who did not. After adjustment, the prevalence of FMD, stress, and fair/poor health was 1.86, 2.29, 1.66 times higher, respectively, among those experiencing food instability than adults who did not. Prevalence for health outcomes were highest among adults experiencing food instability and low social and emotional support [defined as get support sometimes/rarely/never] (range: 41.8-43.9). Adults experiencing food instability and low social and emotional support were 3.93, 5.17, 2.39 times more likely to report FMD, stress, and fair/poor health, respectively, compared to adults experiencing food stability and high social support.

Discussion: These findings highlight the strong associations of food instability with overall well-being and mental health. Presence of strong social and emotional support may buffer some of the negative effects of food insecurity on mental health.

Social

Social isolation and cognitive function and decline in a population-based longitudinal study of aging in India, overall and by education Peiyao Zhu* Peiyao Zhu Emma Nichols Alden L. Gross Jinkook Lee Lindsay C. Kobayashi

Social isolation is a risk factor for dementia, while education is the strongest known protective factor against dementia. Education is thought to enhance cognitive reserve, although a large share of older adults in low- and middle-income countries lack formal education and may be disproportionately vulnerable to additional cognitive risk factors. We estimated the associations between social isolation and cognitive function at baseline and rate of change over time among older adults in India, and whether these associations are stronger among those without formal education. We analyzed baseline data from 3,654 adults (mean age: 69.5) in the population-based LASI-DAD cohort (2017–2019) and follow-up data from 2,291 adults (2022–2024; mean follow-up: 4.2 years). Social isolation at baseline was measured using a 5-point index including living arrangements, social organization participation, and frequency of contact with friends/relatives. General and domain-specific cognitive function (memory, orientation, executive function, verbal fluency) scores were derived at both waves from the Harmonized Cognitive Assessment Protocol. We used a multivariable-adjusted joint modeling approach linking mixed-effects linear regression with survival analysis to account for potential selection bias due to differential mortality and evaluated interactions between social isolation and formal education (yes vs. no). Nearly half of our sample had no formal education (49%). Greater social isolation was associated with lower baseline general cognitive scores (β=-0.04 SD units; 95% CI: -0.06, -0.01, per 1-point increase in isolation), memory (β=-0.06; 95% CI: -0.08, -0.03), and language (β=-0.04; 95% CI: -0.07, -0.01), but not subsequent rates of decline. We found no interaction between social isolation and education in cognitive outcomes. Social isolation is a modifiable risk factor for cognitive function among older adults in India, with similar associations regardless of formal education.

Social

The Geography of Community Integration for Burn Injury Survivors: A Comparative Analysis Across Multiple Metropolises Pyung Kim* Pyung Kim Dohyeong Kim Karen Kowalske

This study investigates geospatial factors associated with community integration through the following research objectives: (1) explore geographic variations in community integration among burn injury survivors in four metropolises with Burn Model System (BMS) centers, (2) identify community-level social and environmental factors that influence integration, and (3) compare how these factors differ across the four cities.

The primary data source for this study is the BMS National Database. Inclusion criteria were limited to adult burn survivors with injuries sustained between 2015 and 2022 and follow-up data at 6 months post-injury to ensure ZIP code availability for spatial analysis, while child burn survivors were excluded to avoid developmental confounding. This resulted in a final sample of approximately 1,500 adult burn survivors. The supplementary geospatial data was obtained from the Urban Institute's Upward Mobility Data, which offers county-level metrics to assess community conditions over time using 19 variables across four categories: (1) Employment Opportunities, (2) Inclusive Neighborhoods, (3) Healthy Environment, and (4) Responsive and Just Governance.

Using this dataset, we performed four analyses: (1) Created county-level maps to illustrate average Community Integration Questionnaire (CIQ) scores before the injury and at 6 months post-injury; (2) Conducted Ordinary Least Squares (OLS) regression to determine which community characteristics were associated with reduced community reintegration outcomes for burn injury survivors; and (3) Examined how these factors varied across the four major metropolitan areas.

By identifying key factors that influence recovery outcomes for burn injury survivors, this research provides actionable insights for physicians and healthcare practitioners involved in burn treatment and recovery.

Social

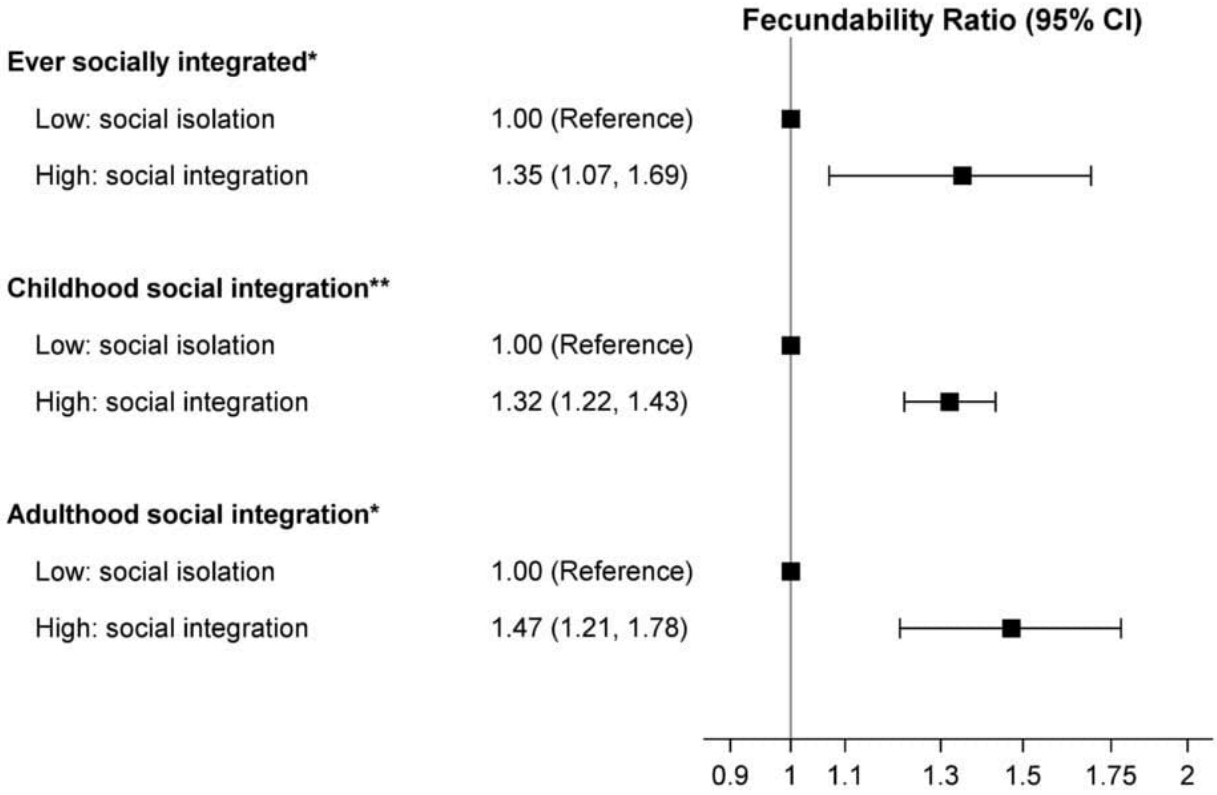
Association of life course social integration with fecundability Molly Hoffman* Molly Hoffman Collette

Background: Social isolation is increasing among U.S. adults and has been associated with adverse health, but the association between social integration and fecundability is not well known.

Methods: We examined the association between life course social integration and fecundability in Pregnancy Study Online (PRESTO), a preconception cohort study of U.S. and Canadian females aged 21-45 years (2013-2024). Eligible participants completed a supplemental questionnaire (SQ) on life course psychosocial factors at baseline (N=8,771). We assessed social integration with an adapted 8-item version of the Berkman-Syme Social Network Index (SNI) during childhood (<18 years) and adulthood (≥18 years) on the SQ. Summed SNI scores were categorized as <5 (socially isolated) and ≥5 (socially integrated). We estimated fecundability, the per-cycle probability of conception, from bimonthly follow-up questionnaires. We used inverse probability-weighted proportional probabilities models to estimate fecundability ratios (FR) and 95% CIs, accounting for confounding and selection bias.

Results: A majority of participants were socially integrated during at least one life stage (97%). Compared with social isolation, being socially integrated during any life stage was associated with increased fecundability (FR=1.35, 95% CI: 1.07-1.69). The association was similar for social integration during childhood (FR=1.32, 95% CI 1.22-1.43), but was notably stronger for social integration during adulthood (FR=1.47, 95% CI 1.21-1.78).

Conclusions: Social integration may have positive effects on fecundability, particularly during adulthood.



*Model weighted to account for childhood social integration and confounders, age, life course trauma, depression and anxiety diagnoses, and parity

**Model weighted to account for parental education, parental divorce, being a twin, number of siblings, being breastfed, and maternal age at birth

LATEBREAKER

Social

A Framework for Examining Community Violence as a Climate-Related Environmental Exposure Jane E Clougherty* Jane Clougherty Ellen J. Kinnee Perry E. Sheffield

Introduction

Violent crime is increasing with climate change and ambient heat. Homicides are expected to increase 6% globally per OC increase in global annual mean temperature, with 2.3 – 3.2 M additional heat-attributable violent crimes in the U.S. by 2099. Greater increases are projected in communities already high in crime, or lacking resources for response, exacerbating inequities. Finally, exposure to community violence (ETCV), as a psychosocial stressor, may exacerbate impacts of climate-related extreme heat and pollution on health.

Methods

We have developed a framework to assess the multiple and complex pathways through which ETCV may impact population health in a warming climate. We are testing that framework using exhaustive data on mental health (MH)-related emergency department visits and hospitalizations among NYC children aged 6-17, for 2005-19, and case-crossover methods, comparing child's risk of MH event on days following violent crimes to their risk on other days.

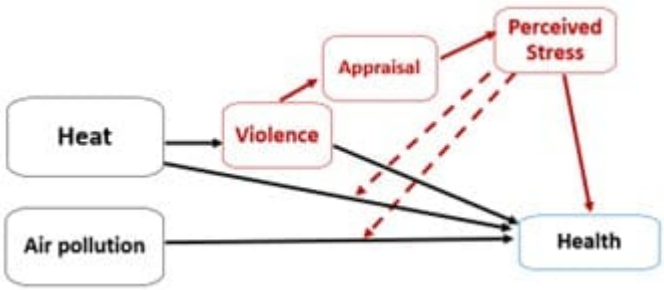
Results

We are refining ETCV metrics by exploring nonlinearity in violence-MH relationships, to identify critical distances and time lags. We are testing the following key pathways in our framework:

- Independent associations between ETCV and risk of child health event, adjusting for extreme heat and pollution.
- Testing whether ETCV, as a stressor, exacerbates heat-health or pollution-health associations.
- Testing whether some portion of heat-health associations may be mediated by (operate via) ETCV.

Discussion

This conceptual model and analysis will help to quantify the impact of community violence on child health, and reveal the multiple pathways through which violence may impact health in coming decades, separately and in combination with other climate-related exposures.



LATEBREAKER

Social

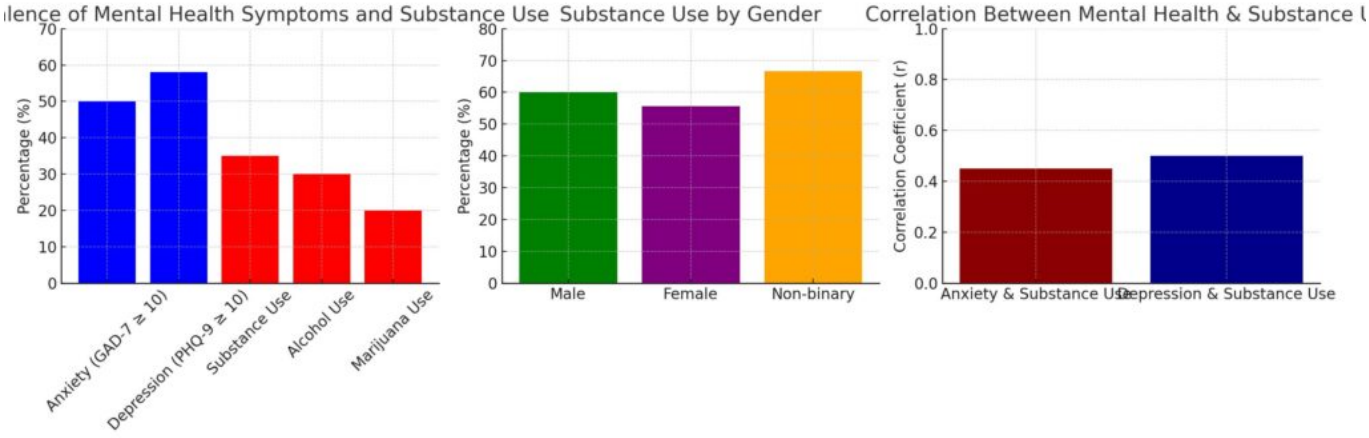
Unmasking the Crisis: Mental Health and Substance Use Trends Among Adolescents During the COVID-19 Pandemic Colette Davis* Amy Macher Colette Davis

Background: The COVID-19 pandemic has profoundly impacted adolescent mental health and substance use, with social isolation, academic disruptions, and uncertainty contributing to rising levels of anxiety, depression, and substance misuse. Understanding these shifts is crucial for developing effective public health interventions.

Methods: This study utilized the 2021 Youth Risk Behavior Surveillance System (YRBSS), a nationally representative dataset, to examine adolescent mental health and substance use trends. The study population consisted of 10,000 adolescents aged 12–18 years. Mental health outcomes were assessed using the Generalized Anxiety Disorder-7 (GAD-7) and the Patient Health Questionnaire-9 (PHQ-9) depression scale. Substance use behaviors—including alcohol, marijuana, and tobacco use—were analyzed alongside social support and school connectedness as potential protective factors. Chi-square tests, multiple linear regression, and correlation analyses were conducted to evaluate associations between COVID-19-related stressors, mental health symptoms, and substance use.

Results: Analysis revealed that 50% of adolescents reported moderate to severe anxiety (GAD-7 ≥ 10), while 58% reported moderate to severe depression (PHQ-9 ≥ 10). Additionally, 35% of participants reported substance use, with alcohol (30%) and marijuana (20%) being the most frequently used substances. Among substance users, 60% had consumed alcohol in the past month. Gender differences were observed, with non-binary adolescents exhibiting the highest rates of substance use (66.7%), followed by males (60.0%) and females (55.6%) ($\chi^2 = 6.45$, $p = 0.040$). Multiple linear regression indicated that the perceived impact of COVID-19 was a significant predictor of anxiety and depression ($\beta = 1.20$, $p < 0.001$), while social support ($\beta = -0.75$, $p < 0.001$) and school connectedness ($\beta = -0.50$, $p = 0.012$) emerged as protective factors against mental health symptoms. Correlation analyses further highlighted a significant positive relationship between anxiety and substance use ($r = 0.45$, $p < 0.01$) as well as depression and substance use ($r = 0.50$, $p < 0.01$), demonstrating that worsening mental health was associated with increased substance use.

Conclusions: The COVID-19 pandemic has intensified mental health challenges among adolescents, leading to a significant rise in substance use. Social support and school connectedness emerged as protective factors, underscoring the importance of school-based mental health initiatives, peer support programs, and targeted interventions. These findings highlight the urgent need for public health efforts to mitigate the long-term mental health consequences of the pandemic on adolescents.


ılence of Mental Health Symptoms and Substance Use
Percentage (%)
Anxiety (GAD-7 ≥ 10)
Depression (PHQ-9 ≥ 10)
Substance Use
Alcohol Use
Marijuana Use
Substance Use by Gender
Percentage (%)
Male
Female
Non-binary
Correlation Between Mental Health & Substance U
Correlation Coefficient (r)
Anxiety & Substance Use
Depression & Substance Use

Social

Associations between socioeconomic characteristics at the end-of-life and place of death among African Americans diagnosed with cancer: Findings from the Detroit Research on Cancer Survivors (ROCS) study Jamaica Robinson* Jamaica Robinson Nora Akcasu Theresa Hastert

Background: Socioeconomic resources at the end-of-life (EoL) may influence elements of EoL care for African Americans diagnosed with cancer, who disproportionately receive expensive EoL care and experience a hospital-based death relative to other cancer patients.

Methods: Our analyses included 511 decedents who participated in the Detroit Research on Cancer Survivors (ROCS) cohort, a population-based study of African Americans diagnosed with incident cancers in Metro Detroit. We measured socioeconomic characteristics – including household income, insurance type (i.e., Medicare, Medicaid, dually eligible), and social risks (i.e., housing instability, food insecurity, utility shutoffs, neighbourhood safety, and not seeking health care because of cost or a lack of transportation) – for the last follow-up survey prior to death. We used these measures in a latent class analysis (LCA) to identify three socioeconomic classes. We assessed place of death via death certificates and categorized decedents as having a hospital- or home-based death. We used modified Poisson models, adjusting for sociodemographics, cancer characteristics, and cause of death, to estimate prevalence ratios (PR) and 95% confidence intervals for associations of socioeconomic class with place of death.

Results: Approximately 35% of decedents were likely to report few social risks, higher annual household income (≥$20K), and Medicare (Class 1); 50% few social risks, lower income (<$20K), and Medicaid or dual eligibility (Class 2); and 15% increased social risks, lower income, and Medicaid or dual eligibility (Class 3). Decedents in Classes 2 and 3 were more marginally more likely than decedents with greater socioeconomic resources to die at home versus in a hospital (PRClass2:1.14, 95% CI:0.89-1.46; PRClass2:1.26, 95% CI:0.91-1.76).

Conclusion: Findings from this study will help to elucidate socioeconomic factors influencing place of death in this socioeconomically and medically marginalized population.

Social

Books, Bonds, and Better Health: Public Libraries as a Third Place for Promoting Health and Wellbeing of Community-Dwelling Older People in Australia Rosanne Freak-Poli* Rosanne Freak-Poli Htet Lin Htun Achamyeleh Birhanu Teshale Alice J. Owen Joanne Ryan Melissa Whitrow James R Baker

Background: Evidence on the impact of community resources, such as public libraries as informal third places for social gathering and learning, on health and wellbeing of older adults is limited.

Aim: To examine longitudinal associations between public library engagement and various health and wellbeing outcomes.

Methods: Data from >12,000 (range:12,124-12,896) healthy community-dwelling older Australians (70+ years) were analysed. Library engagement (frequency of visits) was assessed at baseline and categorised as never, ≤3 times a month, or ≥once a week. An outcome-wide analytical approach was used to examine 44 health/wellbeing outcomes across physical, cognitive/major health events, psychological, social, and health behaviour domains, measured ~2 years post-baseline or >7 years for time-to event outcomes. Gender-disaggregated regressions were performed while controlling for multiple covariates, including prior outcome values.

Results: At baseline, participants were aged 70-95 years (mean:75.2±4.3), and 54.5% were women. Public library engagement was higher among women than men. Compared to non-users, library engagement was associated with better physical and cognitive outcomes (e.g., reduced dementia risk), social wellbeing (e.g., skill sharing in a dose-response relationship), and healthier behaviours (e.g., increased fruit and vegetable intake) at follow-up (Figure). No associations were found with most psychological outcomes.

Gender differences were observed: men had stronger associations with reduced disability and mortality over 7 years, while women showed associations with greater social wellbeing and health-promoting behaviours, and a higher fall risk ~2 years later.

Discussion: Public library engagement was associated with several positive health and wellbeing outcomes. Our findings suggest that integration of public libraries into broader public health strategies to promote various health outcomes could be beneficial.

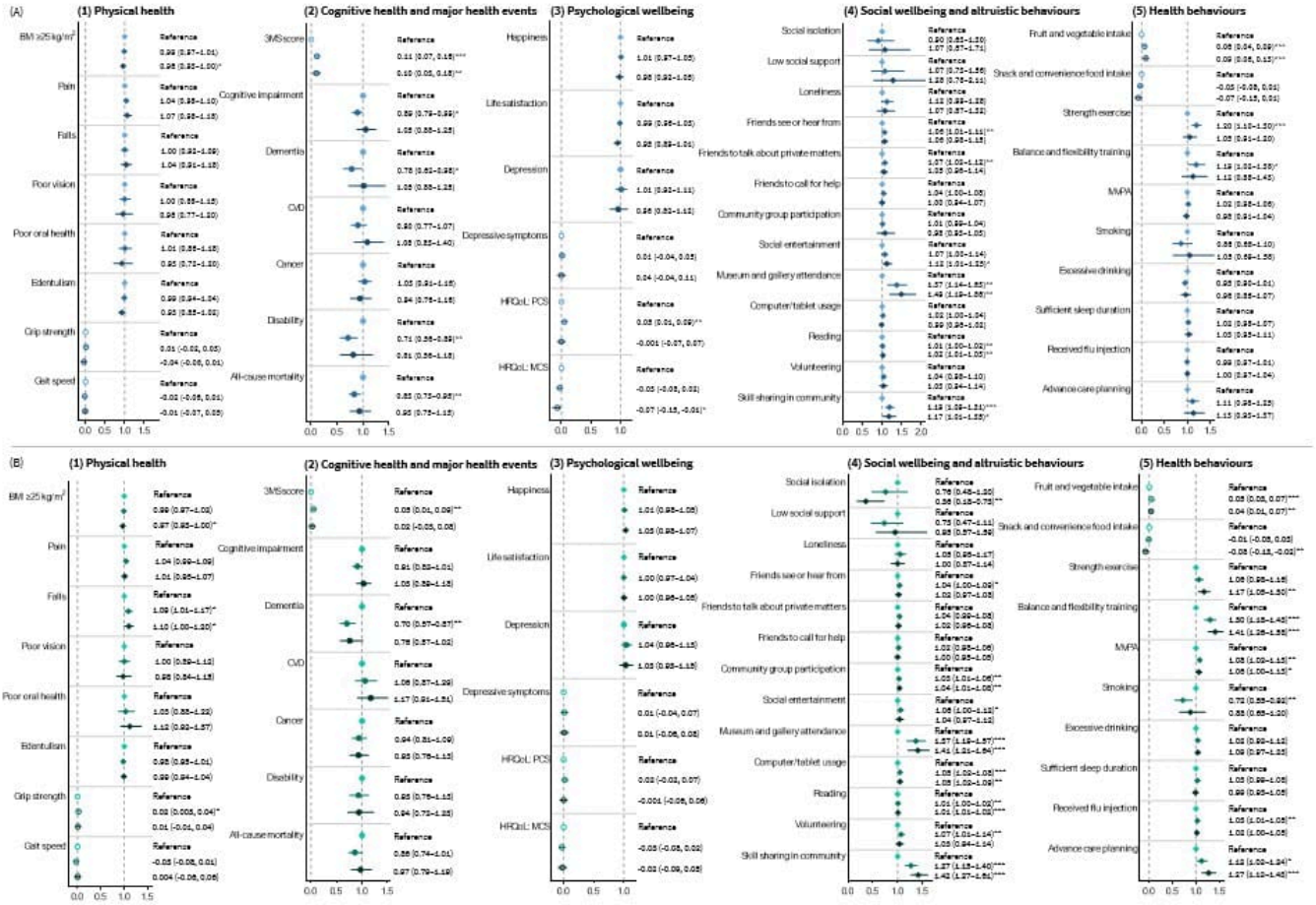


FIGURE. Forest plots showing the association between public library engagement and subsequent health and wellbeing outcomes in (A) men and (B) women. For each outcome, effect estimates are provided for three categories of library engagement: never (reference), ≤3 times a month, and ≥once a week, displayed sequentially from top to bottom.
Abbreviations: 3MS, Modified Mini-Mental State examination; BMI, body mass index; HRQoL, health-related quality of life; MCS, mental component score; PCS, physical component score; MVPA, moderate-to-vigorous physical activity.
Notes: Risk ratio (RR, u), hazard ratio (HR, l), and standardised b coefficient (ı) with corresponding 95% confidence intervals (CI) are reported depending on the type of regression model used

Social

Who is lonelier? An Age-Period-Cohort and Generational Analysis Rosanne Freak-Poli*
Rosanne Freak-Poli Haoxiong Sun Trong-Anh Trinh

When taking office, Surgeon General Murthy heard “if I disappear tomorrow, no one will even notice” repeatedly. Murthy has declared loneliness in America an “epidemic,” identifying it as a root cause contributing significantly to numerous social issues. Unfortunately, the USA is not alone, with the World Health Organization also declaring loneliness a ‘global public health concern’.

Aim

To investigate patterns of loneliness and social isolation across age, period, cohort and generations in a nationally representative longitudinal cohort.

Methods

We use 19 annual waves of data from the Household, Income and Labour Dynamics in Australia (HILDA) Survey, incorporating 337,630 participants aged 15 years and older between 2001 and 2022. Age-Period-Cohort and generational differences in loneliness (≥5/7 for “I often feel very lonely”) and social isolation (meeting friends/relatives outside household ≤2-3 times monthly and being single) were analyzed using logistic regression with $p<0.05$.

Results

Women reported greater loneliness (mean±SD 13%±34 vs 11%±31) and lower social isolation than men (28%±45 vs 29%±45). AGE: Loneliness was greatest among older adults (>18% prevalence) but also high for women aged 15-20 years. Social isolation was greatest for ages 40-60 years (>40%), and for men these high rates continued into later life. PERIOD: Loneliness prevalence decreased from 2001 (13.5%) to 2009 (10.5%), and then increased by 2022 (13.8%). Social isolation steadily increased across the observation period from 24.5% to 35%. Patterns were similar across binary gender. COHORT: More recent birth cohorts report less loneliness and less social isolation, which were consistent across genders. GENERATION: Generational and gender differences in loneliness and social isolation were observed across age groups (Figure).

Discussion

The high rates of loneliness and social isolation are concerning, especially social isolation which is increasing over time with no plateau observed.

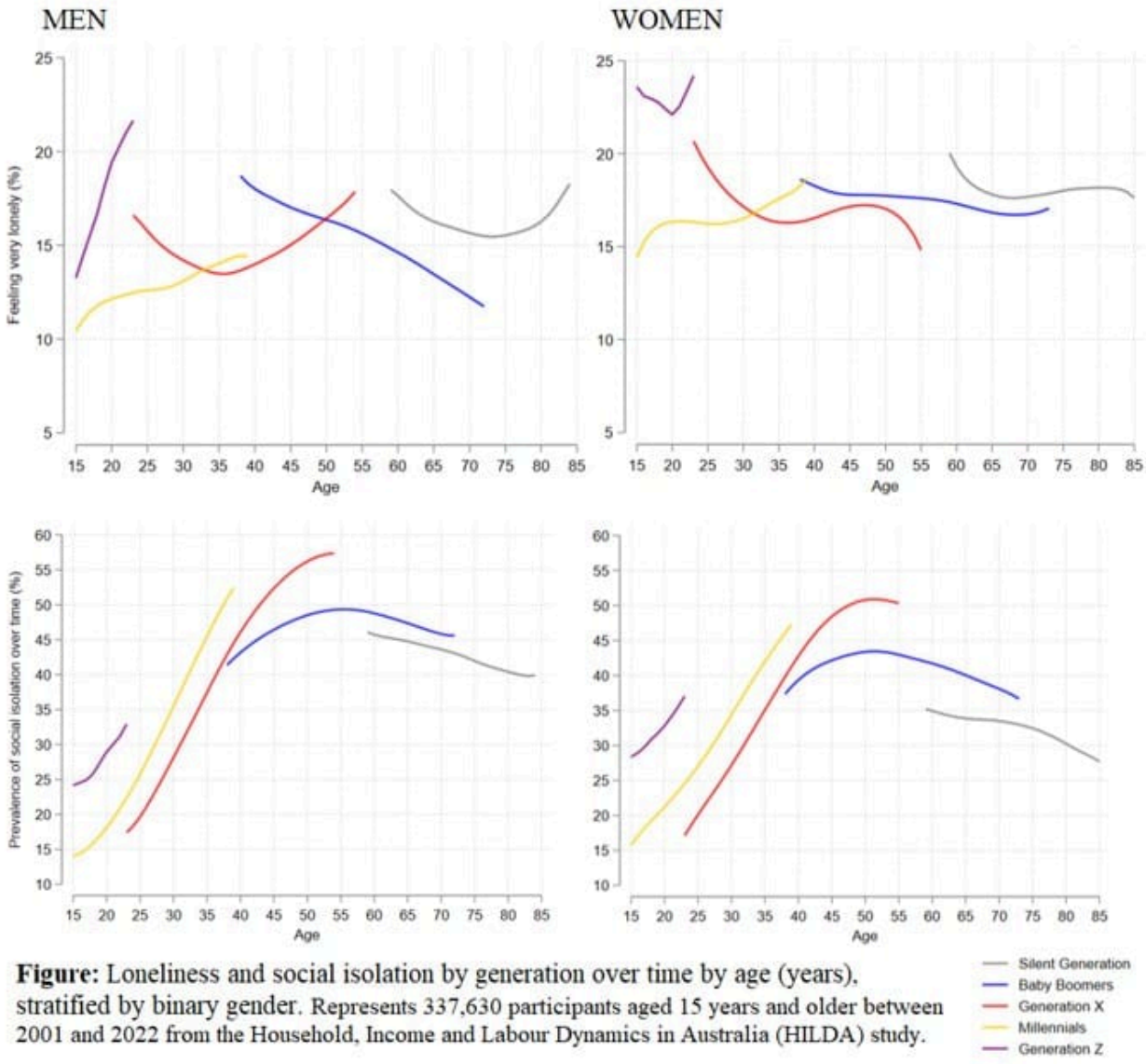


Figure: Loneliness and social isolation by generation over time by age (years), stratified by binary gender. Represents 337,630 participants aged 15 years and older between 2001 and 2022 from the Household, Income and Labour Dynamics in Australia (HILDA) study.

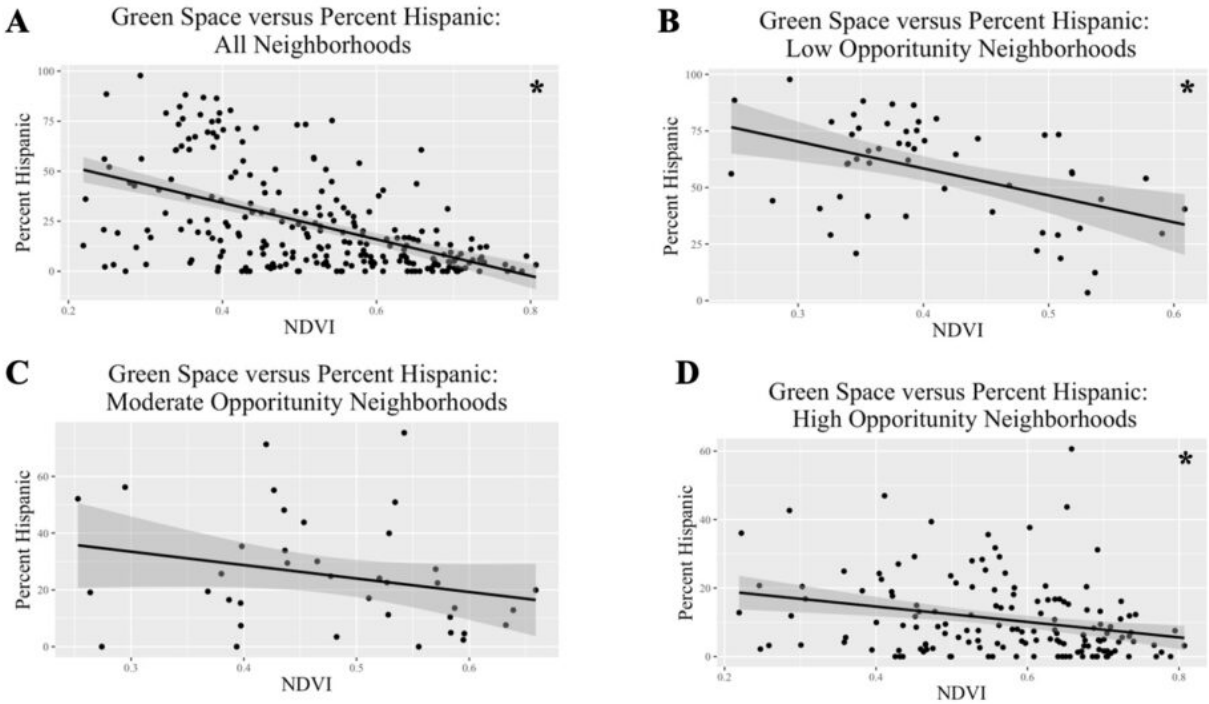
LATEBREAKER

Structural

Examining Associations Between Green Space and Neighborhood Deprivation Among Hispanic and Non-Hispanic Children in Rhode Island Brooke Ury* Brooke Ury Jue Yang Shira Dunsiger Diana S. Grigsby-Toussaint

Socioeconomic factors have been shown to affect children's health, yet the potential of green space to mitigate this is seldom examined. We conducted a cross-sectional analysis to examine the relationship between green space, ethnicity, and neighborhood deprivation among children living in Rhode Island.
Neighborhood deprivation was assessed using the Child Opportunity Index (COI), a census-level metric that evaluates access to resources critical to children's well-being. The COI includes three domains: health and environment, education, and social and economic, measured as low, moderate, or high opportunity. We measured green space using the Normalized Difference Vegetation Index from US Geological Service Landsat satellite data and Tree Canopy Cover data from the US Forest Service. We obtained population data by ethnicity from the American Community Survey. Tukey's test was used to analyze the relationship between green space and neighborhood deprivation, while Pearson correlation coefficients and linear regression models were used to explore the relationship between ethnicity and green space.
Significant associations were found between green space and neighborhood deprivation, with more deprived neighborhoods having less green space ($p < 0.001$). This relationship persisted when focusing solely on COI educational, social, and economic domains ($p < 0.001$). Additionally, there were significant moderate negative correlations between green space and the percentage of Hispanic children in a census tract, with the strength of this relationship growing stronger as neighborhood deprivation increased ($rs = -0.220$ to -0.485, $p < 0.05$).
The findings highlight that Hispanic communities in Rhode Island are negatively impacted by a range of interconnected neighborhood-level factors that compound each other, including access to green space and social and economic resources. Future studies are planned to examine this relationship across the US to ensure the results are robust.

Association Between Ethnicity and Green Space Between levels of Neighborhood Deprivation in Rhode Island

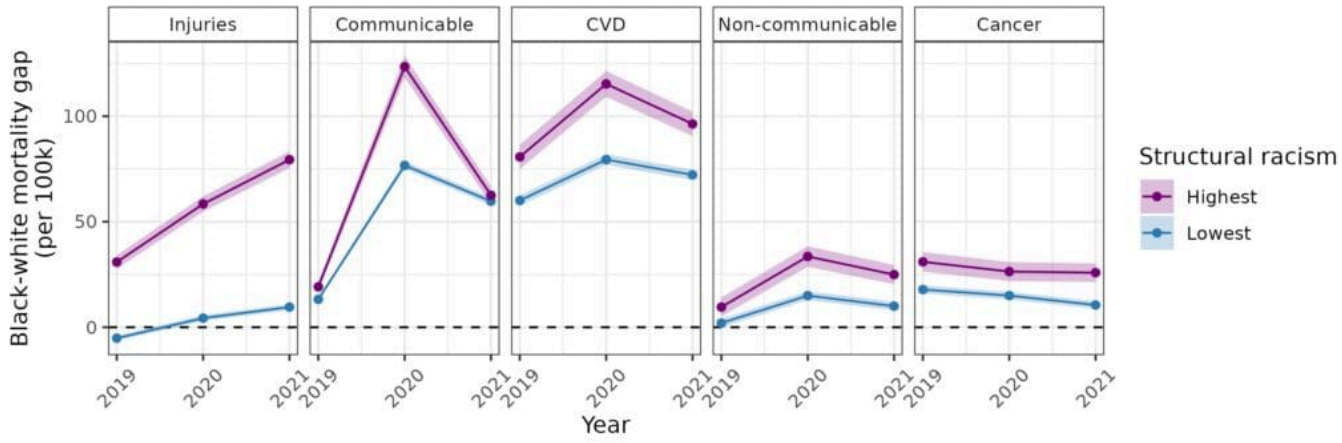


This figure illustrates the relationship between Normalized Difference Vegetation Index and the percentage of Hispanic children in a census tract in Rhode Island for **A** all neighborhoods **B** low opportunity neighborhoods, **C** moderate opportunity neighborhoods and **D** high opportunity neighborhoods * indicates a p-value of less than 0.05 for the Pearson Correlation Coefficient t-test

Structural

The association between structural racism and Black-White health inequities in major causes of death and life expectancy in the United States, 2019-2021 Corinne A Riddell* Corinne Riddell Elleni Hailu Stephanie Veazie Mathew Kiang

We examined the association between state-level structural racism and Black-White health inequities in 2019, 2020, and 2021. We used data from the American Community Survey and the Bureau of Justice Statistics to measure Black-White relative disparities in education, income, homeownership, employment, and incarceration for 2015-2019 in each state. The measures were input into a latent profile analysis to cluster states into five typologies of structural racism. We calculated age-standardized cause-specific mortality rates by race, in each year for each typology of structural racism. We then calculated the absolute difference in mortality rates between Black and White individuals (hereafter “mortality gap”). In 2019, states in the highest structural racism typology had a larger Black-White mortality gap compared to states in the lowest structural racism typology, especially for injuries (See Figure; Low structural racism [SR]: -5 per 100k; High SR: 31 per 100k) and cardiovascular diseases (Low SR: 60 per 100k; High SR: 81 per 100k). In 2020, the Black-White mortality gap increased for all causes except cancer for high and low structural racism typologies. This increase was larger for states with high structural racism. The most disparate increase was for communicable diseases (Low SR: 77 per 100k; High SR: 124 per 100k). In 2021, the mortality gap increased for injuries, but narrowed for communicable diseases and CVD. As a result of the mortality gap, from 2019 to 2021, disparities in Black and White life expectancy widened everywhere, but more in high vs. low structural racism (2019 for men: Low SR: 3.8 years, High SR: 6.2 years vs. 2021: Low SR: 4.9 years vs. High SR: 9.0 years). Patterns highlight the link between structural racism and racial health disparities. The dynamic shifts in health outcomes suggest inequities are not static and racial health equity can be achieved by addressing underlying differences in wealth, opportunity, and power, which shape health.



Study Design

Bayesian methods to evaluate azithromycin mass drug administration for child mortality reduction in Niger Huiyu Hu* Huiyu Hu Ahmed M. Arzika Kieran S. O'Brien Elodie Lebas Ramatou Maliki Travis C. Porco Benjamin F. Arnold Thomas M. Lietman

Background

The MORDOR trial showed an 18% reduction in all-cause mortality among children aged 1–59 months through biannual azithromycin distribution in Niger. Building on these results, the AVENIR trial, a cluster adaptive randomized controlled study, evaluated age-based mass drug administration (MDA) strategies to prevent child mortality. Bayesian methods provide flexibility to incorporate prior knowledge and adapt to evolving data, overcoming limitations of traditional frequentist trials.

Methods

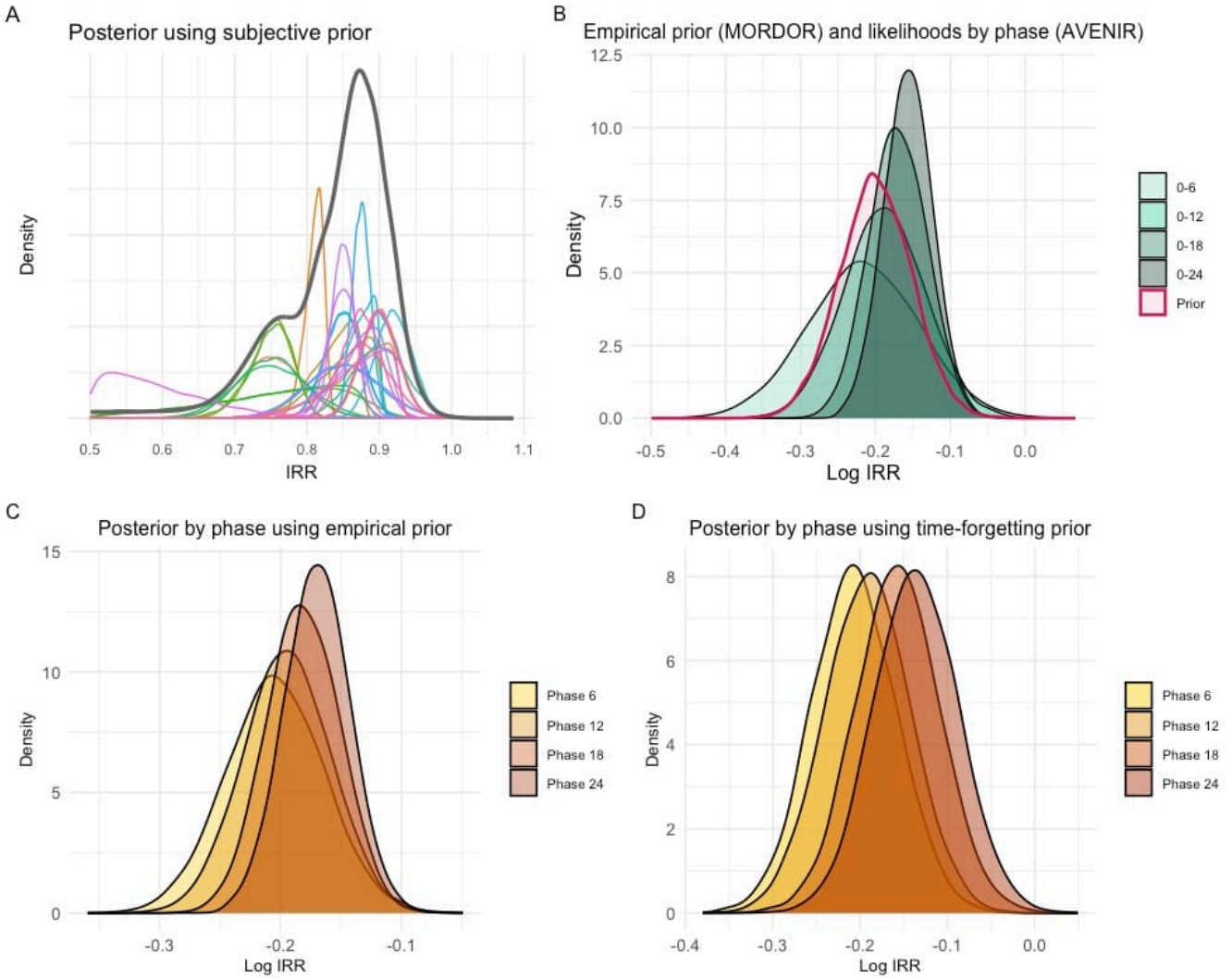
We employed a Bayesian framework with three types of prior distributions—subjective, empirical, and time-forgetting. Subjective priors were collected from 31 public health experts at a topic-specific meeting, fitting a skew-normal distribution to individual's beliefs. Empirical priors were derived from the previous MORDOR trial. With MORDOR data, time-forgetting priors reduced reliance on early data by down-weighting old information as new evidence accumulated, maintaining consistent variance and keeping posterior information constant over time. Mortality data from AVENIR phases (0–6, 0–12, 0–18, and 0–24 months) were sequentially incorporated via Bayes' theorem to estimate posterior distributions of azithromycin's effect.

Results

Posterior estimates confirmed meaningful reductions in child mortality. Subjective priors estimated a 13.6% reduction (95% credible interval [CrI]: 7.7%–19.5%) (Figure A). Using empirical priors from MORDOR (Figure B), posterior estimates showed increasingly precise estimates, with the posterior means decreasing from an 18.1% reduction (95% CrI: 10.0%–25.5%) at 0–6 months to 15.7% (95% CrI: 9.6%–21.5%) at 0–24 months (Figure C). Time-forgetting priors enabled dynamic updates, with posterior means evolving from an estimated 18.7% reduction in mortality (95% CrI: 12.3%–24.8%) at 0–6 months to 12.8% reduction (95% CrI: 8.1%–17.4%) at 18–24 months (Figure D).

Conclusions

Bayesian methods integrating expert beliefs, empirical data, and time-forgetting mechanism provide a framework for evaluating azithromycin MDA efficacy over time. This approach enables real-time updates for on-going trials, supports data-driven decisions, and informs programmatic implementation to reduce childhood mortality in low-resource settings.


A
Posterior using subjective prior
Density
IRR
0.5
0.6
0.7
0.8
0.9
1.0
1.1
B
Empirical prior (MORDOR) and likelihoods by phase (AVENIR)
Density
Log IRR
12.5
10.0
7.5
5.0
2.5
0.0
-0.5
-0.4
-0.3
-0.2
-0.1
0.0
0-6
0-12
0-18
0-24
Prior
C
Posterior by phase using empirical prior
Density
Log IRR
15
10
5
0
-0.3
-0.2
-0.1
Phase 6
Phase 12
Phase 18
Phase 24
D
Posterior by phase using time-forgetting prior
Density
Log IRR
8
6
4
2
0
-0.4
-0.3
-0.2
-0.1
0.0
Phase 6
Phase 12
Phase 18
Phase 24

Study Design

Search for common genetic variants to allow reliable Mendelian randomization investigations into ketone metabolism Zhu Liduzi Jiesisibieke* Zhu Liduzi Jiesisibieke Zhu Liduzi Jiesisibieke Héléne Toinét Cronjé C Mary Schooling Stephen Burgess

Background: Ketone supplementation has been linked to improved cognitive performance and increased risk of insulin resistance. We aim to identify common genetic variants that allow Mendelian randomization investigations into further potential effects of ketone metabolism.

Methods: We set four premises that we believe any valid instrument for ketone metabolism should satisfy. These are: 1) location in a gene region relevant to ketone metabolism, 2) association with all three primary ketone bodies (acetone, acetoacetate, and beta-hydroxybutyrate), 3) no pleiotropic associations, 4) associations with positive control variables (cognitive performance, two-hour glucose, and insulin fold change).

Results: We considered gene regions containing variants previously associated with acetone. Four of these regions had biological relevance to ketone metabolism. Lead variants for three of these four regions (SLC2A4, HMGCS2, OXCT1) associated with all three primary ketone bodies. One region (SLC2A4) was associated with two-hour glucose and insulin fold change; however, this region had strong pleiotropic associations with blood pressure. One region (OXCT1) showed an association with cognitive performance, and thus satisfied all our premises to be a valid instrument for ketone metabolism. In a complementary agnostic approach considering all genome-wide significant predictors of the three primary ketone bodies in turn, genetically-predicted acetoacetate based on 7 variants was associated with improved cognitive performance. However, several variants selected in this approach were not located in biologically-relevant gene regions and were pleiotropic.

Conclusion: Causal claims from Mendelian randomization will be most reliable when the instrumental variable assumptions are plausibly satisfied. We illustrate a framework to identify candidate instruments based on biological considerations.

Study Design

Design and methodological insights from RESONANCE: a US-based registry on the natural history and impact of recurrent pericarditis JoAnn Clair* ALLISON CURTIS Vidhya Parameswaran Paul C. Cremer Sushil A. Luis Michael S. Garshick Ajit Raisinghani Brittany Weber JoAnn Clair Allan L. Klein John F. Paolini

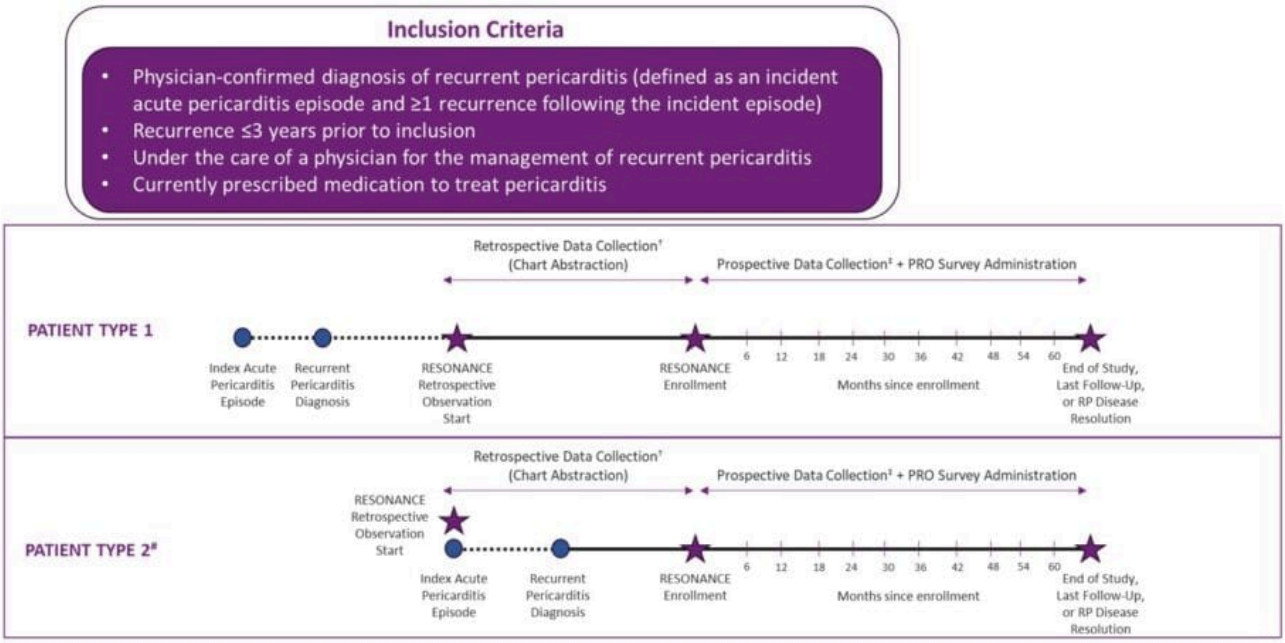
Recurrent pericarditis (RP) is a rare and persistent autoinflammatory disease characterized by serial episodes of chest pain. Treatment often entails years of symptom-suppressive pharmacotherapy (e.g. NSAIDs/colchicine, corticosteroids, and IL-1 pathway inhibition) before resolution of autoinflammation is achieved. Real-world data which capture the long-term RP patient experience are lacking, and registries are susceptible to certain types of bias due to their observational and often retrospective data collection. These biases may include selection (from non-random enrollment), temporal (from inconsistent data collection points), observer (from variability in clinician-recorded data), confounding (from unmeasured factors affecting outcomes), and non-response (from differential participant engagement) biases.

The REgiStry Of the NAtural history of recurreNt periCarditis in pEdiatric and adult patients (RESONANCE), the largest multi-center US-based observational registry, was developed to quantify trends in RP disease burden, management, and outcomes to inform treatment selection and optimize care. The RESONANCE design anticipates and addresses common biases found in registries to ensure the validity and reliability of its findings. An ambispective design combines retrospective (from index acute pericarditis episode or ≤1 year pre-enrollment) and prospective data (collected for up to 5 years) into one observation period (**Figure**).

RESONANCE incorporates robust data collection and post-data collection protocols for missing data, sensitivity analyses to assess dropout patterns, regression/stratification to adjust for confounders, and propensity score matching to compare responders vs. non-responders.

By combining pre- and post-data collection strategies, the impact of identified biases may be mitigated, improving RESONANCE’s accuracy, generalizability, and utility in clinical and research applications.

Figure: RESONANCE Study Design



†Retrospective data collection spans from 1 year pre-enrollment (or at the time of index acute pericarditis episode if the index event is < 1 year prior to enrollment in RESONANCE) until enrollment in RESONANCE. Data collection includes general disease data (e.g., data on recurrent pericarditis diagnosis and symptom onset, number of episodes in the observation period, other relevant recurrent pericarditis conditions and comorbidities, surgical history within the prior 12 months, and recurrent pericarditis medications for each episode) and medical history data (e.g., data on initial recurrent pericarditis diagnosis, initial acute episode, and medications prescribed for first recurrence).

‡ Includes chart abstraction and/or information gathered from patients during telehealth/ in-person clinic visits.

RESONANCE observation may also begin on or before the date of RP diagnosis.

PRO, patient reported outcome.

Substance Use

Family dynamics and environmental factors influencing progression from alcohol experimentation to initiation in youth: Evidence from the Adolescent Brain Cognitive Development (ABCD) Study Maya I. Harwood* Huiru Dong Maya I. Harwood Daniel F. Otero-Leon Mohammad S. Jalali

Early alcohol initiation is linked to the later development of problem drinking and other negative health outcomes. While previous research has identified predictors of alcohol use, few studies have distinguished between the phases of experimentation and initiation – key stages in youth drinking patterns. This study evaluated the influence of sociodemographic, familial, and environmental factors on the time from alcohol experimentation to initiation among preadolescent youth, using data from the Adolescent Brain Cognitive Development (ABCD) Study (2016-2022). For each study participant (N=11,694), alcohol consumption was assessed bi-annually. Experimentation was defined as the first instance of alcohol sipping, while initiation was defined as consuming at least one full drink during the study period. An extended Cox model was used to examine the effects of sociodemographic characteristics, family dynamics, parental alcohol use, alcohol expectancies, and environmental factors on the likelihood of alcohol initiation following experimentation. Among 1,225 youths who reported sipping alcohol during the study, 87 (7.1%) went on to have at least one full drink. Significant factors associated with a higher likelihood of alcohol initiation included older age (hazard ratio [HR] = 1.85, 95% confidence interval [CI]: 1.46-2.35, $p < 0.001$), household rules allowing alcohol consumption (HR = 2.78, 95% CI: 1.58-4.92, $p < 0.001$), family conflict (HR = 1.18, 95% CI: 1.07-1.30, $p < 0.001$), and positive expectancies about alcohol use (HR = 1.13, 95% CI: 1.04-1.23, $p = 0.004$). No significant differences were observed based on sex, race, ethnicity, family income, parental alcohol use, and neighborhood safety. Family and household dynamics emerged as robust influencing factors of early alcohol initiation following experimentation. These findings suggest that environmental interventions should be considered for prevention of alcohol use progression among preadolescent youth.

Substance Use

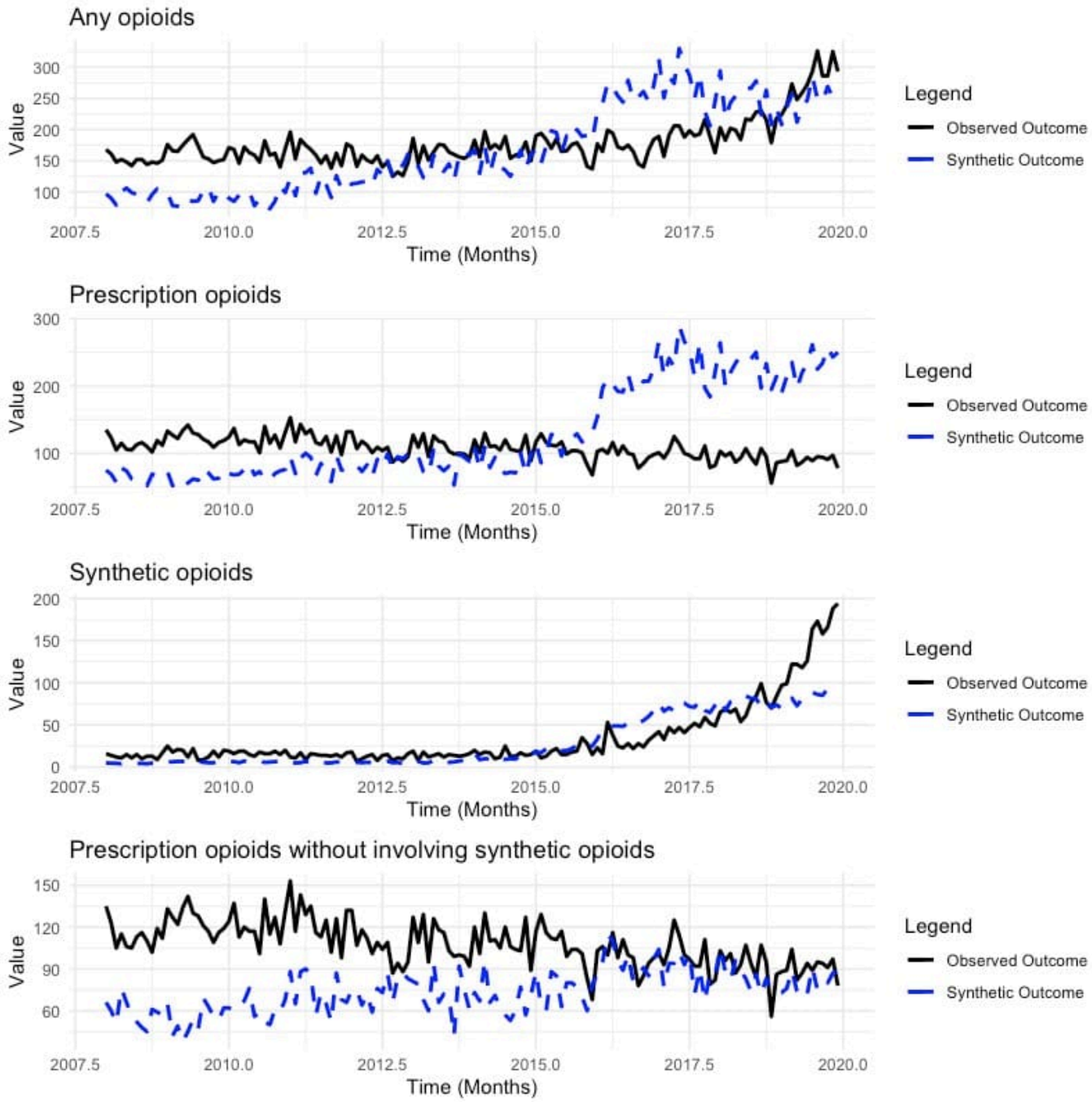
Navigating the Opioid Crisis in California: The Role of Naloxone Access Laws Shutong Huo*
Shutong Huo Abhery Das Zongbo Li Tim Allen Bruckner

Background: To address the rising opioid overdose deaths, California implemented AB 2760 in January 2019. The policy mandated providers to offer naloxone prescriptions alongside opioid prescriptions as a means of reversing potential opioid overdoses. This study aims to evaluate whether AB 2760 corresponds with a reduction in opioid-related overdose deaths.

Methods: We obtained data from the National Vital Statistics System from 2008 to 2019 to calculate monthly prescription opioid-related overdose deaths, prescription opioid-related deaths without involving synthetic opioids, synthetic opioid deaths (i.e., fentanyl), and any opioid deaths in California. We utilized a binary indicator for months before (0) and after (1) policy implementation (Jan. 2019). We generated time series models for outcomes, which incorporated synthetic controls of California based on unexposed states.

Results: Despite the legislation's aim to mitigate opioid overdoses, findings demonstrate an alarming increase in any opioid-related overdose, as well as prescription opioid-related overdose deaths (including synthetic opioids), after the policy's implementation in January 2019. There were 78.31 more opioid-related deaths ($p<0.01$) and 67.15 more prescription opioid (including synthetic opioids) deaths ($p<0.01$) per month above expected, which means 943.72 more deaths due to any opioid and 805.8 more deaths due to prescription opioids in 2019. Exploratory analyses reveal that California's co-prescribing policy corresponds with an increase in synthetic opioid-related deaths, in particular, but not prescription opioid-related deaths without involving synthetic opioids.

Conclusion: Our analysis shows that AB 2760 may not mitigate the trends in fentanyl-related deaths following the 2019 state policy. Our results highlight the need for more comprehensive, targeted interventions, especially addressing the fentanyl epidemic, to effectively combat the opioid crisis in California.


Any opioids
Value
300
250
200
150
100
2007.5
2010.0
2012.5
2015.0
2017.5
2020.0
Time (Months)
Legend
Observed Outcome
Synthetic Outcome
Prescription opioids
Value
300
200
100
2007.5
2010.0
2012.5
2015.0
2017.5
2020.0
Time (Months)
Legend
Observed Outcome
Synthetic Outcome
Synthetic opioids
Value
200
150
100
50
0
2007.5
2010.0
2012.5
2015.0
2017.5
2020.0
Time (Months)
Legend
Observed Outcome
Synthetic Outcome
Prescription opioids without involving synthetic opioids
Value
150
120
90
60
2007.5
2010.0
2012.5
2015.0
2017.5
2020.0
Time (Months)
Legend
Observed Outcome
Synthetic Outcome

Substance Use

Associations of In-Utero Maternal Exposures to Substances and Mood Disorders and Offspring Electroencephalogram (EEG) at Birth Nicolò Pini* Nicolò Pini Lynn Chen J. David Nugent William P. Fifer Michael M. Myers Amy J. Elliott Seonjoo Lee Ayesha Sania

Background: In-utero exposure to substances and maternal mood disorders can adversely affect fetal brain development. We examined the combined impact of exposure clusters on neonatal brain activity, in the Safe Passage Study (PASS).

Methods: We derived clusters of in-utero maternal alcohol (PAE), tobacco (PTE) exposure, and maternal anxiety/depressive symptoms. EEG data from Northern Plains, US, was collected in term newborns at birth (N=824). EEG power was decomposed in delta, theta, low alpha, high alpha, beta, and gamma bands and computed in frontal-polar (FP), polar (PO), temporal (TE), parietal (PA), occipital (OC), frontal-midline (FM), and central-midline (CM) regions. Associations between EEG power and clusters were examined using ANOVA, adjusting for infant sex, hours of life, and gestational age; corrected for false discovery rate.

Results: Analysis yielded 4 groups: Low Risk (67.8%); low PAE, PTE, and anxiety/depression; Mood+ (26.6%); low PAE and PTE, high anxiety/depression; Smoking+ (5.1%); no PAE, high PTE, and moderate anxiety/depression; and Drinking+ (0.4%); high PAE, no PTE, and high anxiety/depression. We detected differences in low frequencies power (delta and gamma) in frontal (FP, PO, TE), and posterior (PA, OC) regions. In frontal regions, average delta power was higher for the low-risk group compared to mood+ ($1.48\times10\text{-}6\pm5.19\times10\text{-}7$, $p<0.05$) or smoking+ ($3.32\times10\text{-}6\pm1.27\times10\text{-}6$, $p<0.05$) or drinking+ ($6.23\times10\text{-}6\pm2.35\times10\text{-}6$, $p<0.05$) groups. In posterior regions, average delta power was lower in the drinking+ group compared to low-risk ($-6.80\times10\text{-}6\pm-2.35\times10\text{-}6$, $p<0.05$) or mood+ ($-5.94\times10\text{-}6\pm-2.36\times10\text{-}6$, $p<0.05$) or smoking+ ($-5.57\times10\text{-}6\pm-2.47\times10\text{-}6$, $p<0.05$) groups. Similar results were found for average theta power.

Conclusion: Prenatal maternal mood and substance use are differentially associated with EEG activity at birth in the offspring. Future work will focus on investigating the contribution of these factors to the trajectories of brain development.

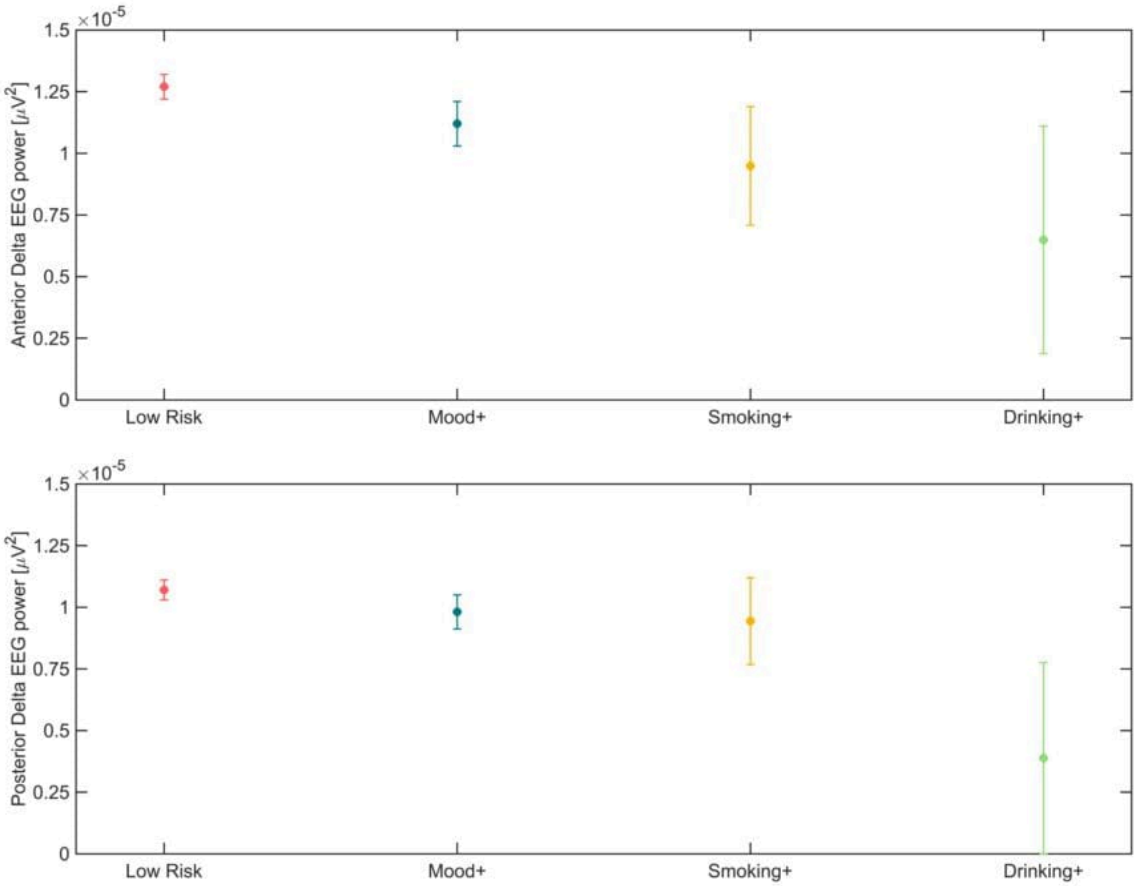


Figure 1. Average EEG delta power in the anterior (top panel) and posterior (bottom panel) brain regions across the exposure clusters (Low Risk, Mood+, Smoking+, Drinking+). Solid black lines connect significant pairwise comparisons, indicating differences in EEG delta power between pairs of exposure clusters.

Substance Use

Risk factors for experiencing substance use-related employment stigma among emergency department patients at high risk of opioid overdose Ralph Welwean* Ralph Welwean Laura C. Chambers Brandon D. L. Marshall Francesca Beaudoin

Abstract

Background: People who use drugs report hesitance to seek employment because of stigma around drug use, which may be compounded by other forms of stigma (e.g., related to race/ethnicity). We evaluated risk factors for substance use-related employment stigma among emergency department (ED) patients who use drugs.

Methods: This was a cross-sectional study among ED patients at high risk of opioid overdose in Rhode Island. The outcomes were three self-reported measures of substance use-related employment stigma. Multivariable log-binomial regression was used to estimate the association between participant characteristics and each outcome.

Results: Among 648 participants, 25.8% reported they had been turned down for a job due to current/past drug use, 40.8% disagreed that most employers will hire someone treated for drug use if qualified, and 77.7% agreed that most employers will pass over applicants treated for drug use in favor of others. Females reported they had been turned down for a job due to drug use less often than males (adjusted prevalence ratio [PR]=0.72, 95% confidence interval [CI]=0.53-0.98). Persons with a history of homelessness (aPR=1.82, 95%CI=1.24-2.66) and addiction treatment (aPR=1.95, 95%CI=1.22-3.12) more often reported having ever been turned down for a job due to drug use. Race/ethnicity was not associated with substance use-related employment stigma.

Discussion: Perceived substance use-related employment stigma was common among ED patients who use drugs, and men, and those with a history of homelessness or addiction treatment may be particularly affected. Employers can help improve employee attitudes and change hiring practices to reduce such stigma.

Substance Use

Polysubstance use during pregnancy and preterm birth Xiaozhong Wen* Xiaozhong Wen Aye Moe Hanchen Jiang Porsche Lee

Objective: We aimed to 1) examine the distributions of polysubstance use during pregnancy and 2) investigate the associations between polysubstance use during pregnancy and the risk of preterm birth.

Methods: We used data from 237,288 mothers enrolled in the U.S. Pregnancy Risk Assessment Monitoring System from 2016-2021. Postpartum mothers reported the status of their use of combustible cigarettes, electronic cigarettes (e-cigarettes), marijuana, alcohol, and drugs in the last 3 months of pregnancy. Our primary outcome was preterm birth, defined as birth before the 37 weeks of pregnancy. We created a correlation matrix to explore the patterns of polysubstance use. We used multivariable logistic regression models to estimate the associations between the different polysubstance use groups during pregnancy with preterm birth, adjusting for socio-demographic and pregnancy-related confounders.

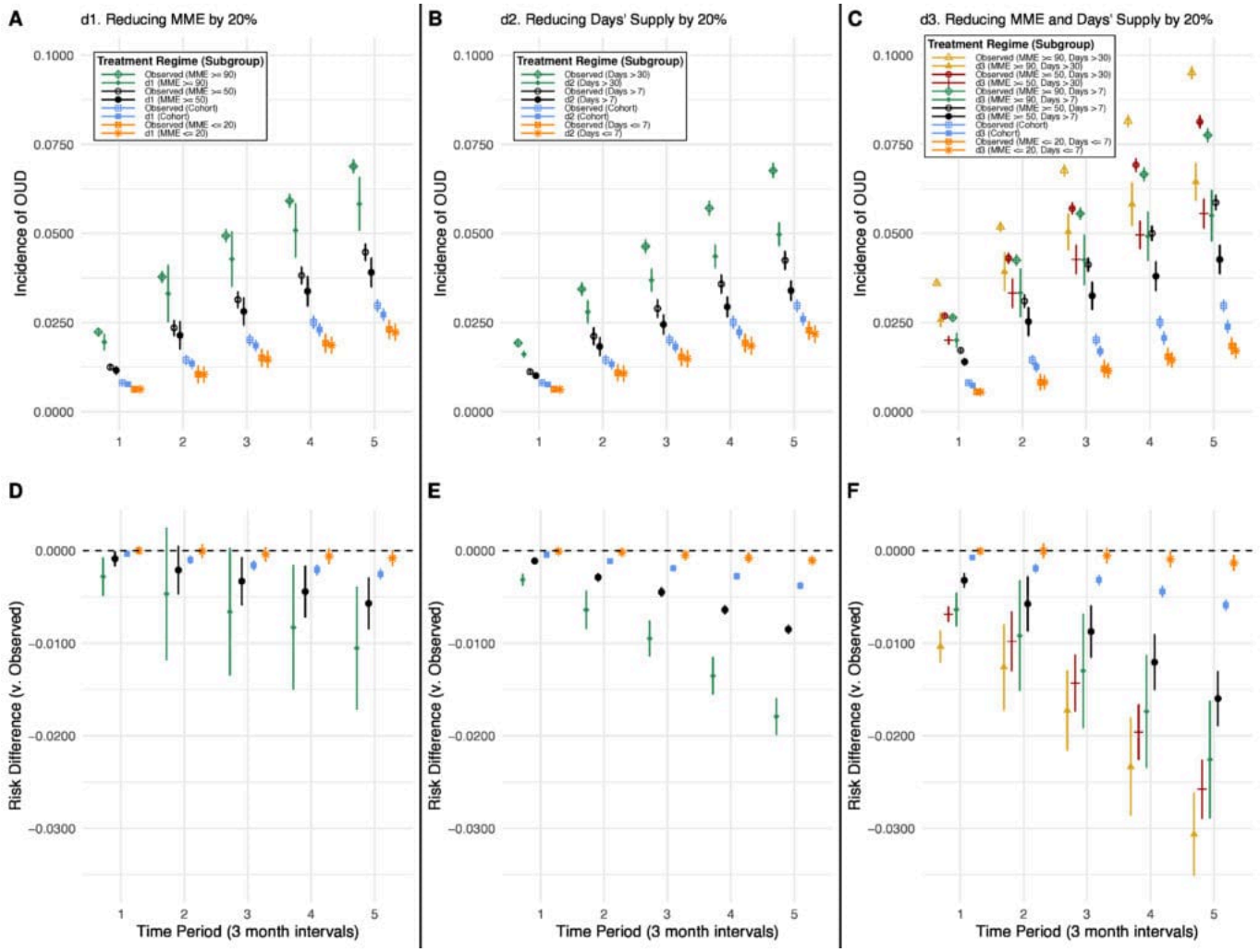
Results: The three most prevalent substances used during pregnancy were alcohol (9.35%), cigarettes (7.11%), and marijuana (4.84%). The highly correlated substance combinations were cigarettes and e-cigarettes (r=0.600), cigarettes and marijuana (r=0.553), cigarettes and amphetamines (r=0.595), cigarettes and methadone (r=0.620), e-cigarettes and methadone (r=.518), marijuana and amphetamines (r=0.635), Adderall and amphetamines (r=.636), and amphetamines and methadone (r=.689). The use of cigarettes and marijuana (confounder-adjusted odds ratio or aOR=1.59 [95% confidence intervention or CI, 1.29-1.95]; p-value <0.001) as well as the use of cigarettes and amphetamines (aOR=1.71 [95% CI, 1.18-2.48]; p-value=0.005) was associated with increased odds of preterm birth compared to non-users. Furthermore, the use of all three cigarettes, marijuana, and amphetamines was also significantly linked to preterm birth (aOR=1.73 [95% CI, 1.06-2.84]; p-value=0.029).

Conclusion: Co-use of cigarettes/marijuana and cigarettes/amphetamines is associated with preterm birth.

Substance Use

Reducing prescription opioid dose and duration to reduce risk of opioid use disorder among patients with musculoskeletal pain Shodai Inose* Shodai Inose Nicholas T. Williams Katherine L. Hoffman Allison Perry Iván Díaz Kara E. Rudolph

Although the U.S. Centers for Disease Control and Prevention's (CDC) opioid prescribing guidelines (2022) recommend initiation of opioids at the lowest effective dose for the shortest required time, they do not discuss the joint effects of these prescribing characteristics and are written to apply broadly to all patients. Due to the prevalence of high-risk levels of opioid prescribing for musculoskeletal (MSK) pain, we examined the effects of applying modest opioid dose and/or duration reduction policies to adult Medicaid patients with newly diagnosed MSK pain who were prescribed opioids (n=229,434) on the risk of developing opioid use disorder (OUD) over 15 months. We divided our cohort into subgroups by prescription "riskiness" based on maximum daily morphine milligram equivalents (MME) and the number of days supplied for all opioid prescriptions in the 3 months following diagnosis, using prescribing cutoffs based on CDC guidelines and state laws limiting opioid prescription. We used a novel approach to estimate the effects of localized modified treatment policies within subgroups (a generalization of the average treatment effect on the treated). Reducing both opioid prescription dose and duration by 20% across the cohort resulted in a statistically significant, but clinically modest, decreased risk of OUD (absolute RD: -0.59%). In contrast, larger, clinically significant reductions in risk >1 percentage point were observed when assessing effects of 20% reductions among the following risky subgroups independently: 1) reducing dose for those with ≥90 MME (RD: -1.05%), 2) reducing days supplied for prescriptions >30 days (RD: -1.79%), and 3) reducing both dose and duration for those with ≥50 MME for >7 days (RD: -1.60%; -3.06% among those with ≥90 MME for >30 days). These findings suggest that reductions in opioid prescribing may have limited impact on OUD risk when applied broadly, but may meaningfully reduce risk when applied to those with riskier prescriptions.


A
d1. Reducing MME by 20%
B
d2. Reducing Days' Supply by 20%
C
d3. Reducing MME and Days' Supply by 20%
Treatment Regime (Subgroup)
Incidence of OUD
0.1000
0.0750
0.0500
0.0250
0.0000
D
E
F
Risk Difference (v. Observed)
0.0000
−0.0100
−0.0200
−0.0300
1
2
3
4
5
Time Period (3 month intervals)

Substance Use

Low Threshold Shelters promote racial equity in housing for chronically unsheltered people with substance use disorder in Boston. Ariela Braverman Bronstein* Ariela Braverman Bronstein Shanyin Yang Sumaiya Miah Jeffrey Desmarais Krystal Garcia Shoba Nair

Background Unsheltered homelessness disproportionately affects communities of color and people with substance use disorder (SUD). In response, Boston implemented seven low-threshold shelters (LTS) in 2022–2023 to house chronically unsheltered individuals with SUD. Guided by Housing First and harm reduction principles, LTS offer transitional housing and support services focused on permanent placement. While these programs may reduce racial disparities, their effectiveness in promoting racial equity remains underexplored. This study examines sociodemographic characteristics, move-out reasons by race/ethnicity, and their association with housing placement. **Methods** We analyzed LTS guests' race/ethnicity, gender, age, and housing placement (January 2022–June 2024) sourced from Boston Public Health Commission systems. Disability status, earned income, and benefits data were sourced from the Homeless Management Information System. A total of 460 LTS guests (80%) had matching records and were included. Descriptive analyses were conducted by race/ethnicity and move-out reason. Competing risk multivariate models assessed associations between sociodemographic characteristics and housing placement. **Results** Among included guests, 24% were Hispanic, 29% Black non-Hispanic, 46% White non-Hispanic, and 4% of another race. Gender and age distributions differed by race/ethnicity but not move-out reasons. Disabilities other than SUD and benefits varied by move-out reasons but not race/ethnicity. Black guests were more likely to be placed in permanent housing (HR = 1.5, 95% CI: 1.0–2.1), as were guests with disabilities other than SUD (HR = 1.3, 95% CI: 1.0–1.6) and earned income (HR = 1.7, 95% CI: 1.0–2.7). **Discussion** LTS may promote equitable housing outcomes, particularly for people of color. Positive trends for Black guests highlight the potential of LTS models, but further research is needed to confirm findings and improve housing stability across diverse populations.

LATEBREAKER

Substance Use

Oral Nicotine Product Use on E-Cigarette Use Persistence in Adolescents and Young Adults: An Analysis Using Augmented Inverse Probability Weighting Dae Hee Han* Dae Hee Han Alyssa Harlow Ming Li Paul Martines Charlotte Duran Jessica Barrington-Trimis Chanita Hughes-Halbert Rafael Meza David Levy Adam Leventhal

Introduction: This study investigated the association between oral nicotine product (ONP) use and e-cigarette use persistence among adolescents and young adults (AYAs) utilizing a doubly robust method with machine learning (ML) to mitigate potential bias from model misspecification while enhancing the precision of the treatment effect estimate.

Methods: We combined data from two separate cohorts of Southern California adolescents (n=269; M=16.3 years, SD=0.6) and young adults (n=449; M=23.4 years, SD=0.4) who reported e-cigarette use within the past 6 months at baseline and were followed up approximately 12 months later in 2022-2023. We employed augmented inverse probability weighting (AIPW) with ML to estimate the average treatment effects of baseline ONP use on e-cigarette use persistence at follow-up, which integrates the robustness of AIPW's doubly robust property with the predictive accuracy of ML algorithms. Analyses were further stratified by cohort, comparing adolescents and young adults. AIPW accounted for confounding by sociodemographic characteristics, e-cigarette use factors, and substance use behaviors. We stacked four ML learners to improve estimation of AIPW, including generalized linear model, multivariate adaptive regression splines, random forests, and extreme gradient boosting.

Results: Of the 718 AYAs who used e-cigarettes at baseline (53.1% female, 58.4% Hispanic), 102 (14.2%) also used ONPs at baseline, with 462 (64.3%) reporting persistent use of e-cigarettes at follow-up. The AIPW+ML analysis did not indicated a statistically significant association between AYA ONP use and subsequent e-cigarette use persistence (risk difference[RD]=-0.01, 95% CI=-0.16, 0.14; risk ratio[RR]=0.98, 95% CI=0.79, 1.22). However, cohort stratified analyses revealed that adolescents who used ONPs (vs. those who did not use) had a lower risk of e-cigarette use persistence (RD=-0.19, 95% CI=-0.34, -0.05; RR=0.67, 95% CI=0.48, 0.94). This association was not observed in the young adult cohort.

Conclusion: Findings suggest that ONPs may serve as a partial nicotine substitute for e-cigarette use among adolescents who use e-cigarettes. Further studies should investigate the association between ONP use and other nicotine product use behaviors in adult populations with chronic nicotine use.

LATEBREAKER

Substance Use

Adolescent depressive symptoms as a potential target for reducing intergenerational smoking transmission Alexandria Andrayas* Alexandria Andrayas

Introduction

Parental smoking is associated with increased offspring smoking, perpetuating cycles of nicotine dependence. Young people with mental health issues are also more likely to start smoking, thereby improving mental health could help break this cycle. However, the extent to which this may occur remains unclear.

Aims

This study investigated whether offspring depression mediates the association between parental smoking at age 12 and offspring smoking at age 16, accounting for intermediate confounding by early substance use at age 13.

Methods

Multiple imputation was used, and analyses adjusted for baseline and mediator-outcome confounders. Multivariable regression was utilised to examine associations between parental smoking, offspring depression, and early substance use. Causal mediation analysis via parametric g-formula with Monte Carlo simulation estimated total, direct, and indirect effects, with 95% confidence intervals derived from 100 non-parametric bootstrap resamples.

Results

Parental smoking at age 12 was associated with offspring early substance use at age 13 (log[OR] = 0.39, 95% CI = 0.20-0.58, $p < 0.001$) and offspring smoking at age 16 (log[OR] = 0.44, 95% CI = 0.24-0.64, $p < 0.001$), but not offspring depression at age 14 (log[OR] = 0.05, 95% CI = -0.14-0.24, $p = 0.6$). Early substance use at age 13 was associated with both offspring depression at age 14 (log[OR] = 0.26, 95% CI = 0.04-0.47, $p = 0.018$) and smoking at age 16 (log[OR] = 1.4, 95% CI = 1.2-1.6, $p < 0.001$). Higher depressive symptoms at age 14 were also associated with smoking at age 16 (log[OR] = 0.25, 95% CI = 0.05-0.46, $p = 0.016$).

Causal mediation analysis provided evidence of a natural direct effect (NDE) of parental smoking at age 12 on offspring smoking at age 16 (MD = 0.058, 95% CI = 0.026-0.091) but no natural indirect effect (NIE) via depression at age 14 (MD = 0.0003, 95% CI = -0.001-0.002). Similar results were found when accounting for intermediate confounding by early substance use at age 13.

Conclusion

Parental smoking in early adolescence increases the likelihood of offspring smoking in later adolescence, but this did not appear to be act via offspring depression.

Substance Use

Modeling Canada’s Opioid Crisis: A Systems Approach to Policy and Intervention Strategies
Zeynep Hasgul* Zeynep Hasgul Hesam Mahmoudi Rebecca Plouffe Tara Sadeghieh Karin Johnson Eva Graham Mohammad S. Jalali

The opioid crisis continues to impose a profound public health burden, with recent trends in Canada paralleling the trajectory of the epidemic in the United States. This study builds on the SOURCE (Simulation of Opioid Use, Response, Consequences, and Effects) model, a system-level quantitative framework developed in collaboration with the U.S. Food and Drug Administration and recommended by the U.S. National Academies of Sciences, Engineering, and Medicine to guide integrated policy decisions. Recognized for its evidence-driven approach, SOURCE incorporates feedback mechanisms—such as drug availability, social influence, and risk perception—that capture the complex, dynamic nature of opioid use and overdose. By adapting and recalibrating SOURCE to the Canadian context, this study enhances our understanding of Canada’s opioid crisis dynamics and provides a robust tool to evaluate tailored policy interventions. This Canadian adaptation incorporates key differences in opioid use patterns, such as the availability and coverage of medications for opioid use disorder (MOUD) and policy contexts. Structural modifications to the model reflect the widespread accessibility of buprenorphine in Canada and the absence of Vivitrol. Using data from Canadian surveys, IQVIA, and public health datasets between 2009 and 2023, the model was recalibrated to estimate Canadian-specific opioid use trajectories, overdose rates, and MOUD treatment outcomes. The adapted model evaluates the future impacts of nine current and new strategies in Canada, spanning harm reduction, MOUD expansion, prevention of misuse, and recovery support, to provide insights into policy and intervention effectiveness. We present portfolios of intervention combinations and their projected reductions in overdose deaths over time with the highest potential reductions observed when integrating multiple strategies across prevention, harm reduction, and treatment.

Substance Use

Opioid Overdose Deaths Among Patients with Pain or Opioid Use Disorder Diagnosis David Fink* David Fink Carol Malte Tracy Simpson Andrew Saxon Deborah Hasin

Chronic pain and opioid use disorder (OUD) are considered drivers of US overdose trends, but lack of opportunity to link mortality files to medical records that include these clinical diagnoses present challenges to comparing magnitude and trends in these relationships. The nationwide Veterans Health Administration (VHA) electronic health records (EHR) system provides a unique opportunity to study opioid overdose trends among patients with chronic pain and OUD diagnoses. Yearly cross-sectional VHA EHR data from 2005 to 2020 were linked with the US Center for Disease Control and Prevention National Death Index to determine opioid overdose death rates among VHA patients with pain or OUD diagnosis, adjusted for age, sex, race and ethnicity. From 2005 to 2020, the overall opioid overdose death rate among patients increased approximately 2.5-fold, from 16.95 to 40.90 per 100,000. In 2005, the opioid overdose death rate was ~1.5 times higher among those with than without chronic pain (21.68 vs. 13.79 per 100,000, respectively). In contrast, 2020 patients without chronic pain had higher overdose death rates than patients with chronic pain (43.77 vs. 37.91 per 100,000, respectively), largely driven by greater increases in deaths from illicit opioids (heroin or synthetic opioids). Among patients diagnosed with OUD, the opioid overdose death rate increased from 344.07 to 790.96 per 100,000 between 2005 and 2020. Among those with OUD, opioid overdose death rates involving prescription opioids remained stable between 2005 and 2020 (218.03 and 190.62, respectively), while overdose deaths rates involving illicit opioids increased 10-fold, from 77.30 to 725.51 per 100,000. VHA patients diagnosed with OUD have opioid overdose death rates substantially higher than patients with chronic pain. The VHA has successfully undertaken many initiatives to reduce prescription opioid harms; however, overdose deaths involving illicit opioids have increased substantially and remain uncontrolled.

Substance Use

Associations between county-level e-cigarette smoke-free air law coverage and e-cigarette use behaviors among US adolescents in the Monitoring the Future Study James Buszkiewicz* James Buszkiewicz Yanmei Xie Catherine A. Vander Woude Steven Cook Bukola Usidame Megan E. Patrick Michael Elliott James F. Thrasher Nancy L. Fleischer

Background: Prior studies have found that e-cigarette smoke-free air laws (SFAL) were associated with lower adolescent e-cigarette use but have not examined whether associations differ by sociodemographic factors.

Methods: We analyzed associations between county-level workplace and hospitality e-cigarette SFAL coverage (100% vs. <100%) and past 30-day e-cigarette use (2014–2022) and first e-cigarette initiation (2015–2022) among US 8th, 10th, and 12th graders using national, cross-sectional Monitoring the Future study data. We used weighted, grade-stratified, modified Poisson regression models adjusted for individual-, county-, and state-level confounding factors. We also examined two-way interactions with sex, race and ethnicity, parental education, and college educational expectations.

Results: E-cigarette SFALs were not associated with adolescent e-cigarette use or initiation in the overall sample but were associated with lower use among some sociodemographic subgroups. Higher (100% versus <100%) workplace e-cigarette SFAL coverage was associated with lower e-cigarette use among 12th-grade males versus females. Higher hospitality e-cigarette SFAL coverage was associated with lower e-cigarette use among 8th and 12th-grade males versus females. Higher hospitality SFAL coverage was associated with lower e-cigarette use among 8th graders and 12th graders of all racial and ethnic groups, except non-Hispanic Black 8th and non-Hispanic White 12th graders. Higher workplace and hospitality SFAL coverage was also associated with lower e-cigarette use among 12th graders whose parents had a high school education or less.

Conclusions: E-cigarette SFALs were not associated with lower adolescent e-cigarette use or initiation in the overall sample. However, given current e-cigarette use disparities, our interaction results suggested that e-cigarette SFAL may widen sex and select racial and ethnic adolescent e-cigarette use disparities while narrowing socioeconomic disparities.

Substance Use

Drug overdose mortality in North Carolina among publicly and privately insured people: 2006-2022 Raana Zakeri* Raana Zakeri Shabbar I Ranapurwala Brian W. Pence Hillary Mortensen Grace Yeboah-Kodie

Background: The drug overdose epidemic costs the US about $1 trillion annually. We aimed to compare the overdose death rates among publicly and privately insured individuals in North Carolina (NC) between 2006-2022.

Methods: Records from Medicaid and privately insured NC individuals were linked to NC State Center for Health Statistics death certificate data, by fuzzy match linkage method using last and first names, date of birth, and sex. Overdoses from all drugs, opioids, and polydrugs were identified using primary cause of death International Classification of Disease Version 10 (ICD-10) codes. Indirect standardization with the NC general population as the reference group, was used to report adjusted rate and standardized mortality ratios (SMRs) adjusted for age and sex per calendar year between 2006-2022.

Results: Between 2013-2022, the adjusted rate and SMR for all drugs, opioids, polydrug overdose deaths among Medicaid population was 67.1, 50.2, and 43.2 per 100,000 person-years (PY), with respective SMRs of 1.6, 2.6, and 1.8 relative to the general population. In contrast, among privately insured population the rates for all drug, opioids, and polydrug overdose deaths were 15.1, 11.3, and 7.9 per 100,000 PY, with respective SMRs of 0.29, 0.49, and 0.32, relative to the general population. The rates for all drug, opioids, and polydrug overdose deaths among Medicaid population peaked in 2013, and then decreased thereafter, while still remaining higher than the general population. However, the rates for the privately insured population remained about a third of the general population throughout the follow up.

Conclusion: People with Medicaid insurance experienced higher overdose rates compared to those with private health insurance. This highlights significant disparities between individuals of different socioeconomic statuses, which must be addressed in any prevention strategies.

Keywords: overdoses, drugs, opioids, polydrugs, Medicaid, health insurance

Veterinary Epidemiology

Neighborhood Effects on Canine Health: Investigating Disadvantage and Preventable Diseases Christopher Pierson* Christopher Pierson Kendra Ratnapradipa Christopher Wichman Elizabeth VanWormer Edward Peters

BACKGROUND: A One Health paradigm suggests that neighborhood disadvantage (ND), known to be associated with negative health outcomes in humans, may have similar effects on companion animals living in the same neighborhood. Veterinarians recommends that dogs be vaccinated for 9 diseases and receive regular heartworm prevention.

PURPOSE: To assess the impact of ND on vaccine preventable diseases in dogs.

METHODS: This study used the Dog Aging Project, a large nation-wide cohort of dogs which asks owners to annually report if their dog developed any health conditions and give information on the dog's lifestyle. This analysis included 15,516 dogs: 8,091 with 1 follow-up and 8,425 with 2 follow-up surveys. ND was measured using the Area Deprivation Index (ADI) of the dog's block group of residence. This analysis focused on the 5 diseases with incident cases: canine influenza, heartworm, kennel cough, leptospirosis, and Lyme disease. We used mixed-effect longitudinal logistic regression to model each disease individually with different covariates for each disease.

RESULTS: After adjusting for vaccination status, flea and tick preventative use, and human Lyme disease incidence in the dog's state, a one percentile increase in nationally ranked ADI was associated with a very slight increase in the odds of a dog having Lyme disease in the past year (OR: 1.01, 95% CI: 1.00 – 1.02). Nationally ranked ADI was not associated with any of the other disease studied, nor was state-ranked ADI associated with any diseases.

CONCLUSION: These findings suggest that ND does not impact vaccine preventable diseases in dogs. While this analysis may not directly inform veterinary care, the findings could be used to inform research on the impacts of a neighborhood on human residents. Factors that affect both canine and human health could be deprioritized in favor of factors that are unique to humans in research trying to understand ND's impact on human health.

Women’s Health

Physician perceptions on oral health for pregnant women: Bangladesh perspective Nabhira Aftabi Binte Islam* Nabhira Aftabi Binte Islam

Background

Hormonal changes during pregnancy can have an impact on dental health. Obstetricians are crucial in providing advice on dental issues and collaborating with dental surgeons to ensure safe and optimal care. This study aimed to investigate obstetricians’ knowledge, attitudes, and practices regarding dental care for pregnant women in Bangladesh.

Methods

A cross-sectional study involving 211 obstetricians, trainees, and residents was conducted in Dhaka, Mymensingh, Chittagong, and Khulna Divisions of Bangladesh from July 1 to December 19, 2023. Eight medical colleges, comprising an equal number of public and private, were randomly selected to ensure a balanced representation across divisions.

Results

Three-quarters of respondents recognized a connection between hormonal changes and an increased risk of gum diseases, while 28.4% highlighted that gum diseases are linked to adverse pregnancy outcomes. Moreover, 87.7% acknowledged a connection between maternal oral health and other health conditions. Additionally, 87.2% of obstetricians advised pregnant mothers to brush twice daily, and 90% recommended dental consultations for tooth and gum problems. However, 52% did not routinely provide oral health advice to expectant mothers. Furthermore, 61.6% reported that their undergraduate curriculum does not include pregnancy-related oral health information. Significant positive associations were also found between standardized knowledge scores and the respondents’ age, job experience, and education and between standardized attitude scores and age and job experience.

Conclusion

Oral health education for obstetricians is essential for improving dental care for expectant mothers. Continuous professional development can enhance their knowledge and practices, ultimately contributing to better health outcomes for mothers and babies

Women’s Health

Disparity of Pregnancy, Childbirth, and Obstetrical Complications between Multicultural Women and Korean Women in Korea: a Nationwide Population-Based Study Bomi Lee* Bomi Lee Soomin Kim Hyemin Jung Jin Yong Lee

Disparity of Pregnancy, Childbirth, and Obstetrical Complications between Multicultural Women and Korean Women in Korea: a Nationwide Population-Based Study

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INTRODUCTION:
In Korea, the number of immigrants and international marriages has steadily increased, with multicu ltural marriages accounting for 10.6% in 2023. However, multicultural women often face limited acc ess to healthcare due to language and cultural barriers. Korea’s universal healthcare system support s various pregnancy and childbirth assistance policies for multicultural women. This study aims to in vestigate differences in pregnancy, childbirth, and obstetrical complications among multicultural wo men in Korea.

METHODS:
Using the data of National Health Insurance (NHI) claims data, we extracted information on women who terminated pregnancy including delivery and abortion from January to December, 2023. We con ducted Pearson’s chi-square test and Student’s t-test to examine the difference between multicultural and Korean women.

RESULTS:
Of the 252,613 pregnancies, 14,540 (5.8%) were among multicultural women. The average age of m ulticultural women (31.0 years) was 2.3 years younger than that of Korean women (33.3 years), but t he proportion of Medical Aids (1.9%) was 3.2 times higher than that of Korean women (0.6%). Howe ver, the abortion rate (24.3% vs. 26.0%) and the cesarean section rate (52.1% vs. 59.3%) were lower among multicultural women compared to Korean women, with no significant differences in most obst etric complications. Notably, the incidence rates of gestational hypertension (1.11% vs. 2.04%) and p lacenta previa (1.35% vs. 1.84%) were lower among multicultural women.

CONCLUSIONS: In most countries, immigrant mothers are reported to receive inadequate prenatal care and experience worse delivery outcomes than their native-born counterparts due to limited access to healthcare. However, these results suggest that the lower rates of abortion and cesarean section among multicultural women may be attributed to their younger maternal age. As this study shows, if universal health coverage is provided to all mothers, the differences can be minimized or even disappear.

Table 1. General characteristics and obstetrical outcomes acccording to multicultural/Korean women

Variables	Total		Multicultural women		Korean women		P value
	No.	(%)	No.	(%)	No.	(%)	
Total	252,613	(100.0)	14,540	(5.8)	238,073	(94.2)	
Age (Mean ± SD)	33.2 ± 4.54		31.0 ± 5.46		33.3 ± 4.45		<.0001
<19	975	(0.4)	127	(0.9)	848	(0.4)	
19-34	156,556	(62.0)	10,334	(71.1)	146,222	(61.4)	
≥35	95,082	(39.6)	4,079	(28.1)	91,003	(38.2)	
Type of insurance							<.0001
NHI	250,800	(99.3)	14,269	(98.1)	236,531	(99.4)	
MA	1,813	(0.7)	271	(1.9)	1,542	(0.6)	
Termination of pregnancy							
Abortion	65,501	(25.9)	3,528	(24.3)	61,973	(26.0)	<.0001
Delivery	187,112	(74.1)	11,012	(75.7)	176,100	(74.0)	
Type of delivery							
Cesarean section	110,195	(58.9)	5,737	(52.1)	104,458	(59.3)	<.0001
Vaginal delivery	76,917	(41.1)	5,275	(47.9)	71,642	(40.7)	
Obstetrical complications							
Gestational hypertension			161	(1.11)	4,863	(2.04)	<.0001
Placenta previa			197	(1.35)	4,375	(1.84)	<.0001

No.=Number, SD=Standard Deviation, NHI=National Health Insurance, MA=Medical Aid

* P value was calculated by chi-square test or t-test between multicultural and Korean women.

Women’s Health

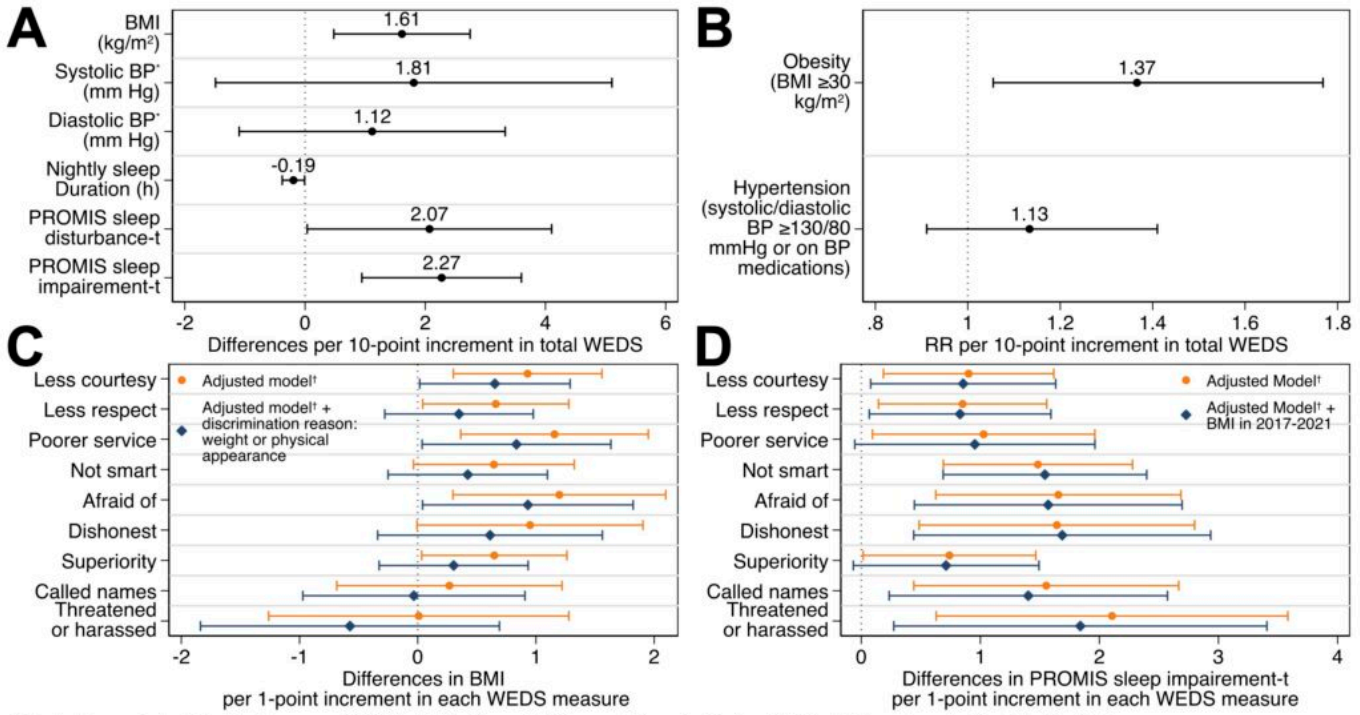
Perceived discrimination and cardiometabolic health in mid-life women: results from the Project Viva cohort Benjamin Grobman* Benjamin Grobman Sheryl L. Rifas-Shiman Izzudin Aris Wei Perng Stephen Juraschek Emily Oken Marie-France Hivert Mingyu Zhang

Background: Understanding how perceived interpersonal discrimination is associated with cardiometabolic health could inform place-based interventions aimed at reducing health disparities.

Methods: Participants are 450 middle-aged women from the Project Viva cohort. In 2021-2022, we assessed perceived interpersonal discrimination using the 9-item, race-neutral Williams Everyday Discrimination Scale (WEDS) via surveys. We also summed the 9-item WEDS into a total score. In 2022-2024, we measured weight, height, blood pressure (BP), and sleep duration (via actigraphy) and quality (via PROMIS Sleep Disturbance forms) during in-person visits. We defined obesity as BMI ≥30 kg/m2 and hypertension as systolic/diastolic BP ≥130/80 mmHg or the use of BP medications. We examined associations of WEDS (total and individual item scores) with cardiometabolic outcomes using linear or modified Poisson models, adjusting for age, household income, and education.

Results: At outcome measurement, women had a median age of 56.1 years (IQR: 53.2-59.2), with 74% self-identifying as White, 10% Black, 7% Hispanic, 7% Asian, and 2% others. At the time of surveys, 74% reported household incomes >$100,000/year. Higher total WEDS scores were associated with higher BMI, shorter sleep duration, greater sleep impairment and disturbance (**Panel A**), and higher obesity risk (**Panel B**). Further adjustment for race and ethnicity slightly attenuated these associations. Most individual WEDS items were consistently associated with BMI (**Panel C**) and sleep impairment (**Panel D**). Adjustment for perceived reasons for discrimination based on weight or appearance reduced, but did not eliminate, associations with BMI (**Panel C**). Adjustment for BMI prior to surveys (measured 2017-2021) did not change associations with sleep impairment (**Panel D**).

Conclusion: Higher perceived interpersonal discrimination was prospectively associated with higher BMI, obesity, and poorer sleep duration and quality among women in midlife.



BMI = body mass index; BP = blood pressure; PROMIS = Patient-Reported Outcomes Information System; WEDS = Williams Everyday Discrimination Scale
*For participants on BP medication, we added 10 mmHg to systolic BP and 5mmHg to diastolic BP. †Adjusted for age at outcome measurement, household income, and education.

Women’s Health

The association between infertility and intimate partner violence among HIV-negative women in low- and middle-income countries Cheyu Zhang* Cheyu Zhang Astha Ramaiya Julia Mandeville Jhumka Gupta

Introduction: Male-perpetrated intimate partner violence (IPV) against women affects one-third of women around the world. This is especially an issue in low- and middle-income countries (LMICs), where a prevalence of 37% was observed. Infertility and childlessness may be factors that influence IPV experiences among women. This paper aims to examine whether women’s infertility and childlessness are associated with IPV experience among HIV-negative women in LMICs.

Methods: Nationally representative Demographic Health Survey (DHS) data from 16 countries (14 from Sub-Saharan Africa) were used. Women aged 20-49 who tested HIV-negative were included in the analysis to minimize reverse causality. Logistic regressions accounting for the survey design factors and weights were used to compare lifetime and past-year IPV experiences (including any IPV, physical IPV, sexual IPV, and psychological IPV) among women who were determined infertile, women with no child, and women with children.

Results: Among all 98,833 women in the study, 41.9% had ever experienced any type of IPV in their lifetime, and 30.0% experienced IPV in the past year. The vast majority of women in this analysis had at least one live birth. Differences in IPV experiences were not significant or borderline significant among infertile women (Lifetime: aOR=0.98, 95%CI 0.75-1.27; Past-year: aOR=0.96, 95%CI 0.72-1.28) and women without children (Lifetime: aOR= 0.78, 95%CI 0.64-0.95; Past-year: aOR=0.82, 95%CI 0.67-1.01) compared to women with children.

Conclusion: The current study showed that the prevalence of male-perpetrated IPV against women was high (41.9% lifetime and 30.0% past-year) among women 20-49 years old in 16 low- and middle-income countries, irrespective of whether they had/did not have children. The results demonstrate the importance of IPV prevention interventions to be inclusive of women with infertility and women without children. Future research is needed to further understand the association between women’s infertility and IPV experiences.

Women’s Health

Relationship Between Kidney Stones and Risk of Incident Cardiovascular Disease Among Postmenopausal Women Mahsa H. Javadi* Mahsa H Javadi Danielle J Harvey Bernhard Haring Nora Franceschini Peter F. Schnatz John Robbins Patrick L Montine Ramesh Mazhari Janani Rangaswami Lorena Garcia

Background:

Kidney stones have been linked to an increased risk for cardiovascular disease (CVD). The relationship between CVD and kidney stones is influenced by interconnected factors like obesity, diet, and sedentary lifestyle. However, existing data lacked adjustment for a wide range of confounding variables. Also, the role of obesity as a potential effect modifier in this relationship remains unknown.

Objectives:

To evaluate whether self-reported kidney stones are associated with incident CVD (coronary heart disease (CHD) + stroke+ peripheral artery disease (PAD)+ Cause-specific mortality due to CVD) in postmenopausal women in the Women’s Health Initiative (WHI).

Methods:

In a prospective cohort study of 110,960 postmenopausal women ages 50-79 years without CVD at baseline, data from the WHI observational study (OS) and clinical trials (CT) were analyzed to assess the association between kidney stones and incident CVD. Kidney stone status was self-reported at baseline and during follow-up, treated as a time-varying, dichotomous variable (with 5,799 women reporting kidney stones at some point and 105,161 reporting no kidney stones). Incident CVD was identified based on self-reported diagnosis of CVD, centrally or locally adjudicated. At baseline, demographic and health history information were self-reported, while dietary data were collected using a validated food frequency questionnaire. Key covariates included: age, metabolic factors (osteoporosis, diabetes, high cholesterol, body mass index (BMI), and waist circumference, Waist-to-hip Ratio (WHR)), lifestyle risk factors (total energy expended from recreational physical activity, history of alcohol use and smoking), and sociodemographic conditions (race, ethnicity, neighborhood socioeconomic status (NSES), and region of residence).

Two-sample t-tests were applied to compare the means of each continuous variable between participants with and without kidney stones. Chi-square tests were used to compare the two groups on categorical variables. Cox proportional hazards models assessed the association of kidney stone and incident CVD adjusting for potential confounders. Cox regression models was conducted with the following models: Model 1adjusted for age at baseline. Model 2 additionally adjusted for metabolic factors. Model 3 added lifestyle-related risk factors to Model 2; Model 4 additionally included sociodemographic covariates.

Results:

Mean age for all participants was 62.8. Mean WHR differed slightly between groups [0.82 (±0.08) in kidney stone group, 0.79 (±0.08) in no kidney stone group, $p<0.0001$]. The racial/ethnic distribution was not significantly different between those with and without a history of kidney stones ($p= 0.5$). Additionally, participants with a history of kidney stones tended to have lower NSES, [73.4 (±8.5) in

kidney stone group, 75.2 (±7.3) in no kidney stone group, p<0.0001]. Over a mean follow-up of 16.5 years in the no kidney stone group, 14.4% developed CVD, with the following specific outcomes: 4.83% developed CHD, 4.24% developed stroke, and 0.77% developed PAD. In the kidney stone group, over a mean follow-up of 14.4 years, 14.7% developed CVD, with 5.06% developing CHD, 4.13% developing stroke, and 0.8% developing PAD.

The crude hazard ratio (HR) for incident CVD was 1.21, 95% confidence interval (CI) (1.15, 1.40), p<0.001, and after adjusting for age, metabolic factors, lifestyle risk factors and sociodemographic conditions, the HR was 1.10 with 95% CI of (1.09, 1.17), p=0.007. The crude hazard ratio (HR) for incident CHD was 1.18, [95% CI: (1.06, 1.30), p<0.01] and the multivariable-adjusted HR was 1.08 [95% CI of (1.01,1.15), p=0.05]. The crude hazard ratio (HR) for incident stroke was 1.18, [95% CI (1.06, 1.30), p=0.05] and the multivariable-adjusted HR was 1.07, [95% CI of (1.01,1.21), p=0.06]. The crude hazard ratio (HR) for incident PAD was 1.07, [95% CI (1.01, 1.19), p=0.6] and the multivariable-adjusted HR was 0.96 [95% CI of (0.88, 1.16), p=0.67].

Conclusion:

Kidney stones are associated with an increased risk of CVD, CHD, and stroke in postmenopausal women but not with PAD. Individuals with a history of kidney stones may represent a high-risk group that could be targeted for early lifestyle/behavioral and other CVD-prevention strategies.

Women’s Health

Physical activity during pregnancy and gestational weight gain among nulliparous women
Tingju Hsu* Tingju Hsu Tsung Yu

Introduction: Excessive gestational weight gain (GWG) is associated with adverse pregnancy outcomes and longer-term obesity in both mother and child. Physical activity (PA) may mitigate these risks, yet optimal timing and quantity remain unclear. **Method:** We analyzed the association between PA and excess GWG among 5724 participants from the Nulliparous Pregnancy Outcomes Study: Monitoring Mothers-to-be (nuMoM2b). Participants reported their PA at 3 study visits: between 6–13 (visit 1), 16–21(visit 2), and 22–29 weeks (visit 3). Weekly PA was summed into metabolic equivalents (MET) and categorized with 3 levels: less than 7.5, 7.5 to less than 21, and 21 or above MET hours. Weights were measured at each visit. Pre-pregnancy weight and weight prior to delivery were also available. Excessive GWG was defined as above 75th percentile on gestational age-specific charts based on participants’ pre-pregnancy BMI. We used logistic regression models to evaluate associations between PA and excessive GWG at visit 2 and prior to delivery. **Results:** There was no difference in the odds of excessive GWG among participants with 3 PA levels in early pregnancy at visit 2. On the other hand, the participants with weekly PA of 21 MET hours or above had a significantly lower risk of excessive GWG (OR=0.74 with 95% CI [0.61,0.90]) compared to participants with weekly PA <7.5 MET hours during later pregnancy prior to delivery. The OR was attenuated and became statistically insignificant but remained in the same direction (adjusted OR=0.83 with 95% CI [0.68, 1.02]) after adjusting for age, race-ethnicity, socio-economic status, alcohol and tobacco consumption, dietary intake and comorbidities. No significant difference in excessive GWG was found between participants with <7.5 and 7.5 to <21 weekly MET hours. **Conclusions**: These findings underscore the nuanced impact of prenatal PA timing and quantity and support the promotion of PA throughout pregnancy to minimize excessive GWG at delivery.

Women’s Health

The association between experiencing racial discrimination and delivery method among women in the United States, PRAMS 2016-2021 Chelse Spinner* Chelse Spinner Lorenzo Hopper Sharon Watson Janaka Lewis Michael Dulin

Introduction: Racial and ethnic disparities in cesarean birth persist, resulting in increased risk of complications. However, the efforts to explain these phenomena have not considered the influence of structural factors. The purpose of this study was to examine the association between experiencing racial discrimination and delivery method, as well as to observe women’s experiences with racial discrimination.

Methods: Data from the 2016-2021 Pregnancy Risk Assessment Monitoring System was used for this secondary data analysis of nulliparous and primiparous women of reproductive age (N=27, 994). The exposure variable was measured using two questions on racial discrimination, and information on the outcome variable was obtained from the birth certificate data. Logistic regression was used to model the association between experiencing racial discrimination and delivery method.

Results: Within the population, minority women (non-Hispanic Black, Hispanic, and non-Hispanic Other women) experienced significantly increased odds of experiencing racial discrimination in comparison to non-Hispanic White women. Racial discrimination was significantly associated with primary cesarean birth in the bivariate analysis (OR, 1.19; 95% CI, 1.03-1.38); however, this relationship became marginally significant after adjustment for confounders (OR, 1.09; 95% CI, 0.94-1.28).

Discussion: Although the association between racial discrimination and delivery method was not statistically significant, even after stratification by race/ethnicity, future research should focus on expanding current measures of racial discrimination in population-based datasets. There is a missed opportunity to understand and explore the experiences of racial discrimination and delivery method, especially during labor/delivery. A comprehensive view of the mechanisms by which racial disparities in cesarean birth continue to operate is critical to reducing health inequities.

LATEBREAKER

Women’s Health

Elucidating the relationships between vulvodynia, immune conditions, and the vaginal microbiome Rebecca Fisher* Rebecca Fisher Julia Bond Bernard Harlow

Background: Vulvodynia is a poorly understood pain condition that affects 7-8% of women by age 40. To shed insight into its complex etiology, we aimed to elucidate the relationship between chronic immune conditions (a known contributor to vulvodynia) and the vaginal microbiome using data from a clinically-confirmed case-control study of vulvodynia. **Methods:** We analyzed data from a case-control study of 213 vulvodynia cases and 220 controls who were recruited from a large healthcare database. We used a directed acyclic graph (DAG) to depict hypothesized relationships between variables. We created a binary variable indicating a history of any chronic immune condition. Vaginal microbiome diversity was assessed using the Shannon diversity index (dichotomized above/below the sample median), and community state types (CSTs) were identified using an unsupervised clustering method. We calculated adjusted odds ratios relating microbiome characteristics to vulvodynia using logistic regression models which we stratified by a history of immune conditions. **Results:** We saw no evidence of effect modification of the association between alpha diversity and vulvodynia by a history of chronic immune conditions. When evaluating CST, stratification by a history of immune conditions resulted in two adjusted odds ratios (aORs) in different directions. The aOR for CST 1-3 vs CST 4-6 was 1.54 (95% CI: 0.91-2.62) among those with an immune condition, whereas the odds of vulvodynia was 0.49 (95% CI: 0.22-1.06) for those without immune conditions, raising the possibility of effect modification. Using our DAG, we did not conduct a planned analysis stratified by microbiome characteristics due to the possibility of collider stratification bias. **Conclusion:** Our findings suggest that there may be an interaction between the vaginal microbiome and history of immune conditions and highlight the utility of DAGs in elucidating complex relationships in this understudied condition.

LATEBREAKER

Women’s Health

Uncovering the Diagnostic Journey of Endometriosis Patients of Color Isabella Caruso*
Isabella Caruso Katherine Reeves

Background:

Despite the significant public health impact, there is minimal research examining endometriosis among racially and ethnically diverse populations. This study aims to gain important perspectives by providing Black women with a space to share their experiences and beliefs about their endometriosis diagnostic journey.

Methods:

Semi-structured, in-depth interviews were conducted virtually to explore the experiences of endometriosis diagnosis and treatment in Massachusetts. Twenty-five self-identified Black women with a self-reported endometriosis diagnosis participated in interviews conducted between June 2023 – August 2023. Interviews were analyzed with a thematic approach to examine emerging key themes.

Results:

The lived experiences of twenty-five participants revealed several key barriers to diagnosis, including cultural beliefs and taboos, normalization of symptoms, and negative interactions with healthcare providers. Additionally, participants shared how endometriosis affects various aspects of their lives, most notably, impacting their intimate relationships, friendships, careers, finances, and mental health.

Conclusions:

Our findings highlight the critical barriers Black women face in obtaining a timely endometriosis diagnosis and receiving compassionate healthcare. More research should be conducted among racially diverse populations to improve our understanding to improve culturally responsive care to address the specific barriers faced among diverse populations.