2024 Annual Meeting

Abstract Book

June 18-21, 2024

Maternal mortality after adolescent and young adult cancer: a population-based study

Caitlin Murphy* Caitlin Murphy Andrea Betts Jennifer Wang Philip Lupo L. Aubree Shay Marlyn Allicock Sandi Pruitt

Background: Adolescents and young adults with a history of cancer (AYAs) have excess risk of adverse birth outcomes, including cesarean delivery and preterm birth. Maternal mortality in this population has not been well-described. To address this gap, we examined maternal mortality in a diverse, population-based sample of AYAs.

Methods: We identified female AYAs diagnosed with cancer at age 15-39 years from January 1, 1995 to December 31, 2015 using data from the Texas Cancer Registry. These data were linked to live birth and fetal death certificates through December 31, 2016 to identify births after diagnosis, excluding births to AYAs diagnosed during pregnancy. We defined maternal mortality as any death within one year of delivery and estimated risk using a Poisson model with robust standard errors.

Results: There were 11,263 births to 8,333 female AYAs after diagnosis. AYAs were commonly diagnosed with thyroid (28.4%), lymphoma (13.2%), and breast (11.2%) cancers; 8.7% were non-Hispanic Black and 29.3% were Hispanic. Mean time from diagnosis to first post-diagnosis birth was 4.3 years (SD=3.0), and mean maternal age at first post-diagnosis birth was 31.0 years (SD=5.5). Risk of maternal mortality was 0.69% (95% CI 0.55%, 0.87%), ranging from 0.03% (95% CI 0.01%, 0.09%) for AYAs with thyroid cancer to 1.51% (95% CI 0.94%, 2.42%) and 1.53% (95% CI 0.64%, 3.67%) for AYAs with breast and gastrointestinal cancer, respectively. Risk also differed by race/ethnicity. For example, non-Hispanic Black (RR 3.38, 95% CI 1.86, 6.17) and Hispanic (RR 1.75, 95% CI 1.05, 2.89) AYAs had higher risk compared to non-Hispanic White AYAs.

Conclusions: Risk of maternal mortality in AYAs is low – less than 1%. However, we observed striking differences in maternal mortality by race/ethnicity, adding to overwhelming evidence on maternal and reproductive health inequities. Additional work is needed to identify mechanisms of disparities and strategies to improve birth equity for AYAs.

Cancer

Pregnancy and cervical cancer: a retrospective study of the associations of age at first pregnancy and parity with non-invasive and invasive cervical lesions among HIV-negative women in Senegal Mariama Bah* Mariama Bah Steve Hawes Rachel L. Winer Selly Ba Qinghua Feng Geoffrey S. Gottlieb Papa Salif Sow Marie Pierre Sy Nancy Kiviat John Lin

Cervical cancer is the leading cause of cancer-related deaths among Senegalese women. There is limited knowledge about the roles of age at first pregnancy (AFP) and parity in developing cervical intra-epithelial neoplasia (CIN) and invasive cervical cancer (ICC) in this population. We investigated the associations of AFP and parity with any CIN and ICC using data from four studies on cervical HPV/dysplasia/cancer conducted in Senegal between 1998 and 2011. Eligibility included being HIV-negative, 18 years or older, not currently pregnant, and having either cervical histology or cytology results. Missing data were imputed with Multiple Imputation by Chained Equations in R. AFP was grouped as 12-14, 15-16, 17-20, 21-24, and 25+, and parity as 0, 1-2, 3-4, 5-6, and 7+, with 21-24 and 1-2 as references, respectively. We conducted multinomial logistic regression in the general and HPV-positive (any type) populations. We adjusted for age, age at sexual initiation, marital status/type, lifetime number of male sex partners, birth control, smoking, and study. Among the 5,588 women in this study, the median AFP was 18 years (range: 12-42) and the median number of live births was 5 (range: 0-16). Younger AFP was associated with higher risks of CIN and ICC compared to older groups in both populations. In the general population, the associations of AFP and CIN were significant for the 12-14 (Odds Ratio (OR)=2.01, 95% CI:1.06-3.83) and 15-16 (OR=1.72, 95% CI:1.02-2.88) AFP groups. Parity was positively associated with CIN and ICC in both populations. Having 3-4 live births was significantly associated with ICC (OR=1.73, 95% CI:1.10-2.71) in the general population, and with CIN (OR=2.20, 95% CI:1.20-4.02) and ICC (OR=2.26, 95% CI:1.12-4.60) in the HPV-positive population. Early AFP had higher risks of CIN and higher parity had higher risks of CIN and ICC among HIV-negative women in Senegal. These findings can help inform future cancer prevention and screening strategies.

Cancer

The Role of HPV E6 oncoprotein as a biomarker in anal cancer screening in persons living with HIV Faiza Faria* Faiza Faria Stephen E. Hawes John Lin Jeffrey Schouten Helen C. Stankiewicz Karita Stephen L. Cherne Anjali Vasavada Ruanne V. Barnabas Judith Wasserheit Qinghua Feng Rachel L. Winer

Persons living with human immunodeficiency virus (PLWH) are at elevated risk for anal cancer compared with the general population. Human papillomavirus (HPV) types 16 and 18 cause most anal cancers; E6 oncoprotein expression plays a key role in anal carcinogenesis. We evaluated the performance of HPV 16/18 E6 oncoprotein for detecting anal high-grade squamous intraepithelial lesions (HSIL) in 125 specimens from 82 PLWH undergoing screening, high-resolution anoscopy (HRA) or treatment in Seattle, Washington (2015-2016). Demographic and clinical data, anal cancer screening, diagnosis, and treatment results, were collected from medical records. Anal brush samples were tested for type-specific high-risk HPV (hrHPV) DNA. Samples positive for HPV 16/18 (n=48) were tested for E6 oncoprotein. We described performance of HPV16/18 E6 oncoprotein, HPV16/18 DNA and any hrHPV DNA as biomarkers for HSIL detection (n=49). We calculated prevalence ratios (PR) for associations between these biomarkers and HSIL using a generalized linear model with a Poisson family and robust variance adjusted for CD4 count, HIV viral load, and age. HPV 16/18 E6 (n=3) was more specific but less sensitive than HPV16/18 DNA and any hrHPV DNA. HPV 16/18 E6+ showed 100% specificity, 100% positive predictive value and an adjusted PR of 6.23 (95% CI: 1.12, 34.50) for HSIL compared to hrHPV negative samples; but low sensitivity (6.1%) and moderate negative predictive value (62.3%). We evaluated HSIL disease extent data from HRA impression and found that 50% of four HSILs with >75% disease extent had E6+ samples, whereas none of 30 HSILs with <25% disease extent had E6+ samples. Results demonstrate that HPV 16/18 E6 oncoprotein is highly specific for identifying HSIL and may be useful for prioritizing lesions at the highest risk for cancer. Longitudinal studies may establish E6 oncoprotein's role in early detection and prevention of anal cancer, either on its own or in combination with other biomarkers.

Cancer

Development of algorithms to identify screen-detected lung, breast, and colorectal cancers in cancer registry-linked claims data Sarah Soppe* Sarah Soppe Sharon Hinton Peacock Allison Verbyla Walker Redd Caroline A. Thompson

Population-level screening is a critical tool to reduce cancer burden through earlier detection and improved survival. While trends in screening rates in the general population can be documented through national surveys, less is known about the proportion of cancer patients whose cancer was diagnosed as a result of screening. The prevalence of "screen-detected cancers" is an underused but important metric that could be abstracted from routine data to evaluate screening effectiveness over time, yet validated algorithms for classifying screen-detected cancers in claims have not been established. Thus, this project aimed to develop cancer site-specific algorithms to classify screen-detected lung, breast, and colorectal cancers in SEER-Medicare data to estimate the proportion of screen-detected cancers. The study population included patients at least 66 years old diagnosed with their first invasive cancer between 2008 and 2017, excluding those not of a screening-eligible age and those without at least 12 months of pre-diagnosis continuous enrollment in fee-for-service Medicare Parts A/B. Algorithmic classification depended on the type and order of procedure codes in the pre-diagnostic lookback period (e.g., codes for low-dose computed tomography in the 3 months before lung cancer diagnosis), considering the commonly used diagnostic investigations for each site. In our representative sample of older adults with cancer, less than 1% of lung cancer diagnoses were screen-detected compared to 83% of breast and 22% of colorectal cancers. Screen-detected cancer prevalence was also examined by calendar year, cancer stage, age at diagnosis, race and ethnicity, and sex, among other clinical and demographic variables. These algorithms will be applied in statewide multi-payer claims linked to registry data to assess their implementation among younger age groups, while validation using electronic health records as a reference standard will enable further algorithm refinement.

Accounting for endoscopic screening in colorectal cancer risk prediction models Bernard Rosner* Esther Wei Kana Wu Graham Colditz Edward Giovannucci Walter C. Willett Andrew T. Chan Minyang Song Bernard Rosner

Colorectal cancer (CRC) risk models routinely adjust for endoscopic screening to account for the presence/absence of adenoma. Also, high-risk adenoma is associated with increased risk of CRC. Thus, inclusion of screening in multivariate models as a confounder does not account for the possibly undetected adenomas among those not screened. In this study, using 45,538 participants from the Nurses' Health Study for whom we have updated endoscopy data from 1986, we defined a subject as screen-covered (SC) if a colonoscopy was performed in the past 10 years, and not screen-covered (NSC) otherwise. A CRC risk model (Model 1) was fit for SC subjects (765 cases, 205,012 person-years (py)) based on adenoma status at colonoscopy and other risk factors. A separate risk model (Model 2) for adenoma (2570 high-risk adenomas, 134,951 colonoscopies) was fit accounting for repeated endoscopies. Models 1 and 2 were used to estimate the direct, indirect (mediated thru adenoma), and total effects of risk factors with CRC risk among SC subjects (yielding ln_HR_SC). We fit a separate ordinary CRC risk model for NSC subjects (454 cases, 317,387 py) without considering their unknown adenoma status (yielding ln_HR_NSC). Finally, we obtained a screening-adjusted HR (HRfull) by taking a weighted average of ln_HR_SC and ln_HR_NSC based on the proportion of screen-covered person-time in the entire population (39%). Comparing HR estimates of unadjusted and fully-adjusted models, we found that effects of screening were small for most risk factors. However, the HR for age became stronger after full adjustment (HRunadjusted= 1.65 (1.53,1.78); HRfull= 1.88 (1.73, 2.05)), while the HR for current PMH use became weaker (HRunadjusted= 0.66 (0.54, 0.82); HRfull= 0.86 (0.71, 1.05)). In summary, we have demonstrated a novel approach to estimate and reduce the confounding effect of screening in estimating associations of CRC risk factors.
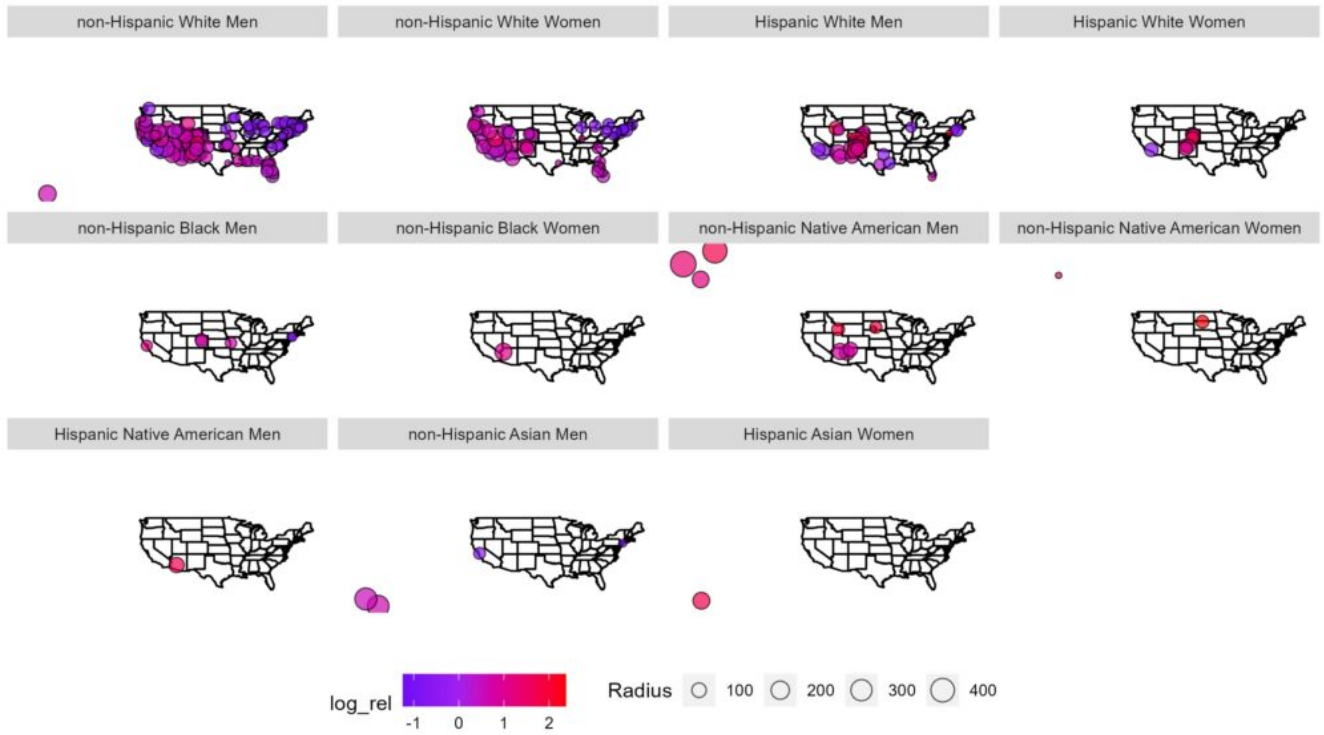
Health Disparities

Intersectional group differences in the spatiotemporal patterning of suicide deaths in the US Amanda Sursely* Amanda Sursely Jonathan Platt

Objective: To identify the spatial and temporal trends in suicide clusters across intersectional social identity groups in the US population from 2005-2020.

Methods: US Vital Statistics data were used to calculate county-level suicide rates from 2005-2020. Rates were calculated for sixteen intersectional groups, defined by unique combinations of racial identity, ethnicity, and gender. We identified spatiotemporal suicide clusters among these groups using the SaTScan space-time statistic to identify areas of lower- and higher-than-expected suicide rates (cold and hot clusters). We also calculated the average proportion of deaths by suicide contained within these clusters to quantify the relative importance of clusters among overall suicide rates.

Results: 275 clusters were identified, comprising 11.4% of total suicides. Patterns of clustering were geographically (see Figure 1) and temporally distinct among intersectional groups. The number of clusters varied across groups, ranging from one in non-Hispanic Black Women to 135 in non-Hispanic White men, comprising a respective 0.4% and 8% of those group suicide deaths. The number and magnitude of hot clusters increased among Hispanic White men and women over time, and the highest overall magnitude clusters were observed in non-Hispanic Native American women. No significant clusters were identified among Hispanic Black Men and Women, or non-Hispanic API Women. Hot clusters were identified in 25 states, particularly in the Western region. Colorado contained the most clusters of any state (31). In contrast, cold clusters were most prevalent in the Northeast.

Conclusions: Suicide rates and clusters have increased since 2005, requiring attention from policy makers, clinicians, and caretakers. Distinct patterns between intersectional groups highlight opportunities to tailor individual- and population-level prevention efforts to prevent suicide deaths in emerging high-risk groups.

non-Hispanic White Men | non-Hispanic White Women | Hispanic White Men | Hispanic White Women

non-Hispanic Black Men | non-Hispanic Black Women | non-Hispanic Native American Men | non-Hispanic Native American Women

Hispanic Native American Men | non-Hispanic Asian Men | Hispanic Asian Women

log_rel
-1 0 1 2

Radius ◯ 100 ◯ 200 ◯ 300 ◯ 400

Evaluating Firearm Violence After New Jersey's Cash Bail Reform Jaquelyn Jahn* Jaquelyn Jahn Jessica T. Simes Jonathan

Background: Reducing pretrial detention (i.e. people incarcerated in jails) has been a cornerstone of movements to end mass incarceration. Across many U.S. cities, there are ongoing public debates on policies that would end pretrial detention due to the inability to afford bail, including oppositional concerns that doing so would increase community violence.

Objective: To evaluate changes in firearm violence after New Jersey's 2017 bail reform policy.

Methods: We used augmented synthetic control models to examine changes in firearm mortality and combined fatal and non-fatal shootings in New Jersey (2014-2019). We focused on New Jersey because it was one of the first states to implement cash bail reform. We compared quarterly rates of fatal and nonfatal firearm assault injuries and firearm self-harm injuries per 100,000 people in New Jersey to a weighted combination of states that did not implement any kind of reform to pretrial detention during the study period. Models matched on a variety of auxiliary covariates, and CIs calculated using the conformal inference method.

Results: New Jersey's pretrial detention population dramatically decreased under bail reform. We did not find evidence of increases in firearm mortality or gun violence, overall or within Black and White racialized groups during the post-policy period, despite rising rates of gun violence nationally during these years. The cumulative ATT for firearm mortality was -0.13 (95% CI: -0.53, 0.23).

Conclusions and relevance: Incarceration and gun violence are significant public health problems impacting racially and economically marginalized groups. Cash bail reform may be an important tool for reducing pretrial detention and advancing health equity without exacerbating community violence.

Social

Historic redlining and accelerated biological aging in U.S. urban adolescents Sarah Laurent*

Sarah Laurent Helen C.S. Meier Lorraine Halinka Malcoe

Background: Historic redlining has shaped present-day neighborhoods, inequitably exposing residents of formerly redlined regions to harmful conditions and stressors. Neighborhood disadvantage can accelerate biological aging measured via DNA methylation epigenetic clocks.

Objective: We examined the association between historic redlining and epigenetic accelerated aging in adolescents.

Methods: Data come from the Future of Families and Child Wellbeing Study. A total of 1,686 adolescents provided saliva samples used to derive DNA methylation accelerated aging (DNAmAA). Historic redlining scores assessed the proportion of census tracts graded by the Home Owners' Loan Corporation (HOLC) "residential security" maps from the early 20th century multiplied by a weighted HOLC grade. Census tracts were categorized as "high" or "low" redlining; areas minimally assessed by HOLC were marked as "ungraded". We used linear regression models to examine the association between redlining categories and DNAmAA using 8 epigenetic clocks, adjusting for age, baseline city, assay type, cell proportion, mother's smoking during pregnancy and household poverty ratio.

Results: Residence in high redlining tracts was strongly racialized ($p<0.001$): 35.1% of Hispanic and 45.3% of non-Hispanic Black adolescents lived in high redlining tracts versus 12.7% of non-Hispanic whites. After adjusting for covariates, adolescents living in high redlining tracts had greater DNAmAA compared to those living in ungraded regions among the GrimAge ($p<0.001$), Horvath ($p=0.008$), PhenoAge ($p=0.019$) and Skin/Blood clocks ($p=0.022$). Sub-sample analyses examining non-Hispanic Black and Hispanic participants alone showed no significant associations.

Discussion: This study is the first to show how historic redlining may become biologically embedded in adolescents living in U.S. urban areas. Findings suggest that historic structural racism drives present-day health inequalities in adolescents via accelerated biological aging.

The relationship between anti-LGBTQ+ legislation and internalized HIV-related stigma among young sexual and gender minorities Nicole K. Kelly* Nicole K. Kelly Shabbar Ranapurwala Brian W. Pence Lisa B. Hightow-Weidman Audrey French Sybil Hosek Audrey Pettifor

Background: A multitude of anti-LGBTQ+ laws targeting young sexual and gender minorities (YSGM) have been introduced in the United States. YSGM experience a high risk of HIV and related stigma, with inequities by race. Stigma is a key barrier to ending the HIV epidemic, but the relationship between structural LGBTQ+ stigma and individual HIV stigma has not been quantified. We examined the association between state-level LGBTQ+ laws and HIV stigma among YSGM, overall and by race and ethnicity.

Methods: Keeping it LITE-1 was a prospective, national cohort of 3,330 HIV-negative YSGM from 2017-2022. Biannual surveys included an internalized HIV stigma scale (range: 7 (low), 28 (high)). Geolocation was linked with state-level LGBTQ+ policy data from the Movement Advancement Project (MAP). LGBTQ+ laws were characterized as less or more discriminatory based on MAP score distributions. We used linear regression with GEE to estimate the longitudinal association between state-level LGBTQ+ policy and individual HIV stigma.

Results: The cohort identified as 10.7% non-Hispanic (NH) Black, 4.6% NH Asian, 19.8% Latine, 53.9% NH White, and 11.0% another race. Living in states with less discriminatory LGBTQ+ policies was associated with a -0.72 mean difference in internalized HIV stigma compared to living in states with more discriminatory laws (95% CI: -0.97,-0.47). NH White YSGM living in less discriminatory states experienced the largest reduction in HIV stigma [White: -1.01 (-1.30,-0.72); Black: -0.36 (-0.90,0.18); Asian: -0.53 (-1.16,0.09); Latine: -0.23 (-0.67,0.21), unknown/multiracial: -0.56 (-1.09,-0.04)].

Conclusions: Living in states with more progressive LGBTQ+ policies was associated with less internalized HIV stigma, particularly among NH White YSGM. Progressive state-level LGBTQ+ policies may not be enough to offset HIV stigma for marginalized racial groups; future studies should examine the intersection of LGBTQ+ laws with ethno-racism, homophobia, and HIV stigma.

Figure 1. Distribution of internalized HIV stigma scores at baseline among a national sample of young sexual and gender minorities, stratified by self-reported race and ethnicity
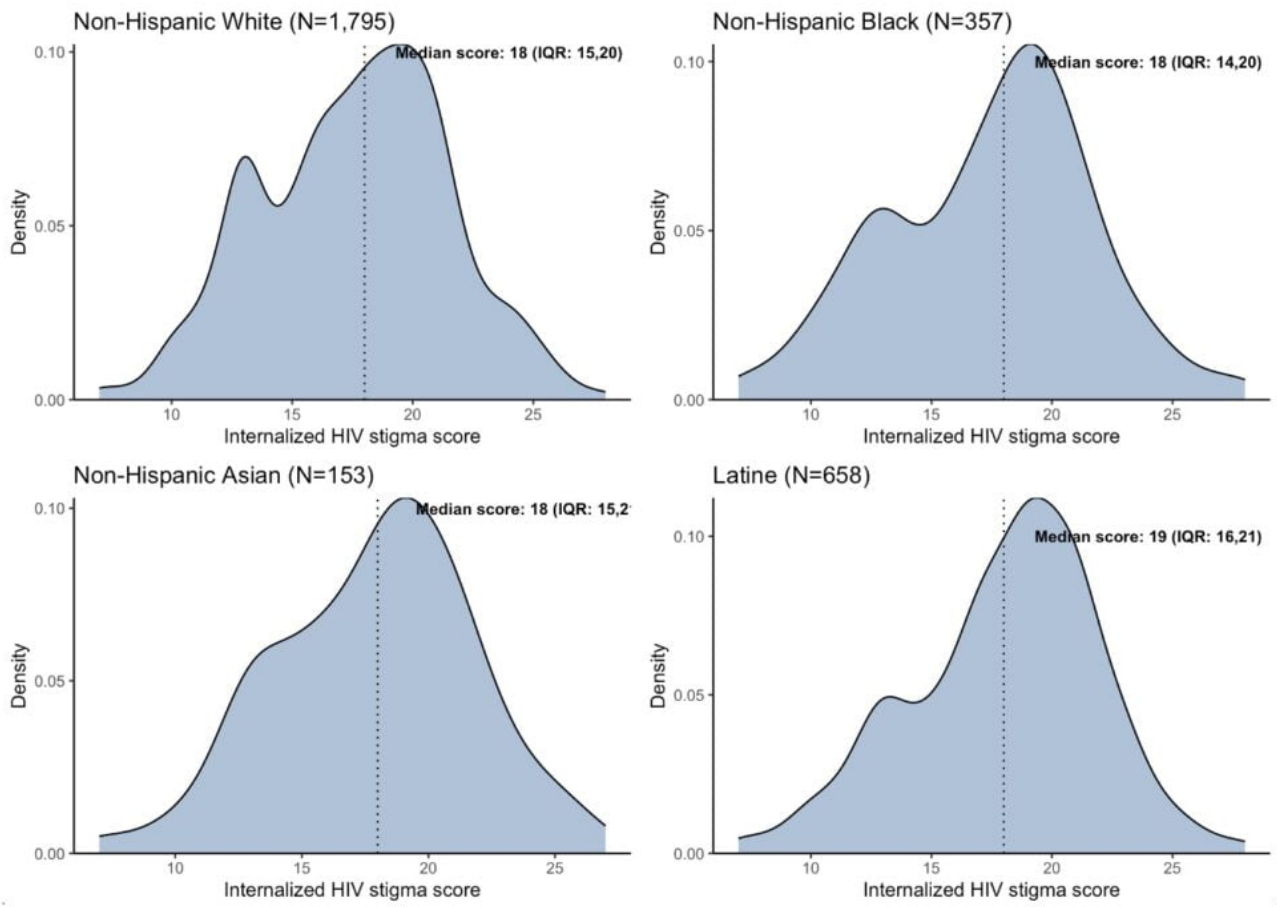
Race adjustment hides systemic racism: Real world example using lifetables Shabbar I Ranapurwala* Shabbar Ranapurwala Serita Coles Scott K. Proescholdbell Shana Geary Brian W. Pence

One of the best methods to calculate the societal burden of a public health problem is to examine the lost societal potential due to the problem, usually conceptualized as the years of potential life lost (YPLL). However, many studies use race-specific lifetables to calculate YPLL to adjust for varying life expectancies in racialized groups. We examined the implications of this race adjustment on YPLL due to suicide and homicide deaths among black and white residents of North Carolina (NC), where suicide and homicide death rates are similar to the US average. We used data from the North Carolina Violent Death Reporting System (NC-VDRS) from 2006-2019 to identify suicide and homicide deaths and used race-adjusted and -unadjusted life tables from the Centers for Disease Control and Prevention from 2006-2019 to calculate YPLL. From 2006-2019, there were 17,385 suicide deaths and 7,668 homicide deaths among black and white NC residents. Using race-unadjusted life tables, the YPLL from suicide deaths was 532,347.5 years (33.7 YPLL/death) for white NC residents and 68,293.4 years (43.1 YPLL/death) for black NC residents. However, when using race-adjusted life tables the total YPLL declined to 63,879.4 (40.3 YPLL/death) among black NC residents but remained almost identical for white NC residents at 532,383.1 (33.7 YPLL/death). With race adjustment, the YPLL/suicide death difference comparing black and white NC residents was 6.6 years (95% CI: 5.9, 7.4) relative to 9.9 years (8.7, 10.2) without race adjustment, with an overall underestimate of 4,414 YPLL for black NC residents. Similarly, the race adjusted YPLL/homicide death difference was 6.4 years (5.8, 7.1) relative to 9.5 years (8.8, 10.2) without race adjustment, an underestimate of 14,907 YPLL from homicides among black NC residents. The race-adjusted YPLL example shows how race adjustment masks and perpetuates systemic racism by hiding the magnitude of the problem and impacting resource allocation.

Figure 1: Potential years of life lost (PYLL) per death by race and race adjustment among homicide and suicide decedents from 2006 to 2019: A - Sucide deaths; B - homicide deaths
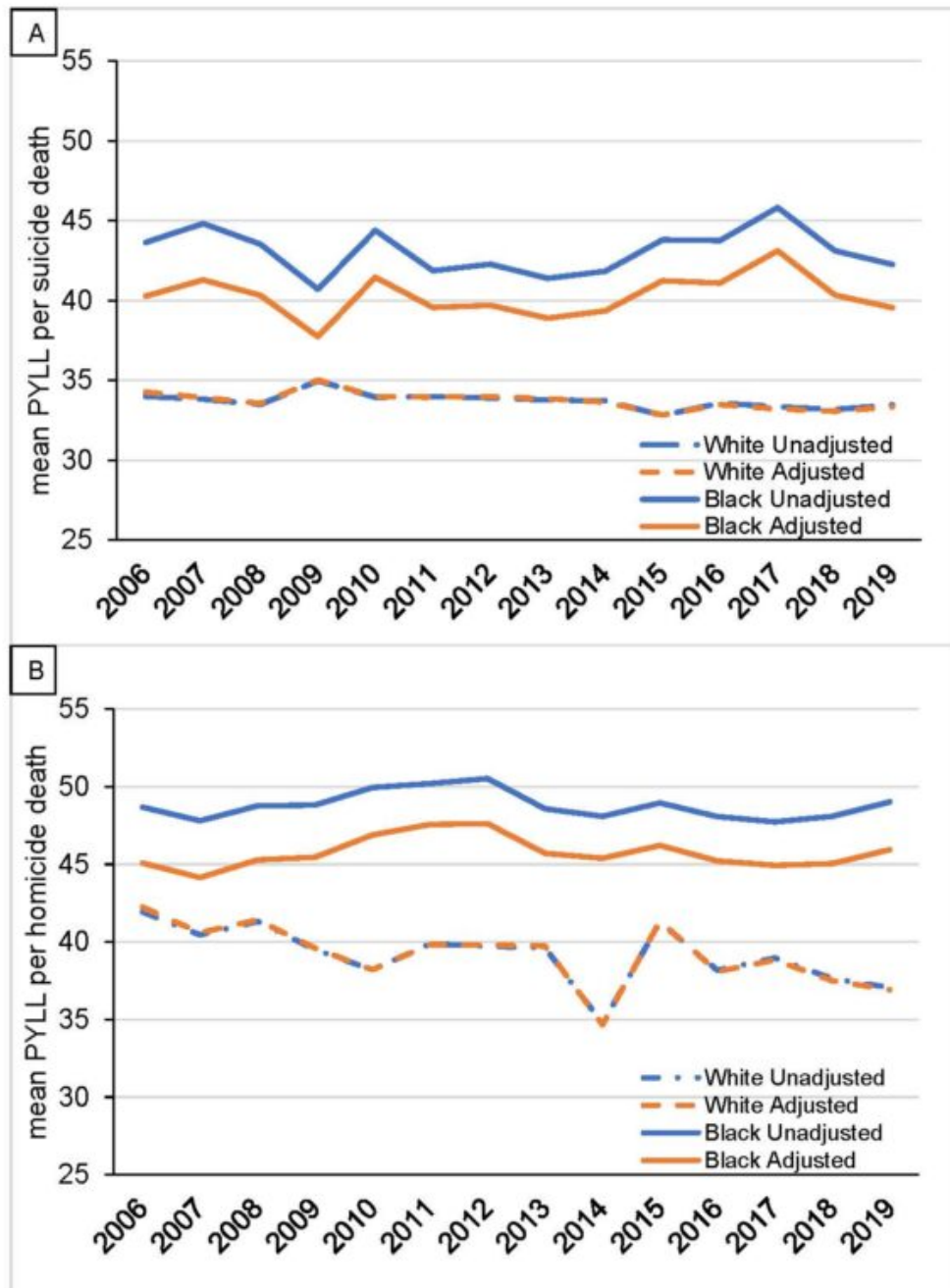
Constructing a multidimensional measure of structural racism: A balancing act between simplicity and complexity Lauren E. Barber* Lauren Barber Maret L. Maliniak Leah Moubadder Jasmine M. Miller-Kleinhenz Jeffrey M. Switchenko Michael R. Kramer Lauren E. McCullough

Structural racism is a complex multidimensional construct. However, prior studies have failed to incorporate this multidimensionality. In this study, we describe methods for operationalizing a multidimensional structural racism measure and consider its challenges.

County-level data on 24 indicators representing six domains (criminal justice, education, employment, healthcare, housing, and political participation) were obtained from sources including the American Community Survey. Indicators were measured separately for Black and White populations in 115 Georgia counties with available data. For each indicator, a racial inequity ratio was calculated such that higher values indicated White advantage. Domain-specific principal component analyses (PCA) were performed to identify indicators for inclusion in the multidimensional structural racism measure. Indicators with loading values >0.4 were selected from each domain and included in a cross-domain PCA. Loading values for the first principal component were assessed and used as weights to derive a multidimensional measure.

Domain-specific PCAs identified 12 indicators for inclusion in the multidimensional measure such as incarceration, household income, mortality, and voting ratios, and school dissimilarity and Thiel's H indices. The first principal component from the cross-domain PCA, which summarized the structural racism construct, explained only 29% of the variation. Employment, healthcare, and housing indicators had the highest loading values (0.32-0.39).

Providing a transparent method for constructing a multidimensional structural racism measure can advance the study of structural racism as a determinant of health. However, researchers may be challenged with balancing potentially oversimplifying the structural racism construct and adequately capturing its underlying complexity. Varying the type and number of indicators may help strike a balance. Ongoing work to develop a valid structural racism measure is critical.

Cancer

Target trial emulation of dynamic surveillance strategies for cancer survivors: an application to non-muscle invasive bladder cancer Emma E. McGee* Emma E. McGee Xabier García de Albéniz Barbra A. Dickerman Kendrick Yim A. Heather Eliassen Mark A. Preston Miguel A. Hernán

More than 60,000 U.S. adults are diagnosed with non-muscle invasive bladder cancer each year. These patients are recommended to undergo surveillance via repeated cystoscopies. However, the ideal frequency of surveillance remains unknown.
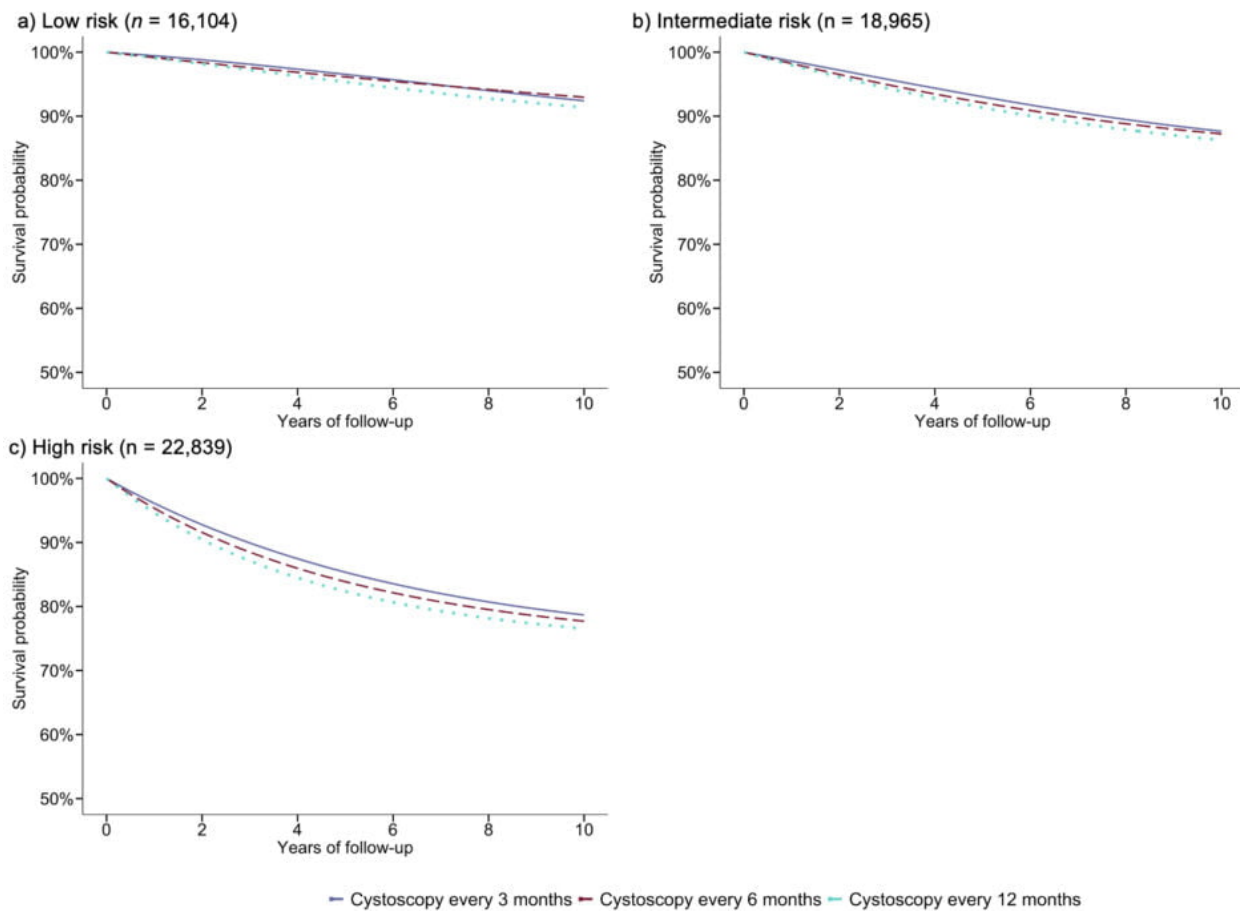
We used observational data from Surveillance, Epidemiology, and End Results (SEER)-Medicare to emulate 3 target trials comparing 10-year risks of bladder cancer mortality under cystoscopy every 3, 6, and 12 months among low, intermediate, and high risk patients. Risks were estimated using inverse probability weighted dynamic marginal structural models.

There were 16,104 low, 18,965 intermediate, and 22,839 high risk eligible individuals. Over 10 years, 5,288 bladder cancer deaths occurred. Among high risk patients, 10-year bladder cancer mortality risks were 21.3% under the 3 month strategy, 22.3% under the 6 month strategy, and 23.5% under the 12 month strategy. Risk differences (95% CI) were 1.0 (-0.9, 2.8) for 6 vs. 3 and 2.1 (0.1, 4.0) for 12 vs. 3 months. For intermediate risk patients, mortality risks were 12.4% under the 3 month strategy, 12.8% under the 6 month strategy, and 13.7% under the 12 month strategy. Risk differences were 0.4 (-1.1, 2.3) for 6 vs. 3 and 1.4 (-0.4, 3.3) for 12 vs. 3 months. For low risk patients, mortality risks were 7.6% under the 3 month strategy, 7.0% under the 6 month strategy, and 8.6% under the 12 month strategy. Risk differences were -0.6 (-2.3, 1.1) for 6 vs. 3 and 1.0 (-1.1, 3.1) for 12 vs. 3 months. When we mirrored the approach of prior observational studies which deviated from a realistic target trial, the direction of effect estimates switched.

We estimated that more frequent cystoscopy may result in reductions in bladder cancer mortality among high risk patients. Among low and intermediate risk patients, surveillance every 6 months may not meaningfully increase mortality as compared with every 3 months. Analyses which failed to emulate a target trial produced starkly different results.

Figure 1. Bladder cancer mortality-free survival curves under different cystoscopy surveillance strategies in low, intermediate, and high risk non-muscle invasive bladder cancer, Surveillance Epidemiology and End Results (SEER)-Medicare linked data (2000 – 2018).

a) Low risk (*n* = 16,104)

b) Intermediate risk (n = 18,965)

c) High risk (n = 22,839)

— Cystoscopy every 3 months — Cystoscopy every 6 months — Cystoscopy every 12 months

Comparison of Breast Cancer Risk Prediction in Models in a Population of Hispanic Women Molly Rogers* Molly Rogers Annie DiFrank Min Shi Clarice Weinberg Mary Diaz-Santana

Background: Among Hispanic women, breast cancer is the most frequently diagnosed malignancy and the leading cause of cancer death. Risk prediction models are used as a tool in precision prevention for risk stratification. However, widely used breast cancer risk prediction tools have been reported to overall either underestimate or overestimate breast cancer risk in Hispanic women. We used data on Hispanic women from the Sister Study to compare the performance of two frequently used breast cancer risk prediction models.

Methods: Using longitudinal data from Hispanic women in the Sister Study (N = 2,462) we compared the predictive performance of two breast cancer risk prediction models, the Breast and Ovarian Analysis of Disease Incidence and Carrier Estimation Algorithm (BOADICEA) and the Breast Cancer Risk Assessment Tool (BCRAT). We compared model performance at 5 years follow-up in all Hispanic women, as well as stratified by country of birth Calibration was assessed by calculating the expected to observed ratios(E/O) and 95% confidence intervals. Model discrimination was examined using ROC curves and c-statistics.

Results: At 5 years follow-up 60 breast cancer cases had accrued. The BOADICEA model had better calibration than BCRAT overall (E/O 0.87(95%CI 0.68-1.12) vs. 0.76(95%CI 0.59-0.98)) and in US-born Hispanic women(E/O 0.74(95%CI 0.52-1.05) for BOADICEA, and 0.47(95%CI 0.33-0.67) for BCRAT). The two models were similarly calibrated in foreign-born Hispanic women(E/O 1.01(95%CI 0.70-1.46) for BOADICEA, and 1.06(95%CI 0.74-1.53) for BCRAT). The estimated c-statistic(AUC) for overall Hispanic women was .64(95%CI 0.57-0.71) for BOADICEA and .57(95%CI 0.50-0.64) for BCRAT.

Conclusions: Our results suggest that both models underestimate BC risk in Hispanic women. However, BOADICEA performs better than BCRAT, particularly within the US-born Hispanic population. Further research should be done to improve risk prediction models specific to Hispanic women.

Performance of the BCRAT and BOADICEA models in terms of the sensitivity and specificity
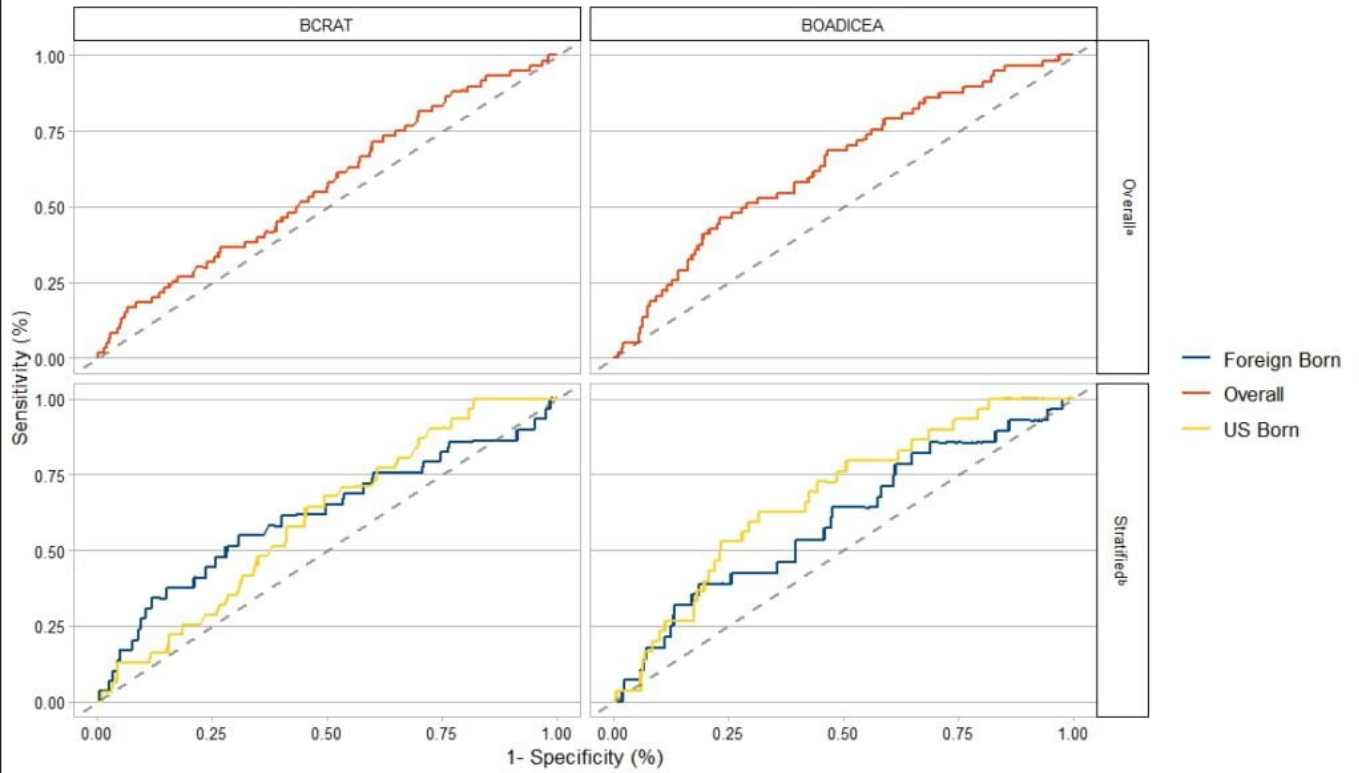
a. Receiver Operator Characteristic curves of each model in the overall population of Hispanic Women
b. Receiver Operator Characteristic curves of each model in the population of Hispanic Women stratified by country of birth

Association between National Area Deprivation Index and Incident Bone Health Outcomes Among Newly Diagnosed Breast Cancer Patients Iridian Guzman* Iridian Guzman Marybeth Ingle

Background: Breast Cancer (BC) patients are susceptible to bone loss. This study aims to evaluate the association between national area deprivation index (ADI), a national ranking of neighborhood sociodemographic disadvantage, and bone health outcomes among newly diagnosed BC patients.

Methods: Newly diagnosed BC patients were retrospectively evaluated from 01/2019-01/2021. Bone health outcomes were osteopenia, osteoporosis & bone fracture. ADI was distributed into quartiles (Q1= least disadvantaged, Q4= most disadvantaged). A multivariable logistic regression model evaluated the likelihood of having a bone health outcome diagnosis using ADI as the primary predictor while adjusting for age, race/ethnicity, employment status, insurance, body mass index (BMI), hypertension, palliative care referrals, vitamin D, hormone therapy, chemotherapy, breast cancer surgery, and bone screening. A multivariable cox proportional hazard model evaluated the association between ADI and time from diagnosis to first bone health outcome diagnosis.

Results: Patients (n=3,011) were older (Median=68), White (55%), non-smokers (63%) with Medicare (58%). 21% of patients had osteopenia, 20% osteoporosis & 1% had bone fractures during follow up. Compared to the least deprived patients, those in Q3 (OR=0.74; 95%CI: 0.56,0.98) and Q4 (OR=0.66; 95%CI:0.49,0.90) were less likely to have an osteoporosis diagnosis. Similarly, time to osteoporosis diagnosis after a BC diagnosis was 27% & 21% longer for Q4 (95% CI: 0.57,0.92) & Q3 (95%CI: 0.63,0.99) patients, respectively compared to Q1 patients.

Conclusion:20% of BC patients also had a diagnosis of osteoporosis. Disadvantaged patients were less likely to have an osteoporosis diagnosis and time to osteoporosis diagnosis after BC diagnosis was longer for disadvantaged patients. Common BC treatments, along with age, impact bone health and survivorship. Future studies should focus on interventions to improve bone health for disadvantaged patients.

Cancer

Military service exposures and the incidence of gynecologic cancers among younger women Veterans from post-9/11 era conflicts Christine Ramsey* Christine Ramsey Erica Abel Allison Gaffey Kathleen Agun Melissa Skanderson Lori Bastian Cynthia Brandt Bevanne Bean-Newberry

Objectives: To examine military service-related risk factors for a new diagnosis of a gynecological cancer among younger women Veterans receiving care in Veterans Affairs (VA) medical centers.

Methods: In a retrospective cohort study of 713,767 women Veterans who entered VA care from 2001–2021 prior to age 50, the primary outcome was a diagnosis of uterine, ovarian, cervical, or other gynecological cancer after entering VA care. The primary exposures were post-9/11-era service vs. participation in other service eras and experiencing military sexual trauma (MST). Poisson models were used to evaluate the associations of post-9/11-era military service, MST, smoking, and body mass index (BMI) and incidence of gynecologic cancers, controlling for demographics (i.e., age, race, and ethnicity).

Results: Overall, 0.7% were diagnosed with a gynecological cancer (N=4,366). Mean age was 33.5 ± 8.9 years at first VA care, mean follow up was 10.7 ± 7.5 years; 21.5% served in the post-9/11 era. Post-9/11 era women were younger (31.0 vs. 34.2 years), less likely current or former smokers (40% vs. 43%), to have a BMI in the obese category (28.1% vs. 35.2%), or to report experiencing MST (31.9% vs. 35.3%) than women from other service ears. In multivariable models adjusting for age, demographics, BMI category and service era, post-9/11 era was associated with 27% less likely diagnosis of a gynecological cancer than women who served in other eras (OR:0.73, CI: 0.66, 0.80). Yet, women who experienced MST were 9% more likely to be diagnosed with a gynecological cancer (CI: 1.02, 1.15) vs. those without MST history. However, there was no significant interaction between service-era and MST on risk of a gynecological cancer diagnosis. Current smoking and having a BMI in the underweight or obese categories were also associated with greater odds of a gynecological cancer diagnosis.

Conclusions: Among women Veterans who began using VA health service before age 50, risk of gynecologic cancers was lower for post-9/11 era Veterans and higher for women who experienced MST.

Impacts: Identifying service era and deployment-related risk factors for gynecologic cancer can improve targeted preventive healthcare for women Veterans.

Disparities by Neighborhood Racial and Ethnic Typology and Neighborhood Poverty in Survival among Adolescents and Young Adults with Cancer in Texas Jennifer Wang* Jennifer Wang Sandi Pruitt Caitlin Murphy

Background: We examined differences in survival by neighborhood racial/ethnic typology and neighborhood poverty among a population-based sample of adolescents and young adults (AYAs, age 15-39 years) diagnosed with cancer.

Methods: AYAs diagnosed with cancer between 1995 and 2015 were identified from the Texas Cancer Registry. Neighborhood racial/ethnic typology (predominantly White [PW], predominately Black [PB], predominately Hispanic [PH], multiethnic neighborhoods) and neighborhood poverty (+/-20% living below poverty) were defined using 2008-2012 American Community Survey data. Five-year survival by racial/ethnic typology and poverty were estimated. Cox proportional hazards models were used to examine associations with mortality, overall and by cancer type, adjusting for age and year at diagnosis, sex, and race/ethnicity (non-Hispanic White [NHW], non-Hispanic Black [NHB], Hispanic).

Results: Among 101,654 AYAs diagnosed with cancer (56.9% NHW, 11.8% NHB, 31.3% Hispanic), common cancer types were breast (15.0%), thyroid (11.4%), and lymphoma (11.2%). Five-year survival ranged from 66.6% (95% CI: 64.3%, 68.7%) for AYAs in PB neighborhoods to 83.2% (95% CI: 82.7%, 83.7%) for AYAs in PW neighborhoods. AYAs in higher (73.9%, 95% CI: 73.4, 74.4) vs. lower (81.5%, 95% CI: 81.2%, 81.8%) poverty neighborhoods had lower 5-year survival. In adjusted analyses, racial/ethnic typology (for example, PB vs. PW: HR 1.18, 95% CI: 1.07, 1.30) and poverty (high vs. low: HR: 1.25, 95% CI: 1.21, 1.29) were associated with worse survival. These associations varied by cancer type. For example, associations were elevated for AYAs with lymphoma (PH vs. PW: HR 1.36, 95% CI: 1.14, 1.63) but not for AYAs with genitourinary cancer (PH vs. PW: HR 0.81, 95% CI: 0.60, 1.09).

Discussion: AYAs in predominantly Black or Hispanic and higher poverty neighborhoods have poor survival. Further research is needed to examine why survival varies by cancer type and identify opportunities for intervention.

Cancer

Beyond BMI: racial and ethnic variation of body size and body composition in individuals with stage II and III breast cancer Ijeamaka Anyene Fumagalli* Ijeamaka Anyene Fumagalli Erica T. Warner Adana Llanos Elizabeth Cespedes Feliciano

Background:

While a common proxy for adiposity, body mass index (BMI) cannot distinguish muscle from adipose tissue and thus may not reflect associations of adiposity with disease outcomes. We examined racial and ethnic differences in body composition among breast cancer patients and associations of multiple physiologically relevant measures of adiposity with survival.

Methods:

We included 3,898 women diagnosed with stage II-III breast cancer from 2005-2019 at Kaiser Permanente with CT scans from which we derived mid-L3 area of skeletal muscle (SKM), subcutaneous (SAT), visceral (VAT), and intermuscular (IMAT) adipose tissue. Adjusting for age at diagnosis, we examined body composition distributions among Asian/Pacific Islander (API) (N=754), Non-Hispanic (NH) Black (NHB) (N=331), Hispanic (N=534), and NH-white (N=2279) women. We then fit Cox proportional hazard models to estimate hazard ratios and 95% confidence intervals for the associations of body composition with survival within strata of BMI and race/ethnicity.
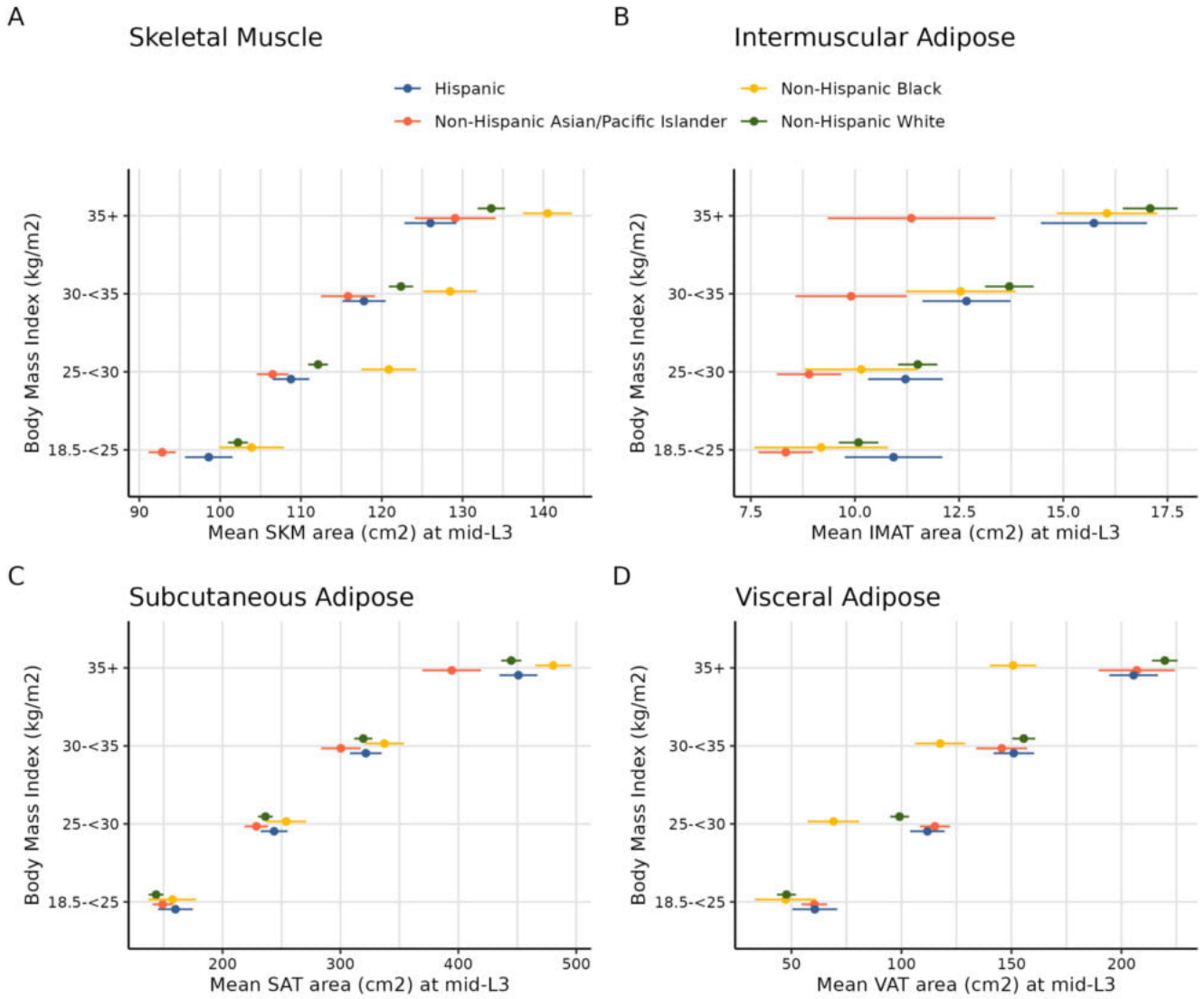
Results:

API women had the lowest mean BMI (mean±SD, 26±9) and NHB women had the highest mean BMI (32±7). Adjusting for age at diagnosis and BMI, NHB women with higher BMI had higher SAT (eg, BMI 30-<35 kg/m2: 337 [NHB] vs 300 [API], 322 [HISP], 319.4 [NHW]) and SKM (eg, BMI 30-<35 kg/m2: 129 [NHB] vs 116 [API], 118 [HISP], 122 [NHW]) but lower VAT (eg, BMI 30-<35 kg/m2: 118 [NHB] vs 146 [API], 151 [HISP], 156 [NHW]) area in cm2 than other groups. Over a median follow-up of 6.8 years, 742 breast cancer deaths occurred. Associations of each tissue with breast-cancer mortality varied by race/ethnicity and BMI with the most consistent associations for greater risk with increasing VAT among NHB and API women, but confidence intervals were imprecise.

Conclusion:

BMI obscures differences in body composition by race and ethnicity. Examining adipose tissue distribution within strata of BMI reveals differing associations within and amongst racial and ethnic groups.

Adiposity and muscle estimates amongst population of stage II and III breast cancer patients
Adjusting for age at diagnosis, race/ethnicity, and BMI

A   Skeletal Muscle

B   Intermuscular Adipose

C   Subcutaneous Adipose

D   Visceral Adipose

Legend:
- Hispanic
- Non-Hispanic Asian/Pacific Islander
- Non-Hispanic Black
- Non-Hispanic White

Social

Association between discrimination and spontaneous abortion in a preconception cohort

Sharonda M. Lovett* Sharonda M. Lovett Lauren A. Wise Jasmine Abrams Molly N. Hoffman Chad M. Coleman Ruth J. Geller Renée Boynton-Jarrett Collette N. Ncube

Introduction: Discrimination may increase risk of spontaneous abortion (SAB, pregnancy loss <20 weeks' gestation) via pathways such as heightened stress, limited access to societal resources, and exposure to adverse environments.

Methods: We examined associations of discrimination with SAB incidence among 5,586 participants who conceived in Pregnancy Study Online, a preconception cohort study (2013-2023). Eligible participants were 21-45 years, assigned female sex at birth, and U.S. or Canadian residents. We collected data on pregnancies and SABs at baseline and follow-up. Starting in 2019, we invited participants to recall discriminatory experiences using Williams' Everyday Discrimination and Major Experiences of Discrimination scales. We used age and race/ethnicity-adjusted Cox models to estimate hazard ratios (HR) and 95% CIs with gestational weeks as the time scale. We also explored effect modification by race/ethnicity.

Results: Seventeen percent of participants reported very high scores of everyday discrimination and 47% reported ≥1 event of lifetime discrimination. Job discrimination was the most prevalent lifetime experience (34%) while the most prevalent everyday experiences included others perceiving the participant as not smart (64%) and being treated with disrespect (63%). Everyday discrimination was positively associated with SAB. Relative to no everyday discrimination, HRs for low, medium, high, and very high scores of everyday discrimination were 1.11 (CI 0.90-1.37), 0.93 (CI 0.76-1.15), 1.13 (CI 0.91-1.39), and 1.20 (CI 0.97-1.49), respectively. Lifetime discrimination was also associated with higher SAB incidence (1 event: HR=1.02, CI 0.86-1.20, ≥2 events: HR=1.24, CI 1.07-1.45 vs. none). HRs for everyday discrimination, but not lifetime discrimination, were similar across race/ethnicity strata.

Conclusions: This is the first study of discrimination and SAB. Our findings suggest everyday and lifetime discrimination are associated with SAB incidence.

Tracking the Anatomy of a Disparity: Four Unique Typologies of Changing NHB-NHW Disparities in Preterm Birth Rates Across U.S. Counties Allison Stolte* Allison Stolte Joan A. Casey Alison Gemmill Hedwig Lee Brenda Bustos Ralph A. Catalano Tim A. Bruckner

Non-Hispanic Black – Non-Hispanic White (NHB-NHW) disparities in preterm birth (PTB; gestational age <37 weeks) are persistent in the US. Studies and programs addressing such disparities often target changes in NHB-NHW rate ratios or absolute differences. Whereas these measures offer important benchmarks for examining shifts in the relative burden of PTB, they mask absolute changes in subgroup rates. NHB-NHW disparities can decrease even as group-specific rates increase, such that decreasing disparities may not indicate improved population health. In this paper, we dissect the anatomy of a disparity—separately considering changes over time to NHB and NHW PTB—to develop a typological framework for assessing disparity trends. Figure 1 presents the classification of US counties into four typologies based on changes to their NHB-NHW absolute differences between two periods: 1995-1999 and 2015-2019. Institutional Progress counties, located around metropolitan areas (and especially in Maryland and California), experienced improvements in NHB and NHW PTB and in NHB-NHW disparities. These counties had the lowest NHB and NHW PTB rates in 2015-2019, serving as success stories for addressing disparities while improving population health. Politics of Despair counties, the largest group, experienced reductions in NHB-NHW disparities driven by faster increases in NHW PTB rates. This typology closely aligns with documented trends of increasing mortality rates unique to NHW adults primarily in the US South and rural areas. In Racism as a Fundamental Cause counties, improvements in PTB rates concentrated among NHW births. This process increased NHB-NHW disparities. These counties compose the smallest group and have relatively high 2015-2019 rates of NHB PTB. Finally, Institutional Harm counties experienced increases in NHB and NHW rates and in NHB-NHW disparities. These counties serve as 'cautionary tales' in which widespread harm concentrated among socially disadvantaged (here, NHB) groups. The four typologies uncover the many ways disparities change and can be used to study 'exemplary' counties, understand causes for these changes, and devise strategies for future improvements.

Figure. Four typologies of county-level changes in NHB-NHW disparities in preterm birth rates between 1995-1999 and 2015-2019

■ Institutional Harm ■ Racism as a Fundamental Cause ■ Politics of Despair ■ Institutional Progress □ NA
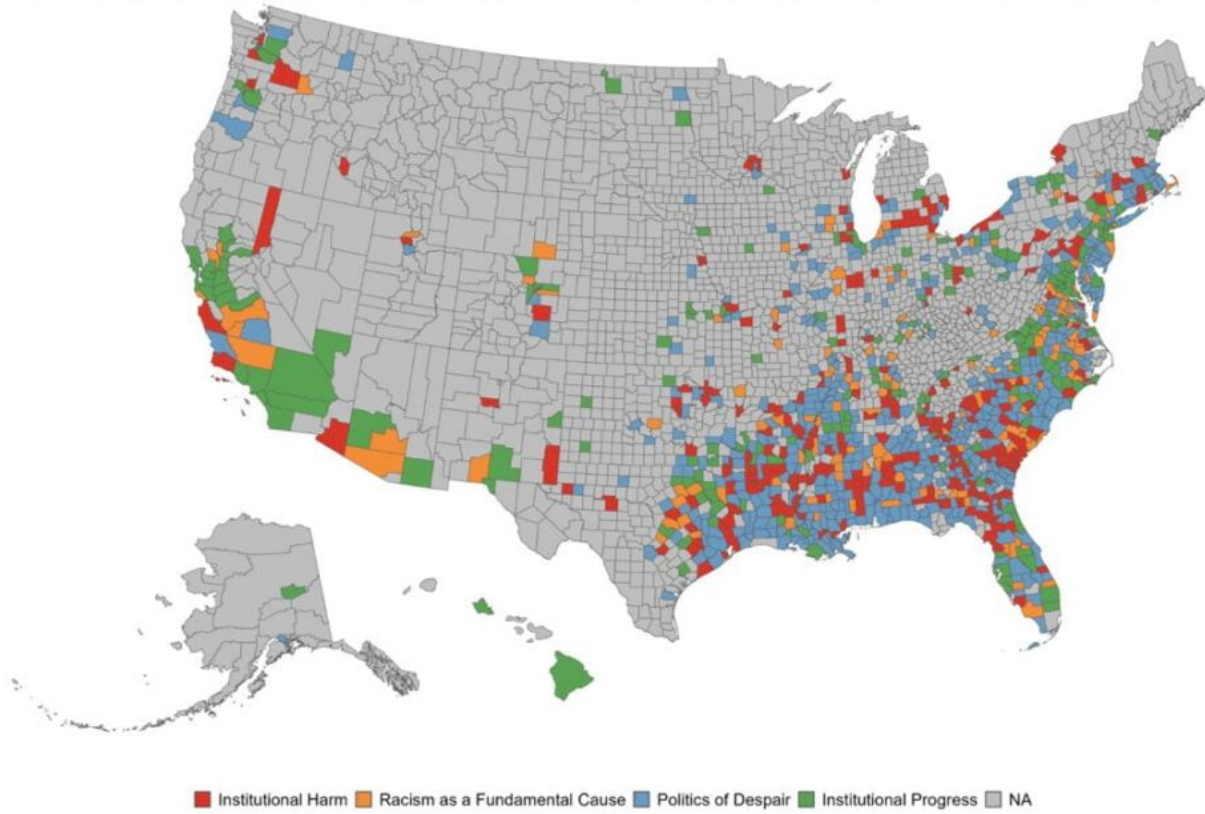
Notes: Counties with at least 100 NHB and 100 NHW births in each aggregated period are included in the analysis. NHB-NHW absolute differences in PTB rates are calculated using individual-level birth data from the National Center of Health Statistics. Institutional Progress (N=232), Politics of Despair (N=491), Racism as a Fundamental Cause (N=147), and Institutional Harm (N=257).

Using spatial Bayesian models to estimate associations between structural racism and severe maternal morbidity disparities in Georgia Jasmin Eatman* Jasmin Eatman Katherine Campbell Kait Stanhope Sheree Boulet

The maternal health crisis is especially profound in the state of Georgia, where 35% of births are to Black-identifying people, and rates of severe maternal morbidity (SMM) exceed national averages. Our goal was to estimate associations between contemporary and historic indicators of structural racial discrimination (SRD) and Black-white county-level SMM disparities.

We used Georgia linked live birth/fetal death certificate and hospital discharge data for deliveries to Black and white birthing people for 2013-2020. Instances of SMM during hospitalization occurring intrapartum, delivery, or up to 42 days postpartum were included as an outcome event. Structural racism was defined at the county-level using multiple domains: residential processes, political representation, criminal justice, and historic oppression. We estimated the association of the change in SMM rate difference between Black and White birthing people with measures of SRD using Bayesian spatial models.

The sample included 709,335 deliveries to Black and White individuals and prevalence of SMM was higher among births to Black individuals (31.7 per 1,000) compared to White (18.0 per 1,000) with mean rate difference of 13.7 per 1,000 deliveries. Results of the SRD-SMM regression showed differences solely among residential processes measures comparing spatial polarization of income and the combination of race and income distributions. The estimated change in SMM rate difference between Black and white birthing people increased by 4.5 per 1,000 deliveries in the lowest income counties compared to the highest (B: 4.5, 95% CI: 1.1, 8.0) and increased by 3.8 per 1,000 for concentrated racial/economic disadvantage (B: 3.8, 95% CI: 0.2, 7.4).

Ecologic processes did not fully capture the relationship between SRD and SMM, highlighting the need for further research to elucidate the drivers of disparities in adverse maternal health outcomes.

DOMAINS OF STRUCTURAL RACISM

HISTORIC

CRIMINAL JUSTICE

RESIDENTIAL

POLITICAL

Percentage of Enslaved Residents in the 1860S

Ratio of Felony Incarcerations

Index of Concentration at the Extremes

Ratio of Black to White Voting Persons

Racial Violence and Terrorism

Disruption of Social Networks

De jure Segregation and Disenfranchisement

Unequal Legislative Representation

Documented Lynchings 1865-1950

Fatal Police Encounters

Dissimilarity Index

Racial Composition of Elected Officials

PATHWAYS OF EMBODIMENT
OVER THE LIFE COURSE

Manifestations of Multigenerational Stress (Weathering Hypothesis)

Encounters with Carceral System in Multiple Societal Domains

Health Promoting Resources and Opportunities

Acquisition of Resources in the Community including Social Support

Risk Potentiators	Risk Mitigators
• Scientific research interpreting race as biologic variable. • Chronic activation of biologic stress response mechanism	• Observed outcomes in research contextual-ized by lived experience of racism • Application of context to clinical care and patient counseling.

Risk Potentiators	Risk Mitigators
• Prison industrial complex targeting Black communities. • Experiences of internalized and interpersonal racism.	• Police reform encompass-ing increased access to social support. • Prosecution of racial terrorism and legalized structural racism.

Risk Potentiators	Risk Mitigators
• Resources sequestered within white communities. • Unequal valuation of property and systemic barriers to Black homeowner-ship.	• Racially homogenous community: protective role against structural racism. • Circulating economic wealth in Black communities.

Risk Potentiators	Risk Mitigators
• Partisan political manipulation of legislative jurisdictions • Multi-generational voter suppression and disenfran-chisement.	• Representati on of Black elected officials' lived experience of racism to inform policy. • Improved access and relevance of public services.

MACRO-LEVEL: ENVIRONMENTAL
MEZZO-LEVEL: CONTEXTUAL
MICRO-LEVEL: BIOLOGIC

DISPARITIES AND RATES OF SEVERE MATERNAL MORBIDITY

Mental Health

White supremacist murders of Black persons and Black youth suicides in the US, 2010-2019: A Time Series Analysis.

Parvati Singh* Parvati Singh Marquianna Griffin Rania Badran Nisha Saranat Amy Fairchild Kamesha Spates

Over the past two decades, the incidence of suicide among Black youth under the age of 25 in the United States has increased substantially. Scholars attribute this alarming trend to racism and discrimination, in conjunction with greater psychiatric vulnerability of Black youth to racist events. White supremacist incidents of violence resulting in murder arguably form one of the most extreme and visible forms of racism. These events may manifest like a contagion, rippling across communities, and correspond with rapid proliferation of racial discrimination, aggression and violence targeted towards minority groups that, in turn, may increase risk factors for suicide and suicide mortality among Black youth. We examined temporal association between monthly trends in white supremacist murders of Black individuals and suicide mortality among Black youth aged 5-24 from 2010 to 2019. We retrieved national monthly counts of white supremacist murders of Black persons (exposure) from the Anti-Defamation League hate and extremism incidents database, from 2010 to 2019. For our outcome, we retrieved monthly counts of suicides among black and white youth (age 5-24 years), by sex (male, female) suicides from the CDC's Restricted Use National Vital Statistics Mortality database from 2010 to 2019. We used Autoregressive Integrated Moving Average (ARIMA) time-series methods to examine the proximate relation between our exposure (0-3 month lags) and outcome. Results from time-series analysis show an increase in Black male youth suicides two months following an increase in White supremacist murders of Black persons (coeff= 3.9, p < 0.01; fail to reject the null among Black female youth). These findings suggest approximately 72 additional suicides among Black male youth statistically attributable to white supremacist murders of Black person over our study period. Our findings underscore the potential impact of white supremacist events on the disturbing rise in Black youth suicides.

Investigating the Role of Chronic Stress and Perceived Discrimination in Racial Disparities in Incident Dementia among US older adults: A Causal Mediation Analysis Mina Habib* Mina Habib Nicola Churchill Roch A Nianogo

Background: The rising prevalence of cognitive decline and dementia in the general population necessitates the need to identify and address factors that contribute to racial disparities in dementia outcomes.

Objective: This study investigates the role of ongoing chronic stress (OCS) and perceived everyday discrimination (PED) in the association between race and incident dementia (ID) among Non-Hispanic (NH) Black and White populations and aims to identify intervention pathways to reduce these disparities.

Methods: Utilizing the Health and Retirement Study—a longitudinal, nationally-representative study of Americans over 50—G-computation based parallel mediation analysis was performed on 5,602 participants (4,913 NH White, 689 NH Black). Multiple imputation (MI) and inverse probability of censoring weights (IPCW) addressed incomplete covariates and loss to follow-up. ID was identified using validated Lange-Weir Classification, and PED and OCS scores were obtained from established indices. Analysis included socio-demographic characteristics, baseline mediator values, and Apolipoprotein E4 status. Results from 100 MI/IPCW datasets were combined via Rubin's rule, with 95% confidence intervals estimated via bootstrapping.

Results: NH Black participants demonstrated a higher dementia risk compared to NH Whites, with an adjusted risk ratio of 2.21 (95%CI: 1.69 – 2.73). Neither OCS or PED directly mediated the race-dementia association. However, we observed substantial proportions attributable to interaction (27% for OCS and 26% for PED) and proportions eliminated (27% for OCS and 26% for PED), indicating significant excess ratios due to interaction (ERINTref) between OCS and race (ERINTref: 0.32; 0.06 – 0.58) and PED and race (ERINTref: 0.3; 0.13 – 0.48).

Conclusions: Our findings, notably proportions attributable to interaction and eliminated, suggest racial disparities in ID due to OCS and PED can be eliminated through race-specific interventions targeting both pathways.

Mediation of the Association of Race and Incident Dementia by Chronic Stress and Perceived Everyday Discrimination, 2006-2016 HRS (N=5,602)
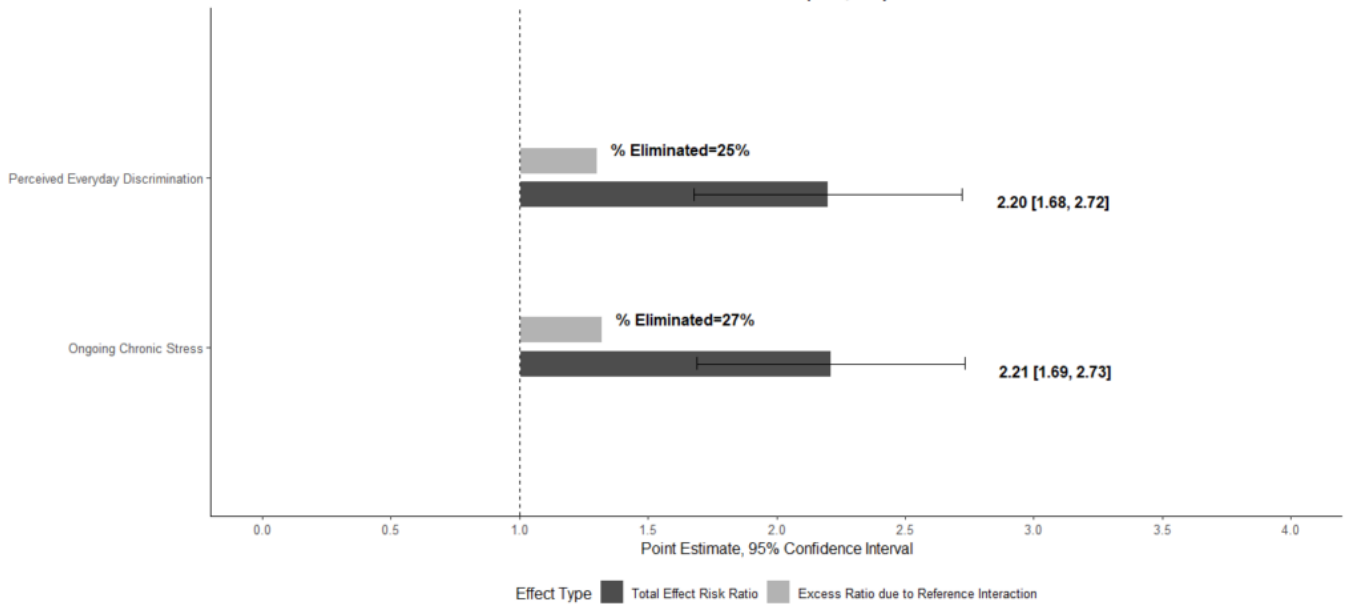
Risk Ratios were obtainted via g-formula based causal mediation analysis and adjusted for age, gender, participant's years of education, mother's years of education, employment status, whether participant's household income fell below the federal poverty line, whether participant tested positive for Apolipoprotein E4 gene, and respective baseline mediator.

Meta-analyses of nutritional exposures must identify and distinguish between study estimands: a pilot study of an illustrative review Natalia Ortega* Natalia Ortega Peter Tennant Octavio Pano Georgia Tomova

Background: Answering causal questions is a common aim of nutrition research. Meta-analyses (MAs) aim to produce definitive estimates of causal effects by synthesising findings from multiple studies. Unfortunately, few nutrition studies are explicit about their target causal estimands, making it challenging to appropriately pool their estimates and interpret them. In dietary data, it is particularly important to consider the energy adjustment strategy; because adjusting for, or dividing by, total energy will change the effect from an additive to a substitutive effect. It is unclear, however, whether such issues are widely considered in primary or secondary research.

Methods: To explore the reporting of target estimands in nutrition research, and the extent that MAs pool different estimands, we systematically searched for all MAs on the illustrative topic of saturated fats and cardiovascular disease incidence. For this pilot study, we identified the most cited MA and doubly-extracted data from all contributing primary studies.

Results: Among the 21 primary studies included in the illustrative MA, only one defined a target estimand within their aim. Thirty-eight unique models were examined, of which 32 targeted substitutive effects and 6 additive effects. Among the studies with substitutive models, 70% did not mention the energy adjustment strategy of choice, nor mentioned a comparator. Substitution models typically adjusted for alcohol, fiber, vegetables, fruits and intake of different types of fat. Only 5 out of 32 models were correctly interpreted as substitutive by the authors, and 2 out of 6 as additive in the results. Twenty out of 38 models did not provide an interpretation for the estimate.

Conclusion: MAs should differentiate between study estimands and aim to pool estimates for the same estimand where possible, or as a minimum – differentiate between substitutive and additive effects.

Maternal magnesium intake and hypertensive disorders of pregnancy among nulliparous women Yijia Zhang* Yijia Zhang Meghan Angley Uma Reddy Ka Kahe

Background and Objectives Magnesium assists muscle relaxation and helps maintain normal blood pressure, and may play a role in the development of hypertensive disorders of pregnancy (HDP). This study examined the associations between magnesium intake, C-reactive protein (CRP), a biomarker for inflammation, and HDP in a large cohort of nulliparous women in the United States.

Methods This study used data from the Nulliparous Pregnancy Outcomes Study: Monitoring Mothers-To-Be (NuMoM2b). After excluding women with pre-existing health conditions, i.e., chronic hypertension and pre-gestational diabetes, and women without dietary magnesium data, a total of 7,976 participants were included in the final analysis. Modified Block 2005 Food Frequency Questionnaire was used to assess the intake of magnesium in the three months prior to pregnancy. Women were considered to have HDP if they were diagnosed from 20 weeks' gestation onwards for new-onset antepartum gestational hypertension, preeclampsia, eclampsia, or superimposed preeclampsia. A subset of the population (n = 2916) had data on serum CRP. We classified CRP levels as either low risk or intermediate-to-high risk for global cardiovascular disease using a cutoff of 1 mg/L. Multivariable logistic regression was used to calculate odds ratios (ORs) and 95% confidence intervals (CIs) for the associations between magnesium intake (in quartiles) and the outcomes.

Results The range of magnesium intake (mg/day) for four quartiles were Q1: 4.98–180.02, Q2: 180–241.67, Q3: 241.77–318.27, and Q4: 318.33–1943.27. After adjustment for potential confounders, magnesium intake was associated with lower odds of HDP (Q4 vs. Q1: OR = 0.62, 95% CI = 0.49–0.79; ptrend < 0.001). Higher magnesium intake was also inversely associated with CRP levels (Q4 vs. Q1: OR = 0.61, 95% CI = 0.41–0.90; ptrend = 0.01).

Conclusion Magnesium intake may be associated with a lower risk of HDP, potentially through its anti-inflammatory properties.

Nutrition/Obesity

The Role of Vegetarian Diets on Pregnancy and Live Birth among Couples Undergoing Infertility Treatment Quynh Long Khuong* Quynh Long Khuong Stefanie Hinkle Ellen Caniglia Enrique Schisterman Julia DiTosto Chanele Lomax Erica Johnstone Pauline Mendola Jim Hotaling Ginny Ryan Matthew Peterson Douglas Carrell Bradley VanVoorhis Sunni Mumford

Introduction: In recent years, many people have followed vegetarian diets due to the potential benefits for metabolic diseases. However, evidence on the effect of vegetarian diets on fertility outcomes is scarce, especially the combined impact of both partners. This study investigated the association of female and male partner vegetarian diets on pregnancy, pregnancy loss, and live birth.

Methods: We used data from the Folic Acid and Zinc Supplementation Trial (FAZST) conducted among couples seeking infertility treatment (females aged 18-45, males aged 18+ years). Individuals self-reported whether they followed a vegetarian diet. We grouped couples based on whether both partners, only one partner, or neither partner followed a vegetarian diet. Log-binomial models evaluated associations between vegetarian diets and pregnancy outcomes, including β-hCG-detected pregnancy, clinical pregnancy, and pregnancy loss, and live birth, adjusting for relevant confounders. Models for pregnancy loss utilized inverse probability weights to account for selection bias.

Results: Of 2120 couples, 19 followed a vegetarian diet together, while 60 had one partner who followed this diet. Of these 60 couples, 9 vegetarians were male and 51 were female. Compared to couples with neither partner on a vegetarian diet, couples where both partners followed a vegetarian diet had higher probabilities of pregnancy and live birth, with RR (95% CI) of 1.27 (0.97–1.66), 1.27 (1.03–1.55), and 1.36 (0.91–2.06) for β-hCG-detected pregnancy, clinical pregnancy, and live birth, respectively. No association was observed for pregnancy loss, with an RR of 1.08 (0.60–1.97). No differences were observed comparing couples with one vegetarian partner to those with no vegetarians.

Conclusion: Our findings suggest a potential benefit on pregnancy and live birth if both partners follow a vegetarian diet. Future studies with larger sample sizes are needed to confirm these findings.

Timing of introduction to fruits and vegetables during infancy and intake in childhood

Priscilla Clayton* Priscilla Clayton Diane L. Putnick Ian R. Trees Jordan N. Tyris Tzu-Chun Lin
Edwina H. Yeung

Most children in the US do not meet daily recommendations for fruits and vegetables. Early infant feeding practices may influence dietary preferences in childhood. However, little is known about how timing of introduction to fruits and vegetables may impact their intake in childhood.

Parents from the Upstate KIDS cohort reported whether they introduced solids or liquids (e.g., vegetables, fruits, meats, juice, dairy, etc.) other than breastmilk or formula to their infants at 4, 8, and 12 months of age. All singletons and one randomly selected multiple from each family with information on feeding practices and diet at 30-36 months (n=2770) and 7-9 years of age (n=1429) were included. We used Poisson regression to model the associations between introduction of fruits and vegetables and intake in childhood. Models were adjusted for mother's age, race/ethnicity, education, insurance status, pre-pregnancy BMI, child's gestational age, parity, WIC participation, frequency of fast-food intake, and breastfeeding duration.

About 34% of infants were introduced to fruits and vegetables by 4 months, 61% around 8 months, and 5% around 12 months. Mothers introducing by 4 months had lower educational attainment, higher pre-pregnancy BMI, and a higher WIC participation relative to mothers introducing later (p <.0001). Compared to those introducing fruits and vegetables by 4 months of age, introduction around 12 months of age was associated with 10% (adjusted RR: 0.90; 0.81, 1.00) lower daily subsequent fruit and vegetable intake at 30-36 months but not with introduction around 8 months (aRR: 0.96; 0.92, 1.00). Similar but attenuated associations around 12 months (aRR: 0.90; 0.76, 1.06) and 8 months (aRR: 0.97; 0.90, 1.04) relative to 4 months for fruits and vegetable intake at 7-9 years were observed.

Delaying an infant's introduction to fruits and vegetables to 12 months was associated with lower intake in childhood, although other complementary foods require further investigation.

Associations of night shift work with weight gain in female nurses in The Netherlands: results of a prospective cohort study Henriette M. van Duijne* Michael Schaapveld Henriette M. van Duijne Nina E. Berentzen Roel C.H. Vermeulen Jelle J. Vlaanderen Hans Kromhout Katarzyna Jóźwiak Anouk Pijpe Matti A. Rookus Flora E. van Leeuwen

Background: Working night shifts has been associated with increased risk of diabetes and cardiovascular disease, which may (partly) be explained by weight gain. We assessed associations of working night shifts and weight gain in the Nightingale Study.

Methods: This study included 36,273 (former) nurses, who completed questionnaires in 2011 and 2017. Night shift exposures (cumulative number (no.) nights, mean no. nights per month, consecutive no. nights per month) between 2007-2011 were categorized into tertiles. Poisson regression was used to estimate incidence rate ratio (IRR) of >5% weight gain among all participants and IRR of overweight/obesity (≥25 kg/m2) among women with healthy baseline BMI. Effect modification by age or menopausal status was assessed using likelihood-ratio (LR) tests.

Results: Working night shifts between 2007-2011 was not associated with >5% weight gain (IRR=1.04, 95% Confidence interval (CI)=0.97-1.12) compared to never working nights. However, the association between working nights and weight gain differed by menopausal status in 2011 (Pinteraction=0.040), with increased risk of gaining >5% weight (IRR=1.19, 95%CI=1.06-1.34) for postmenopausal women who worked nights compared to those who never worked nights. Postmenopausal women had increased risk of >5% weight gain when they worked ≥4 nights (IRR=1.26, 95%CI=1.05-1.51) or ≥4 consecutive nights (IRR=1.43, 95%CI=1.17-1.74) per month. Neither pre- nor postmenopausal women who worked nights had increased risk of overweight/obesity (IRR= 1.01, 95%CI=0.90-1.14 and IRR=1.22, 95%CI=0.99-1.49, respectively). However postmenopausal women who worked ≥241 nights (IRR=1.35, 95%CI=1.04-1.76) or ≥4 consecutive nights (IRR=1.38, 95%CI=1.07-1.77) had increased risk of overweight/obesity compared to those who never worked nights.

Conclusion: Working nights was associated with a slightly increased risk of weight gain and development of overweight/obesity for women who were postmenopausal at study inclusion.

Acute impact of air pollution on fetal death in the San Joaquin Valley, California: a time-stratified case-crossover study Sneha Ghimire* Sneha Ghimire Alec M. Chan-Golston Asa Bradman Valerie Martinez

Background: Fetal death affects approximately 0.57% of pregnancies. Recent research suggests that air pollution may affect fetal development and mortality. The San Joaquin Valley (SJV) of California is an underserved region with a significant air pollution burden but the impacts of air pollution on fetal death in this area is unclear.

Methods: In this case-crossover study, we identified 1,343 singleton fetal deaths (>20 weeks gestation) in the SJV from 2016 to 2019. Daily zip-code level concentrations of ozone (O3) and particulate matter < 2.5 microns (PM2.5) were derived from Community Multi-scale Air Quality models by the San Joaquin Valley Air Pollution Control District and geospatially linked to the maternal zip codes at delivery. Using conditional logistic regression models, we compared exposures during case periods shortly before the event with control periods when the event did not happen, within the same mother to eliminate time-invariant confounding. Case periods were the day of the event and each of the 14 days prior (lag0-lag14). Control periods were selected using the time-stratified approach. OR and 95% CI were calculated for each 10-unit increase in exposures while adjusting for temperature and humidity.

Results: PM2.5 and O3 were positively associated with higher odds of fetal death in the cold (Nov-Apr) and warm (May-Oct) seasons, respectively. Each 10-unit increase in cold season PM2.5 and warm season O3 was associated with 5% (aORlag6 1.05, 95% CI 1.00,1.12) and 7% (aORlag6 1.07, 95% CI 1.02,1.13) increased odds of fetal death six days post-exposure, respectively. The associations appeared stronger in Asian, Hawaiian/Pacific Islander, low-income, and older mothers.

Conclusions: Air pollution may contribute to fetal death risk. In the changing climate where air pollution exposure is expected to increase in certain areas, efforts to reduce exposure in pregnant people are critical and should be strengthened, especially in underserved populations.

Vaginal Microbiome Structure in Pregnancy and Host Factors Predict Preterm Birth: Results from the ECHO Cohorts Kimberly McKee* Kimberly McKee Christine M. Bassis Jonathan Golob Beatrice Palazzolo Ananda Sen James E. Gern Sarah S. Comstock Christian Rosas-Salazar Tom O'Connor Nigel Paneth Anne L. Dunlop Environmental Influences on Child Health Outcomes (ECHO) Program

The vaginal microbiome is a dynamic system, typically shifting over the course of pregnancy toward increased enrichment of Lactobacillus to support pregnancy maintenance. Proliferation of Lactobacillus may be absent among women with preterm births although specific signatures robust across populations have not been identified. Using vaginal data from the first to third trimester from pregnancy cohorts with available data in the Environmental Influences on Child Health Outcomes Program, we meta-analyzed 16S rRNA gene amplicon sequence data to identify robust vaginal microbiota signatures in pregnancy that along with host factors predicted preterm birth (<37 weeks gestation). We classified community state types and employed penalized logistic regression models, applying Firth's correction, and mixed models for assessing the association between vaginal community state types and preterm birth. To compare the most predictive combination of vaginal taxa and host factors, we generated supervised random forest model plots with receiver operating curves and validated them using a train (20%) and test (80%) approach. Of N=683 births, 12% were preterm, most of which were spontaneous. Vaginal community types were strongly associated with spontaneous preterm birth (adjusted odds ratio= 3.86[95%CI= 1.57-11.3] for Diverse, non-Lactobacillus dominant communities; adjusted odds ratio= 3.03 [95%CI=1.25-8.78] for L. iners-dominant compared to those L.crispatus dominant). Although strongly associated with preterm birth, after adjustment for vaginal community types and level of maternal education, self-identified race was no longer a robust predictor(p=0.58). We calculated the highest area under the curve (0.72) for the most discriminant vaginal taxa (Shuttleworthia satelles, Prevotella amnii, Gardnerella vaginalis) combined with host age, providing insight into potential predictive risk scoring and targets for preterm birth prevention strategies that may be robust across populations.

Paid Family Leave and Prevention of Acute Respiratory Infections in Young Infants

Katherine Ahrens* Katherine Ahrens Teresa Janevic Erin C. Strumpf Arijit Nandi Justin R. Ortiz
Jennifer A. Hutcheon

Introduction: Acute respiratory tract infections are the leading cause of emergency department (ED) visits and hospitalizations in US children, with highest risks in the first two months after birth. Group childcare settings can increase the frequency and spread of respiratory tract infections. Our aim was to determine if New York State's 2018 paid family leave policy, which provided eligible workers with ≤8 weeks of paid time off, lowered acute care encounters for respiratory infections in young infants.

Methods: We used acute care encounters (hospitalizations and ED visits) in New York State and New England control states (Massachusetts, New Hampshire, Vermont, Maine), Oct 2015- Feb 2020. We conducted a controlled time series analysis using Poisson regression to estimate the impact of the paid family leave policy on acute care encounters for respiratory infections in infants aged ≤8 weeks, comparing observed counts during respiratory virus season (Oct-Mar) to those predicted in the absence of the policy. Our primary outcome was encounters for upper or lower respiratory tract infections or associated symptoms (fever, cough). Our secondary outcome was acute care encounters for respiratory syncytial virus (RSV) bronchiolitis. Acute care encounters for respiratory infections in one-year olds (who would not be expected to benefit from the policy) was modelled as a placebo test.

Results: There were 52 943 acute care encounters for respiratory infection among infants aged ≤8 weeks. Encounters were 18% lower than predicted (relative percentage change= -17.9 [95% CI: -20.3 to -15.7]) after the introduction of paid family leave. RSV encounters were 27% lower [95% CI: -31 to -24] than predicted. No such reductions were observed in one-year olds after the introduction of paid family leave (relative percentage change= -1.5 [95% CI: -2.5 to -0.6]).

Conclusions: New York's paid family leave policy reduced acute care encounters for respiratory tract infections in young infants.
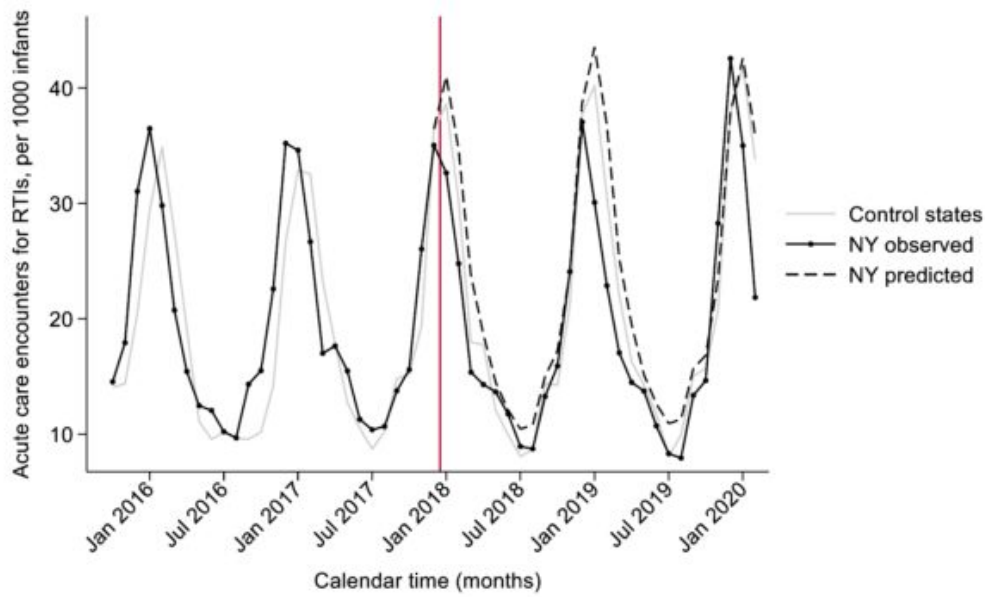
Figure: Observed and predicted monthly rates of acute care encounters per 1000 infants ≤8 weeks of age for any respiratory tract infection and associated symptoms after the introduction of paid family leave in New York State compared with control states (Maine, Massachusetts, New Hampshire, Vermont), Oct 2015-Feb 2020

Prenatal air pollution exposure and risk of autism: findings from ECHO cohorts Akhgar Ghassabian* Akhgar Ghassabian Aisha Dickerson Yuyan Wang Joseph M Braun Kristen Lyall Lisa A Croen Rima Habre Deborah H Bennett Jean A Frazier Hannah C Glass Stephen R Hooper Robert M Joseph Catherine J Karr Jiwon Oh Susan Korrick Kaja Z LeWinn Christine Loftus Craig Newschaffer Mike O'Shea Thomas G O'Connor Adam Szpiro Frederica Perera Heather E Volk

The influence of prenatal exposure to low-level air pollution on child neurodevelopment is unclear.
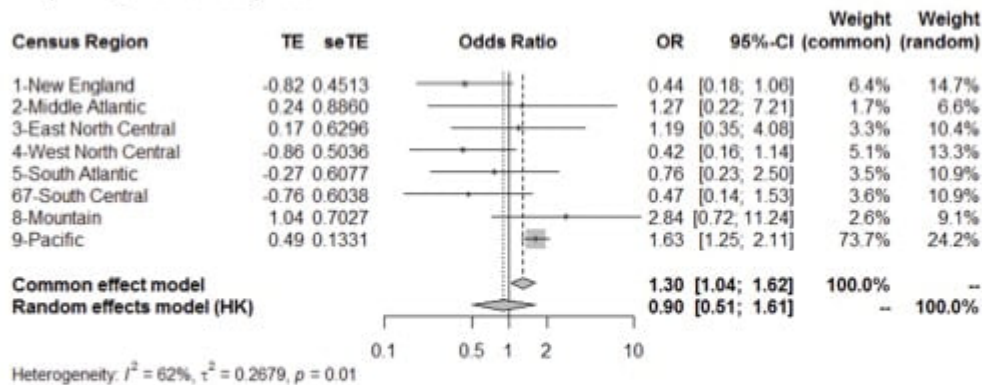
We used data from 7398 mother-child pairs from 39 cohorts (recruitment 2000-2016) in the Environmental influences on Child Health Outcomes (ECHO) to examine the association of prenatal exposure to fine particulate matter (PM2.5), nitrogen dioxide (NO2), and ozone (O3) with autism. An ensemble model integrating machine learning algorithms and predictors estimated daily exposure at residential addresses. Parents rated children's autism-related traits at mean age 8.9 years (SD=3.3) using the Social Responsiveness Scale (SRS) and reported on physician-diagnosed autism spectrum disorder (ASD). We used quantile regression to examine associations at different levels of SRS (25th, 50th, and 75th quantiles) and logistic regression for ASD diagnosis. Models included 3 pollutants and were adjusted for sociodemographic and lifestyle factors, urbanicity, season, and year of birth. Models were run at census divisions and coefficients were pooled in a meta-analysis. We tested for modification by sex.

Average pregnancy exposure for PM2.5 was 9.0 µg/m3 (SD=2.6), 22.0 ppb (SD=9.0) for NO2, and 40.6 ppb (SD=5.9) for O3 (8hr max), with variations across divisions. The median SRS T score was 46 (interquartile range [IQR]=42, 52) and 451 children (6.1%) were diagnosed with ASD. Higher O3 was associated with higher SRS score on average (β per IQR increase in O3=1.11, 95%CI: 0.18, 2.04) and at the lowest quantile of SRS (β=0.95, 95%CI: 0.32, 1.58), but not at the highest quantile. Higher O3 was also associated with ASD (OR=1.43, 9%CI: 1.19, 1.72). There was heterogeneity across divisions for associations of PM2.5 and NO2 with SRS and for NO2 with ASD. Higher PM2.5 was associated with higher odds of ASD in girls only. Associations of O3 with SRS or ASD were stronger in girls.
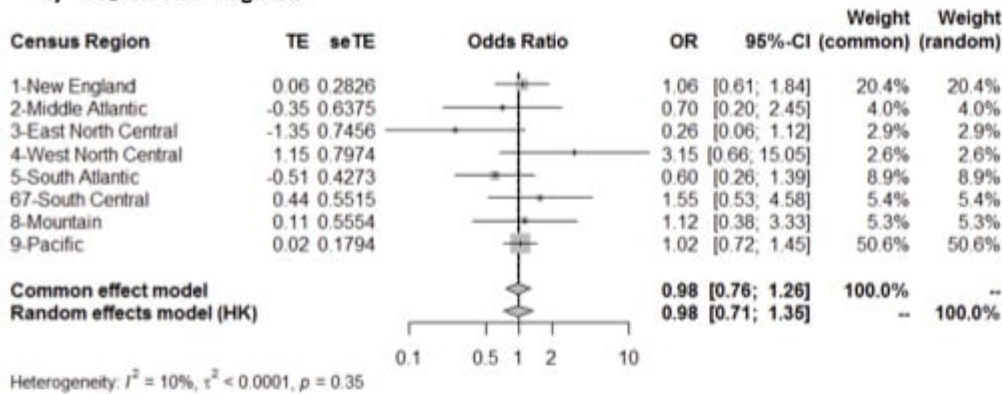
Low-level air pollution exposure may be a risk factor for autism, even for traits in the non-clinical range.

Figure. Associations between prenatal air pollution exposure (averaged across pregnancy) and child risk of autism.
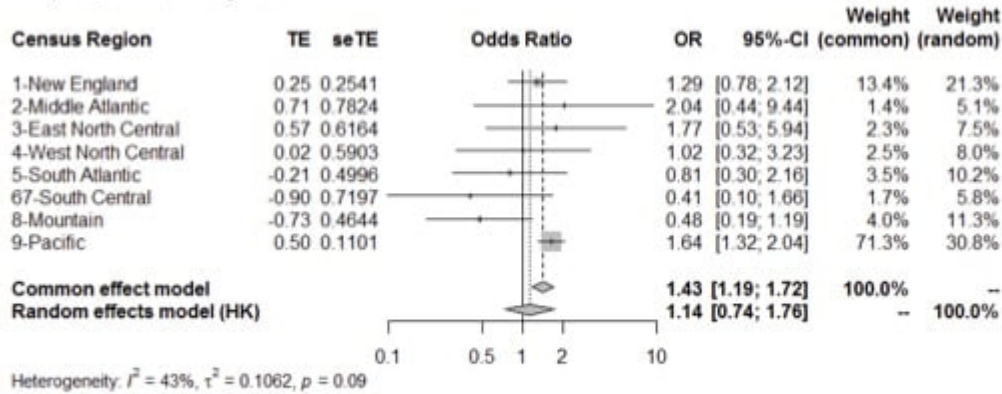
a) PM$_{2.5}$ and ASD diagnosis

Census Region	TE	seTE	Odds Ratio	OR	95%-CI	Weight (common)	Weight (random)
1-New England	-0.82	0.4513		0.44	[0.18; 1.06]	6.4%	14.7%
2-Middle Atlantic	0.24	0.8860		1.27	[0.22; 7.21]	1.7%	6.6%
3-East North Central	0.17	0.6296		1.19	[0.35; 4.08]	3.3%	10.4%
4-West North Central	-0.86	0.5036		0.42	[0.16; 1.14]	5.1%	13.3%
5-South Atlantic	-0.27	0.6077		0.76	[0.23; 2.50]	3.5%	10.9%
67-South Central	-0.76	0.6038		0.47	[0.14; 1.53]	3.6%	10.9%
8-Mountain	1.04	0.7027		2.84	[0.72; 11.24]	2.6%	9.1%
9-Pacific	0.49	0.1331		1.63	[1.25; 2.11]	73.7%	24.2%
Common effect model				**1.30**	**[1.04; 1.62]**	**100.0%**	**--**
Random effects model (HK)				**0.90**	**[0.51; 1.61]**	**--**	**100.0%**

Heterogeneity: $I^2 = 62\%$, $\tau^2 = 0.2679$, $p = 0.01$

b) NO$_2$ and ASD diagnosis

Census Region	TE	seTE	Odds Ratio	OR	95%-CI	Weight (common)	Weight (random)
1-New England	0.06	0.2826		1.06	[0.61; 1.84]	20.4%	20.4%
2-Middle Atlantic	-0.35	0.6375		0.70	[0.20; 2.45]	4.0%	4.0%
3-East North Central	-1.35	0.7456		0.26	[0.06; 1.12]	2.9%	2.9%
4-West North Central	1.15	0.7974		3.15	[0.66; 15.05]	2.6%	2.6%
5-South Atlantic	-0.51	0.4273		0.60	[0.26; 1.39]	8.9%	8.9%
67-South Central	0.44	0.5515		1.55	[0.53; 4.58]	5.4%	5.4%
8-Mountain	0.11	0.5554		1.12	[0.38; 3.33]	5.3%	5.3%
9-Pacific	0.02	0.1794		1.02	[0.72; 1.45]	50.6%	50.6%
Common effect model				**0.98**	**[0.76; 1.26]**	**100.0%**	**--**
Random effects model (HK)				**0.98**	**[0.71; 1.35]**	**--**	**100.0%**

Heterogeneity: $I^2 = 10\%$, $\tau^2 < 0.0001$, $p = 0.35$

c) O$_3$ and ASD diagnosis

Census Region	TE	seTE	Odds Ratio	OR	95%-CI	Weight (common)	Weight (random)
1-New England	0.25	0.2541		1.29	[0.78; 2.12]	13.4%	21.3%
2-Middle Atlantic	0.71	0.7824		2.04	[0.44; 9.44]	1.4%	5.1%
3-East North Central	0.57	0.6164		1.77	[0.53; 5.94]	2.3%	7.5%
4-West North Central	0.02	0.5903		1.02	[0.32; 3.23]	2.5%	8.0%
5-South Atlantic	-0.21	0.4996		0.81	[0.30; 2.16]	3.5%	10.2%
67-South Central	-0.90	0.7197		0.41	[0.10; 1.66]	1.7%	5.8%
8-Mountain	-0.73	0.4644		0.48	[0.19; 1.19]	4.0%	11.3%
9-Pacific	0.50	0.1101		1.64	[1.32; 2.04]	71.3%	30.8%
Common effect model				**1.43**	**[1.19; 1.72]**	**100.0%**	**--**
Random effects model (HK)				**1.14**	**[0.74; 1.76]**	**--**	**100.0%**

Heterogeneity: $I^2 = 43\%$, $\tau^2 = 0.1062$, $p = 0.09$

Models were adjusted for maternal age, educational levels, marital status, smoking and drinking alcohol in pregnancy, pre-pregnancy body mass index, and psychiatric diagnosis, parity, and a child's birth year, birth season, race and ethnicity, and urbanicity of residential address.

Perinatal & Pediatric

State-level payday loan bans and preterm births in the US, 2000 to 2019 Parvati Singh*

Parvati Singh Samantha Gailey Tim A. Bruckner Rania Badran

Payday loans refer to high-interest, short-term loans. These loans can provide immediate financial relief for individuals with limited access to traditional credit. However, the predatory nature of payday loans may portend increased financial strain and adverse public health consequences. Payday lending may contribute to elevated risk of preterm birth- a leading cause of infant mortality- in an exposed population. In line with expectations from the Social Ecological Model of Health, payday lending may not only reduce individual assets but also reduce community resources, divert investments away from health care systems, and worsen economic inequality and increase social and economic distress. We examine whether state-level temporal variation in payday loan restrictions over a 20-year period (2000–2019) corresponds with a reduction in preterm births in the US. Between 2000 and 2019, 10 US states and the District of Columbia imposed restrictions on payday lending at varied time points. We use data on preterm births provided by the CDC Wonder database (2000–2019) and apply staggered difference-in-difference and event study approaches to examine whether preterm births (per 100 live births) declined among states that imposed payday lending restrictions, relative to states that never imposed restrictions. We also control for state-specific time propensity of preterm births, derived through time-series analysis. Results indicate a decline in the preterm births by approximately 2% (95% CI: -0.40, -0.03)) within the first 3 years of payday loan restrictions, which corresponds to more than 4500 fewer than expected preterm births. Our findings suggest that ecological mechanisms that potentially reduce toxic macroeconomic exposure to payday lending may correspond with a reduction in preterm births at the population level.

Event study graph showing the Average Treatment effect for the Treated (ATT) for 0, 1, 2, 3 years post enactment of payday lending bans (Treatment) on preterm births (per 100 live births) across 46 US states (excluding CT, MA, NY, NJ, VT), 2000-2019
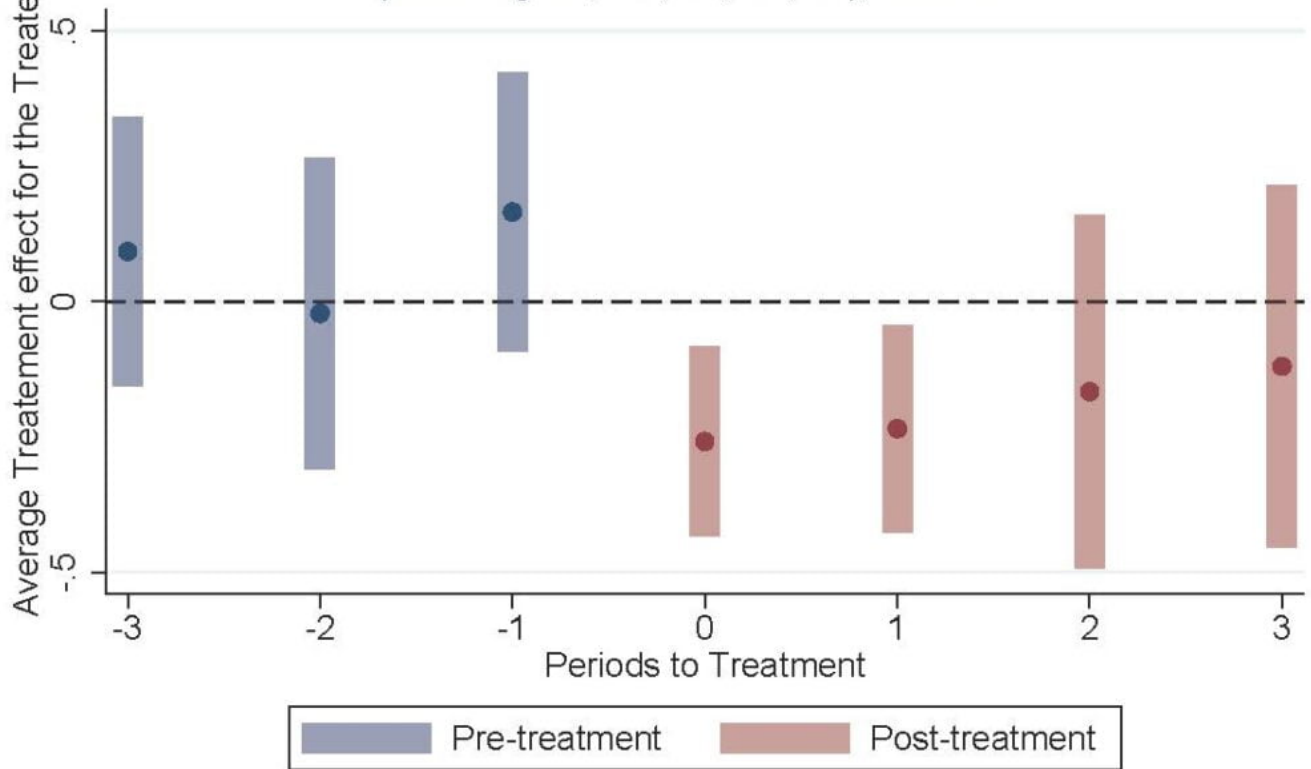
Maternal early pregnancy body mass index and sleep apnea in the offspring Mia Zhu* Mia Zhu Sven Cnattingius Louise M. O'Brien Eduardo Villamor

Objectives: To investigate the association between maternal early pregnancy body mass index (BMI) and offspring sleep apnea diagnosis.

Methods: We conducted a nationwide cohort study among 3,281,803 singleton live births in Sweden born 1983-2015. Using national registries with prospectively recorded information, we followed participants for a sleep apnea diagnosis from 2 to up to 35 years of age. We compared sleep apnea risks by early pregnancy BMI categories using hazard ratios (HR) with 95% confidence intervals (CI) from adjusted Cox models. We also conducted sibling-controlled analyses among 1,724,473 full siblings.

Results: There were 17,830 sleep apnea diagnoses over a median follow-up age of 17.9 years. Maternal early pregnancy BMI was positively associated with offspring sleep apnea risk; compared with women with normal BMI (18.5-24.9), adjusted HR (95% CI) of offspring sleep apnea for maternal BMI categories overweight (BMI 25.0-29.9), obesity class I (BMI 30.0-34.9), and obesity classes II or III (BMI ≥35.0) were, respectively, 1.14 (1.09, 1.19), 1.28 (1.20, 1.36), and 1.40 (1.27, 1.54). Corresponding HR (95% CI) in sibling comparisons were, respectively, 1.13 (1.01, 1.26), 1.17 (0.97, 1.42), and 1.32 (0.97, 1.80). Pregnancy, birth, and neonatal complications were associated with risk of sleep apnea in offspring, but did not substantially mediate the association between maternal obesity and offspring sleep apnea.

Conclusions: Maternal overweight and obesity are associated with offspring sleep apnea risk in a dose-response manner.

The impact of targeted regulation of abortion provider laws on birth rates among minors in the U.S. Kaya Van Roost* Kaya Van Roost Nichole Austin Alissa Koski

Background–In the decades preceding Dobbs, many states were tightening access to abortion through supply-side abortion restrictions, including targeted regulation of abortion provider (TRAP) laws. Evidence on the impact of TRAP laws on abortion provision is mixed, and no study has investigated effects among subgroups, such as minors. TRAP laws may add to the difficulties that minors face in accessing abortion, increasing their likelihood of carrying pregnancies to term. Given the well-known negative consequences of early childbearing, understanding the impact of these laws on minors is crucial. We quantified the impact of two types of TRAP laws–ambulatory surgical center (ASC) and admitting privilege laws–on birth rates among girls aged 15-17.

Data & methods–We identified treated states that enforced a TRAP law between 2000 and 2022 through a comprehensive database of the laws. We used CDC birth data and census population information to calculate birth rates. We compared changes in birth rates post-TRAP law enforcement among treated states to the same changes in untreated states using the Calloway and Sant'Anna difference-in-differences method for contexts with variations in treatment timing.

Results–The mean birth rate in states that later enforced an ASC or admitting privilege law was 24 and 21 per 1000 girls aged 15-17, respectively, in pre-treatment years. The enforcement of an ASC law led to a 14% increase in the birth rate (0.14, 95% CI: 0.073, 0.20), while admitting privilege laws increased birth rates by 12% (0.12, 95% CI: 0.050, 0.19) on average across post-enforcement years.

Discussion–As the restriction of abortion intensifies post-Dobbs, it will be critical to consider the effects on minors, who face additional barriers to accessing abortion and for whom giving birth carries unique risks. Our results show that prior, less restrictive regulation of abortion through TRAP laws led to small increases in birth rates among girls aged 15-17.

Relative Effect of TRAP laws on Birth Rates Among Minors
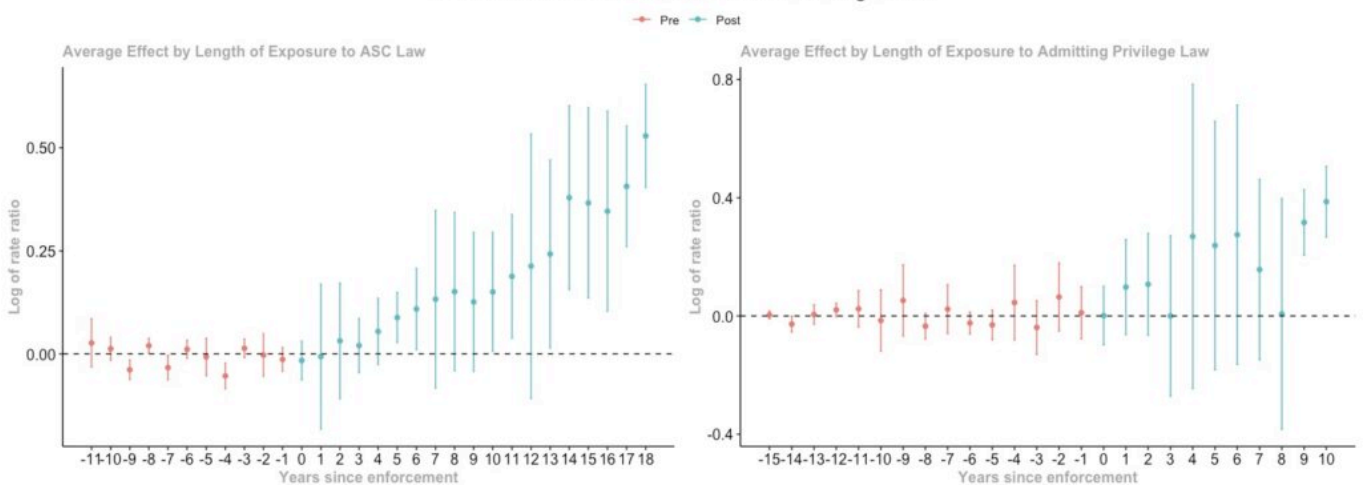
The association between hospital and obstetric unit closures on postpartum acute care in rural North Carolina Mekhala Dissanayake* Mekhala Dissanayake Mollie Wood John Jackson Chantel Martin Michele Jonsson-Funk Rachel Urrutia

Background: Hospital and obstetric (OB) unit closures are concentrated in the rural Southern United States, often where marginalized racial/ethnic groups reside and access to maternal healthcare is strained. Objective: Estimate the effect of hospital/OB closures on postpartum acute care (PPAC) among rural North Carolina (NC) Medicaid beneficiaries by county racial composition. Data: NC birth certificate/Medicaid claims, births from 01/01/2014-12/31/2019. Methods: We categorized rural counties as lower (LNHW, <80% White) or higher (HNHW, ≥80% White) Non-Hispanic White, reflecting the racial/geographic stratifications of rural NC. Our outcome was PPAC: any maternal emergency department or inpatient hospital admission up to 6 weeks after birth. We used comparative interrupted time series analyses of births (with a 1-year baseline) to estimate the effect of living in closure counties (any closure) vs. control counties (with hospital, no closure) on the monthly risk of PPAC over 1-year follow up. We stratified analyses by county racial composition and maternal race/ethnicity (Non-Hispanic White (NHW) and Non-Hispanic Black (NHB)). Results: In LNHW counties there was 1 eligible OB/2 hospital closures (N=16,973 births). Immediately after closure, overall effect estimates of PPAC risk were near zero (-0.7 percentage point, 95% confidence interval (CI): -8.6, 7.2). We observed similar risk for NHW births (1.6, 95% CI: -9.2, 12.3), but a 6.1 percentage point decrease (95% CI: -13.3, 1.1) for NHB births. In HNHW counties there was 1 eligible hospital/4 OB closures (N=5,098). Estimates were near zero overall (-1.0, 95% CI: -4.1, 2.1) and for NHWs (-0.04, 95% CI: -3.5, 3.4), but for NHBs we observed a large but imprecise increased risk (15.2, 95% CI: -39.7, 70.2). Conclusion: The risk of PPAC after closure changed the most among NHB births, though imprecisely estimated due to small sample size. If valid, the effect may result from differential access to healthcare resources.

Social

Relationships between the length of exposure to state-level eviction moratoria and birthweight among Medicaid and uninsured birthing people 2020-2021 Kaitlyn Stanhope*
Kaitlyn Stanhope Sara Markowitz Michael R Kramer

Introduction: Limited data exists on how housing policies may impact outcomes for birthing people. In March and April 2020, 43 states implemented eviction moratoria. Our goal was to estimate associations between the length of exposure to moratoria and birthweight among Medicaid/uninsured people conceiving in March-May 2020 and giving birth to a live born infant.

Methods: We used data from United States natality files, 2020-2021. We defined the exposure as the number of months for which the individual was exposed to a state-level eviction moratoria, categorized as 0 (referent, no state-level moratoria), 1, 2, 3, 4, 5 or more. We estimated differences in birth weight in grams and 95% confidence intervals using quantile regression with generalized estimated equations. We included individual (age, parity, race, ethnicity, likely single parenthood), county (rurality), and state-level covariates (unemployment, poverty, median household income, governor's party affiliation, Medicaid expansion, COVID-19 death rate through July 2020) as potential confounders.

Results: We included 376,622 births. The results of the quantile regression show a pattern of stronger associations between eviction moratoria length and birthweight in the lower and upper tails of the birthweight distribution (Figure 2). In states with a moratorium of five or more months, the 5th and 10th quantiles were 45.8, 95% CI: (9.1, 82.5) and 25.8, 95% CI: (0.5, 51.1) grams higher than states who never implemented a moratorium. At the higher end, the 90th and 95th quantiles were 28.5, 95% CI: (4.3, 52.7) and 28.1, 95% CI: (5, 51.1), respectively. The pattern was similar for moratoria of four months. There were no meaningful associations for moratoria of one to three months.

Conclusions: People birthing in states with longer moratoria in place had higher birth weight, with gains concentrated on the extremes of the birth weight spectrum, independent of the economic and political climate of the state.

Social
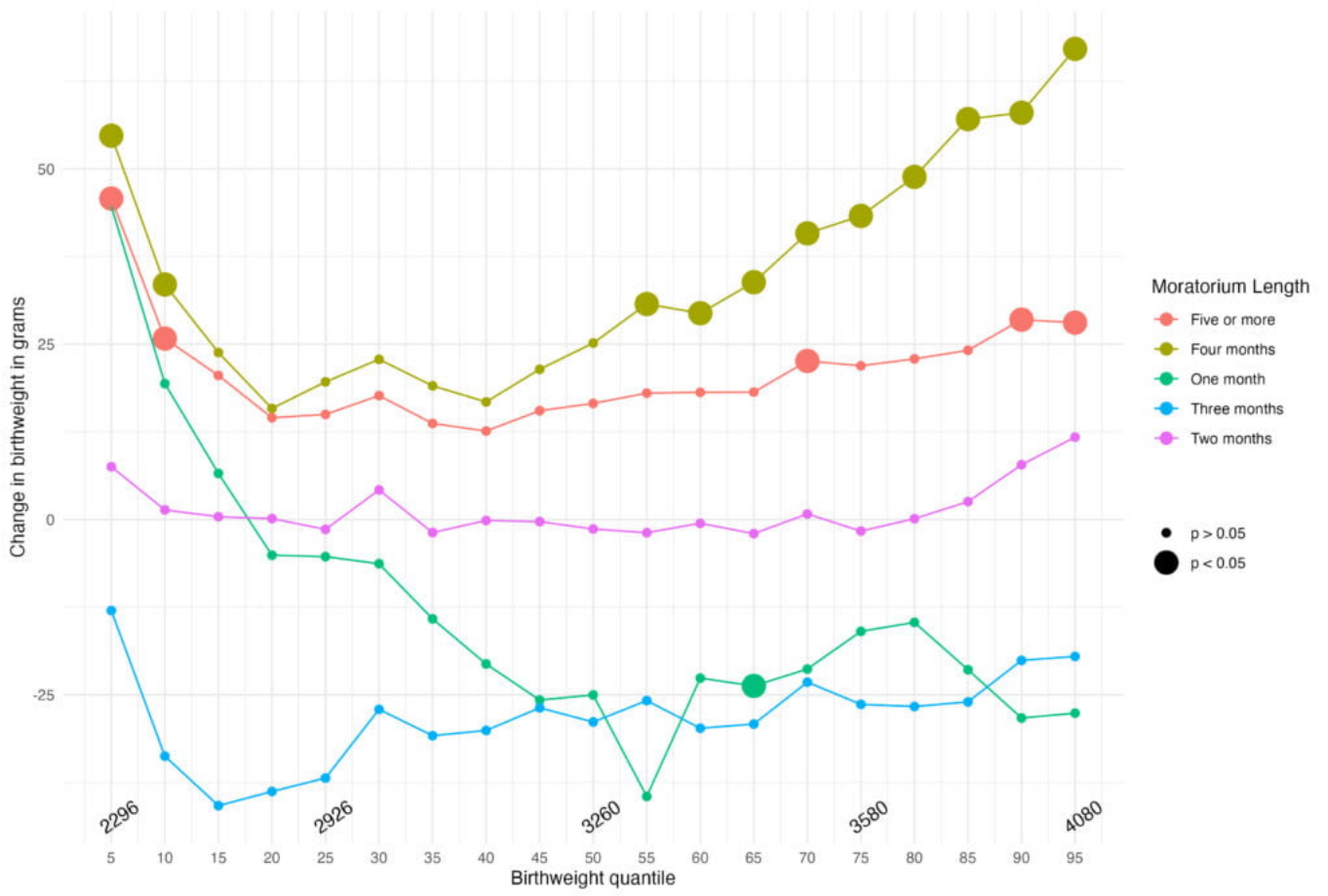
Increased food insufficiency after COVID-era SNAP emergency allotments expired: A quasi-experimental study Whitney Wells* Whitney Wells Kaitlyn Jackson Cindy W. Leung Rita Hamad

In response to economic distress and food insecurity during the COVID-19 pandemic, the US Congress expanded the Supplemental Nutrition Assistance Program (SNAP) by introducing Emergency Allotments (EAs) to increase monthly benefits starting in March 2020. In March 2023, EAs expired in the 35 states/territories still providing them. We provide some of the first evidence of the impacts of this loss of nutrition support—in some cases over $250/month—for economically disadvantaged households.

We examined the effects of SNAP EA expiration on food insufficiency, mental health, and financial well-being, using data from the US Census Household Pulse Survey. In difference-in-differences analyses, we compared pre-post differences among SNAP participants to pre-post differences among SNAP-eligible non-participants. We also examined subgroup effects by race/ethnicity and income.

The SNAP EA expiration led to a substantial increase in food insufficiency (8.4 percentage points; 95%CI: 5.5, 11.3). Black SNAP participants experienced a greater increase in anxiety symptoms (0.47; 95%CI: 0.13, 0.80) compared with White SNAP participants (-0.06; 95%CI: -0.25, -0.13) (p=0.01).

This study has implications for ongoing policymaking with respect to US nutrition and safety net programs to support vulnerable families, especially amidst inflated food prices.

Effect of SNAP emergency allotment expiration on health and financial well-being

Panel A: Binary Outcomes

Outcome		Effect (95% CI)
Household food insufficient		8.4 (5.5, 11.2)
Use of food pantries		2.4 (-0.1, 4.9)
Somewhat/very difficult paying expenses		1.7 (-1.3, 4.6)
Behind on rent/mortgage		-0.5 (-3.5, 2.4)

Percentage point change: -4, -2, 0, 2, 4, 6, 8, 10, 12
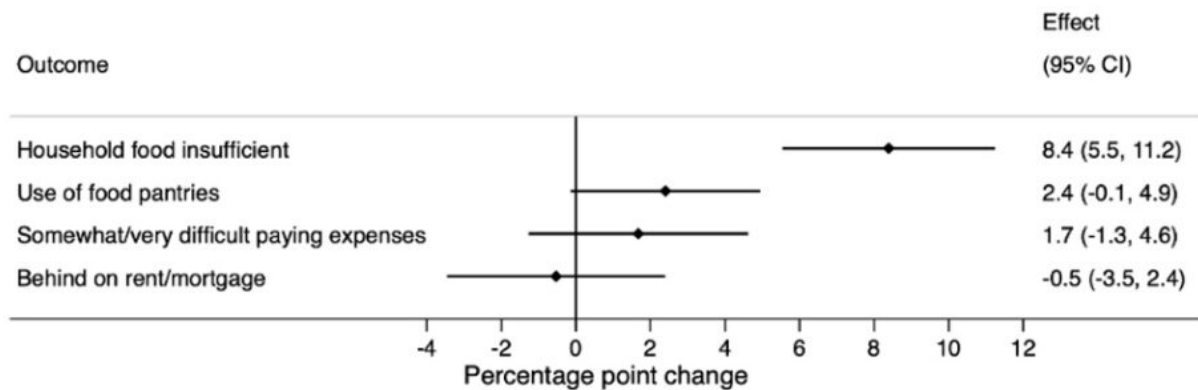
Panel B: Continuous Outcomes

Outcome		Effect (95% CI)
Anxiety symptoms score (GAD-2)		0.05 (-0.08, 0.19)
Depressive symptoms score (PHQ-2)		0.00 (-0.13, 0.13)

Change in score: -.2, -.1, 0, .1, .2
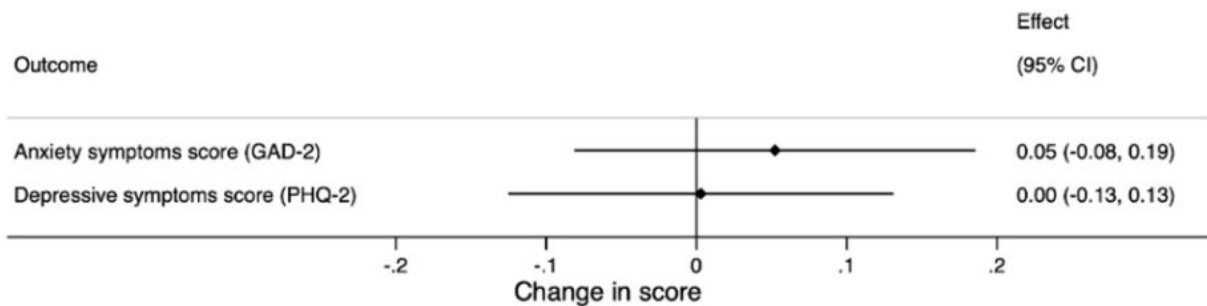
SOURCE: Authors' calculated based on data drawn from US Census Bureau Household Pulse Survey, November 2022 – July 2023 waves.
NOTES: N=15,585. Abbreviations: Supplemental Nutrition Assistance Program (SNAP); Generalized Anxiety Disorder 2-item scale (GAD-2); Patient Health Questionnaire 2-item scale (PHQ-2). All models are adjusted for sex, income, marital status, household size, education, age, and work loss in the past 4 weeks fixed effects for survey week and state of residence and include robust standard errors. For binary outcomes, coefficient represents percentage point change from linear probability model.

From redlining to reproduction: Examining the influence of historical neighborhood disinvestment on fertility Sharonda M. Lovett* Sharonda M. Lovett Lauren A. Wise Andrea S. Richardson Collette N. Ncube Erin J. Campbell Kipruto Kirwa Kenneth J. Rothman Amelia K. Wesselink Mary D. Willis

Background: Redlining, a historic racist practice that systematically diverted wealth away from Black and Hispanic into White neighborhoods, has been associated with adverse birth outcomes. However, redlining's influence on fertility is not known. Our objective was to estimate the association between historical redlining and fecundability, the per-cycle probability of conception.

Methods: We analyzed data from 1,358 female participants aged 21-45 in Pregnancy Study Online (PRESTO; 2013-2023), an online preconception cohort study of couples attempting spontaneous conception without fertility treatment. Participants completed a baseline questionnaire on sociodemographic and reproductive factors, and bimonthly follow-up questionnaires for up to 12 months to ascertain pregnancy status. We linked participants' geocoded addresses to neighborhoods graded by the U.S. Home Owners' Loan Corporation (HOLC) during the 1930s for perceived riskiness of mortgage lending: A+B (best or still desirable), C (declining), and D (hazardous; i.e., redlined). We used proportional probabilities regression models to estimate fecundability ratios (FR) and 95% confidence intervals (CI), adjusting for age and calendar year of enrollment.

Results: Most participants resided in neighborhoods with higher-risk HOLC grades: 41% grade C and 21% grade D. Black and Hispanic participants were less likely to live in grade A+B neighborhoods compared to non-Hispanic White participants. FRs were 0.84 (95% CI 0.73-0.97) and 0.77 (95% CI 0.65-0.92) for neighborhoods graded C and D, respectively, compared with neighborhoods graded A+B. Associations persisted among nulliparous females and those with <3 cycles of pregnancy attempt time at enrollment.

Discussion: In this preconception cohort study, residence in historically redlined neighborhoods was associated with reduced fecundability. Historical redlining may have reinforced neighborhood processes that yielded persistent place-based inequities in fecundability.

Figure 1. Association between historical redlining (measured via a grading system by the U.S. Home Owners' Loan Corporation during the 1930s) and fecundability among self-identified female participants trying to conceive in the United States, Pregnancy Study Online 2013-2023

Fecundability Ratio*
(95% CI)

Overall (N=1,358)

Best or still desirable neighborhoods	1.00 (Reference)
Definitely declining neighborhoods	0.84 (0.73-0.97)
Hazardous neighborhoods	0.77 (0.65-0.92)
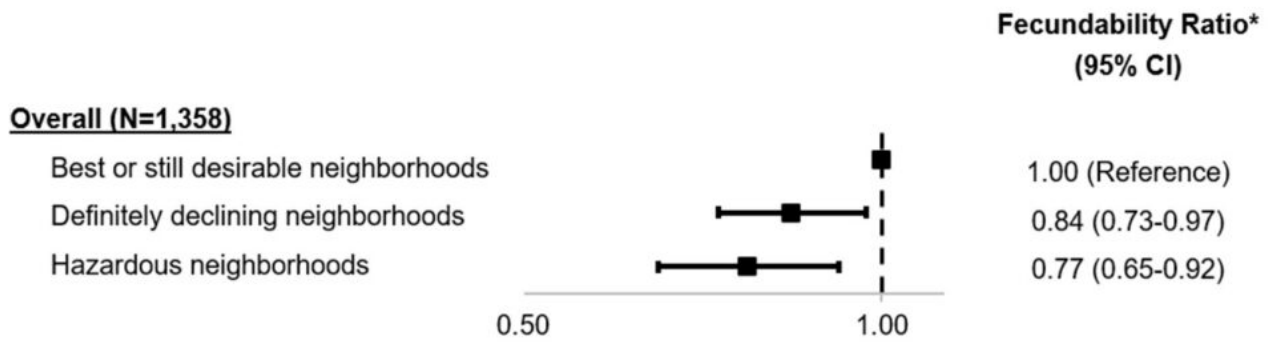
*Adjusted for age and calendar year of enrollment

Exploring the impact of PM2.5 on lung function trends among Black adolescents in Jackson, Mississippi Nina Lee* Nina Lee Erica Walker

Particulate Matter 2.5 (PM2.5) is a pervasive air pollutant that can penetrate deep into the lungs and lead to adverse respiratory effects. PM2.5 poses a great concern for children, given their developing respiratory systems. Hyperlocal air monitoring enables researchers to uncover address-level health disparities. Jackson Mississippi is an understudied city with a deep-seated history of racial disparities and environmental injustices. **Aim:** To understand the relationship between daily PM2.5 and lung function of Black adolescents living in Jackson. **Methods:** 60 participants were enrolled in the Mississippi Adolescent Environmental Health Study (MAEHS), the first longitudinal study of children in Greater Jackson, examining the individual and joint impact of air, noise, water, soil quality on environmental health. 37 participants completed a survey and lung function was tested using spirometry. A representative sample of 40 week-long air quality measurements were collected across Jackson from June 2022-Dec 2023. We used the ordinary Kriging method to interpolate prediction surface maps from the average daily PM2.5 at each site. The average PM2.5 value at the home address of participants were extracted from the kriging raster using bilinear interpolation. The average FEV1/FVC ratio (Forced Expiratory Volume in one second to Forced Vital Capacity ratio) was compared for participants exposed daily to PM2.5 levels above and below the median. **Results:** The average FEV1/FVC ratio for adolescents experiencing daily average PM2.5 levels below the median (6.25 µg/m3) was 82.1 and 76.2 for those above the median. The average difference of 5.9 (95% CI: 0.2-11.6) is significant with a p-value of 0.04. **Conclusion:** Our study reveals a significant average difference in lung function among Black adolescents in Jackson exposed to daily PM2.5 levels above and below the median, emphasizing the urgency of addressing environmental disparities to safeguard health in vulnerable populations.

Environment/Climate Change

Running on Fumes: An Analysis of Fine Particulate Matter's Impact on Finish Times in Ten Major US Marathons, 2003-2019 Elvira Fleury* Elvira Fleury Gray Bittker Allan Just Joseph Braun

Objective: Assess the effect of race-day fine particulate matter air pollution (PM2.5) on marathon finish times.

Methods: Using a spatiotemporal machine-learning model, we estimated the average daily PM2.5 concentration along ten major US marathon courses (2003-2019). For the 157 included event-years, we web-scraped 1,630,170 male and 1,182,732 female finish times. We used multivariable quantile regression to estimate the temperature, humidity, and windspeed-adjusted association of one µg/m3 higher race-day PM2.5 with net finish times in each decile and the 1st, 25th and 75th percentiles (%ile) of finishers in sex- and marathon-stratified samples. We pooled estimates for the 1st percentile of finishers across the ten events using random-effects meta-analysis.

Results: In the 1st percentile of finishers, pooling estimates from the ten races, one µg/m3 higher race-day PM2.5 was associated with 7.25 seconds (s) (95% CI: -2.2 – 16.7 (s)) and 13.3 seconds (95% CI: -0.3 – 26.9 (s)) slower finish times in men and women, respectively. In eight of the ten marathons, PM2.5 was consistently associated with increased finish time in faster-than-median female runners (Range Estimates: β10th %ile: 10.8–44.4 (s); β20th %ile: 11.5–57.5 (s); β25th %ile: 8.2–56.7 (s); β30th %ile: 7.3–58.2 (s); β40th %ile: 2.7–65.3 (s)). In six of the ten marathons, PM2.5 was consistently associated with increased finish time for the first quartile of male finishers (Range Estimates: β10th %ile: 13.2–58.2 (s); β20th %ile: 10.5–60.4 (s); β25th %ile: 5.1–66.9 (s)). The association of PM2.5 with finish time was inconsistent at other percentiles.

Conclusion: Greater race-day PM2.5 estimates were associated with slower finish times in faster-than-average marathoners. While more research is needed to characterize the potential benefits of interventions that reduce race-day PM2.5, events seeking to facilitate record-breaking performances should consider strategies to limit PM2.5 emissions on race days.

Grouped mixtures of air pollutants and seasonal temperature anomalies and cardiovascular hospitalizations among US residents Yaguang Wei* Yaguang Wei Heresh Amini Tingfan Jin James Healy Brent Coull

Background: Air pollution is a recognized risk factor for cardiovascular disease (CVD). Temperature is also linked to CVD, with a primary focus on acute effects. Despite the close relationship between air pollution and temperature, their effects are often examined separately, potentially overlooking their synergistic effects.

Methods: We obtained hospitalization records for residents of 14 US states between 2000–2016 from the Health Cost and Utilization Project. We used a grouped weighted quantile sum regression, a novel approach for mixture analysis, to simultaneously evaluate cumulative and individual associations of annual exposures to four grouped mixtures: air pollutants (elemental carbon, ammonium, nitrate, organic carbon, sulfate, nitrogen dioxide, ozone), deviations of summer and winter temperature means from the long-term averages (i.e., seasonal temperature mean anomalies), deviations of summer and winter temperature standard deviations from the long-term averages (i.e., seasonal temperature variability anomalies), and interactions between air pollutants and seasonal temperature mean anomalies. Outcomes are hospitalization rates for four prevalent CVD subtypes: ischemic heart disease, cerebrovascular disease, heart failure, and arrhythmia.

Results: Chronic exposure to air pollutant mixtures was associated with increased hospitalization rates for all CVD subtypes, with heart failure being the most susceptible subtype and sulfate, nitrate, nitrogen dioxide, and organic carbon being the most toxic pollutants. Mixtures of interactions between air pollutants and seasonal temperature mean anomalies were associated with increased hospitalization rates for all CVD subtypes.

Conclusions: The most toxic pollutants identified would inform source-specific emission control policies. Hotter summers and colder winters jointly exacerbated adverse effects of chronic exposure to air pollution on cardiovascular health.
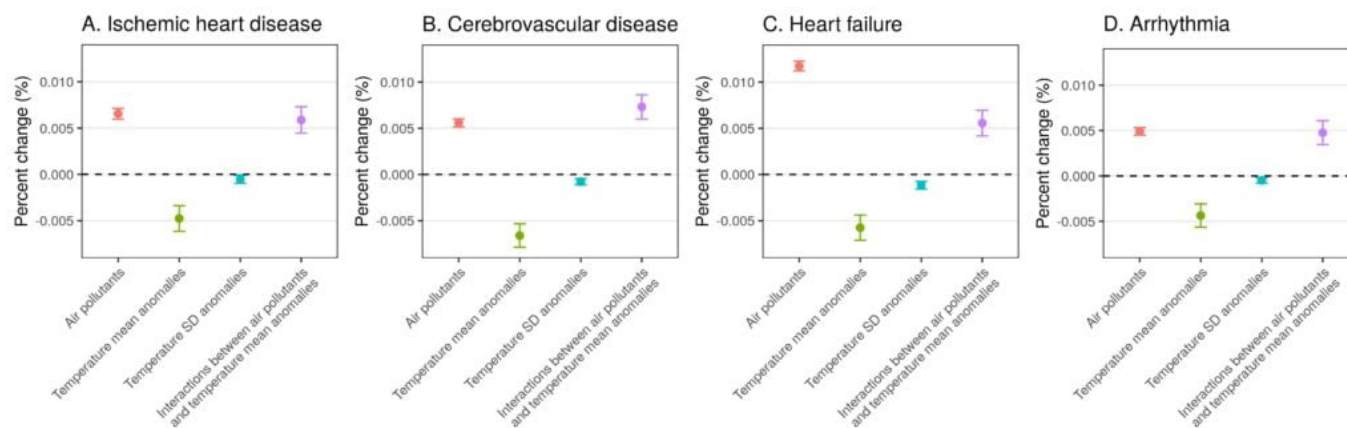
Heat Exposure During Susceptible Windows of Spermatogenesis and Sperm Epigenetic Age

Carrie J Nobles* Carrie Nobles Timothy P Canty Pauline Mendola Lindsey M Russo Kaniz Rabeya Karen C Schliep May Shaaban Akanksha Singh Allison M Ring Rachael Hemmert Neil J Perkins C Matthew Peterson Erica B Johnstone James A VanDerslice J Richard Pilsner

Introduction: Spermatogenesis is uniquely susceptible to redox stress, with age-related disruption of the blood-testes barrier associated with changes in sperm DNA methylation linked to reduced fecundity and pregnancy complications. Heat stress may cause similar disruptions, presenting a route through which high temperatures may impair men's reproductive health.

Methods: We evaluated exposure to high ambient temperatures and sperm epigenetic age in the Folic Acid and Zinc Supplementation Trial (2013-2018). Sperm epigenetic age, the acceleration or deceleration of age-related changes in sperm DNA methylation, was calculated in 1220 men enrolled near Salt Lake City, Utah. Utilizing local hourly temperature data, hours per day exceeding the 98th, 95th, 90th, and 75th percentile thresholds for dry bulb temperature (ambient air) and wet bulb temperature (relative temperature with 100% humidity) were calculated across spermatogenesis and susceptible windows of mitosis, meiosis I+II, spermiogenesis, and spermiation. Generalized linear models adjusted for season, fine particulate matter, and participant characteristics.

Results: During spermatogenesis, an additional 2 hours/day exposure to wet bulb temperatures ≥90th (16.1°C), ≥95th (17.2°C), and ≥98th (17.8°C) percentile thresholds was associated with 0.11 (95% CI 0.04-0.17), 0.18 (95% CI 0.08-0.28) and 0.33 (95% CI 0.12-0.53) years accelerated sperm epigenetic age, respectively. Associations were strongest during the windows of meiosis I+II and spermiogenesis (e.g. 0.08 [95% CI 0.02-0.14] and 0.08 [95% CI 0.03-0.14] years, respectively, for ≥95th percentile). Associations for dry bulb temperature were similar, although moderately attenuated.

Conclusions: Associations of high wet bulb temperatures, capturing impaired efficiency of sweating for cooling body temperature, and accelerated sperm epigenetic age adds evidence that heat-related disruption of spermatogenesis may adversely impact men's reproductive health.

Investigating the relationship between lead in private drinking well water and climate change factors on preterm birth risk in North Carolina Eric Brown Jr.* Eric Brown JR. Rebecca Fry Lauren Eaves

Prenatal exposure to various environmental chemicals, including lead in drinking water, is associated with increased risk of preterm birth. With a rapidly changing climate, the toxicity and distribution of environmental chemicals are projected to increase. The effects of these varied exposures on the health of infants are understudied. North Carolina birth certificates between 2003-2014 (n = 1,148,438) were geocoded based on maternal residence at delivery. Pregnancies were assigned exposures for air toxicants (e.g., PM2.5 and ozone), average tract-level lead well water concentrations, and ambient temperature. We evaluated associations between single climate change-related factors and preterm birth using adjusted logistic regression models. Climate change-related mixtures were assessed using quantile-based g-computation. Individually, air pollutants exposure within the first trimester increased the risk for preterm birth (PM2.5: 1.48 OR (1.48, 1.49), Ozone: 1.01 OR (1.01,1.01)). Exposure to a mixture of PM2.5, ozone and lead was modified by heat; with pregnancies exposed to average ambient temperature above 70.7°F in the last two weeks of pregnancy having the greatest risk of preterm birth (7.15 OR (6.27, 8.16)). Socioeconomic factors, specifically neighborhood deprivation, enhanced this risk, with higher deprived areas having 7.17 OR (5.97, 8.62). In a cohort of over 1 million births, this study identified that individual climate-related stressors are associated individually and in mixtures with preterm birth. This study is among the first to examine how a mixture of climate change-related factors (heat and air pollution) and a chemical exposure (lead in drinking water) are associated with preterm birth.

Racial/Ethnic Disparities in the Neighborhood Walking Environment and Sleep Health: A Nationally Representative Sample of the United States Dzifa Adjaye-Gbewonyo* Dzifa Adjaye-Gbewonyo Amanda E. Ng Dayna A. Johnson Chandra L. Jackson

Background: Access to walkable environments and amenities that may improve sleep health varies by race/ethnicity. Thus, identifying associations between neighborhood walkability and sleep can inform interventions and policies and address disparities.

Methods: Data from the 2020 National Health Interview Survey (N=27,521) assessed neighborhood measures (pedestrian access: walking paths, sidewalks; amenities: shops, transit stops, entertainment/services, places to relax; unsafe walking conditions: traffic, crime) and sleep measures (short (<7 hours/day) and long (9+ hours/day) duration; the frequency of waking up not well-rested; trouble falling asleep; trouble staying asleep; and sleep medication use). Adjusted for sociodemographic and health covariates, we estimated PRs assessing associations between neighborhood characteristics and sleep stratified by racial/ethnic group (non-Hispanic White, non-Hispanic Black, non-Hispanic Asian, and Hispanic) from multivariable logistic regression models with robust variance.

Results: For White adults, neighborhood was associated with favorable (e.g. places to relax, waking up not well-rested, PR=0.93; 95% CI 0.89-0.97) and unfavorable sleep health (e.g. walking paths, sleep medication, PR=1.24;95% CI 1.05-1.46). Among Black adults, sidewalks were associated with favorable outcomes (e.g. short sleep duration, PR=0.85; 95% CI 0.74-0.97). For Asian adults, neighborhood was related to both favorable (e.g. places to relax, long sleep duration, PR=0.53; 95% CI 0.31-0.91) and unfavorable (e.g. traffic, short sleep duration, PR=1.32; 95% CI 1.05-1.66) sleep health. Among Hispanic adults, walking paths were associated with favorable sleep health (e.g. short sleep duration PR=0.80; 95% CI: 0.65-0.99) while unsafe walking conditions were related to unfavorable sleep health.

Conclusion: Features of the neighborhood environment have differing associations with sleep by race/ethnicity. Future research may identify the determinants.

Loneliness, discrimination, mental health, and immigration status David Adzrago* David Adzrago Faustine Williams

Introduction: Loneliness and discrimination have increased risks for physical and mental health problems, reduced quality of life, and mortality. Vulnerable groups, including immigrants, those who experienced discrimination, and with mental health, are more burdened with loneliness. However, sparse literature examined the effects of discrimination on loneliness through mental health among immigrants, a population largely understudied. We examined the mediation effects of anxiety/depression on the relationship between discrimination and loneliness based on immigration status, adjusting for resilience and sociodemographics.

Methods: We used a 2021-2022 national cross-sectional survey data on adults aged > 18 years (N= 4,740). We conducted mediation analyses with multivariable linear regression and bootstrapping. We analyzed loneliness (Scores 3-9; >4 as higher loneliness) as the dependent variable; discrimination (Scores 0-20; >1 as higher discrimination) as the independent variable; and anxiety/depression (Scores 0-12; >1 as higher anxiety/depression) as the mediator.

Results: In the immigrant sample (n= 1,029), the total (not accounting for anxiety/depression) (β= 0.124, p< 0.001), direct (after accounting for anxiety/depression) (β= 0.055, p< 0.001), and indirect (discrimination's effect explained by anxiety/depression) (β= 0.069, p< 0.001) effects of discrimination on loneliness were significantly positive. Anxiety/depression mediated 55.65% of the total effect of discrimination on loneliness.

In the U.S.-born (n= 3,711), the total (β= 0.161, p< 0.001), direct (β= 0.059, p< 0.001), and indirect (β= 0.102, p< 0.001) effects of discrimination on loneliness were positive. Anxiety/depression mediated 63.35% of the total effects.

Conclusions: Anxiety/depression mediates the effect of discrimination on loneliness, especially in the U.S.-born. Mental health and immigration status should be considered in efforts aimed at reducing discrimination and loneliness disparities.

Trends and Socioeconomic Inequalities in Mental Health Service Use in Canada over a 16-year Period Jasleen Arneja* Jasleen Arneja Arijit Nandi

One in five Canadians experiences a mental illness every year. In Ontario, Canada's most populous province, hospitalizations and emergency department visits for mental health increased from 2009 to 2017. However, these estimates are not available at the national level. We aim to examine pan-Canadian trends in mental health service use from 2004 to 2019, and document socioeconomic inequalities in the use of mental health services among adults in Canada over this 16-year period.

Linked survey and health administrative data available through Statistics Canada's Research Data Centres will be used. Adults surveyed in the 2005–2019 cycles of the Canadian Community Health Survey (CCHS) who agreed to data linkage (approximately N= 765,649) will be linked to annual income from tax data in the T1 Family File, hospital discharges from the Discharge Abstract Database, and emergency department visits from the National Ambulatory Care Reporting System from 2004–2019.

We will examine trends in the prevalence of hospitalizations and emergency department visits for mood disorders, anxiety disorders, substance use disorders, schizophrenia, and intentional self-harm. We will estimate income-based socioeconomic inequalities in mental health service use using the relative index of inequality (RII) and slope index of inequality (SII). The RII and SII consider both the population size and the relative socioeconomic position of individuals/groups by regressing the prevalence of the outcome (e.g., ED visits) on individuals' relative position in the social hierarchy. The RII and SII will be used to examine the relation between ranked post-tax income from the T1FF and two dependent variables modeled separately, hospitalizations and emergency department visits for mental health, for each year from 2004–2019 using logistic and linear regression models, respectively. Results will be presented both overall, and stratified by age category, sex, and province.

Inequities in access to mental healthcare at intersections of race and ethnicity, gender identity, and gender modality: An application of Multilevel Analysis of Individual Heterogeneity and Discriminatory Accuracy (MAIHDA) Arieh Lisitza* Arieh Lisitza Amanda Swarr Katarina Guttmannova Anjum Hajat

Inequities in access to mental healthcare at intersections of race and ethnicity, gender identity, and gender modality: An application of Multilevel Analysis of Individual Heterogeneity and Discriminatory Accuracy (MAIHDA)

Transgender populations, and particularly transgender women of color, are burdened by high rates of both mental illness and healthcare avoidance. Despite this, research examining the patterns of non-use of mental healthcare within this community is lacking, and is further hampered due to the difficulty of collecting large, population-based samples of transgender adults in general, and transgender people of color in particular. We therefore use data from the Census Bureau's new Household Pulse Study in conjunction with the novel MAIHDA method to assess the prevalence of unmet mental healthcare needs at critical intersections of gender modality, gender identity, and race and ethnicity. Participants were 699,843 U.S. adults who completed the Household Pulse Survey between July 2021 to May 2022. Participants were sorted into intersectional strata by race/ethnicity (Asian, Black, White, Hispanic, and mixed/another race), gender modality (dichotomized as transgender or cisgender) and gender identity (dichotomized as masculine vs feminine). We then fit a multilevel binomial regression model with strata and participant-level random intercepts to assess the main effects, and calculated stratum-level residuals as a measure of intersectional effects. Unmet mental health needs were most prevalent among transgender people (PR=2.57, 95% CI= 2.49, 2.66), women (PR=1.75, 95% CI=1.73, 1.78), and people who self-identified as Black (PR=1.28, 95% CI=1.25, 1.31), Hispanic (PR=1.30, 95% CI=1.27, 1.33) mixed/another race (PR=1.60, 95% CI= 1.55, 1.65). The largest protective intersectional effect was for Black transgender women and the largest detrimental intersectional effect was for Black cisgender women. These preliminary findings suggest that although racism, transphobia, and misogyny might each independently increase the prevalence of unmet mental health needs, there may be an additional resiliency effect associated with experiencing multiple marginalized identities.

Stratum-level residuals by gender identity, gender modality and race and ethnicity
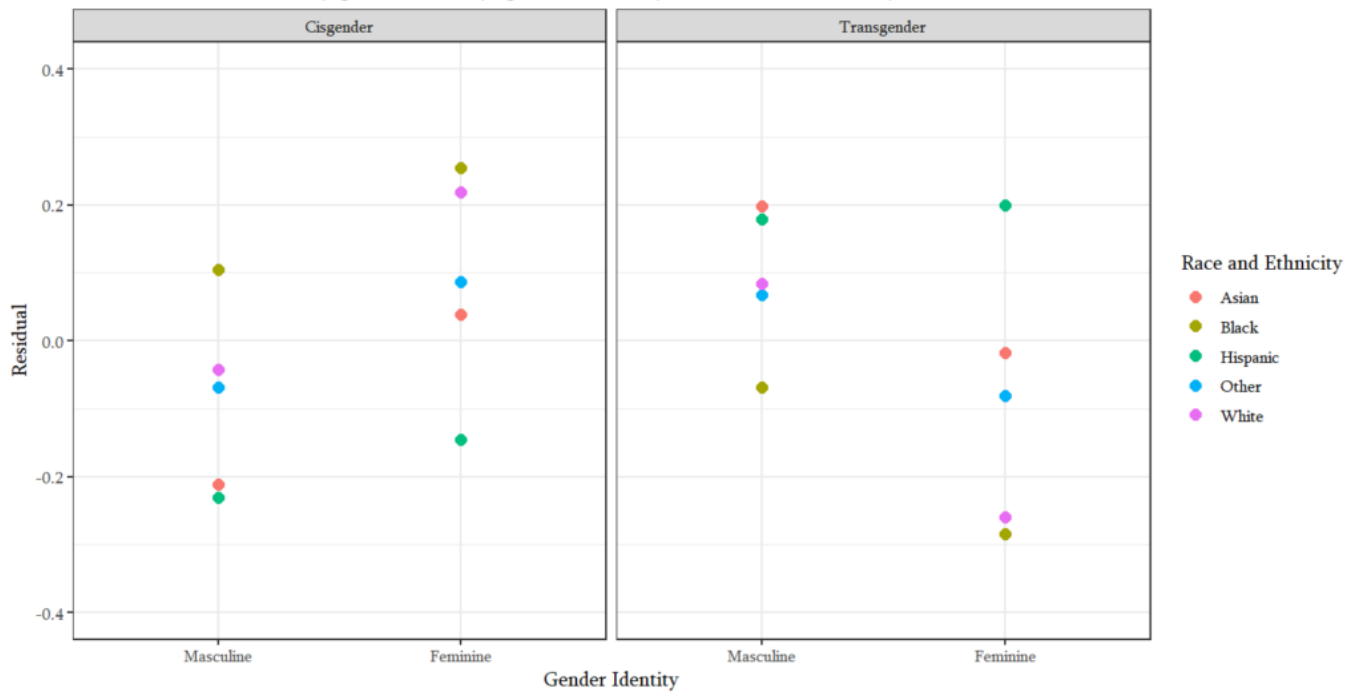
Parents' education modifies the association between neurodevelopmental disability and bullying victimization in children aged 12-17 in the United States. Adaeze Anamege* Adaeze Anamege Juan Perez-Carreno Delano Brooks

Introduction: The prevalence of bullying among adolescents in the United States is disproportionately high. While recent studies have explored the effects of neurodevelopmental disabilities on bullying prevalence, research on whether external factors such as parents' education influence the association between their children having a neurodevelopmental disability and experiencing bullying is sparse.

Methods: We characterized a representative sample of adolescents experiencing bullying using the 2021 National Health Interview Survey. We further determined whether parents' education modifies the effect of attention-deficit disorder, attention-deficit/hyperactivity disorder, intellectual disability, learning disability, and autism on bullying victimization. Bivariate and multivariable analyses were conducted to quantify the associations, controlling by age, sex, race, and health status. Predicted probabilities were calculated based on logistic regression models. All analyses were conducted in SAS version 9.4 and STATA-SE 17.

Results: Among 3,207 adolescents aged 12-17 years the prevalence of neurodevelopmental disabilities and bullying was 19.9% (95% CI: 18.3%-21.4%) and 22.4% (95% CI: 20.6%-24.2%), respectively. Neurodevelopmental disabilities were associated with decreased odds of experiencing bullying (aOR = 0.41, 95% CI: 0.32–0.53). Conversely, having parents with a high school education or less was associated with higher odds of being bullied (aOR= 1.87, 95% CI: 1.32-2.64). There was a significant interaction between parents' education and neurodevelopmental disabilities on the probability of experiencing bullying (interaction p < 0.001).

Conclusion: Future studies should explore the integration of anti-bullying educational programs within public health interventions targeted at parents with lower educational attainment. These programs should focus on increasing bullying awareness and developing strategies to foster adolescent social well-being.

Understanding the impact of selection biases inherent in pregnancy research across different causal inference approaches: a simulation study Basma Dib* Basma Dib Ellen Caniglia Sean Brummel Roger Shapiro Sonja Swanson

Randomized trials and observational studies that study the effect of pre-/during-pregnancy treatments on maternal and neonatal outcomes often have inherent forms of selection or collider-stratification bias. For example, these studies often restrict analyses to those who had a livebirth, those with a specified gestation duration, and/or those with complete follow-up. These selection factors and the outcome of interest frequently have unmeasured or even unknown shared causes which may induce bias in estimating the effect of treatment. Though such selection biases can affect all causal inference approaches, what is unknown is the extent to which the biases meaningfully impact different analytic approaches in pregnancy studies. We conducted a simulation study to assess and compare the magnitude and direction of selection biases in a hypothetical study of treatment effect on pregnancy outcomes across three different causal inference methods: inverse probability weighting (IPW), instrumental variable (IV), and sibling comparison design (SCD) analysis. We generated simulated data for various scenarios under two main conditions: (1) presence of loss to follow-up and (2) presence of a competing event. For each scenario, we generated 500 samples of data, each with a sample size of 10,000, and estimated an average causal effect. In presence of loss to follow-up, the mean bias in the risk difference estimates increased with a stronger association of loss to follow-up with treatment and outcome, with estimates obtained from IPW analysis and SCD analysis biased to nearly the same extent and in the same direction. The estimates obtained from IV analysis were consistently more biased by about one percentage point in the same direction. The mean bias varied across which causal estimand was targeted in light of the competing event. Our simulation study provides insight on the extent to which different analytic methods are impacted by selection bias in pregnancy research.

A series of emulated target trials to estimate the safety of antihypertensives for the management of non-severe gestational hypertension among pregnant individuals in Botswana Julia DiTosto* Julia DiTosto Rebecca Zash Denise Jacobson Modiegi Diseko Gloria Mayondi Judith Mabuta Mompati Mmalane Joseph Makhema Shahin Lockman Roger Shapiro Ellen Caniglia

Antihypertensive therapy is critical for management of non-severe gestational hypertension (HTN), yet potential fetal consequences are unclear. Standard analyses may be subject to immortal time and selection bias. Conducting a series of emulated target trials (ETT) can avoid these biases by aligning start of follow-up with therapy initiation.

The Tsepamo Study has evaluated birth outcomes at government delivery sites in Botswana since 2014. We investigated antihypertensive therapy initiation ≥24 weeks gestation for management of non-severe gestational HTN on stillbirth and small-for-gestational-age (SGA) by conducting 16 sequential ETT of therapy initiation versus no initiation during each week from 24-39 weeks' gestation. For each ETT, pregnant individuals with no history of HTN were eligible if they had not previously initiated therapy and had ≥1 elevated non-severe blood pressure reading (140-159 mm Hg systolic or 90-109 mm Hg diastolic) within 1 week of each ETT start. Log-binomial models were used to calculate RR and 95% CI. Results were pooled across all trials with bootstrapping to obtain CIs. Sensitivity analyses applied more stringent eligibility criteria (i.e., excluding preeclampsia and requiring >1 elevated blood pressure at baseline).

Of 28,608 individuals, 9,524 (33.3%) initiated antihypertensives between 24-39 weeks' gestation. Comparing initiation to no initiation, the pooled RR was 1.18 (1.07-1.40) for stillbirth and 1.15 (1.08-1.27) for SGA. RRs varied by week of ETT start (**Fig**) and were sensitive to definition of eligibility criteria. For stillbirth, the pooled RR was 1.07 (0.87, 1.23) when excluding preeclampsia and 0.90 (0.34, 1.32) when requiring >1 elevated blood pressure at baseline.

Our results suggest initiation of antihypertensive therapy for non-severe gestational HTN may increase risk of stillbirth and SGA. Results were sensitive to eligibility criteria definitions, suggesting potential for unmeasured confounding by HTN severity.

Figure
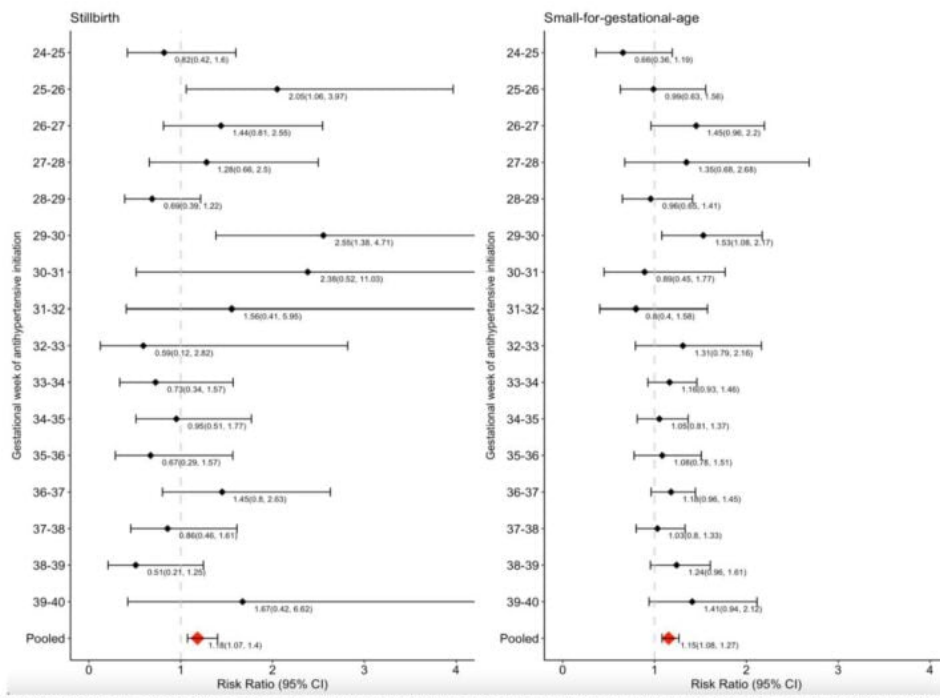
Models were adjusted for age, parity, history of preterm delivery or stillbirth, education, employment, HIV-status, GA at 1st antenatal visit, HbA1C, and systolic and diastolic blood pressure at trial start.

Exposure to gestational diabetes and hypertension in offspring: A triangulation approach

Nicole Brunton* Nicole Brunton Heather J. Prior Randy Walld Allison Dart Nathan Nickel Todd A. Duhamel Jonathan McGavock

Background: Exposure to gestational diabetes mellitus (GDM) is associated with increased risk for cardiovascular morbidity including adolescent hypertension. Whether this association represents a causal in utero mechanism remains unclear.

Methods: This study leveraged administrative health data from 418,169 singleton born offspring from 224,963 families in Manitoba, Canada. GDM and adolescent hypertension were determined using ICD codes and validated algorithms. We conducted three complimentary analyses. First, we compared rates of hypertension between offspring exposed to GDM and controls that were exact-matched on birthyear, socioeconomic index, maternal age, parity, residence, and health region using a Poisson model with person-years of the denominator as an offset. Second, we repeated these analyses using paternal type 2 diabetes status as a negative exposure control. Lastly, a sibling analysis compared the incidence of hypertension between siblings discordant for GDM exposure.

Results: Between unrelated families (n=209,461), risk of hypertension was 35% higher in GDM exposed vs unexposed offspring (RR:1.35, 95%CI: 1.19,1.54). After matching on covariates (n=11,612), there was a similar increased risk of hypertension among offspring exposed to GDM (RR:1.41, 95%CI: 1.16,1.72). Among all paternal-offspring pairs (n=145,318), hypertension risk was 1.7-fold higher for offspring whose fathers lived with diabetes (RR:1.70, 95% CI: 1.28, 2.27). The sample was considerably smaller after matching (n=2,022); however, the effect size remained similar, though it was less precise (RR:1.50, 95%CI: 0.96,2.24). There was no difference in risk for hypertension among sibling-pairs discordant for GDM exposure (n=12,204; OR:1.01, 95%CI: 0.83,1.21).

Conclusion: Collectively, these findings suggest that previously documented associations between exposure to GDM and increased risk of offspring hypertension may be due to family-based confounding rather than a direct in utero mechanism.

Childhood cancer risk in the offspring in relation to paternal occupational exposure to hydrocarbon solvents Yixin Chen* Yixin Chen Julia Heck Beate Ritz Johnni Hansen

Background: Paternal occupational exposures to hydrocarbon solvents are suspected risk factors for childhood cancer in offspring. However, prior studies are inconsistent.

Methods: This Danish population-based case-control study examined childhood cancer risk associated with paternal exposure from 3 months pre-conception to birth to aromatic (ARHC), aliphatic/acyclic (ALHC) and chlorinated hydrocarbons (CHC) as well as the specific solvents, dichloromethane, perchloroethylene, trichloroethylene, 1,1,1-trichloroethane, and toluene. Exposure estimates were based on Job Exposure Matrices. We included children born 1968-2013, aged <20 years old, with 10442 cases and 261050 matched cancer-free controls (25:1 matching ratio by sex and birth date). We employed conditional logistic regression models to estimate associations between hydrocarbons (any or high/low exposure stratified by median) and offspring cancer risk, adjusted by child's birthplace, paternal age and country of birth. Trend tests were used to assess exposure-response relationships.

Results: Paternal exposure to ARHC (high: OR: 1.31; 95% CI: 0.95, 1.81; P trend = 0.024) and CHC (high: OR: 1.82; 95% CI: 1.18, 2.82; P trend = 0.0028) was associated with an increased risk of glioma and an exposure-response was observed. The risk of childhood leukemia (high: OR: 1.29; 95% CI: 1.06, 1.56; P = 0.007), especially acute myeloid leukemia (high: OR: 1.87; 95% CI: 1.24, 2.82; P trend = 0.005) was higher when fathers were highly exposed to ALHC. Toluene increased the risk of leukemia (high: OR: 1.28; 95% CI: 1.05, 1.55; P trend = 0.01) and exhibited an exposure-response as did 1,1,1-trichloroethane for children's malignant bone tumors (OR: 1.79; 95% CI: 1.13, 2.86; P trend = 0.042) including osteosarcoma (OR: 2.29; 95% CI: 1.25, 4.18; P trend = 0.0084).

Conclusions: Our findings in Denmark suggest that paternal hydrocarbon exposure may increase the risks of glioma, leukemia, and malignant bone tumors in their offspring.

A randomized controlled trial to reduce endocrine disrupting chemical exposure in children Alan Fossa* Alan Fossa Katherine Manz George Papandonatos Aimin Chen Mark J. LaGuardia Robert C. Hale Bruce Lanphear Alexandra Pagano Kurt Pennell Kim Yolton Joseph Braun

Endocrine disrupting chemical (EDC) exposures during childhood may lead to adverse health outcomes, but few studies have explored the efficacy of dust control on EDC exposure. We conducted a secondary analysis of a randomized controlled trial, originally designed to reduce lead exposure, to see if the intervention lowered EDC loadings in household dust and biomarker concentrations in 2- and 3-year-olds. We also explored whether effects on biomarker concentrations were mediated through dust loadings. Study participants were maternal-child pairs from the Cincinnati, Ohio metropolitan area enrolled between 2003 and 2006 (n=250). Prenatally, families received either a housing intervention that included paint stabilization and dust mitigation or, as a control, injury prevention measures. At 24- or 36-months we measured organophosphate esters (OPEs), perfluoroalkyl substances (PFAS), and phthalates or their metabolites in dust, urine, and serum. We assessed associations between dust and corresponding biomarker EDCs, characterized EDC mixtures, and investigated treatment effects using Spearman correlations, principal components analysis, and linear regression, respectively. To adjust for selection bias due to attrition, we fit all statistical models using inverse probability of retention weights. Correlations between EDCs in dust and analogous biomarkers were weak ($\rho \leq 0.3$). The intervention was most notably associated with lower PFAS in dust (as high as -41%; 95% CI: -71, 19 for PFOA) and lower urinary concentrations of OPE and phthalate metabolites (as high as -22%; 95% CI: -38, -3 for DEHP metabolites). Almost all 95% confidence intervals included the null. There was some evidence that lower PFAS in serum was mediated through dust loadings (proportion mediated as high as 86% for PFOA). Housing interventions that mitigate dust could be effective in reducing childhood exposure to EDCs but larger studies with more tailored interventions are needed.

Spearman correlations between EDCs in dust, urine, and serum

Injuries/Violence
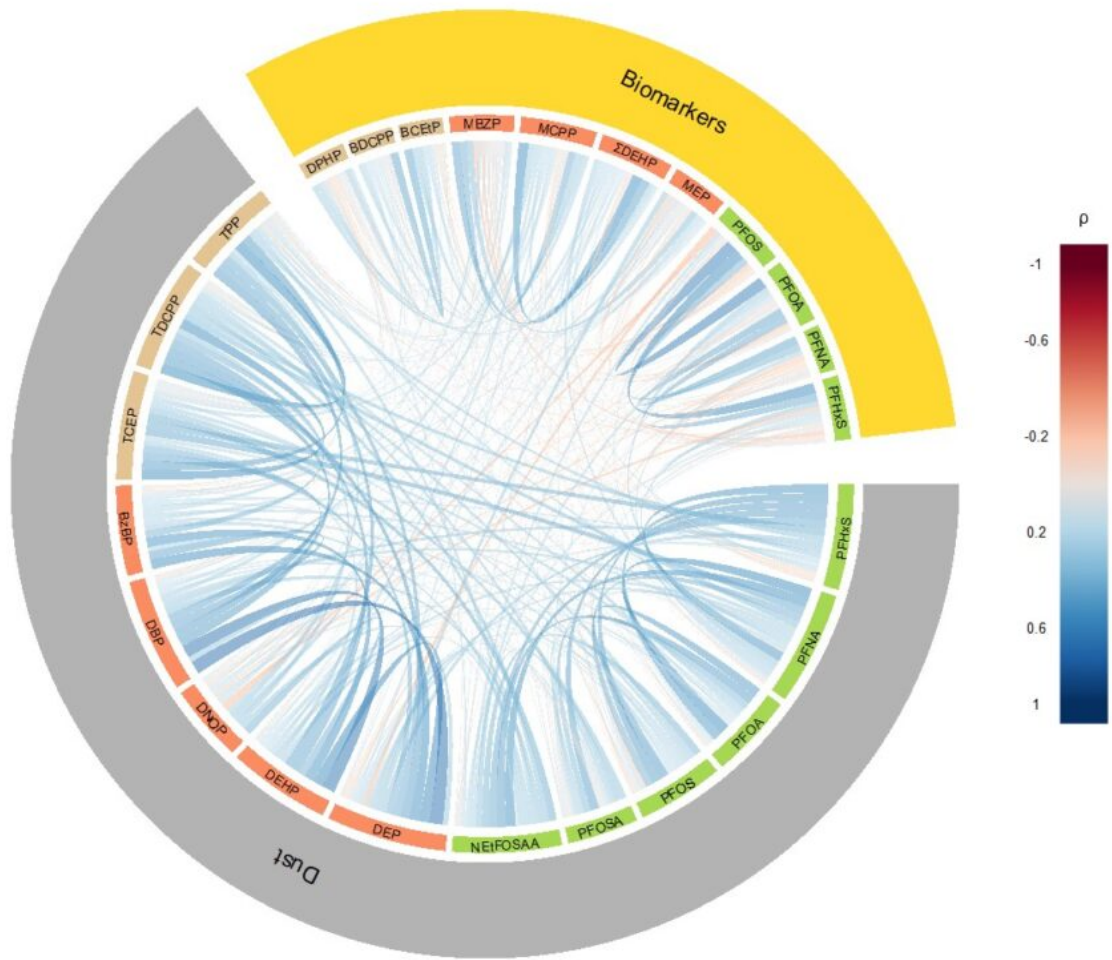
Individual, handgun, and purchasing characteristics and risk of firearm-related violent crime perpetration: a nested case-control study Hannah Laqueur* Hannah Laqueur Julia Schleimer Aaron Shev Rose Kagawa

Statement of Purpose: Firearm purchasing records offer a potentially critical administrative data source to identify individuals at elevated risk of perpetrating firearm violence. In this study, we describe individual, handgun, and transaction characteristics of purchasers in California who went on to perpetrate firearm violence as compared to the general population of registered handgun purchasers in the state.

Methods/Approach: We link individuals with handgun transactions records in California (1996- 2020) to criminal history records (1980-2021) to identify those who perpetrated a firearm-related violent crime. We enroll a dynamic cohort of individuals over a 24-year period (from 1996-2020). To avoid bias due to missing purchase history, we enroll only those for whom we can capture the full legal purchase history (the legal age of purchase in California is 21): e.g., those age 21 in 1996, individuals aged 21-22 in 1997, etc., up to those age 21-45 who purchased a handgun in 2020. Using incidence density sampling, we gender-match purchasers who perpetrated a firearm related violent offense to ten purchasers (controls) who remained "at risk" at the time that the case perpetrated the crime. We examine firearm purchasing patterns, handgun characteristics and criminal history. We analyze the data using conditional logistic regression.

Results/Conclusions: There were a total of 6,153 handgun purchasers arrested for a firearm-related violent crime. The largest risk factor was a prior criminal history: purchasers were roughly four times as likely to be arrested for a firearm-related violent crime if they had any prior criminal history (OR: 3.93, CI: 3.69-4.19). Controlling for criminal history, the type of transaction was still significant: risk increased if the handgun was redeemed at a pawn shop (OR:1.52, CI: 1.17-1.97) or was a low-cost handgun (OR:1.73, CI: 1.52, 1.98). However, when we examine interactions, handgun and purchase characteristics are only significant among those with no prior criminal history.

Significance: We identify several firearm and transaction level risk and protective factors. However, criminal history remains the most important risk factor for subsequent firearm violence.

Importance of Violence Prevention Approach Type for Predicting Neighborhood Violence

Rose Kagawa* Rose Kagawa Veronica Pear Colette Smirniotis Alex Kwong Hannah Laqueur

Background

Violence is a leading cause of death, disability, and despair, and the effectiveness of efforts to intervene on the social determinants of violence is not well understand. This study sought to determine what types of violence prevention efforts contribute most to the prediction of neighborhood violence rates.

Methods

Our study population included all census tracts in Cleveland, Ohio with complete data and >0 residents (N=169). The primary outcome of interest was the rate of major violent crime (homicide, rape, robbery, and aggravated assault) in 2019. Our main exposures were counts of 16 different violence prevention approaches (e.g. family relationship programs; anti-poverty policies, job readiness programs). To identify violence prevention approaches, we conducted an extensive review of public facing documents, resulting in 2,522 distinct intervention-locations that met our eligibility criteria. We grouped interventions by approach type following the CDC Technical Package for the Prevention of Youth Violence and other sources, then aggregated these approaches by year and census tract for the years 2015-2019. An additional 54 variables described the demographic, social, and physical features of Cleveland's census tracts over the study period (e.g. education levels, walkability, building type, age distribution). We used random forest to identify the violence prevention approaches that were most predictive of the rate of violent crime in 2019 and the degree to which the inclusion of these approaches improved the predictive ability of the model.

Results (preliminary)

Including violence prevention approaches in the prediction model improved model performance (MSE with=50.6 vs MSE without=64.7). However, no violence prevention approaches were ranked in the top 10 for variable importance. Among violence prevention approaches, investments in the physical environment were ranked as most important, following by approaches that reduced community-level risk factors (e.g. anti-poverty policies), and career training opportunities.

Conclusions

This study identifies specific approaches to violence prevention that are most important for predicting future violence rates for a single city. This information can guide future evaluation efforts attempting to identify causal effects.

Interpersonal violent injury and psychiatric disorder: Retrospective analysis of population-based, longitudinal Norwegian register data Sidra Goldman-Mellor* Sidra Goldman-Mellor Ping Qin

Interpersonal violent injury is a major public health problem, with potential adverse impacts on population mental health. However, rigorous epidemiologic research on this topic remains lacking. We aimed to examine how exposure to violent injury is associated with treatment for psychiatric disorder using nationwide longitudinal registry data from Norway. We identified all Norwegians presenting to emergency services in 2010-2018 with violent injury, along with sex- and age-matched control individuals from the general population. The primary outcome was subsequent outpatient or inpatient treatment for psychiatric disorder, observed through December 31, 2018. Psychiatric treatment rates in each study group were compared using stratified multivariable Cox regression models, controlling for sociodemographic characteristics and psychiatric history. Secondary analyses tested for moderation by sex, age, and prior psychiatric treatment, and examined congruence between pre- and post-violence psychiatric diagnoses. We found that violence-injured patients (n=28,276) had substantially higher rates of subsequent psychiatric treatment (102.8 per 100,000 person-years) when compared to controls (26.9 per 100,000), even after accounting for covariates (HRadj: 2.36; 95% CI: 2.29, 2.42). The association between violence injury and psychiatric treatment increased with age. Substance use, mood, and anxiety disorders were the most common diagnoses among violence-injured patients at follow-up. Twenty percent of violence-injured patients, vs. 6% of controls, had a history of prior psychiatric treatment, with high rates of pre- and post-violence diagnostic congruence. Our results suggest that violence-injured patients face substantial burden of psychiatric disorder, especially for substance use and mood/anxiety disorders. Clinical and public health strategies are needed to address this burden, which precedes violent injury in some cases but is likely provoked or exacerbated by it in others.

Injuries/Violence

: Independent and Joint Impacts of Alcohol and Cannabis Outlet Densities on Self-Harm Injuries in California: A Bayesian Spatiotemporal Analysis Rafael Charris* Rafael Charris Ellicott Matthay

Background: With the rapid expansion of state recreational cannabis legalization in the US, it is vital to understand its impact on alcohol-related harms, including self-harm injuries. This study explores the interactive impacts of changes in the physical availability of recreational cannabis and alcohol on self-harm injuries in California.

Methods: We integrated statewide data on self-harm injuries (2017-2019) across 1604 ZIP Code Tabulation Areas (ZCTAs), incorporating death, emergency department visits, and hospitalization records alongside geocoded alcohol outlet listings and storefront recreational cannabis outlet listings. We used Bayesian spatiotemporal models to account for small-area spatial dependence, modeling quarterly ZCTA-level self-harm rates. The models examined alcohol and cannabis outlet densities and their interaction, adjusted for sociodemographic confounders. From the multiplicative differences that the model returns, we applied g-computation to calculate additive risk differences (RDs) corresponding to hypothetical interventions on alcohol and cannabis outlet densities.

Results: Adjusted models indicated that eliminating cannabis outlets was associated with a slight but imprecise reduction in nonfatal self-harm injuries (nonfatal RD: -0.37; 95% CI: -1.31, 0.60). Regarding alcohol outlets, a 30% reduction in these outlets' densities was associated with a 2.5 per 100,000 decrease in nonfatal self-harm injuries (95% CI: -3.6, -1.44). These trends varied by demographic subgroup and injury means. Notably, no interaction was observed between alcohol and cannabis outlet reductions.

Conclusions: The introduction of storefront recreational cannabis outlets in California does not appear to have contributed to changes in rates of nonfatal self-harm injuries, but alcohol outlet densities were strongly correlated with rates of nonfatal self-harm injuries. Reducing alcohol outlet density is a candidate intervention for reducing self-harm. This analysis illustrates a novel approach for leveraging the posterior distributions of multiplicative-scale Bayesian spatiotemporal models to report policy-relevant additive-scale risk differences that account for spatial autocorrelation.

Injuries/Violence

Predicting US suicide death rates over time using measures of structural inequity Jonathan Platt* Jonathan Platt Amanda Sursely Avinash Mudireddy

Introduction: Suicide is the leading cause of violent death in the US, and death rates have been increasing especially among historically marginalized groups. Despite congressional calls, research focusing on social inequities and suicide is limited. This project aimed to identify key social inequities to accurately predict suicide death rates, utilizing an intersectional framework to account for multidimensional social structures, and machine learning methods to model that complexity with statistical efficiency.

Methods: US Vital Statistics data were used to calculate county-level suicide rates from 2005-2020 (n=5603). We assembled a dataset of 36 indicators of structural inequities across racial, sex/gender, and class domains. For prediction, we specified a time-series regression model with a Convolutional Neural Network (CNN) layer, Gated Recurrent Unit (GRU) layers, and dense layers. The integrated CNN-GRU structure utilizes a hybrid loss function and applies regularization techniques to enhance the model's ability to capture local patterns and temporal ordering.

Results: Model fit and error rates suggest good prediction accuracy (Mean Absolute Error=3.95, Root Mean Squared Error=5.54, R-squared=0.77; see figure). The final model contained 10 inequity indicators; structural classism indicators included income inequality and receipt of public assistance, while structural sexism indicators included sex disparities in education attainment, employment, poverty, political representation, and state laws restricting domestic violence perpetrators from possessing firearms. No indicators of structural racism were retained.

Discussion: An effective population health approach to suicide prevention must account for both historical and emerging inequities to identify high risk groups and prevent disparities. The indicators of structural classism and sexism we have identified highlight key targets for equity-promoting interventions to reduce preventable suicide deaths.

The accuracy of predicting US county-level suicide rates, comparing observed vs. predicted values from indicators of structural inequity.
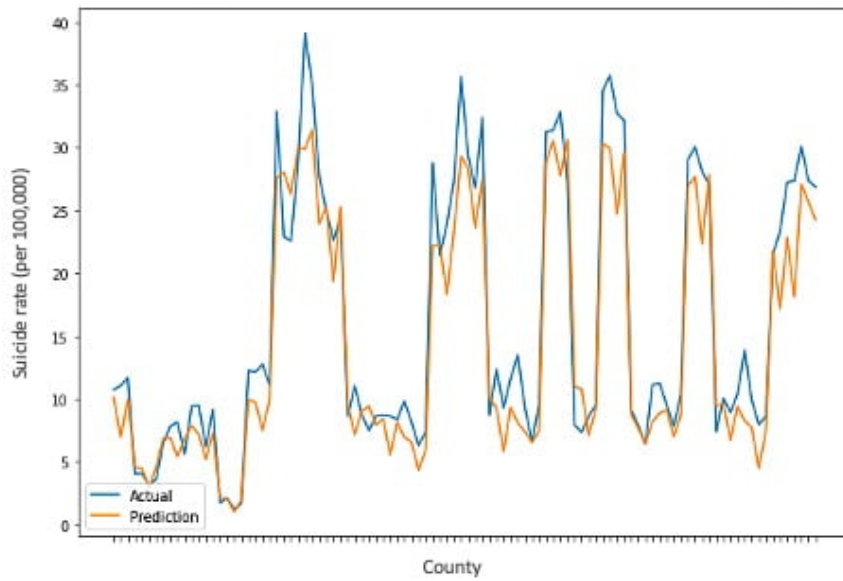
State minimum wage laws and state-level rates of new HIV diagnoses among Black, Latine, and White U.S. women and men, 2010-2019 Dougie Zubizarreta* Dougie E. Zubizarreta Jarvis T. Chen Ariel L. Beccia S. Bryn Austin Scott Burris Lindsay K. Cloud Madina Agénor

Racialized inequities in HIV are marked and persistent. Structural racism-related laws, including economic policies that disproportionately affect people of color, are potential drivers of these inequities. Yet, research is lacking on the impact of specific US state laws.

Data on inflation-adjusted state minimum wage laws from Temple's Center for Public Health Law Research was linked to data on state-level rates of new HIV diagnoses among US adults aged 13-59 from AIDSVu (N=51 states/DC). Linear models with state and year fixed effects were fit to examine associations between changes in state minimum wage laws and changes in state-level rates of new HIV diagnoses per 100,000 from 2010-19 among racialized groups (Black, Latine, White), overall and by gender, adjusting for time-varying state-level covariates (Medicaid expansion status, voter political lean, political ideology of elected officials). Sensitivity analyses lagged state minimum wage laws and time-varying covariates by one year to account for any delays in the effect of changes in state minimum wage laws.

Findings show a consistent pattern of decrease in HIV rates associated with increases in state minimum wages across all racialized groups. We observed the largest effects for Black adults, for whom a $1 increase in the state minimum wage was associated with a 5.5 per 100,000 decrease in HIV rate, followed by Latine adults (2.7/100,000), and White adults (1.5/100,000). We identified similar patterns within gender groups. Among men, the impact of increasing state minimum wages on HIV rates was greater for Black men (6.3/100,000) followed by Latine men (4.7/100,000) and White men (2.9/100,000). Among women, the effect was largest for Black women (5.9/100,000) but small for Latine women (0.9/100,000) and null for White women. Findings from lagged analyses were consistent with non-lagged analyses.

State minimum wage laws are a critical intervention for mitigating racialized HIV inequities among US men and women.

Figure 1. State minimum wage in dollars and state-level rates of new HIV diagnoses per 100,000 among Black, Latine, and White U.S. adults, 2019
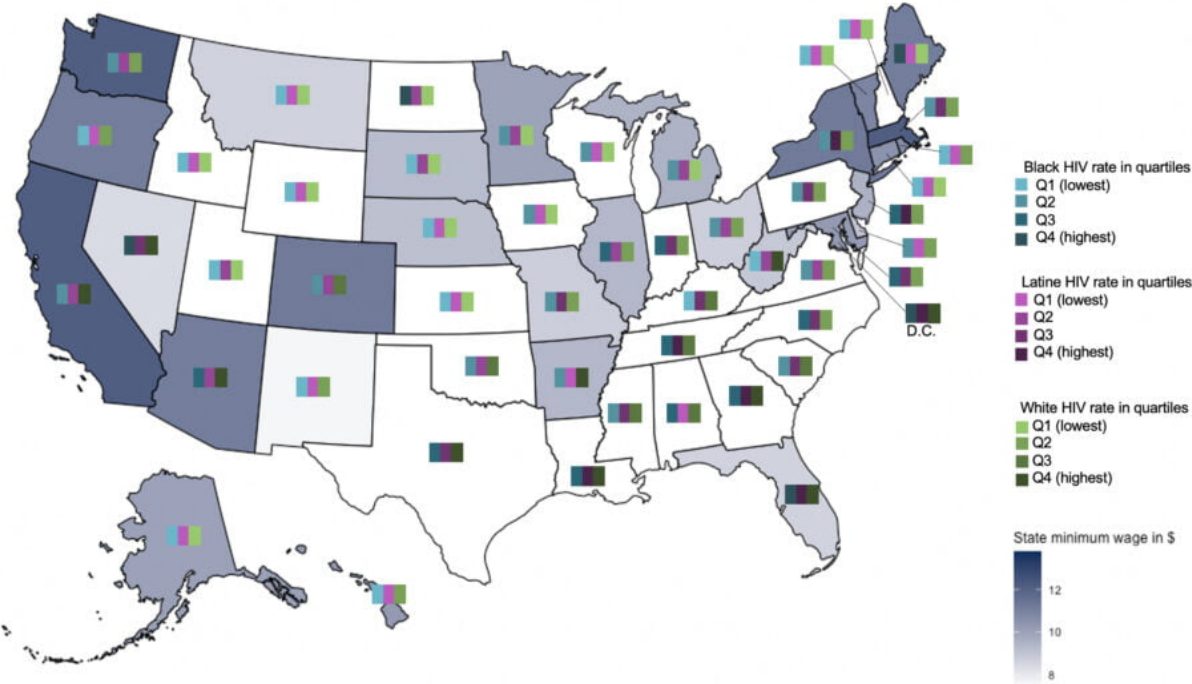
Income inequality and comorbid overweight/obesity and depression among a large sample of Canadian secondary school students: The mediator effect of social cohesion Jason Mulimba Were* Jason Were Stephen Hunter Karen A. Patte Scott T. Leatherdale Roman Pabayo

Background: Comorbid overweight/obesity (OWO) and depression is emerging as a public health problem among adolescents. Income inequality in a community is a structural determinant of health that independently increases the risk of both OWO and depression among youth. However, no study has examined the association between income inequality and comorbid OWO and depression or tested potential mechanisms in the relationship.

Objectives: 1) To identify the association between income inequality and comorbid OWO and depression; and 2) To test whether social cohesion mediates this relationship.

Methods: We used data from the 2018-2019 Cannabis, Obesity, Mental health, Physical activity, Alcohol, Smoking and Sedentary behavior (COMPASS) project. Our sample was composed of 46,171 adolescents from 136 schools distributed in 43 census divisions in 4 provinces in Canada (BC, AB, ON, QC). Comorbidity was determined by a participant being simultaneously classified as having OWO (BMI-Z > 1) and depression (≥10 points on the 10-item Center for Epidemiologic Studies Depression scale Revised). Income inequality was measured using the Gini coefficient at the census division level for school postal codes. Social cohesion was assessed using a school connectedness scale. Sex-stratified multilevel path analyses models were used to examine the study objectives.

Results: The direct effect between income inequality and OWO-depression comorbidity was not significant (Figure 1). However**,** income inequality was significantly associated with increased risk of comorbidity via social cohesion. One standard deviation increase in the Gini coefficient was associated with a 9% and 8% increase in the odds of comorbidity in girls (OR=1.09; 95% CI = 1.03, 1.15) and boys (OR=1.08; 95% CI = 1.03, 1.13), respectively.

Conclusion: Policies aimed at reducing income inequality, and interventions to improve social cohesion, may contribute to reducing the risk of OWO-depression comorbidity among adolescents.
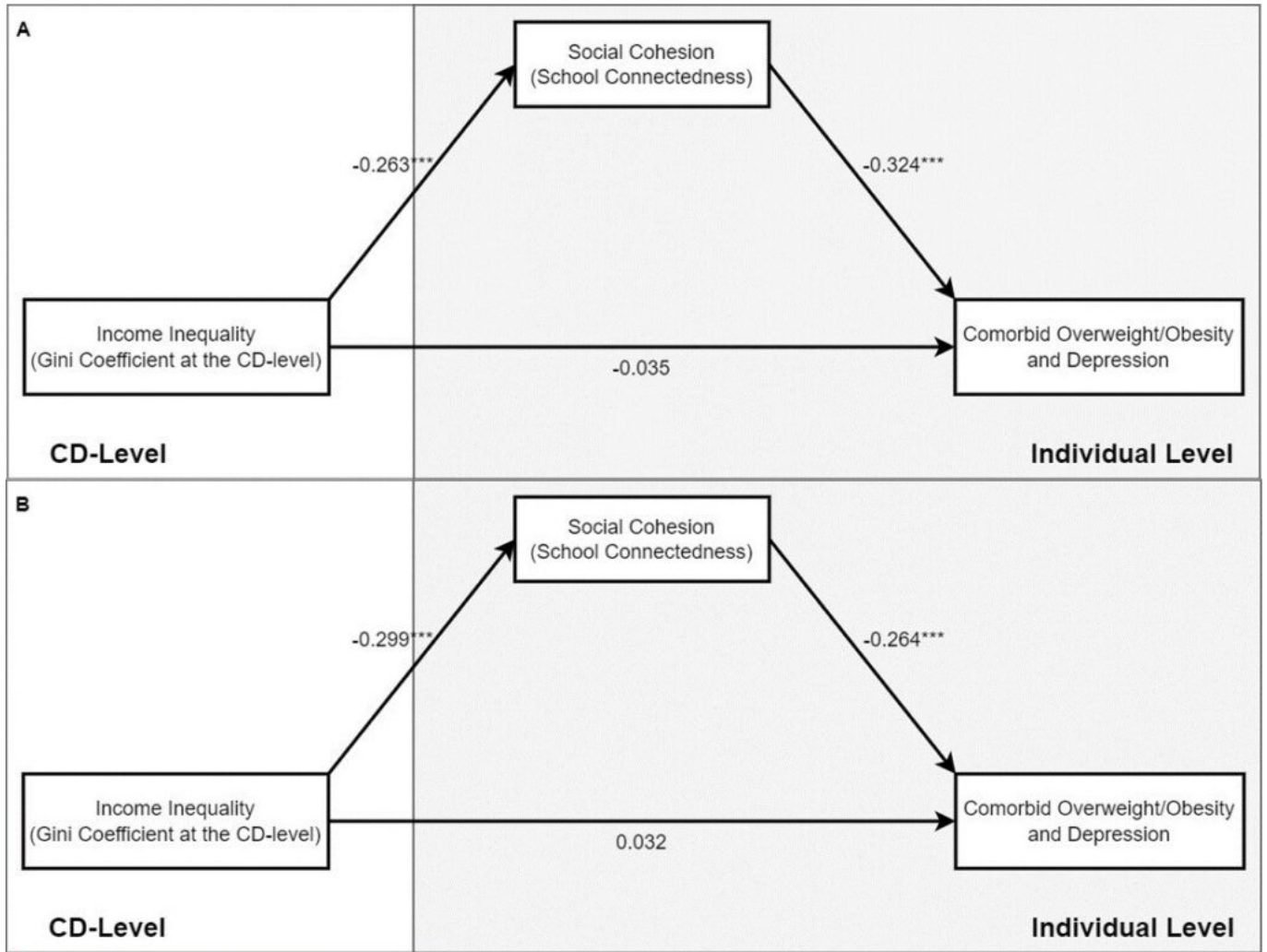
*= p < 0.05, ** = p < 0.01 *** = p < 0.001

Figure 1: Unstandardized coefficients of the multilevel path analysis models of comorbid by sex: A) Girls and B) Boys
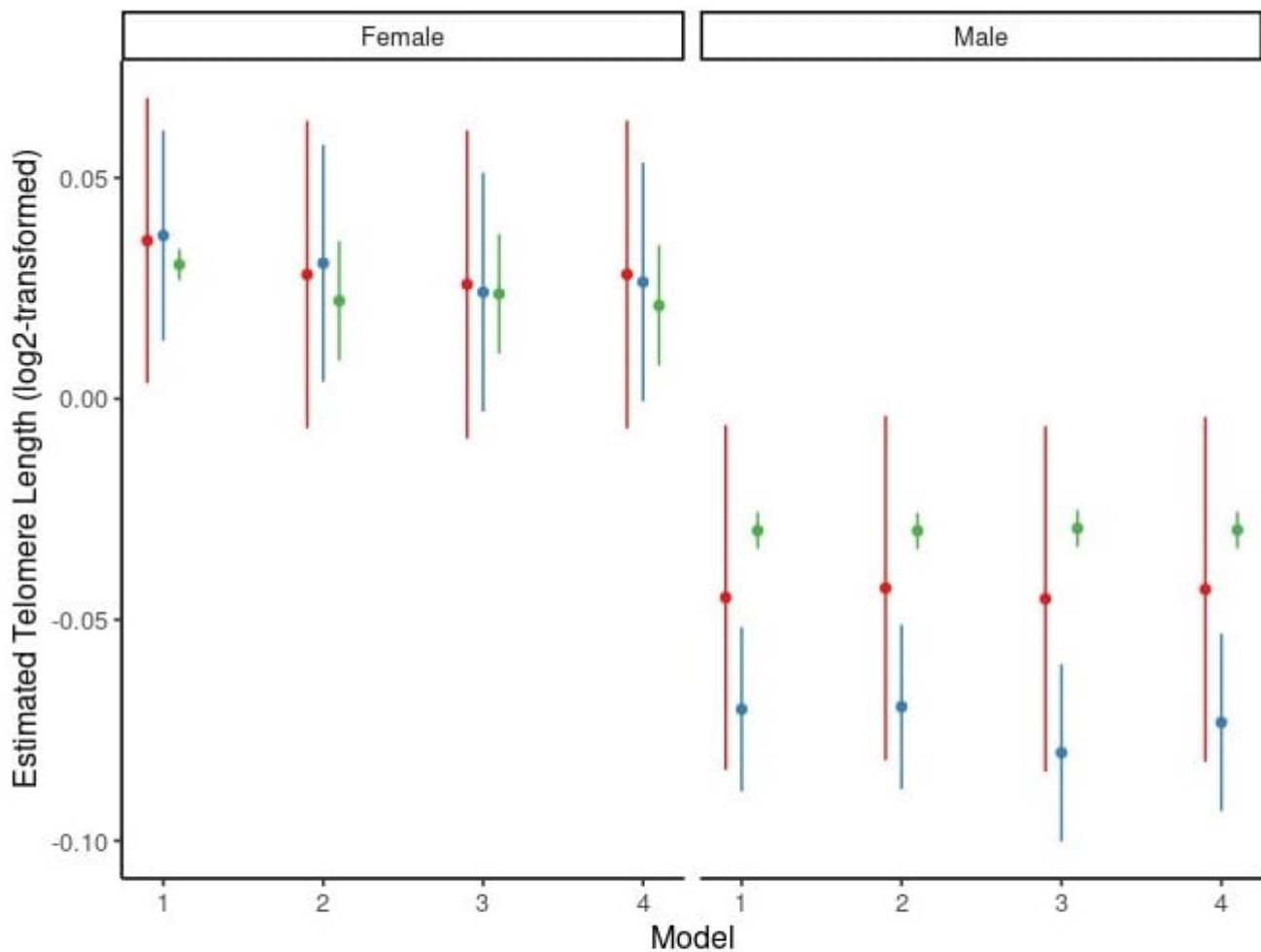
Aging

Telomere Length Differences by Sexual Orientation in Adults from the Resource for Genetic Epidemiology Research on Aging Cohort Adovich S. Rivera* Adovich Rivera Chun R. Chao Rulin C. Hechter

Background: The weathering hypothesis proposes that marginalized people experience faster biologic aging due to lifelong experience with stigma and stress which translates to chronic disease disparities. Prior studies have shown disparities in telomere length (TL) by race & ethnicity and socioeconomic status. We assessed differences in TL by sexual orientation in a cohort of insured adults from California.

Methods: We used cross-sectional data from the Resource for Genetic Epidemiology Research on Aging (2008-2011). TL was expressed as log2-transformed telomeric DNA to beta-globin single copy gene ratio (LTS). With linear regression models stratified by binary gender/sex, we calculated differences by sexual orientation (bisexual, gay/lesbian, straight) after adjusting for baseline age and socio-demographics. Oaxaca decomposition was used to explore drivers of significant disparities.

Results: We included 102,258 eligible individuals with mean baseline age of 63.4 years (SD: 14.5). The cohort was 58% female and 7.6% sexual minorities. Females showed no significant differences in age-adjusted LTS by sexual orientation (bisexual: 0.04, 95%CI: 0.004, 0.07; lesbian: 0.04, 95%CI: 0.01, 0.06; straight: 0.03, 95%CI: 0.027, 0.034) and the lack of difference persisted even after adjustment for all socio-demographic variables. Gay (-0.07, 95%CI: -0.09, -0.05) but not bisexual (-0.04, 95%CI: -0.08, -0.01) men had significantly shorter age-adjusted LTS compared to straight men (-0.03, 95%CI: -0.034, 0-0.026). This difference persisted even after full adjustment (gay-straight difference: -0.04, 95%CI: -0.06, -0.02). Decomposition showed that smoking and marital status were drivers of the gay-straight disparity.

Conclusion: Gay men had significantly shorter telomeres than straight men. Other sexual minorities had values comparable to their straight counterparts. Confirmatory studies using other aging measures and studies on health implications and social mechanisms are warranted.

Note: Models 1 to 4 are nested: Model 1 adjusted only for age at sample. Model 2 added race & ethnicity, nativity, & survey year. Model 3 added income, education, marital status, employment, & living alone. Model 4 added smoking and BMI.

Birth outcomes and pregnancy complications among US service members by disaggregated Asian, Native Hawaiian and Pacific Islander, and American Indian and Alaska Native race and ethnicity, 2010-2021 Celeste Romano* Celeste Romano Clinton Hall Monica Burrell Anna Bukowinski Jackielyn Lanning Sandra Maduforo Sandra Michelle Magallon Zeina Khodr Gia Gumbs Ava Marie Conlin

Introduction: A dearth of health disparities research has disaggregated data for US service members identifying as Asian and Native Hawaiian and Pacific Islander (NHPI) or reported health outcomes for racial and ethnic subgroups. Group representation is also underestimated when restricting group counts to those identifying as single race and non-Hispanic, especially for American Indian and Alaska Native (AIAN) and NHPI populations. Disaggregated estimates of health outcomes are needed to illuminate the experiences of military members identifying as Multiracial and Native and to elucidate patterns indiscernible in aggregated data.

Methods: Live births among pregnant service members were captured in Department of Defense Birth and Infant Health Research program data, 2010–2021. Self-reported race and ethnicity were obtained from personnel records. The prevalence of select birth outcomes and pregnancy complications, identified from medical encounter data, were calculated by disaggregated race and ethnicity.

Results: Overall, 216,017 births were identified among pregnant US service members and an increasing proportion occurred among Asian and Multiracial service members. Adverse birth outcomes and pregnancy complications varied in prevalence across racial and ethnic groups, particularly across Asian subgroups: Asian Indian and Filipino service members had consistently higher rates of adverse outcomes compared with other Asian subgroups and the total Asian population (eg, cesarean birth: 37.3% Asian Indian, 33.2% Filipino, 28.6% Asian). Multiracial AIAN and NHPI service members had higher rates of select adverse outcomes than their single-race, non-Hispanic counterparts (eg, low birth weight: 4.4 vs 3.8% AIAN; 4.9 vs 4.1% NHPI).

Conclusions: Increased attention should be paid to the disaggregation of racial and ethnic health outcomes among service members, especially given recognized disparities among racial and ethnic subgroups and the Multiracial population.

Sexual orientation disparities in adverse pregnancy outcomes Payal Chakraborty* Payal Chakraborty Ellis Schroeder Colleen A. Reynolds Sarah McKetta Juno Obedin-Maliver S. Bryn Austin Bethany Everett Sebastien Haneuse Brittany M. Charlton

Background: Sexual minority (SM) individuals have health profiles—e.g., health behaviors; limited resources due to structural, interpersonal, and individual stigma—that may place them at higher risk for adverse pregnancy outcomes (APOs), yet little research has examined sexual orientation disparities in APOs.

Methods: We used pregnancy data from the Nurses' Health Study 3, an ongoing cohort of nurses and nursing students in the US/Canada. Pregnancies occurred from 1978–2023. We analyzed 6 self-reported APOs: preterm birth (PTB), low birthweight (LBW), and macrosomia (MAC) among live births (N=25,877) and gestational hypertension (gHTN), gestational diabetes (GDM), and preeclampsia (PRE-E) among pregnancies ≥20 weeks (N=26,176). We examined disparities among 5 sexual orientation groups: completely heterosexual (reference), heterosexual with same-sex experience; mostly heterosexual; bisexual; and lesbian. We used log-binomial models to estimate risk ratios (RRs) fit via weighted generalized estimating equations to account for multiple pregnancies per person and informative cluster sizes.

Results: Compared to pregnancies to completely heterosexual participants, those of SM groups combined had higher risks of GDM (RR[95%CI]: 1.15[1.00–1.34]), gHTN (1.33[1.18–1.50]), and PRE-E (1.23[1.07–1.42]); no significant differences were observed for PTB, LBW, and MAC. Pregnancies to heterosexual participants with same-sex experience and mostly heterosexual participants had a higher risk of gHTN (1.34[1.08–1.66]; 1.30[1.12–1.51]), respectively) and PRE-E (1.40[1.09–1.79]; 1.20[1.00–1.44]) and lesbian participants had a higher risk of gHTN (1.68[1.11–2.52]). Bisexual and lesbian participants had RRs with high magnitudes for most APOs.

Conclusions: SM individuals experience disparities in many APOs, and disparities differ by SM subgroup. Elucidating the pathways to reduce disparities (e.g., structural barriers, health care needs) is critical for achieving reproductive health equity.

Figure. Risk ratios of adverse pregnancy outcomes by sexual orientation using log-binomial models with weighted generalized estimating equations (unit of analysis is pregnancies).*
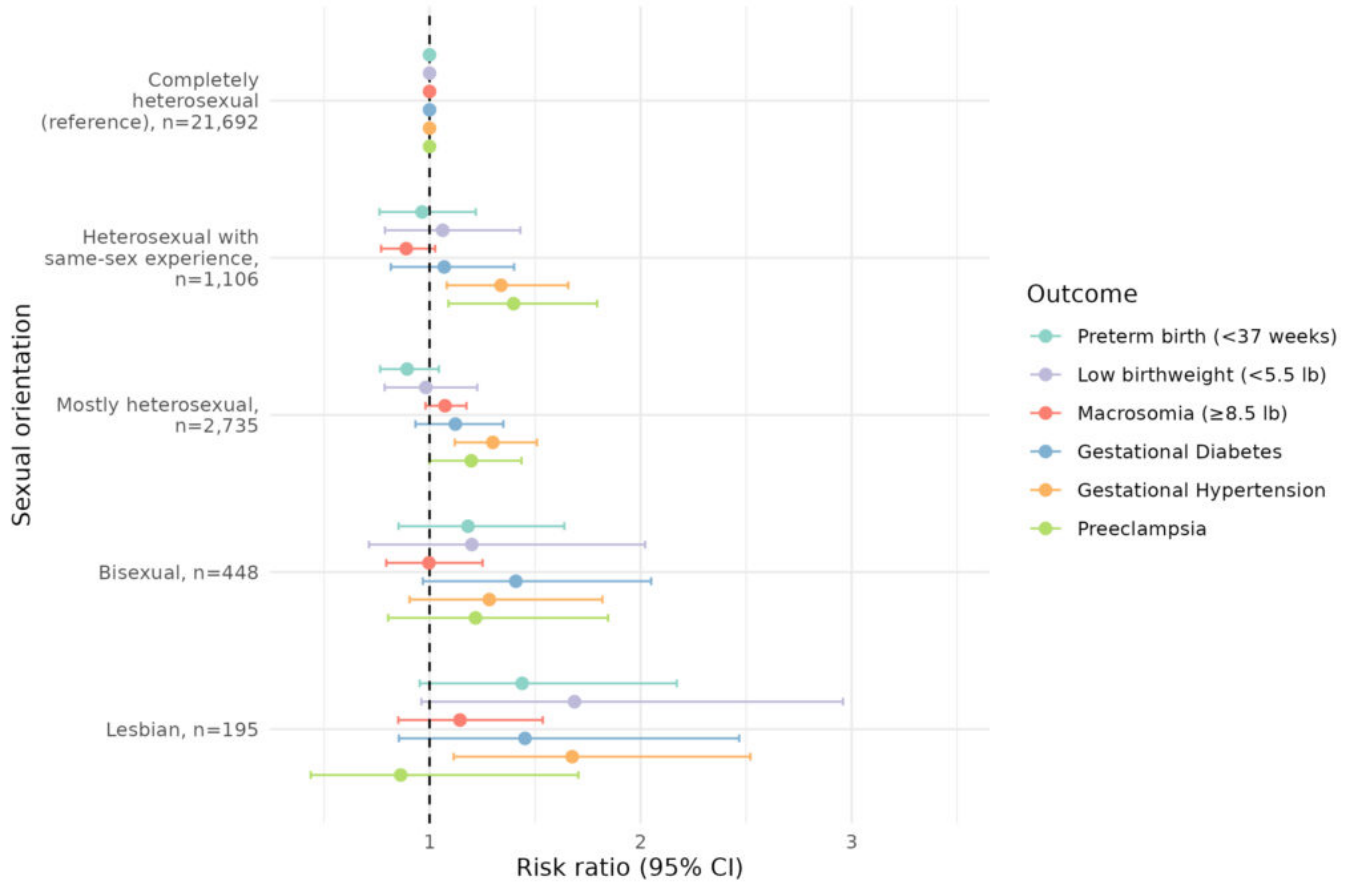

*Analyses for preterm birth (overall prevalence=10%), low birthweight (5%), and macrosomia (24%) were restricted to live births. Analyses for gestation diabetes (6%), gestational hypertension (8%), and preeclampsia (6%) were restricted to pregnancies ≥20 weeks gestation.

Addressing nonpositivity using statistical and mathematical models Paul Zivich* Paul Zivich
Jessie K Edwards Bonnie Shook-Sa Eric Lofgren Justin Lessler Stephen R Cole

Transportability methods can be considered when the desired target population and available study population differ on measured covariates. Most transportability methods rely on a positivity assumption, such that all relevant covariate patterns in the target population are also observed in the secondary population from which the available data was selected. Strict eligibility criteria, particularly in the context of randomized trials, may lead to violations of this assumption. Common approaches to nonpositivity are to restrict the target population, restrict the adjustment set, or extrapolate from a statistical model. Instead, we propose a synthesis of statistical (e.g., g-methods) and mathematical (e.g., microsimulation, mechanistic) models that avoids limitations of the alternative methods. Briefly, a statistical model is fit for the regions where positivity holds, and a mathematical model is used to fill-in, or impute, across the nonpositive regions. To implement our approach, we propose two estimators, one based on a marginal structural model and the other on the conditional average causal effect. The proposed synthesis method is illustrated by transporting the effect of antiretroviral therapy on CD4 cell count from the AIDS Clinical Trial Group (ACTG) 175 to the Women's Interagency HIV Study. Due to inclusion criteria in ACTG 175, nonpositivity occurs by baseline CD4 cell count. Using the synthesis approach and contemporaneous information on the conditional average causal effect, bounds on the effect of antiretroviral therapy are estimated for the nonpositive regions. Our results indicate that two-drug ART would have been beneficial on short-term CD4 cell counts in the target population without relying on the more restrictive assumptions of the other non-synthesis approaches. The synthesis approach sheds light on a way to address positivity violations and unifies different methodological areas to address a single scientific question.
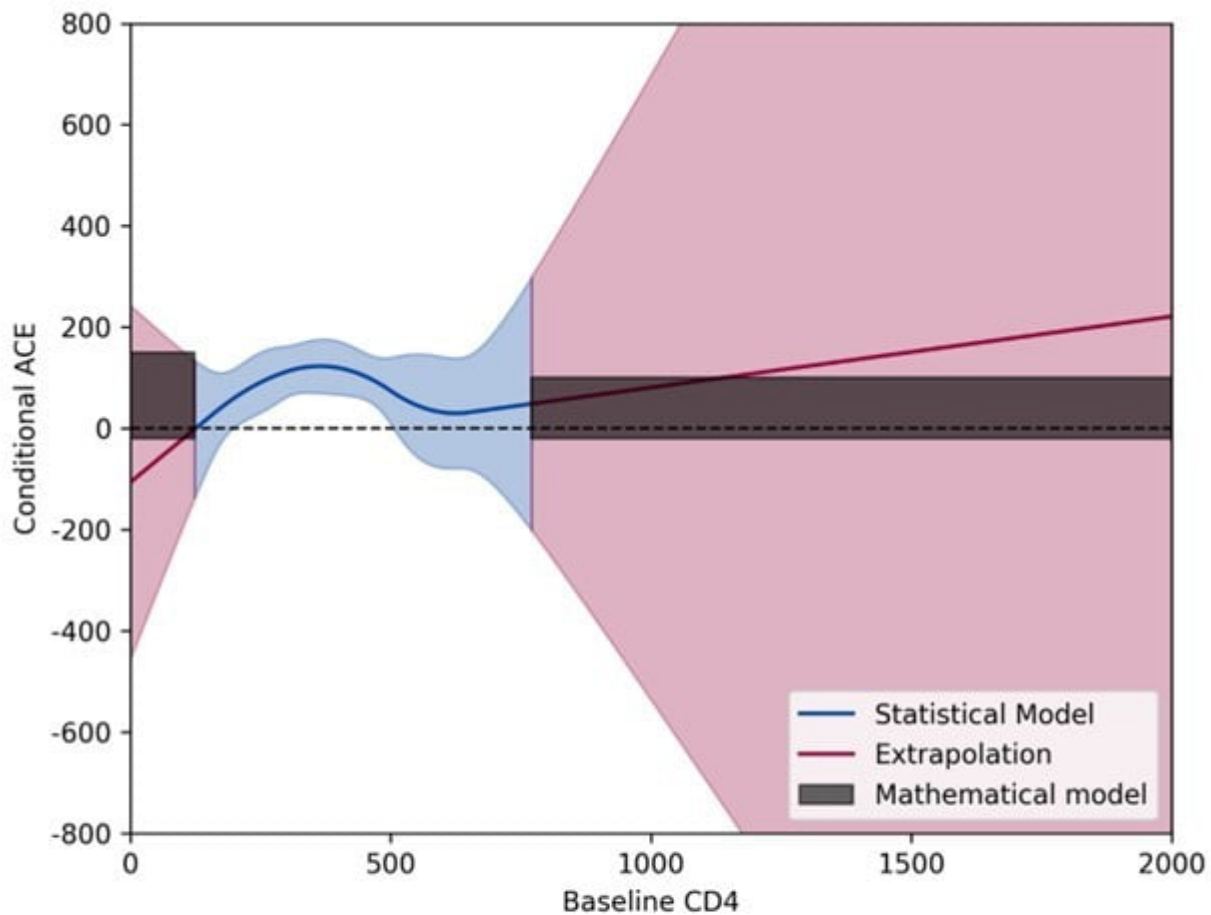
The blue region indicates the estimated conditional average causal effect in the target population in the regions where the positivity assumption holds (i.e., overlap in baseline CD4 between the ACTG 175 and WIHS participants). The red region indicates the extrapolations from the estimated statistical model to the regions of nonpositivity in the target population. The gray region corresponds to ranges of plausible values for the conditional average causal effect in the nonpositive regions based on pharmacokinetic studies external to both data sources.

A common-cause principle for eliminating selection bias in causal estimands through covariate adjustment Maya Mathur* Maya Mathur Ilya Shpitser Tyler VanderWeele

Average treatment effects (ATEs) may be subject to selection bias when they are estimated among only a non-representative subset of the target population. Selection bias can sometimes be eliminated by conditioning on a "sufficient adjustment set" of covariates, even for some forms of missingness not at random (MNAR). Without requiring full specification of the causal structure, we consider sufficient adjustment sets to allow nonparametric identification of conditional ATEs in the target population. Covariates in the sufficient set may be collected among only the selected sample. We establish that if a sufficient set exists, then the set consisting of common causes of the outcome and selection, excluding the exposure and its descendants, also suffices. We establish simple graphical criteria for when a sufficient set will not exist, which could help indicate whether this is plausible for a given study. Simulations considering selection due to missing data indicated that sufficiently-adjusted complete-case analysis (CCA) can considerably outperform multiple imputation under MNAR and, if the sample size is not large, sometimes even under missingness at random. Analogous to the common-cause principle for confounding, these sufficiency results clarify when and how selection bias can be eliminated through covariate adjustment.

Identifying vaccine effectiveness in the test-negative design under an equi-confounding assumption Christopher Boyer* Christopher Boyer Kendrick Li

The test-negative design (TND) is often used to monitor the effectiveness of vaccines under real-world conditions. In a TND study, individuals who develop the same symptoms and seek care are tested for the infectious disease of interest and effectiveness is estimated by comparing the vaccination history of test-positive and test-negative controls. Traditional approaches have justified the TND under the assumption that either a) receipt of a test is a perfect proxy for unmeasured (binary) health-seeking behavior or b) vaccination is unconfounded conditional on measured covariates, both of which are likely to be violated in practice. Here, we return to original motivation for the TND and show that the design may alternatively be justified under a scale-invariant assumption that unmeasured confounder(s) act equivalently for test positive and test negative illnesses, i.e. odds ratio equi-confounding. We discuss the implications of this assumption for the design of TNDs. In addition to providing alternative justification for the conventional logistic regression estimator, we derive estimators for the marginal risk ratio based on outcome modeling and inverse probability weighting using the generalized propensity score. We also derive a doubly-robust estimator allowing for the use of more flexible machine learning models. We provide proofs of our results as well as simulations to examine the finite sample performance of our estimators and illustrate the consequences when our assumptions are violated.

Causal Inference

Transporting treatment effects from difference-in-differences studies Audrey Renson*
Audrey Renson Ellicott C. Matthay Kara C. Rudolph

D

Difference-in-differences (DID) is a popular approach for estimating causal effects of treatments and policies in the presence of unmeasured confounding. If all assumptions are met, DID identifies the sample average treatment effect in the treated. However, a goal of such research is often to inform decision-making in target populations outside the treated sample. Transportability methods have been developed to extend inferences from study samples to external target populations; these methods have primarily been developed and applied in settings where identification is based on conditional independence between the treatment and potential outcomes, such as in a randomized trial. We present a novel approach to identifying and estimating effects in a target population, based on DID conducted in a study sample that differs from the target population. We present a range of assumptions under which one may identify causal effects in the target population and employ causal diagrams to illustrate these assumptions. In most realistic settings, results depend critically on the assumption that any unmeasured confounders are not effect measure modifiers on the scale of the effect of interest. We develop several estimators of transported effects, including g-computation, inverse odds weighting, and a doubly robust estimator based on the efficient influence function. Simulation results support that the proposed estimators are approximately unbiased when the stated assumptions are met. As an example, we apply our approach to study the effects of a 2018 US federal smoke-free public housing law on air quality in public housing across the US, using data from a DID study conducted in New York City alone.

Neighborhood disadvantage and menstrual disturbances among pregnancy planners in the U.S. Ruth J. Geller* Ruth Geller Mary D. Willis Collette N. Ncube Donna D. Baird Lauren A. Wise Amelia K. Wesselink

Introduction: Neighborhood disadvantage is associated with adverse reproductive outcomes, but its relation to menstruation is largely unknown. We hypothesized that neighborhood disadvantage would be associated with higher prevalence of abnormal uterine bleeding (AUB) and dysmenorrhea.

Methods: We analyzed baseline data from the Pregnancy Study Online, an internet-based preconception cohort study of pregnancy planners not using contraceptives or fertility treatments. We included 5,525 U.S. participants aged 21-39 years who enrolled during 2013-2019, lived at their current residence for ≥1 years before baseline, and reported on their typical menstrual cycle characteristics in the absence of hormonal contraceptive use. We linked participants' baseline residential addresses to the 2015 Area Deprivation Index (ADI), a Census block group measure of within-state neighborhood disadvantage. We defined AUB as cycle length <24 or >38 days, duration of flow ≥7 days, irregular cycles, and/or heavy flow. We defined dysmenorrhea as the report of severe cramps requiring medication and bed rest. We used log-binomial regression to estimate prevalence ratios (PR) and 95% CIs for the associations of ADI tertiles with AUB and dysmenorrhea, adjusting for age (21-24, 25-29 [ref.], 30-34, or 35-39 years) as a potential confounder and multivitamin use, season, and calendar year as precision variables. Covariates were modeled using indicator variables.

Results: The median ADI was 5 (IQR 2-7; higher scores represent greater disadvantage). The frequencies of AUB and dysmenorrhea were 34% and 8%, respectively. Adjusted PRs comparing the highest versus lowest ADI tertiles were 1.22 (95% CI 1.11-1.34) for AUB and 1.53 (95% CI 1.22-1.92) for dysmenorrhea.

Conclusions: Living in a disadvantaged neighborhood was associated with a higher prevalence of AUB and dysmenorrhea. Further investigation in longitudinal studies could inform interventions that improve menstrual health at the population level.

Reproductive
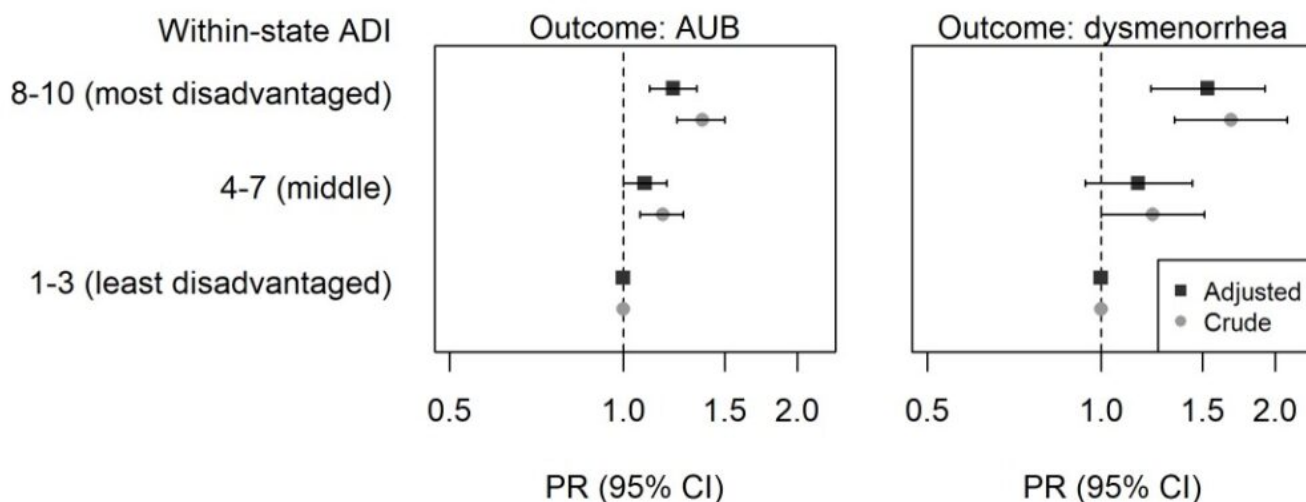
A probabilistic estimate of anovulation using basal body temperature recorded in a mobile phone application (app) Anne Marie Jukic* Anne Marie Jukic D. Robert McConnaughey Carlotta Favaro Eleonora Benhar Agathe van Lemsweerde Jack T Pearson Allen J Wilcox Donna D Baird Anne Marie Z Jukic

Factors that increase anovulation have been difficult to study. We propose a method of ascertaining likely anovulation from basal body temperature (BBT). We use test data from the Natural Cycles mobile app (NC app) to calculate the difference in mean temperature between two portions of the menstrual cycle that are iteratively created by dividing the cycle on each cycle day from day 5 (from cycle start) to -5 (from next cycle start). The maximum temperature difference (MTD) among these differences was retained for each cycle. We hypothesized that a small MTD is correlated with anovulation as defined by a proprietary NC app algorithm. Our test sample of cycles (N=114,004) excluded those of extreme lengths or with a high proportion of missing BBT days, and those impacted by pregnancy, breastfeeding, illness, or hormone use. When we stratified the MTD distribution by the NC app's definition of anovulatory and ovulatory, there was little overlap between the two (median MTDs of 0.26 °F and 0.63°F, respectively). Using a receiver operator characteristic (ROC) curve, the MTD was highly concordant with the NC app's measure of anovulation (area under the curve: 0.89). Using the Youden point of the ROC curve, we identified the optimal MTD cut point below which a cycle was likely to be anovulatory. We used generalized linear regression and binomial regression with a compound symmetric covariance structure to estimate associations of MTD and MTD-defined anovulation with older age. Older participants had lower estimated MTDs, and the risk of anovulation was also higher. (Table) These findings replicated in a second sample of NC app cycles. The MTD is the first estimate of anovulation based solely on daily BBT. It is predictive of NC app-defined anovulation and shows the expected association with older age. The MTD could be useful across many digital platforms to understand factors associated with anovulation.

Table. Association of age with the MTD and with the risk of anovulation*.

	Cycles	Change in MTD, °F x 10^4 (95% CI)	RR
Age			
18-19	565	-146 (-242, -50.0)	2.53 (1.94, 3.30)
20-24	13543	-41.5 (-68.2, -14.8)	1.63 (1.47, 1.81)
25-29	38375	40.1 (18.4, 61.7)	1.17 (1.07, 1.29)
30-34	35083	50.5 (28.9, 72.1)	0.94 (0.86, 1.04)
35-39	16912	0	1
40-44	7039	-125 (-158, -92.0)	1.23 (1.07, 1.41)
45-50	2232	-334 (-388, -280)	1.99 (1.68, 2.36)
>50	255	-854 (-1003, -705)	4.22 (3.08, 5.78)

*Anovulation defined by the optimal MTD cut point based on the Youden point of the ROC curve.

Reproductive

Influence of preconception Chlamydia trachomatis seropositivity on fecundability, pregnancy loss and live birth among women attempting pregnancy with a history of pregnancy loss Yajnaseni Chakraborti* Yajnaseni Chakraborti Stefanie N. Hinkle Jørgen Skov Jensen Catherine L. Haggerty Toni Darville Sunni L. Mumford Enrique F Schisterman Brandie De Paoli Taylor

Background: Chlamydia trachomatis (CT) can lead to innate-immune dysregulation and is associated with tubal factor infertility, yet the impact of prior exposure to CT on other reproductive outcomes is understudied. Given the unprecedented increase in CT infections in the U.S. and the high prevalence of pregnancy loss, we examined the association between CT seropositivity and conception, live birth, and pregnancy loss.

Method: Using data (n=1228) from a prospective cohort study – the Effect of Aspirin in Gestation and Reproduction (EAGeR), preconception CT seropositivity was determined using a multi-peptide ELISA test at baseline. Time-to pregnancy (fecundability) defined as number of menstrual cycles to β-hCG-detected pregnancy, was modeled using discrete Cox proportional hazard models, accounting for left truncation and right censoring. Live births were determined from medical records, and pregnancy loss was defined as any loss post positive β-hCG test. Inverse-probability (via a Generalized Boosted Model) weighted quasi-Poisson and unweighted log-binomial models, were used for assessing risks of pregnancy loss and reduced live birth, respectively. All models were adjusted for baseline demographic and reproductive history variables.

Results: Seropositivity (~11%) was associated with a reduction in live birth (RR: 0.66, 95% CI: 0.50,0.87), and an increased risk of pregnancy loss (RR: 1.15, 95% CI: 1.05,1.26), but was not associated with reduced fecundability (HR: 0.83, 95% CI: 0.63,1.08).

Conclusions: The above findings support our overarching hypothesis that prior exposure to CT among women with a history of pregnancy loss may impact future reproductive outcomes. This is important as therapies to target recurrent pregnancy loss are limited. Our results edict the need of future studies exploring mechanisms by which CT may influence long-term reproductive function, as this may identify treatments to improve outcomes among those with a history of infection.

Reproductive

Physical Activity and Risk of Spontaneous Abortion in a Danish Preconception Cohort Marie Dahl Jørgensen* Marie Dahl Jørgensen Ellen M. Mikkelsen Mette Aadahl Søren Brage Jakob Tarp Elizabeth E. Hatch Kenneth J. Rothman Lauren A. Wise Anne Sofie Dam Laursen

Background: About 15-30% of all pregnancies end with spontaneous abortion (SAB), making it one of the most common pregnancy complications. The evidence on the extent to which physical activity (PA) influences risk of SAB is inconsistent.

We evaluated the association between hypothetical replacement of pre-pregnancy sedentary time with different intensities of PA and the risk of SAB using data from a Danish preconception cohort.

Methods: We included 4,724 participants who conceived after entry in the SnartForældre.dk cohort from 2011 to 2023. Participants reported their PA levels via the International Physical Activity Questionnaire at baseline and on bimonthly follow-up questionnaires during preconception. We used data from the most recently completed questionnaire prior to conception. Pregnancy outcomes were identified via follow-up questionnaires, the Danish National Patient Registry, and the Medical Birth Registry.

We used Cox proportional hazards regression models to calculate hazard ratios (HR) and 95% confidence intervals (CI) with gestational weeks as the time scale. We used isotemporal substitution models to examine the effect of replacing durations of sedentary time with walking, moderate PA, and vigorous PA.

Results: The overall risk of SAB was 18% and median gestational age at loss was 7 weeks. The HRs for substitution of 30 minutes of sedentary time/day with 30 minutes of walking, moderate PA, or vigorous PA were 1.01 (95% CI 0.99-1.03), 0.98 (95% CI 0.89-1.09), and 0.91 (95% CI 0.79-1.04), respectively. Among participants with ≥7 hours of sedentary time/weekday, the association for replacement of sedentary time with vigorous PA was stronger (HR 0.80, 95% CI 0.64-1.00).

Conclusion: Replacing 30 minutes of sedentary time/day with walking or moderate PA had little association with risk of SAB. However, replacing sedentary time with vigorous PA was associated with a slightly lower risk of SAB, mainly among participants with ≥7 hours of daily sedentary time.

Endometriosis and hypertriglyceridemia, why we care about severity and typology? Karen Schliep* Karen Schliep Leslie Farland Anna Pollack Emmanuel Adediran Rachel Myrer Maggie Fuzak Kathryn Rexrode Michael Varner C. Matthew Peterson Madeline Paulson

While plausible mechanisms exist for an association between endometriosis and hypertriglyceridemia, prior studies have shown inconsistent findings, possibly due to the inability to assess endometriosis severity or subtypes. Among 473 premenopausal individuals undergoing gynecologic laparoscopy, regardless of clinical indication, the present study assessed the association between non-fasting serum triglycerides and incident endometriosis. Participants were recruited in Salt Lake City and San Francisco (2007–2009). Surgeons completed an operative report immediately after surgery to capture revised American Society for Reproductive Medicine staging (I−IV) and typology of endometriosis (superficial endometriosis [SE], ovarian endometrioma [OE], and deep infiltrating endometriosis [DE]). We collected biospecimens, anthropometrics, and self-reported sociodemographics at baseline. We evaluated the association between endometriosis diagnosis, stage, typology, and triglyceride concentrations using non-fasting female cutpoints (normal <175mg/dL vs hypertriglyceridemia ≥175mg/dL) via generalized linear models. Among the cohort, 108 women (23%) had high triglycerides. Endometriosis was associated with a slightly higher prevalence of high triglycerides (adjusted prevalence ratio (aPR): 1.41, 95% CI: 0.93, 2.12, Table 1). We found stronger associations by stage and type. Compared to no endometriosis, women with moderate to severe stage endometriosis had 2.03 (95% CI: 1.13, 3.63) higher adjusted aPR for hypertriglyceridemia. Women who were diagnosed with DE combined with OE had a 4.01 higher aPR (95% CI: 2.56, 6.29) for hypertriglyceridemia. In sum, we found that endometriosis staging and typology correlated more strongly with hypertriglyceridemia compared to diagnosis alone. A limitation of this study is not having fasting blood draws; however, prior research has shown that non-fasting triglyceride levels are a better predictor of cardiovascular risk than fasting triglycerides.

Table 1: Endometriosis diagnosis, staging, and typology and hypertriglyceridemia

Endometriosis	Hypertriglyceridemia n (%)	Unadjusted PR (95% CI)	Adjusted[1] PR (95% CI)
No	64 (22.6)	REF	REF
Yes	44 (23.2)	1.02 (0.73, 1.43)	1.41 (0.93, 2.12)
Endometriosis Stage			
No endometriosis	64 (22.6)	REF	REF
Stage I/II	26 (18.7)	0.83 (0.55, 1.25)	1.16 (0.73, 1.84)
Stage III/IV	18 (35.3)	1.56 (1.02, 2.40)	2.03 (1.13, 3.63)
Endometriosis Subtype			
No endometriosis	64 (22.6)	REF	REF
SE	25 (21.6)	0.94 (0.63, 1.42)	1.28 (0.80, 2.04)
OE or DE	8 (15.4)	0.69 (0.35, 1.34)	0.84 (0.35, 2.00)
OE & DE	11 (50.0)	2.20 (1.37, 3.50)	4.01 (2.56, 6.29)

Abbreviations: prevalence ratio (PR), superficial peritoneal endometriosis (SE), ovarian endometriomas (OE), deep infiltrating endometriosis (DE)

[1]Adjusted for age at baseline, race/ethnicity, marital status, BMI, serum cotinine, and stage of menstrual cycle (follicular vs luteal)

Neighborhood socioeconomic position and use of preconception folic acid-containing supplements in the National Birth Defects Prevention Study, 1997-2011 Anne Marie Darling*
Anne Marie Darling Eirini Nestoridi Rashida Smith-Webb Wendy Nembhard Jenil Patel Bailey Wallace Shannon Evans Suzan Carmichael Gary Shaw Mahsa Yazdy

Background: Neighborhood socioeconomic position has been associated with the occurrence of neural tube defects (NTDs). Our objective was to determine any differences in folic acid-containing supplement use, which reduces the risk of NTDs, by neighborhood. **Methods:** This study included 10,504 control participants from the National Birth Defects Prevention Study who gave birth to liveborn infants between 1997-2011. The neighborhood-level socioeconomic position indicator (nSEPI) was derived through a principal components analysis that incorporated 17 census socioeconomic indicators pertaining to the census tract in which participants lived longest during the 3 months prior to conception. The nSEPI was categorized into tertiles, with the highest tertile representing the lowest socioeconomic position. Folic acid-containing supplement use was defined as any use of folic acid or multivitamins containing folic acid during the 3 months prior to conception. Generalized estimating equations accounting for census-tract clustering and adjusted for individual-level socioeconomic and demographic factors were used to estimate the association between nSEPI tertiles and preconception folic acid-containing supplement use. Associations with individual components of the nSEPI were also examined. **Results:** Participants residing in low socioeconomic neighborhoods (nSEPI tertile 3) were less likely to report preconception folic acid-containing supplement use (Odds Ratio [OR] 0.66, 95% Confidence Interval [CI] 0.56, 0.77). Individual components of the nSEPI were consistently associated with supplement use, including census tracts with high unemployment ratio (T3 vs. T1: OR 0.61, 95% CI 0.52, 0.72), and high ratio of female headed households with dependents (T3 vs. T1: OR 0.61, 95% CI 0.52, 0.71). **Conclusions:** Neighborhood socioeconomic inequalities in preconception folic acid-containing supplement use are present and highlight potential opportunities for policy and community level interventions to address these inequalities.

Maternal antibodies to fetal brain antigens in relation to a mixture of five classes of environmental chemicals Kimberly* Kimberly Berger Kristen Michelle Lauren Heather Paul Judy Lisa

Maternal antibodies (MA) pass through the placenta to protect the immunologically naive neonate, and in some cases, can be reactive to fetal tissue. Previous work supports impacts of MA to fetal brain proteins on child neurodevelopment, but limited work has examined MA in relation to environmental pollutants, which have also shown associations with adverse neurodevelopment. We analyzed data from 411 general population controls from an Autism Spectrum Disorder case-control study of Californian children born in 2000-2003. Second trimester serum was assayed for environmental chemicals: eleven polychlorinated biphenyls, two organochlorine pesticides, six per- and polyfluoroalkyl substances, and six brominated flame retardants were detected in at least 60% of specimens. Particulate matter 10 and 2.5 microns in diameter, nitric oxide (NO), nitrogen dioxide, and ozone data for 30 days preceding specimen collection were downloaded from monitoring stations near maternal addresses. MA reactivity to eight highly expressed fetal brain antigens (CRMP1, CRMP2, GDA, NSE, LDHA, LDHB, STIP1, and YBOX) was measured by ELISA. Bayesian Hierarchical Modeling (BHM) and Bayesian Kernel Machine Regression (BKMR) analyses estimated overall mixture and individual chemical associations with MA accounting for co-exposures. In BHM models, each doubling of ozone concentrations was associated with an increase in MA reactivity to CRMP2, GDA, LDHB, NSE, and STIP1. Ozone (odds ratio: 6.72, 95% CI: 1.56, 30.05) and NO (odds ratio: 1.83, 95% CI: 1.15, 2.92) were associated with the highest quartile of the combination CRMP1 & CRMP2, which are crucial in neurodevelopment and may co-generate. BKMR models showed higher quantiles of combined exposures were associated with increased MA reactivity to STIP1 and CRMP2. Our results suggest environmental chemicals may increase maternal immune reactivity to fetal brain antigens, which may have longer-term neurodevelopmental impacts.

Prenatal Exposure to Mixtures of Non-persistent Chemicals and Childhood Obesity through Preadolescence: A Meta-analysis across 8 European Birth Cohorts Nuria Güil-Oumrait* Nuria Güil-Oumrait Martine Vrijheid Vincent Jaddoe Charline Warembourg Barbara Heude Sabrina Llop Loreto Santa-Marina

Background: Experimental studies have shown potential obesogenic effects resulting from early-life exposure to non-persistent chemicals commonly found in plastics and personal care products. However, epidemiological studies examining this association have been inconsistent, often limited by sample size or lacking a longitudinal approach. This study aimed to evaluate the associations between exposure to phenols and phthalate metabolites during pregnancy and offspring obesity outcomes in 8 birth cohorts spanning from north to south Europe.

Methods: We used harmonized data from over 5000 mother-child pairs with maternal urinary concentrations of 3 bisphenols, 4 parabens, benzophenone-3, triclosan, and 10 phthalate metabolites. Body Mass Index (BMI) z-scores were derived for three key developmental periods (early childhood: 2-5 y, adiposity rebound: 5-9 y, and preadolescence: 9-13 y). Adjusted associations were examined using DataSHIELD, employing linear mixed-effects models fitted separately for each cohort and combined through random effects meta-analysis. Interactions by age were tested, and linear fixed effects models assessed associations at each outcome time-point.

Results and conclusions: Preliminary findings, based on 3045 mother-child pairs from 4 cohorts, reveal an association between prenatal exposure to mono-ethyl phthalate (MEP) and an increase in childhood BMI z-score ($\beta = 0.08$, 95%CI: 0.00, 0.18). Fixed effects models indicate more pronounced associations between phthalate metabolites and BMI at older stages, specifically during preadolescence. These results suggest that prenatal exposure to MEP, a metabolite of diethyl phthalate widely used in fragranced cosmetics, is associated with increased BMI in childhood. Over the next 2 months, we anticipate definitive results, including the remaining 4 cohorts and an assessment of sex interactions.

Exposure-response relationships between chronic exposure to fine particulate matter and hospitalization risks for major cardiovascular diseases Yaguang Wei* Yaguang Wei Yijing Feng Edgar Castro Adjani A. Peralta Joel D. Schwartz

Objective: To estimate exposure-response (E-R) relationships between chronic exposure to fine particulate matter (PM2.5) and risks of first hospitalizations for ischemic heart disease, cerebrovascular disease, heart failure, cardiomyopathy, arrhythmia, valvular heart disease, thoracic and abdominal aortic aneurysms, and composite of these cardiovascular disease (CVD) subtypes.

Methods: We conducted a cohort study within Medicare fee-for-service beneficiaries aged ≥ 65 years in the contiguous US between 2000–2016. For each outcome, participants were followed each year until the first hospitalization, death, or end of study. Estimated PM2.5 levels at ZIP codes were calibrated to reduce exposure error. A causal framework that allowed confounders to have different impacts in different exposure ranges was developed, incorporating uncertainty of exposure estimates to reduce biases from exposure error.

Results: Three-year average PM2.5 exposure was associated with increased relative risks of first hospitalizations for ischemic heart disease, cerebrovascular disease, heart failure, cardiomyopathy, arrhythmia, and thoracic and abdominal aortic aneurysms. For composite CVD, the E-R curve demonstrated monotonically increased risk associated with PM2.5: compared to exposures ≤ 5 μg/m3, the WHO air quality guideline, the relative risk was 1.29 (95% CI, 1.28 to 1.30) at exposures between 9–10 μg/m3, which encompassed the US national average of 9.7 μg/m3. On absolute scale, ischemic heart disease, cerebrovascular disease, heart failure, and arrhythmia presented significantly increased risks associated with PM2.5. The effects persisted at least for three years after PM2.5 exposure. Age, education, healthcare accessibility, and neighborhood deprivation level modified the susceptibility to PM2.5.

Conclusions: No "safe threshold" exists for chronic effect of PM2.5 on CVD. Significant benefits could be attained through compliance with the WHO air quality guideline.
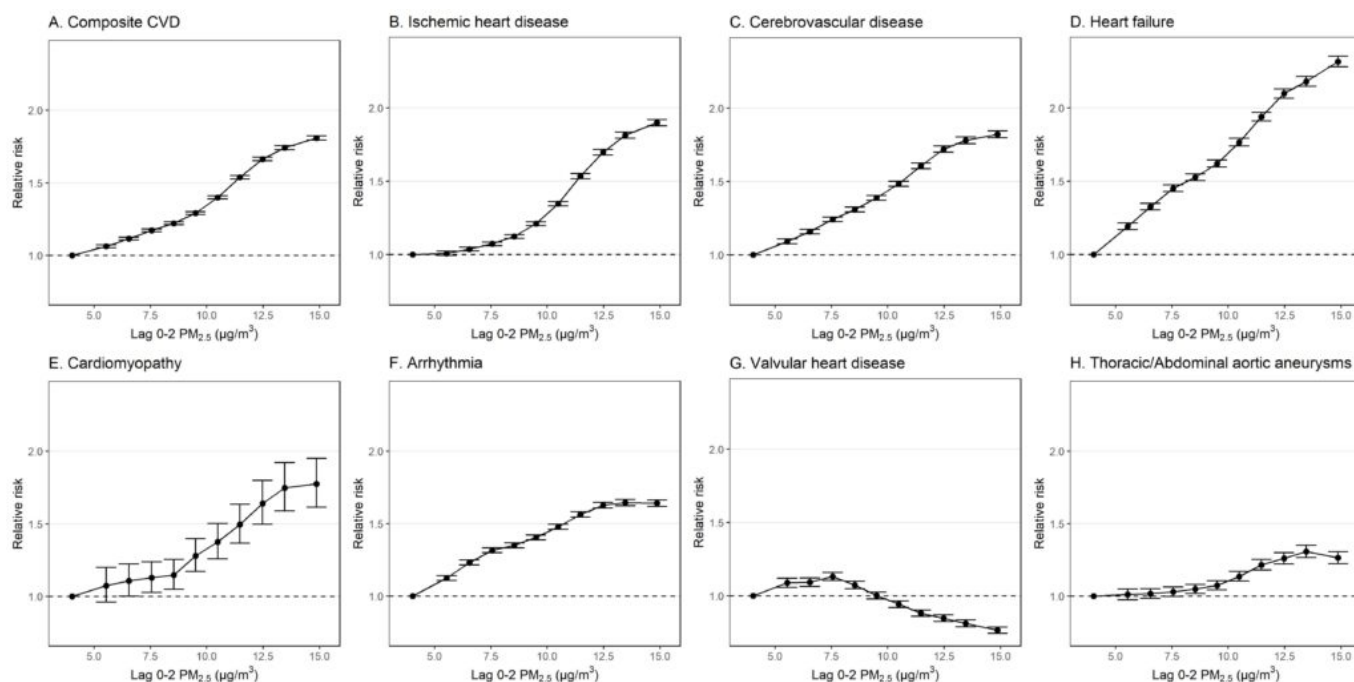
Carcinogenic industrial air pollution and breast cancer risk in the NIH-AARP Diet and Health Study Caroline Pruitt* Jessica Madrigal Caroline Pruitt Jared A. Fisher Linda M. Liao Barry I. Graubard Gretchen L. Gierach Debra T. Silverman Mary H. Ward Rena R. Jones

Background: Emissions from industrial facilities include known mammary carcinogens, but these exposures are not well studied with respect to breast cancer. We evaluated associations between air emissions of multiple carcinogenic chemicals and post-menopausal breast cancer risk in a large prospective U.S. cohort.

Methods: We used the US Environmental Protection Agency's Toxics Release Inventory to estimate historical airborne emissions (1987-1995) of 19 known and probable carcinogens for participants enrolled (1995-1996) in the NIH-AARP Diet and Health Study. A total of 15,124 breast cancers were diagnosed among 170,402 women through 2018. We constructed inverse distance- and wind-weighted average emissions metrics within 5 and 10km of the enrollment address for each chemical. We estimated multivariable adjusted HRs and 95% CIs for quintiles of each chemical in association with breast cancer overall and separately by disease type [invasive vs. ductal carcinoma in situ (DCIS)] and estrogen receptor (ER) status.

Results: We observed a suggestive association between asbestos emissions within 10km and breast cancer (HRQ5 vs. non-exposed=1.08, 0.97-1.20; p-trend=0.10) that was stronger for invasive disease (HRQ5 vs. non-exposed=1.12, CI=1.00-1.26; p-trend=0.02); but there was no association with DCIS (HRQ5 vs. non-exposed=0.89, CI=0.67-1.19; p-trend=0.50). We found a non-statistically significant increased risk of DCIS associated with trichloroethylene (TCE) in the top exposure quintiles at 10km (HRQ3=1.15, CI=0.99-1.34 and HRQ4=1.14, CI=0.97-1.33; p-trend=0.15), and a pattern of elevated risk across TCE quintiles for ER+, but not ER- tumors; these associations were stronger within 5km, though less precise. Associations with other chemicals were generally null or lacked clear patterns.

Conclusions: Our novel investigation suggests a small increased risk of breast cancer in association with asbestos and TCE emissions from industrial sources that warrants additional study.

Association of Midlife Air Pollution Exposures and Residential Road Proximity with Cognitive Decline over 28 Years: The Atherosclerosis Risk in Communities (ARIC) Study

Ziwei Song* Ziwei Song Katie Lynch Naa Adoley Parker-Allotey Erin E. Bennett Xiaohui Xu Eric A. Whitsel Richard Smith James D. Stewart Eun Sug Park Qi Ying Emma Stapp Melinda C. Power

Background: Limited research has explored the associations between midlife ambient air pollution exposures and cognitive decline, despite the potential etiologic relevance of midlife exposures. We therefore considered whether midlife exposure to air pollutants and traffic are associated with 28-year cognitive decline from mid- to late-life in the Atherosclerosis Risk in Communities (ARIC) study.

Methods: Our sample included Black and White ARIC participants from four sites, Forsyth County, North Carolina; Jackson, Mississippi; Washington County, Maryland; and the suburbs of Minneapolis, Minnesota, who were free of dementia and completed cognitive testing at Visit 2 (1990-1992). Participants were asked to complete 3 cognitive tests — Delayed Word Recall Test (DWRT), Digit Symbol Substitution Test (DSST), and Word Fluency Test (WFT) – at Visit 2, Visit 4 (1996-1998), Visit 5 (2011-2013), Visit 6 (2016-2017), and Visit 7 (2018-2019). At participant addresses, we estimated: [1] 1990-1992 average ambient air pollutant concentrations by combining output from the Community Multiscale Air Quality (CMAQ) chemical transport model fused with observed annual concentrations and [2] distance to major roads and road density within 500m radius as measures of traffic exposure. We used adjusted linear mixed-effects models to quantify associations between exposures and 28-year cognitive change.

Results: Among 12,700 eligible participants, median age was 57 years, 56.0% were female, 24.2% identified as Black, and 78.9% had attained at least a high school education at baseline. Higher levels of nitrates, copper, and lead were marginally associated with greater 28-year decline in DSST performance; no other exposures were associated with cognitive decline in adjusted models.

Conclusions: Higher midlife exposure to select components of airborne PM2.5 including neurotoxic trace metals may be linked to decline in processing speed.

Geographic Variation and Disparities in Hypertensive Disorders of Pregnancy Katherine Campbell* Katherine Campbell Lance Waller Penelope Howards Anne Dunlop Michael Kramer

Small area estimates of hypertensive disorders of pregnancy (HDP) (e.g. chronic vs gestational hypertension) are not readily available for county and local areas. Documenting local rates of disorders are of interest but generating statistically robust small area estimates can be difficult when local population and event counts are small. We use Bayesian spatial analysis to address challenges in describing county-level patterns of HDP subtypes and identifying characteristics of counties with high risk.

We abstracted birth certificate data for births to individuals ages 18 to 44 years in the US between 2009 and 2019. We model counts of each HDP subtype at the county-level via Poisson-Gamma Bayesian spatial model to estimate stable local rates of HDPs, account for spatial dependency, and identify counties exceeding the expectation of disease risk. We describe demographic and socioeconomic context based on county-specific measures to characterize counties identified as "high risk" (posterior probability of exceeding the national average) for each HDP.

Among 42 million live births in 2,869 counties, gestational hypertension rates were (7.5%) in 521 counties. Chronic hypertension rates were higher than expected (2.7%) in 513 counties and more consistently located in the southeastern US. The results revealed 204 counties exhibiting co-occurrence of high-risk for both chronic and gestational hypertension, but more than 300 counties showed subtype discordance. Differences in contextual factors were evident in counties with high-risk chronic hypertension compared to those without, whereas high-risk gestational hypertension was less strongly associated with racial density of counties and did not exhibit a clear correlation with rurality. This study underscores the question of combining HDPs for surveillance and research, given their distinct geographic distributions and the variation in their relation to place-based characteristics.

Women's Health

Overactive bladder 5 years after the Mid-Urethral Sling Tensioning (MUST) Trial : prospective cohort study following a multi-centre randomized control trial in Alberta, Canada Taylor Hughes* Taylor Hughes Amy Metcalfe Miranda Fidler-Benaoudia Kirsten Fiest Erin Brennand

Background: Mid-urethral slings (MUS) are the preferred surgical treatment for female stress urinary incontinence, yet a small subset of MUS patients experiences overactive bladder (OAB) sometimes needing further treatment. The Mid-Urethral Sling Tensioning (MUST) Trial provides an opportunity to gage OAB after MUS through follow-up of a randomized clinical trial which used patient reported and administrative health data.

Objective: To holistically assess the burden of OAB 5 years after MUS insertion using medication, surgical intervention and patient-reported OAB outcomes, and to compare OAB outcomes by MUS tensioning technique.

Methods: MUST Trial participants provided 5-year post-MUS data via patient-reported questionnaires linked to administrative health data. OAB burden was assessed by analyzing changes in pre- and 5-year post-op scores on validated OAB questionnaires, post-op OAB medication use and incidence of bladder Botox procedures.

Results: Of the 318 MUST Trial participants, 259 had complete questionnaire data; among them, 211 (81.5%) had OAB 5 years post-MUS. 225 (86.9%) had OAB pre-MUS. Few experienced clinically significant worsening in OAB symptoms; 19.0% in daily urination, 22.5% in urgency, 18.1% in urine leakage. Conversely, 38.7%, 40.3% and 47.6% showed significant improvement in the respective symptoms. 1/5 of total participants used OAB medication (all were naïve) with median start at 151 days post-op for a median duration of 319 days. 7 underwent a Botox procedure. The Babcock Clamp tensioning technique provided less frequent nightly urination and less leakage than the Mayo Scissor.

Conclusion: After MUS, some patients experienced improved OAB symptoms, while a minority report worsening. 20% of patients will trial OAB medications after MUS, but not all continue. Despite this rarity, medication is a crucial point of discussion for MUS candidates. Surgeons can freely choose tensioning techniques, expecting no significant difference in OAB outcomes.

Trends in self-reported infertility risk factors among fertility mobile app users trying to conceive Katie Noddin* Katie Noddin Eddye Golden Shannon Malloy Leslie Saltzman

Background: Today, up to one in four women trying to conceive experience infertility or impaired fecundity. Factors associated with infertility and impaired fecundity include age, gynecological disorders, race, ethnicity, and socioeconomic status, among others.

Reproductive health mobile apps have grown in number and popularity to support women's fertility goals. In the U.S., about one-third of women use apps to track their reproductive health. These apps present a unique opportunity to understand infertility risk factors among people trying to conceive (TTC) at a large scale.

Objective: To assess the incidence of self-reported infertility risk factors over time among individuals trying to conceive using a fertility tracking app.

Design: Self-reported infertility risk factors, race, ethnicity, age, and other demographic variables were collected from a sample of 2.6M users from 2017 to 2023 who indicated actively TTC. Trends in self-reported infertility risk factors and demographic information were assessed using multivariate descriptive analyses.

Results: Between 2017 to 2023, the average age of users who were TTC rose by 8.4%. Younger age groups showed an increase in self-reported risk factor incidence over time while older age groups decreased. There was a 14% increase in the proportion of users TTC indicating any risk factor for infertility, leading to 29% reporting at least one risk factor in 2023. PCOS was the most commonly indicated risk factor and increased the most year over year. Conversely, the incidence of users who were TTC with diagnosed infertility decreased by 42% over the 6 years. The sample closely mirrored the U.S. at large in race.

Summary: As infertility rises, understanding changes in risk factors is imperative to designing successful interventions that reduce preventable risk and optimize fertility. This large-scale analysis offers a unique view into the infertility risk factors of fertility app users trying to conceive.

Women's Health

The relationship between sexual orientation and race/ethnicity and preventive health care utilization among Illinois women 21-65: Is intersectionality at play? Caitlin Meyer Krause*
Caitlin Meyer Krause Kristin Rankin Arden Handler William Barshop Madison Levecke Brenikki Floyd

Background: Generally, lesbian, gay, and bisexual (LGB) women are less likely to receive routine health care including the well-woman visit (WWV), which provides an opportunity to receive cervical cancer screening (CCS). This study assessed the relationship between sexual orientation and receipt of preventive health services, including modification by race/ethnicity, among Illinois women aged 21-65.

Methods: The study used 2016, 2018, and 2020 Illinois Behavioral Risk Factor Surveillance System data among women aged 21-65 to examine rates of CCS within 3-5 years per US Preventive Services Taskforce guidelines (n=2848) and 2016-2018 and 2020-2021 data to examine WWV use (n=5863) by sexual orientation (heterosexual vs. LGB; not asked in 2019). Self-reported race/ethnicity was tested as an effect modifier to assess intersectionality. Using Poisson regression models, adjusted prevalence ratios (aPR) and 95% CIs were estimated with specialized techniques for the survey design and weighting. Covariates included age, education, marital status, employment, health insurance coverage, and race/ethnicity by sexual orientation.

Results: Overall, 4.6% of Illinois women aged 21-65 self-identified as LGB. Heterosexual and LGB women had a similar prevalence of receipt of both a WWV (77.1% and 71.7%, respectively; aPR=1.04, 95% CI: 0.95, 1.15) and CCS (85.3% and 83.4%, respectively; aPR=1.03, 95% CI: 0.93, 1.13). When stratified by race, Non-Hispanic (NH) Black heterosexual women had a higher prevalence of both services compared to LGB women; however, adjusted associations included the null. NH White and Hispanic women had similar prevalence of both visit types by sexual orientation.

Conclusion: In Illinois overall, heterosexual and LGB women receive preventive care screenings at similar rates. However, WWV and CCS receipt may differ between NH Black heterosexual and LGB women which may indicate missed opportunities for some women to receive preventive care.

Women's Health

The Contribution of Contextual Factors to Geographic Variation in Pregnancy-Related Mortality: A Multilevel Analysis Chloe M. Barrera, PhD, MPH* Chloe Barrera David A. Goodman, PhD, MS Sarah Blake, PhD, MA Lauren Christiansen-Lindquist, PhD, MPH Alex Peahl, MD, MSc Michael R. Kramer, PhD, MMSc

Background Racial and geographic disparities in US pregnancy-related mortality are significant and persistent. This analysis assesses geographic variation in pregnancy-related deaths and the role of individual and county-level factors.

Methods Pregnancy Mortality Surveillance System data were linked with publicly available county-level indicator data. Three-level Poisson regression models (individuals, counties, regions) stratified by non-Hispanic Black/White race were used to estimate associations between county-level indicators and pregnancy-related mortality. We calculated median rate ratios (MRRs) from the estimated variance of the random effects for county and region to quantify the magnitude of the between geographic variance unexplained by the variables in each model. Model 1 was adjusted for individual characteristics and Models 2-6 were additionally adjusted for county-level indicators of economic stability, neighborhood environment, education and literacy, social context, and health.

Results Our analysis included 3,561 pregnancy-related deaths and 22,822,719 live births, representing 88% of all known pregnancy-related deaths and 99% of all known live births during 2014-2019. In Model 1, we found intercounty and interregional variation in pregnancy-related mortality among both Black and White populations. When county-level indicators were adjusted for, there was attenuation of the MRR that was generally greater among the White compared to Black population. For example, the introduction of county-level health indicators reduced the regional MRR from 1.35 to 1.09 among the White population and from 1.37 to 1.25 among the Black population.

Conclusion Geographic inequities in pregnancy-related deaths are experienced differently by non-Hispanic Black and non-Hispanic White women living in the same geographic units. Strategies are needed to address inequities in pregnancy-related deaths at different geographic levels.

Mental Health

Involuntary Psychiatric Commitments among Non-Western Immigrants During the Muhammad Cartoon Controversy in Denmark Tim Bruckner* Tim Bruckner Parvati Singh Camilla Hvidfelt Lars Andersen

Persons deemed a danger to themselves, others, or gravely disabled may receive involuntary psychiatric commitment if family, other residents, law enforcement, or clinicians initiate this process. On September 30, 2005, a Danish newspaper published cartoons depicting the Prophet Muhammad. This publication led to the worst foreign policy crisis in Denmark since the second World War. Whereas protests within Denmark against the cartoon remained peaceful, this cartoon controversy—including the attacks on four Danish embassies outside of Denmark—may have reduced societal tolerance for threatening or deviant behavior among non-Western immigrants. We test whether this cartoon controversy preceded greater than expected counts of new involuntary psychiatric commitments among non-Western immigrants. Rigorous interrupted time-series methods support this hypothesis in that new involuntary psychiatric commitments rose by 10.5 per quarter (95% Confidence Interval: 3.95, 17.03), which equates to a 43% rise, during the controversy (p<.01). Changes in help-seeking overall for mental health services do not appear to account for this rise in new involuntary commitments. In addition, the pattern of results indicates that anti-immigrant sentiment in the broader community, rather than within the police force, likely contributed to this rise. Findings cohere with the notion that population-wide controversies may lower societal tolerance for behavior deemed deviant—and in this case, specifically among non-Western immigrants.

Mental Health

Post Dobbs: Distance to abortion facilities and depressive symptoms among racially/ethnically minoritized women of reproductive age Abhery Das* Abhery Das Allison Stolte Samantha Gailey

On June 24, 2022, the US Supreme Court's decision on Dobbs v. Jackson Women's Health transformed the landscape of abortion access in the US by granting states the power to ban abortion. In the following months, several states implemented restrictive abortion laws that limited women's fertility decisions and hindered their access to comprehensive reproductive care. The symbolic dis/empowerment framework suggests that these new sociopolitical contexts may disempower women in ways that harm their psychological well-being. Indeed, one study reports greater mental distress among women of reproductive age following the Dobbs decision. The psychological burdens of Dobbs, however, likely manifest heterogeneously. Previous studies find that racially/ethnically minoritized women experienced disproportionate harms from pre-Dobbs restrictive reproductive health laws. More recently, many abortion-related lawsuits have targeted racially/ethnically minoritized women, which may heighten feelings of disempowerment among these groups. We test whether state-level disempowerment related to women's reproductive health, proxied as distance to abortion facilities, coincide with greater depressive symptoms among racially/ethnically minoritized women of reproductive age after the Dobbs decision. As our exposure, we utilize quartiles of within-state average driving distance (miles) to abortion facilities, captured at the county-level. For our outcome, we use the Patient Health Questionnaire-2, a clinically valid measure of depressive symptoms among 49,361 racial/ethnic minoritized women of reproductive age (18-49). We use biweekly surveys (repeat cross-section) from August 2020 – July 2023 from the nationally representative Census Household Pulse Survey. We find that women of color the furthest away from abortion facilities (quartile 4; >103 miles) show slightly greater depressive symptoms (Coeff: 0.13; SE: 0.04; p=0.003) than women of color closer to abortion facilities (quartile 1; <28 miles) after the Dobbs decision. Increased distance to abortion facilities may reflect feelings of restricted bodily autonomy and overall disempowerment that hinder the mental health of women of color at reproductive age.

Associations between Maternal Nativity and Prenatal Depression by Racial and Ethnic Subgroups Kendria Kelly-Taylor* Kendria Kelly-Taylor Sara Aghaee Joshua Nugent Ayesha Sujan Nina Oberman Ai Kubo Elaine Kurtovich Charles P. Quesenberry Jr Kathryn Ridout Mibhali Bhalala Lyndsay Avalos

US born persons present more adverse perinatal outcomes compared to non-US born, yet less is known how maternal nativity (US born vs. non-US born) is associated with prenatal depression among racial and ethnic subgroups (e.g., Mexican, Hmong). This study examined differences in prenatal depression diagnosis and severity by maternal nativity among a large cohort of pregnant persons universally screened for depression. A retrospective cohort study of pregnant persons receiving prenatal care at Kaiser Permanente Northern California from 2013 to 2019 (n=258,452) was conducted. Twenty racial and ethnic groups, and nativity were obtained from birth records, and depression diagnosis, severity (measured using Patient Health Questionairre-9 [PHQ-9]), and covariates (maternal age, parity, delivery year, education, and neighborhood deprivation) were captured via electronic health records. We calculated age-adjusted prevalence rates and used modified Poisson regression models to estimate adjusted relative risks. Among race/ethnic subgroups, non-US-born persons had lower prevalence of prenatal depression compared to US-born persons (PRrange:3.9-20.3%; PRrange:4.8-25.4%, respectively). Adjusted models documented equivalent or lower risk among non-US born persons. In contrast, the prevalence of severe depression (PHQ-9 score: 15+) varied. Non-US born persons (vs. US born) had higher rates among Chinese (3.2% vs. 1.9%) and Hmong (4.6% vs. 3.2%) persons, yet lower rates among Black (3.9% vs. 8.1%) and Puerto Rican (1.9% vs. 6.8%) persons, for example. Adjusted models for severe depression showed non-US born Japanese, Chinese, and Vietnamese persons had significantly higher risk compared to US born (aRR:3.45, 95%CI:1.16-10.27; aRR:2.31, 95%CI:1.71-3.14; aRR:1.90, 95%CI:1.24-2.90, respectively). Future research should continue to explore the relationship between nativity, prenatal depression and severity among racial and ethnic groups and investigate mechanisms for these associations.

Mental Health Disparities Among Rural LGBTQ+ Youth in Kentucky Meredith Cahill*
Meredith Cahill Robert Illback Lisa Crabtree Ben Birkby

In 2023, Kentucky mandated that schools prohibit transgender students from utilizing facilities in alignment with their gender identity. The mandate also banned school staff from using student-requested pronouns and instruction on gender identity and sexual orientation. This raised concerns about subjecting already vulnerable LGBTQ+ youth to further discrimination, and subsequent increased risk for poor mental health outcomes, especially in rural communities. The current study examined mental health disparities experienced by rural LGBTQ+ youth in Kentucky through a secondary analysis of 2021 data from a statewide behavioral health survey of middle and high school students. Self-reported data on sexual orientation and gender identity, 30-day serious psychological distress, past year suicidal ideation, and past year suicide attempts were analyzed using multivariate logistic regression, controlling for student grade level and race/ethnicity to compute odds ratios (ORs) and 95% confidence intervals. Analyses were stratified by rurality using federal designations. The prevalence of 30-day serious psychological distress, suicidal ideation, and suicide attempts was 22%, 14%, and 8%, respectively. Prevalence rates for these indicators varied by gender and sexual orientation, with students outside of the gender binary reporting the highest rates. For LGBTQ+ students, significantly higher odds of 30-day serious psychological distress (OR:8.6;95%CI:7.9-9.3), past year suicidal ideation (OR:8.0;95%CI:7.5-8.7), and past year suicide attempt (OR:5.4;95%CI:5.0-5.9) were seen. These disparities were heightened for LGBTQ+ youth in rural counties for suicidal ideation (OR:9.1; 95%CI:8.2-10.1) and attempted suicides (OR:6.2;95%CI:5.6-7.0). Kentucky LGBTQ+ students, especially in rural areas, had increased odds of poor mental health compared to their peers. These findings highlight the urgent need for policies supporting safe and affirming school environments throughout the state.

Does history repeat itself? Racial disparities in emergency department visits for schizophrenia/psychosis following the police killing of George Floyd. Parvati Singh* Parvati Singh Geoffrey Carney-Knisely Kamesha S. Spates Marquianna Griffin Amy Fairchild Tim A. Bruckner

In the United States, Black persons are disproportionately diagnosed with schizophrenia relative to Whites. Clinician bias stemming from racialized diagnostic criteria for schizophrenia/psychosis, and inappropriate contextualization of attributes among Black persons as pathological, may underlie this disparity. Symptoms of schizophrenia such as agitation, delusion, and non-compliance, were part of the (now discontinued) disorder termed the "protest psychosis" as a type of reactive psychosis stemming from racial tensions during the Civil Rights movement in the 1950s and 1960s. This disorder included the rejection of "Caucasian values" and a "repudiation of white civilization", and was utilized to characterize Civil Rights protestors as severely mentally ill. The legacy of these targeted and discriminatory diagnostic criteria may continue to permeate the modern context. In May 2020, the police killing of George Floyd sparked widespread protests through the Black Lives Matter Movement against police brutality and racial injustices in the US. Given the historical precedence of "protest psychosis" in response to the Civil Rights Movement, we sought to examine disparities in schizophrenia-related Emergency Department (ED) visits immediately following the police killing of George Floyd in May 2020. We used monthly data on ED visits from January 2016 to December 2020 across 5 University of California health systems and examined whether ED visits with a diagnosis of schizophrenia increased selectively among Black persons in June 2020, controlling for (1) all other psychiatric ED visits among Black persons, and (2) ED visits for schizophrenia among White persons. Results from time-series AutoRegressive Integrated Moving Average (ARIMA) analyses indicate 47 additional ED visits for schizophrenia/psychosis among Black persons in June 2020 (p<0.01). These results indicate perpetuation of historical trends and align with expectations from the legacy of "protest psychosis".
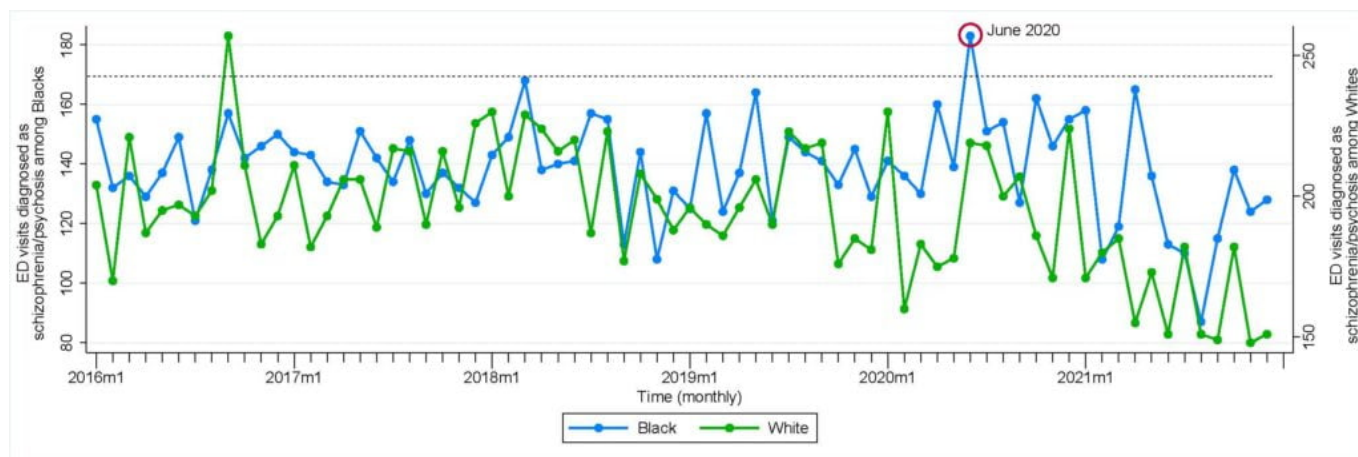
Inter-relations of Education, Social Participation, and Cognitive Function. A Longitudinal Analysis of Taiwanese Middle-Aged and Older Adults Yu-Tien Hsu* Yu-Tien Hsu Ichiro Kawachi Jarvis T. Chen

Social participation is associated with maintenance of cognitive function in older persons and could be a potential mediator of the association between educational attainment and late-life cognitive function. Moreover, social participation could interact with educational attainment on cognitive function. However, few studies have formally tested these relationships within a causal mediation framework.

We used data from the Taiwan Longitudinal Study in Aging, a nationally representative sample. The sample comprised participants aged 50 or above and recruited in 1989 (n = 4,400), stratified by age group (aged 50-64 years versus 65 or above). We used sequence analysis and optimal matching technique to define clustered patterns of social participation and work history in 1996, 1999, 2003, 2007, and 2011. We then used four-way decomposition to identify the effects of educational attainment, social participation pattern, and their interaction on the cognitive function in 2015, measured bythe Short Portable Mental Status Questionnaire.

We found a strong association between education and late-life cognitive function for both subgroups. As we decomposed the underlying pathway, the mediating pathway through social participation only accounted for 5% or less of the total effect for both subgroups, none of them were statistically significant. Notably, comparing college or above group to no formal education group in the younger subgroup, the reference interaction effect was a statistically significant component of the total effect (-0.58, 95% C.I. = -1.13, -0.11). Furthermore, under a hypothetical intervention scenario among younger participants, there could be 25% (95% C.I. = 0.01, 0.49) and 37% (95% C.I. = 0.12, 0.71) reductions in educational disparity in late-life cognitive function if we could set the participants without formal education to have a same level of social participation as those with middle/high school or college education.

Our results indicate that testing interventions encouraging more active patterns of social participation or stable involvement in employment could be valuable to mitigate educational disparities in late-life cognitive function. Moreover, people with higher level of educational attainment may benefit more from social participation than those without.

Ten-year cognition transitions in older cancer survivors in the National Health and Aging Trends Study (NHATS) Emilie D Duchesneau* Emilie D Duchesneau Zhang Zhang Michelle M Mielke Heidi D Klepin Amresh D Hanchate

Background

Aging, cancer, and cancer treatments are risk factors for cognitive impairment. While studies have described cognition transitions during the period surrounding cancer diagnosis and treatment, few have focused on the long-term survivorship period. We described 10-year cognition transitions in older cancer survivors.

Methods

We used Rounds 1-10 of NHATS, a prospective cohort of adults 65+ years with annual assessments of cognition and age-related conditions. We included 1303 older adults reporting any cancer history at Round 1 (2011). Cognition was assessed annually for 10 years using a validated measure based on self-report, the AD8 Dementia Screening Interview, and objective assessments of memory, orientation, and executive function. Cognition was categorized as "possible", "probable", or "no dementia". One-year transitions between the 3 cognition states were described using Sankey diagrams and an age- and sex-adjusted Markov transition probability matrix, including death as its own state. We used multiple imputation and inverse probability of censoring weights to account for missing data and attrition.

Results

In Round 1, 12% had probable, 14% possible, and 74% no dementia. The **Figure** visualizes transitions across cognition states. One-year probabilities of death were 6%, 13%, and 23% for those with no, possible, and probable dementia. The 1-year probability of remaining in the current state at any round was high for those with probable (69%) and no dementia (84%). Transitions were common among those with possible dementia, with a 17% probability of transitioning to probable and 44% to no dementia.

Conclusions

One-year transitions were uncommon in older cancer survivors with probable or no dementia. Transitions were more common in those with possible dementia. Research is needed to identify risk factors for cognition transitions, particularly among those with possible dementia who may benefit from interventions to prevent further cognitive decline.

Sankey diagram depicting transitions across cognition states and death in older cancer survivors in the National Health and Aging Trends Study
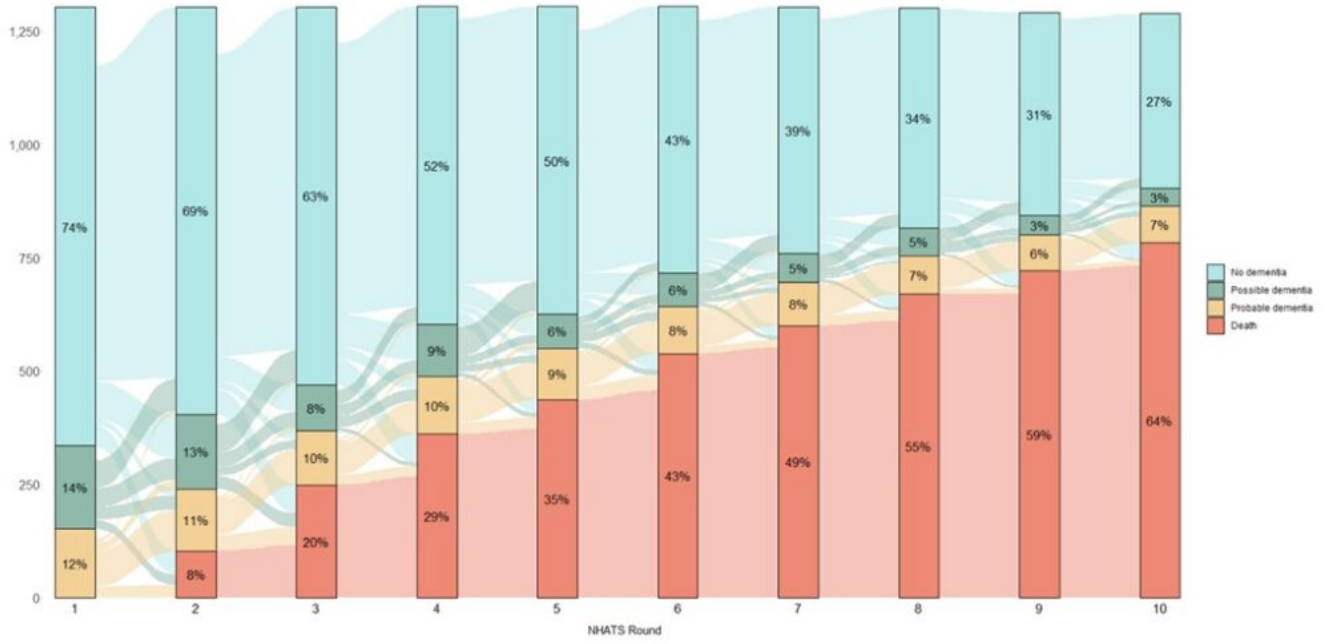
Evaluating Linked ICD-10 Medicare Claims Data as a Method of Dementia Case Ascertainment in Research Settings Joya Bhattacharyya* Joya Bhattacharyya Yi Chen Kan Z. Gianattasio Francine Grodstein Bryan D. James Ali Moghtaderi Christina Prather David Rein Raj C. Shah Emma K. Stapp Melinda C. Power

Background: The United States transitioned to use of ICD-10 in 2015. Limited previous research validating use of Medicare claims data as a case-finding strategy for identifying persons living with dementia has considered ICD-10 code definitions.   Here, we identified six ICD-10 code definitions for dementia from recent high-impact work and aimed to compare their sensitivity, specificity, and accuracy relative to research-based dementia ascertainment.

Methods: Eligible participants from 5 Rush Alzheimer's Disease Center (RADC) cohort studies were aged 65 years or older, enrolled in Medicare fee-for-service, and consented to Medicare claims data linkage. We compared dementia status at each annual RADC cohort study visit between 2015 and 2019 to dementia status based on presence of ICD-10 codes denoting dementia within a 12 month period centered on the RADC cohort study visit for six ICD-10 code definitions for dementia identified from the literature.

Results: All six code definitions had high accuracy (>85%). Five of the six code definitions had high specificity (>90%) but low sensitivity (<60%), while one code definition had greater sensitivity (80%) at the expense of slightly lower specificity (87%). For all code definitions, Black participants were more likely to meet research-based but not claims-based criteria for dementia (i.e., be underdiagnosed in clinical settings) than their White peers. Age was negatively associated with accuracy.

Conclusions: ICD-10 Medicare claims data can be used to ascertain dementia cases, but selection of code definition impacts sensitivity, specificity, and accuracy of results, and performance varied by participant characteristics. Understanding the measurement properties of the code definition used may help inform bias mitigation strategies in studies using Medicare claims data to ascertain dementia.

Association Between Retirement and Cognitive Decline Among Older Black/African Americans: A STAR Study Nancy Chen* Nancy Chen Elizabeth Rose Mayeda Paola Gilsanz M. Maria Glymour Lisa L. Barnes Kristen George Yi Lor Claire Meunier Alexander Ivan B. Posis Rachel Whitmer

Background: Whether retirement negatively impacts cognitive decline is unclear, especially among diverse populations. We investigated this relationship in a cohort of Black/African American adults.

Methods: The Study of Healthy Aging in African Americans comprises community-dwelling Black Americans ages 50+ who are long-term Kaiser Permanente Northern California members. Verbal episodic memory (VEM) and executive function (EF) were assessed at three interview waves using the Spanish and English Neuropsychological Scales. We categorized baseline retirement status as 1) retired and 2) not retired. Participants who were retired with disabilities were excluded to reduce possible reverse causation. Linear mixed models with random intercepts and slopes estimated associations of retirement status with VEM and EF over time. All models adjusted for baseline age, gender, education, parental education, and interview mode (in-person or phone). Sensitivity analyses categorized retirement status as 1) retired before age 65, 2) retired at age 65+, and 3) not retired.

Results: Participants' (N=552) mean age was 68.8 (SD=9) years at baseline, mean follow-up time was 2.2 (SD=0.6) years, 68% were women, 64% had <college education, 63% had a parent with <high school education, 62% were retired, 45% retired before age 65, and 17% retired at age 65+. Baseline retirement status was not associated with baseline VEM and EF scores or decline in VEM scores. Retirees had faster decline in EF than adults who were not retired (b=–0.04, 95% CI –0.09, –0.001; Figure 1). Adults who retired at 65+ had slower decline in VEM (b=0.08, 95% CI –0.01,0.16) but faster decline in EF (b=–0.07, 95% CI –0.13, –0.01) than those who retired before 65 (Figure 1). Adults who retired at 65+ had faster decline in EF than those not retired (b=–0.09, 95% CI –0.15, –0.03; Figure 1).

Conclusion: Retirement and retirement age were associated with faster decline in executive function in middle-aged and older Black adults.

Figure 1. Predicted cognitive decline in verbal episodic memory and executive function by retirement status with 95% confidence limits.
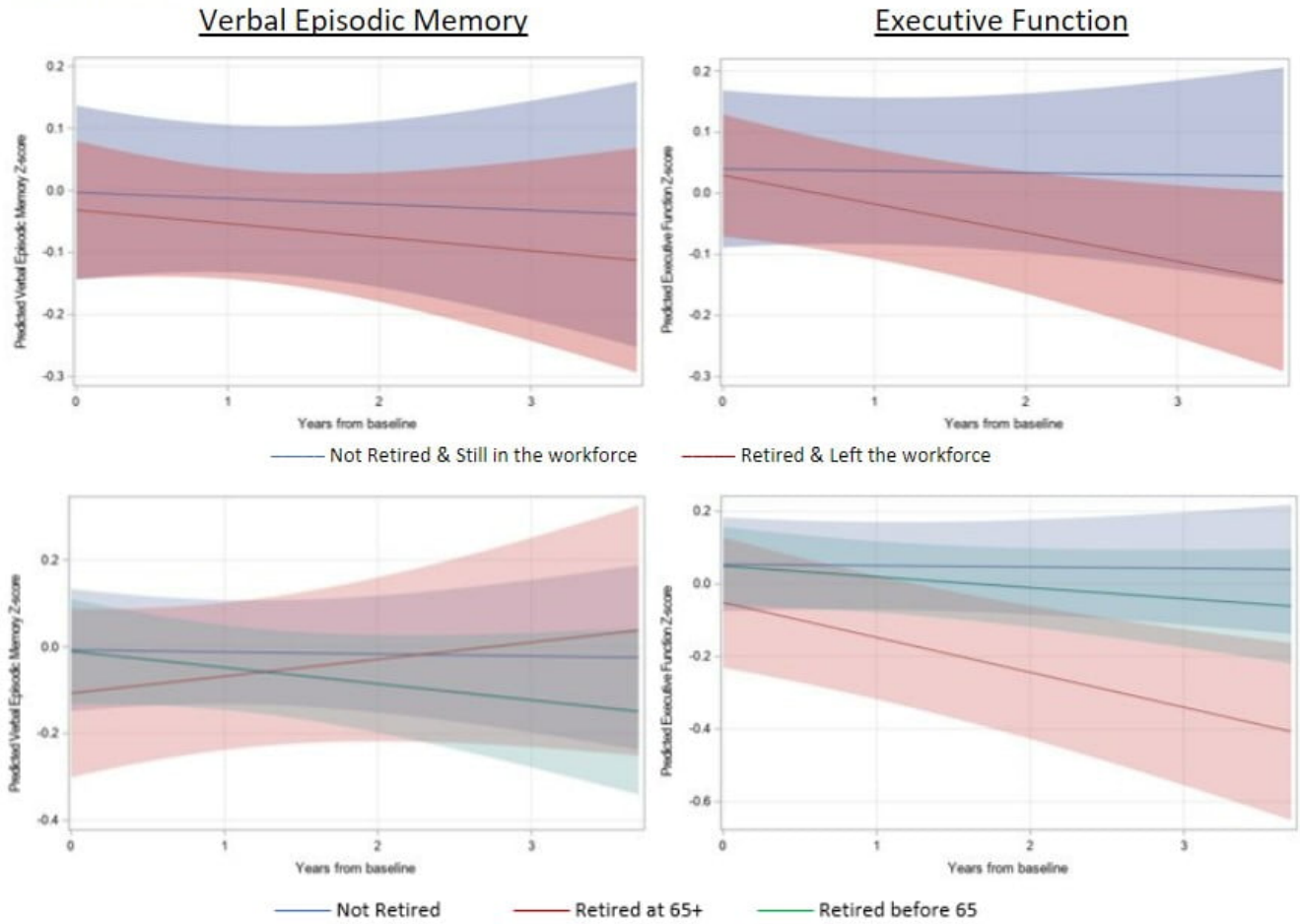
Impact of the South African Child Support Grant on memory decline and dementia probability in rural and low-income mothers, 2014-2021 Erika T. Beidelman* Erika Beidelman Rishika Chakraborty Janet Jock Chodziwadziwa Whiteson Kabudula Meredith Phillips Kathleen Kahn Katherine Eyal Darina T. Bassil Lisa Berkman Lindsay C. Kobayashi Molly Rosenberg

Introduction: Aging populations across sub-Saharan Africa are rapidly expanding, leading to an increase in the burden of Alzheimer's disease and related dementias (ADRD). Cash transfer interventions are one plausible mechanism to combat ADRD at a population level in low-income settings. We exploited exogenous variation in eligibility for South Africa's Child Support Grant (CSG) to estimate the longitudinal association between eligibility duration and cognitive function in rural mothers with age-eligible children (n=855).

Methods: South Africa's CSG delivers monthly cash payments to primary caregivers, predominantly mothers, to offset the costs associated with raising children. This study utilized data collected between 2015 and 2021 from a rural, low-income cohort in the Agincourt research area of South Africa. We fit linear mixed effects models and generalized linear models to estimate the association of CSG eligibility duration with memory decline and dementia probability, respectively. We stratified all models by the mother's total number of children (1-4 and 5-9) and examined effect modification by socioeconomic status and education level.

Results: Among mothers with 1-4 children, those with high CSG exposure (~>19 years) experienced slower rates of memory decline, with this effect being strongest among women with low levels of educational attainment ($\beta = 0.07$, 95% CI = 0.01, 0.12). For mothers with 5-9 children, high CSG exposure was associated with higher dementia probability and faster memory decline.

Conclusions: Our findings support the use of large-scale cash transfers as a promising intervention to promote healthy cognitive aging in some sub-groups of mid-life women from low-income settings. However, we found evidence that the CSG in its current structure may not be sufficient support for women with more than four children to derive measurable cognitive benefits.

Plot of predicted memory scores (with 95% confidence intervals) across time (in years) for women with 1 to 4 children (Panel a) and 5 to 9 children (Panel b)

Aging
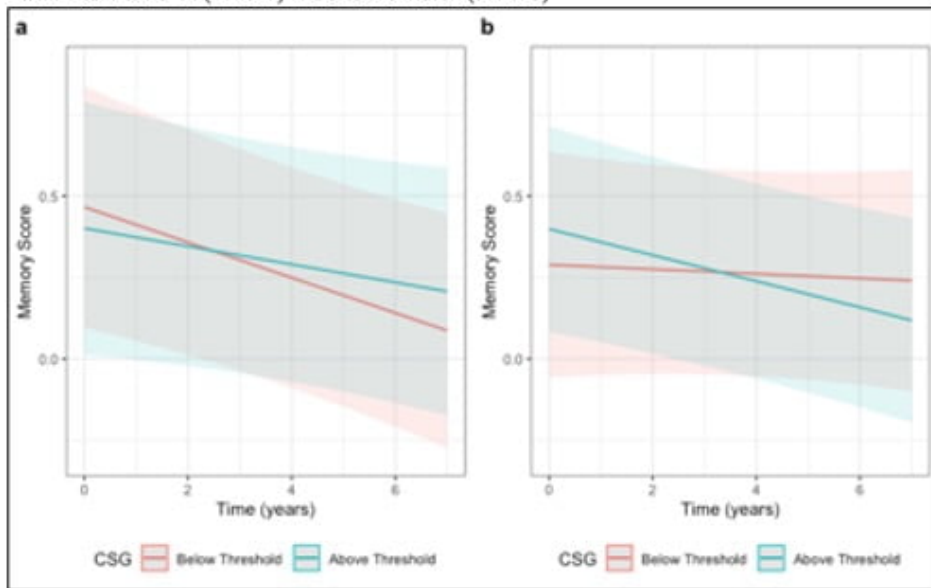
Evaluating heterogeneity in the association between hypertension and dementia by age and race/ethnicity in a diverse cohort of Asian American and non-Latino white older adults

Natalie Gradwohl* Natalie Gradwohl L. Paloma Rojas-Saunero Yingyan Wu Eleanor Hayes-Larson Yixuan Zhou Rachel Whitmer Paola Gilsanz Ron Brookmeyer Elizabeth Rose Mayeda

Introduction: The association between hypertension and dementia may vary by age, with robust associations between midlife hypertension and higher dementia risk and null or inverse associations between later-life hypertension and dementia risk. However, prior research is inconclusive and has minimal representation of Asian Americans.

Methods: We followed a cohort of 132,180 Kaiser Permanente Northern California members (4,848 Chinese, 4,130 Filipino, 2,786 Japanese, 823 South Asian, and 123,593 non-Latino white) aged 60 years and above at baseline, using electronic health records (EHR) from 2002-2020. Hypertension (yes/no) was defined as a diagnosis in EHR ≥5 years before baseline. We ran Cox-proportional hazards models (time on study as timescale) to calculate hazard ratios (HR) relating hypertension and dementia stratified by baseline age <75 vs. ≥75 years and race/ethnicity. Models were adjusted for baseline age, sex/gender, years of education, and baseline age-hypertension interaction.

Results: Prevalence of hypertension 5 years before baseline was high, ranging from 47% among non-Latino whites to 62% for Filipinos. For those <75 at baseline, rate of dementia was higher in hypertensive vs. non-hypertensive individuals for all groups except South Asians (White HR = 1.33 95% CI [1.26-1.40]; Chinese HR = 1.51 [1.10-2.08]; Filipino HR = 1.64 [1.19, 2.25]; Japanese HR = 1.28 [0.85-1.93]; South Asian HR = 1.03 [0.57, 1.84]). Associations were weaker in those ≥75 years at baseline (Figure).

Discussion: Participants with prevalent hypertension at baseline were more likely to develop dementia over follow-up for all racial/ethnic groups except South Asians, for whom estimates were imprecise; this association was larger for those who were younger at baseline. More data on the health of Asian American older adults is needed to understand risk factors for dementia across different ethnicities.

Race/ethnicity-specific hazard ratios for dementia incidence (hypertension vs. no hypertension) at ≥5 years prior to baseline
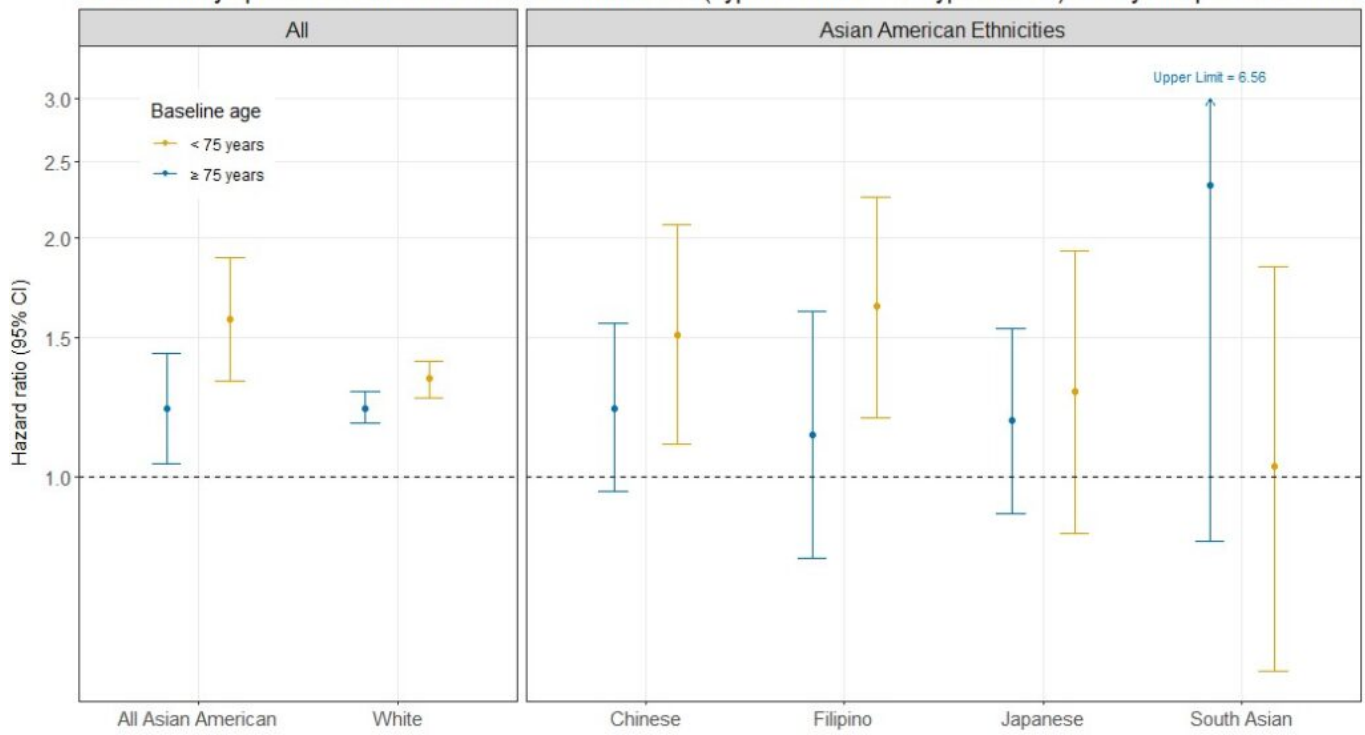
Organochlorine insecticide use and mosaic loss of chromosome Y in a study of male farmers Lauren Hurwitz* Lauren Hurwitz Vicky Chang Laura Beane Freeman Mitchell Machiela Weiyin Zhou Gabriella Andreotti Nathaniel Rothman Sonja Berndt Stella Koutros Jonathan Hofmann

Background: Organochlorine (OC) insecticides are a class of environmentally persistent chemicals linked to risk of several cancers, including prostate cancer and non-Hodgkin lymphoma. In vitro and animal studies suggest some OCs may be genotoxic, but evidence in humans is limited. Mosaic loss of chromosome Y (mLOY) is a marker of genomic instability that has been associated with cancer and may reflect intermediate effects of pesticide exposure. We examined associations between OC use and mLOY in circulating blood of male farmers.

Methods: This investigation included 1,653 male farmers from Iowa and North Carolina in the Biomarkers of Exposure and Effect in Agriculture study, a subcohort of the Agricultural Health Study. Ever use and intensity-weighted lifetime days of use of 7 OCs were derived from questionnaires. mLOY was detected using genotyping array intensity data in the pseudoautosomal regions of the sex chromosomes. Logistic regression was used to estimate associations between OC use and mLOY, adjusted for pre-specified confounders. Stratified analyses were performed by other mLOY risk factors (age, smoking status, obesity [BMI ≥30 kg/m2]) and state of residence.

Results: mLOY was detected in 357 farmers (22%). We observed positive associations with mLOY for ever use of DDT (OR 1.44 [1.08-1.92]) and lindane (OR 1.30 [0.99-1.72]). Associations were stronger among farmers without obesity (DDT: OR 1.61 [1.12-2.33], p-interaction=0.20; lindane: OR 1.80 [1.26-2.56], p-interaction<0.01). For lindane, there was evidence of exposure-response among farmers ≥70 years of age (p-trend=0.03) and those without obesity (p-trend=0.07). Other OCs were not associated with mLOY overall.

Conclusions: Use of DDT and lindane were associated with mLOY, particularly in certain subgroups of farmers (e.g., non-obese or ≥70 years of age). Our findings suggest that these pesticides could confer genotoxic effects and provide new mechanistic evidence for their associations with cancer risk.

Use of Non-steroidal Anti-inflammatory Drugs, Aspirin, Ibuprofen, and Acetaminophen in Relation to Biliary Tract Cancers in the Biliary Tract Cancers Pooling Project (BiTCaPP)

Ilona Argirion* Ilona Argirion Crystal Najib Katherine McGlynn Peter Campbell

Background: Non-steroidal anti-inflammatory drugs (NSAIDs) have been reported to reduce the risk of several cancers, leading to their proposed use as chemopreventive agents; nevertheless, their relationship with biliary tract cancers (BTCs) remains to be fully elucidated.

Methods: Data from thirteen prospective studies in the Biliary Tract Cancers Pooling Project (BiTCaPP) were harmonized to investigate the association between NSAIDs (aspirin and ibuprofen), acetaminophen, and BTCs. Hazard ratios (HR) and 95% confidence intervals (CI) were estimated using Cox proportional hazards regression after adjustment for sex, race, education, smoking, alcohol use, body mass index, and cardiovascular disease. Sensitivity analyses were conducted to assess the role of duration and intensity of use, presence of gallstones, and cholecystectomy on the observed associations.

Results: During 19,036,644 person-years of follow up, 494 gallbladder cancer (GBC), 339 intrahepatic bile duct cancer (IHBDC), 499 extrahepatic bile duct cancer (EHBDC), and 291 ampulla of Vater cancer (AVC) cases occurred. NSAIDs were inversely associated with IHBDC (HR=0.57 [95%CI: 0.44-0.73]) and EHBDC (HR=0.76 [95%CI: 0.62-0.94]); similar results were found for aspirin (HRIHBDC=0.58 [95%CI: 0.45-0.75]; HREHBDC=0.80 [95%CI: 0.64-0.98]). Ibuprofen use was inversely associated with IHBDC (HR=0.71 [95%CI: 0.52-0.97]) and AVC (HR=0.61 [95%CI: 0.43-0.86]). Increasing intensity of NSAID use was associated with decreased EHBDC risk (ptrend=0.04), and increased intensity of aspirin use was associated with decreased IHBDC risk (ptrend=0.02), while increasing intensity of acetaminophen use was associated with increased IHBDC and EHBDC risk (ptrend=0.003 and 0.02, respectively). Results did not vary by cholecystectomy or gallstone status.

Conclusion: NSAIDs mitigate chronic inflammation and could protect against IHBDC and EHBDC. Conversely, acetaminophen use may increase the risk of IHBDC and EHBDC.

Oral contraceptive use and risk of melanoma: results from a prospective cohort study among 59,407 nurses Linske de Bruijn* Henriette M. van Duijne van Duijne Linske de Bruijn Henriette M. van Duijne Nina E. Berentzen Roel C.H. Vermeulen Jelle J. Vlaanderen Hans Kromhout Katarzyna Jóźwiak Flora E. van Leeuwen

Background: The incidence of melanoma increases worldwide, which cannot be entirely explained by exposure to UV and other risk factors. Oral contraceptive (OC) use may also influence melanoma risk, although studies which evaluated this association reported conflicting results. We therefore assessed the association of OC use with melanoma risk in a large cohort of female nurses.

Methods: The Nightingale Study comprises 59,947 Dutch female nurses, aged 18-65 years in 2011 (mean age: 46.9 years). Participants provided data on OC use in the baseline questionnaire (2011) and were followed for cancer occurrence up to August 2021. Missing exposure and covariate data (e.g. lifestyle factors including UV exposure) were imputed using multiple imputation by chained equations. Associations of OC use with risk of melanoma were assessed using proportional hazard models with attained age as timescale while adjusting for age at baseline. Women who never used OC or used OC before 2011 for ≤five years were used as reference group.

Results: During follow-up, 302 women were diagnosed with melanoma. In comparison to the reference group, melanoma risk was significantly increased for participants who ever used OC (Hazard ratio (HR)=1.36, 95%Confidence Interval (CI)=1.00-1.85) or currently used OC (HR=2.14, 95%CI=1.43-3.18). Risk was not significantly increased among former users who had used OC for >5 years (HR=1.23, 95%CI=0.90-1.69), even when last OC use was <2 years before baseline (HR=1.14, 95%CI=0.57-2.27). Among current OC users, risk did not increase with longer duration of use (HRper one year increase=0.97, 95%CI=0.93-1.00).

Conclusion: Current OC use, but not duration or recency of OC use, was associated with increased melanoma risk among nurses. Future studies should focus on the type and dose of OC in relation to melanoma risk to further clarify potential mechanisms behind the increased risk of melanoma associated with current OC use.

Cancer

Exposure to nitrosatable drugs in pregnancy and pediatric cancer risk: a population-based cohort study in Taiwan Chuanjie Deng* Chuanjie Deng Ya-Hui Hu Pei-Chen Lee Anupong Sirirungreung Eugenia Yupei Chock Zeyan Liew Beate Ritz Julia E. Heck

Background: Nitrosatable drugs, including secondary and tertiary amines and amides, have been implicated in the endogenous formation of N-nitroso compounds (NOCs) in the human stomach, with experimental evidence linking NOCs to carcinogenicity in animals. However, the association between maternal nitrosatable drug use and pediatric cancer risk remains inconclusive.

Methods: We conducted a population-based retrospective cohort study based on the Taiwan Maternal and Child Health Database (N=2,199,302) from 2004-2015 to investigate the potential association between maternal nitrosatable drug use in pregnancy and pediatric cancer risk among offspring. Nitrosatable drug prescriptions were identified from the National Health Insurance Program using Anatomical Therapeutic Chemical (ATC) codes, and cancer cases were ascertained through linkage to the Cancer Registry (1979-2017). Cox proportional hazards regression was employed with adjustment for parental age and socioeconomic status.

Results: In 2,659 cancer cases we identified, maternal nitrosatable drug use in pregnancy was associated with an elevated risk of overall cancer (HR=1.25, 95% CI: 1.04-1.50) and astrocytoma (HR=3.21, CI: 1.02-10.07) in offspring. Secondary amines exhibited a positive association with hepatoblastoma (HR=1.65, CI: 1.12-2.44), while children of mothers who took tertiary amines had a higher risk of overall cancer (HR=1.11, CI: 1.03-1.21), hepatoblastoma (HR=1.99, CI: 1.32-2.98) and germ cell tumors (HR=1.33, CI: 1.02-1.74), particularly among males (HR=1.50, CI: 1.04-2.16). Amides were strongly associated with medulloblastoma (HR=2.16, CI: 1.08-4.32).

Conclusions: Maternal nitrosatable drug use in pregnancy increases risk of astrocytoma, hepatoblastoma, and germ cell tumors in offspring in our study. The findings underscore the importance of further exploration into the potential carcinogenic effects of maternal nitrosatable drug use in pregnancy on offspring.

Cancer

Disparities in Utilization of Immune Checkpoint Inhibitor Therapy among Older Patients with Advanced Non-Small Cell Lung Cancer: A SEER-Medicare Analysis Danting Yang*

Danting Yang Shama D. Karanth Hyung-Suk Yoon Jae Jeong Yang Lusine Yaghjyan Dejana Braithwaite

Background and purpose: Socioeconomic and racial/ethnic disparities exist in access to care among patients with non-small cell lung cancer (NSCLC) in the United States. Immune checkpoint inhibitor (ICI) therapy has emerged as a promising treatment option for advanced NSCLC (aNSCLC). In this study, we investigate the associations of race/ethnicity with ICI therapy utilization among older patients with aNSCLC.

Methods: This retrospective study used data from the Surveillance, Epidemiology, and End Results (SEER)-Medicare-linked database. The cohort included patients (aged 66 years or older) diagnosed with aNSCLC (stage III/IV) between March 2015 to December 2017, followed through December 2019. Race/ethnicity was categorized as non-Hispanic (NH)-White, NH-Black, Hispanic, and Other. ICI therapy utilization was determined by identifying any usage of the following ICI agents (Nivolumab, Pembrolizumab, Atezolizumab, Durvalumab, Ipilimumab, and Cemiplimab-rwlc) from the Medicare database. Multivariable logistic regression models assessed the association between race/ethnicity and ICI therapy utilization (yes, no). Effect measure modification analyses were conducted by sex, socioeconomic status, and comorbidity.

Results: The final sample included 26,836 patients, 76.2% were NH-White, 10.1% NH-Black, 5.7% Hispanic, and 8.0% Other. The overall ICI therapy utilization rate was 17.8%, varying across ethnicities: NH-Black 14.1%, Hispanic 16.3%, NH-White 18.4%, and Other 18.5%. In comparison to NH-White patients, NH-Black patients were 15% less likely to receive ICI therapy (adjusted odds Ratio: 0.85, 95% CI: 0.75, 0.96). Furthermore, the association between race/ethnicity and utilization of ICI therapy was modified by comorbidity status, sex, and socio-economic status (SES).

Conclusion: NH-Black patients with aNSCLC were less likely to receive ICI therapy than their NH-White counterparts.

Variations in Treatment Utilization Rates Among Race/Ethnicity Groups
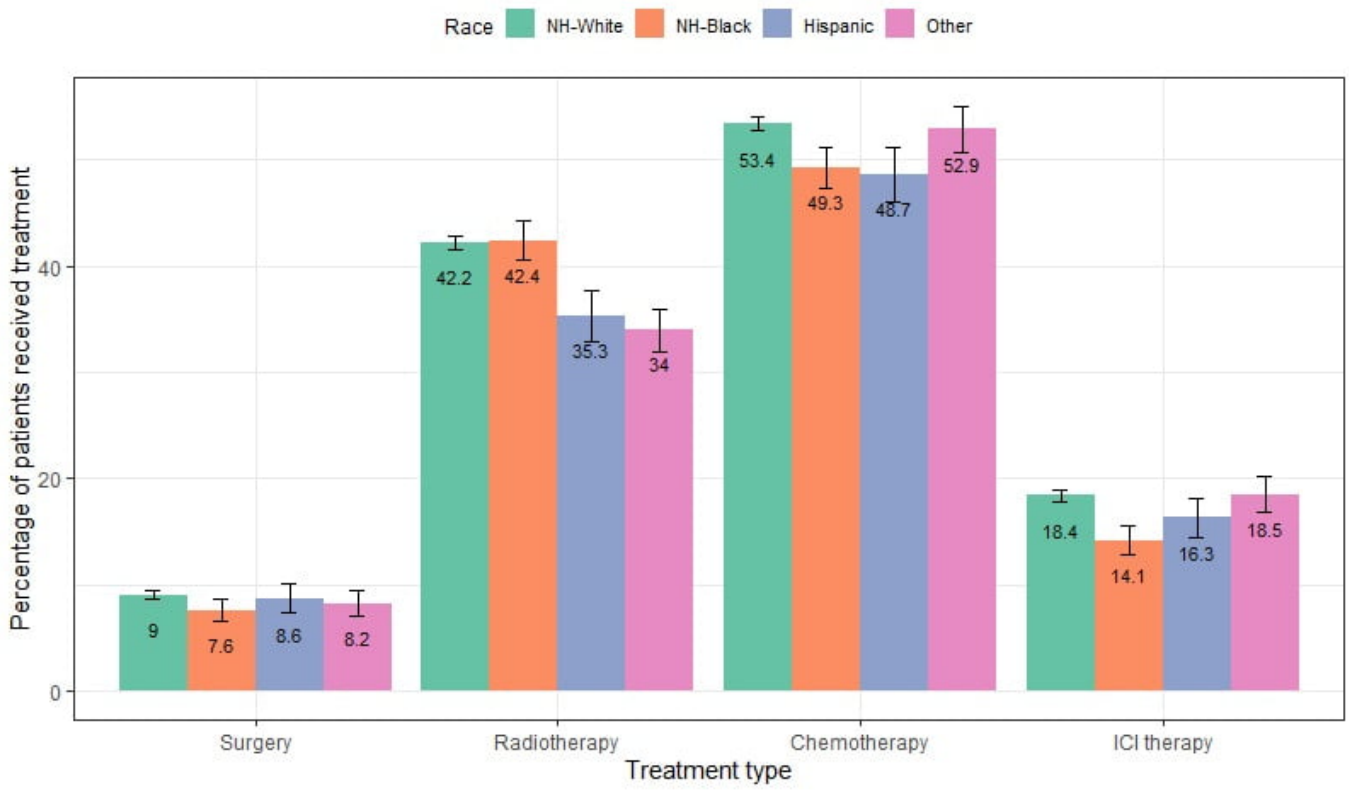
Examining the joint effect of multilevel resilience and covid-19 distress on viral suppression among african american/black adults living with hiv in the southeastern united states Tariz D. Viera-Rojas* Tariz Viera-Rojas Jason R. Gantenberg Jee Won Park Marta G. Wilson-Barthes Joseph W. Hogan Michael P. Carey Sannisha K. Dale Valerie A. Earnshaw Sarah Dougherty-Sheff Deana Agil Akilah J. Dulin Chanelle J. Howe

Background: African American/Black persons living with HIV (AA/B-PLWH) in the southeastern U.S. experience disparities in HIV outcomes, including viral suppression. The COVID-19 pandemic disrupted HIV care and caused distress (e.g., economic, mental) that may have impacted HIV viral suppression among AA/B-PLWH. However, availability of multilevel resilience resources (MRR) may have buffered against COVID-related distress. The potential impacts of a joint intervention on MRR and distress on HIV viral suppression warrants investigation.

Objective: Estimate the joint effect of MRR and COVID-19 distress on HIV viral suppression among AA/B-PLWH.

Methods: Prospective cohort study of 103 AA/B-PLWH aged ≥18 years old enrolled in two parent HIV clinic cohorts in the southeastern U.S, with relevant complete data. MRR and COVID-19 distress were assessed based on self-report using the Multilevel Resilience Resource Measure Long Form and the Modified Stanford Measure, respectively, and considered as binary exposures. The outcome was a binary indicator of viral suppression (≤50 copies/mL) during post-exposure follow up (18-month maximum). We estimated unadjusted and adjusted RDs using modified Poisson models.

Results: Focusing on findings most compatible with the data, compared to those with no distress and greater MRR, patients with no distress but lesser MRR were equally likely to be virally suppressed (adjusted RD: -0.00; 95% CL: -0.20, 0.19). Patients with any distress but greater MRR (adjusted RD: -0.12; 95% CL: -0.36, 0.11) or lesser MRR (adjusted RD: -0.03 95% CL: -0.28, 0.21) were less or slightly less likely to be virally suppressed.

Conclusion: We found weak evidence that a dual intervention to increase MRR and decrease COVID-19 distress could improve HIV viral suppression. Effect estimates were imprecise and did not provide strong evidence for interaction on the additive scale. Studies with a larger sample size are needed to examine this joint effect more robustly.

Table: Risk differences for the joint effect of multilevel resilience resources and COVID-19-related distress on viral suppression among African American/Black adults living with HIV in the southeastern United States (n=103).

COVID-19 Related Distress	Multilevel Resilience Resources	N	HIV Viral Suppression (%)	Risk Difference (95% CL)	
				Crude	Adjusted [a]
Any	Lesser	16	87.5	-0.01 (-0.20, 0.19)	-0.03 (-0.28, 0.21)
	Greater	33	81.8	-0.06 (-0.23, 0.11)	-0.12 (-0.36, 0.11)
None	Lesser	20	95.0	0.07 (-0.08, 0.21)	-0.00 (-0.20, 0.19)
	Greater [b]	34	88.2	0	0
Coefficient for product term (p-value)				0.01 (0.93)	-0.09 (0.63)

Abbreviations: CL, confidence limits

[a] Adjusting for date at dual exposure measurement, age at dual exposure measurement, gender at enrollment, sexual orientation at enrollment, neighborhood disadvantage at enrollment, neighborhood murder index at enrollment, drug use at or in the 3 months prior to dual exposure measurement, depression at or in the 2 weeks prior to dual exposure measurement, AIDS-defining illnesses at or in the 2 years prior to dual exposure measurement, years since antiretroviral therapy initiation, last CD4 cell count in the 2 years prior to dual exposure measurement, and most recent viral suppression status in the 2 years prior to dual exposure measurement.

[b] Reference category

A geospatial analysis of public transit access to HIV pre-exposure prophylaxis (PrEP) providing clinics in metro-Atlanta Noah Mancuso* Noah Mancuso Patrick Sullivan
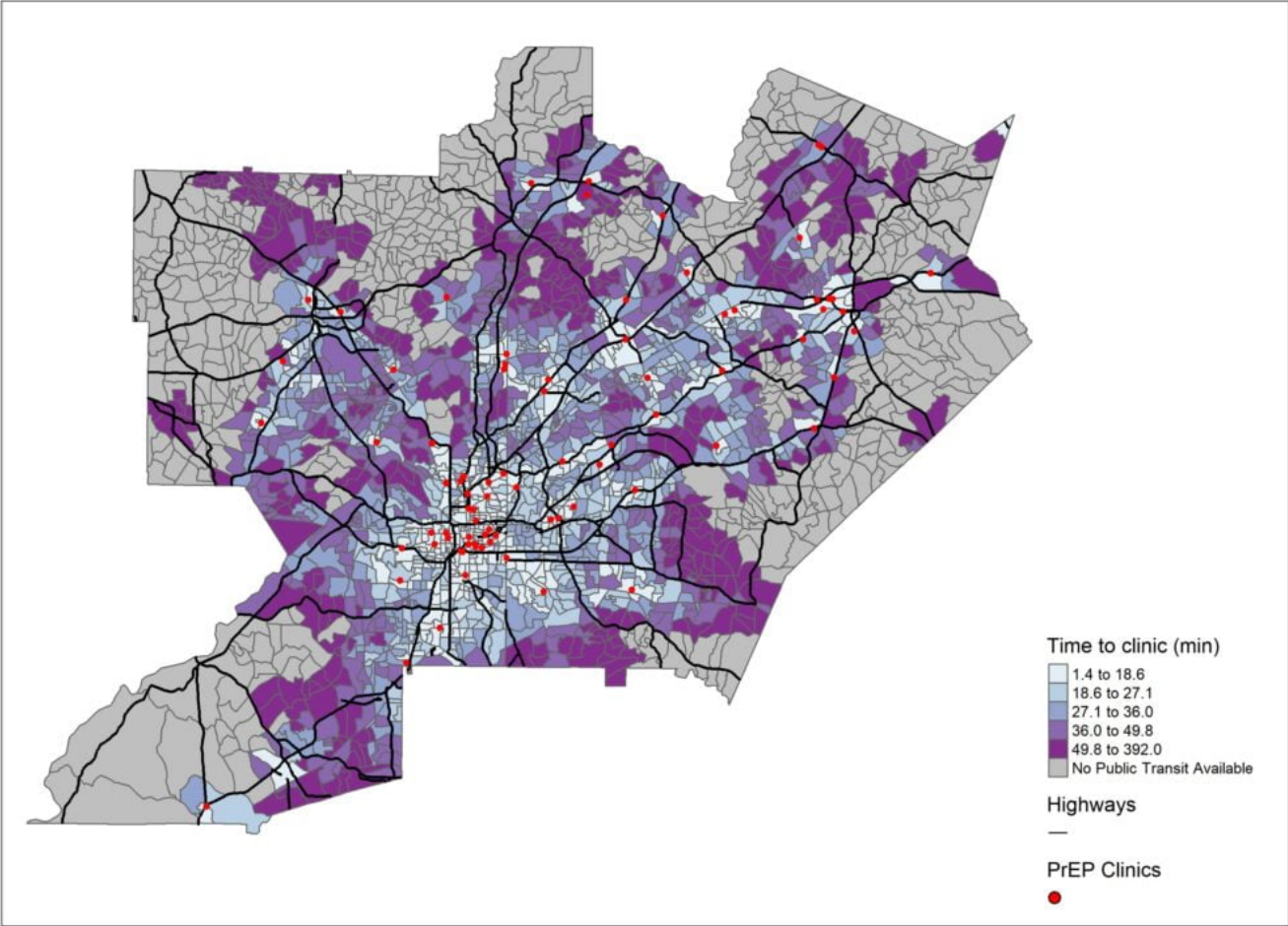
Background: Young Black and Hispanic men experience high HIV incidence in the US and rely on public transit more than White men. HIV pre-exposure prophylaxis (PrEP) is a highly effective HIV prevention method, but challenges with access remain. We describe public transit access to PrEP providing clinics in the metro-Atlanta region.

Methods: Census block groups (CBGs) from four Atlanta counties were joined with CBG-level sociodemographic data from the 2016-2020 American Community Survey. PrEP clinics in Georgia were identified in a national directory. Population-weighted centroids of each CBG were used to calculate the 10 closest PrEP clinics; the Google Maps Distance Matrix API was used to calculate travel time by public transit. CBGs were considered public transit deserts if no public transit option was available or if transit time was >45 minutes. Multivariable log-binomial regression was used to describe associations between public transit deserts and CBG-level race, ethnicity, age, and income.

Results: Of the 2,466 Atlanta CBGs, 23% had no access to a PrEP clinic by public transit. The average transit time to the nearest PrEP clinic was 37 minutes; 489 CBGs housing 729,941 residents had transit times >45 minutes. A 5% increase in the proportion of males aged 25-34; of people living under the poverty line; or of Hispanic people living in a CBG were each associated with a decreased prevalence of being defined as a public transit desert [aPR=0.61 (0.56, 0.66); aPR=0.75 (0.71, 0.78); aPR=0.96 (0.94, 0.98)]. There was no association with Black race.

Conclusion: Many Atlantans do not have access to a PrEP clinic by public transit. Public transit access to PrEP is better for CBGs with more HIV prevention priority populations. To increase PrEP access in public transit deserts, the geographic spread of PrEP clinics should be expanded, travel subsidiaries should be provided for ride-sharing services, and telemedicine and pharmacy PrEP programs should be widely available.

Transit time to nearest PrEP clinic

Time to clinic (min)
- 1.4 to 18.6
- 18.6 to 27.1
- 27.1 to 36.0
- 36.0 to 49.8
- 49.8 to 392.0
- No Public Transit Available

Highways
—

PrEP Clinics
●

The anxiety care continuum and its clinical relevance for people living with HIV Lauren Zalla* Lauren Zalla Heidi Hutton Anthony Fojo Oluwaseun Falade-Nwulia LaQuita Snow Jeanne Keruly Richard Moore Catherine Lesko

Background: Anxiety is prevalent among people with HIV, but we know little about how it affects viral suppression (VS). We aimed to examine the anxiety care continuum and its association with VS in a large urban HIV clinic in the United States.

Methods: Johns Hopkins HIV Clinical Cohort participants contributed clinical and patient-reported outcome data from 2014-2023. Anxiety symptom severity was self-reported using standard scales (GAD-7 and PHQ-PD). We defined anxiety care continuum stages as: no anxiety (no anxiety symptoms or diagnosis); untreated anxiety (symptoms or diagnosis but no treatment); and treated anxiety (prescribed an anti-anxiety medication and/or engaged in mental health care). We fit generalized logit models to estimate crude and adjusted associations with the six-month probability of VS. We stratified models by sex and race/ethnicity (non-Hispanic White, non-Hispanic Black) and adjusted for age, years in care, and depressive symptoms using augmented inverse probability weights. We accounted for missing data using multiple imputation and estimated nonparametric bootstrap-based 95% confidence intervals (CI).

Results: Of 7,395 surveys from 1,967 patients, 46% were receiving anxiety treatment and 24% reported anxiety symptoms. Patients with untreated mild anxiety had a similar probability of VS as those with no anxiety (absolute difference: -0.4%; 95% CI: -3.7, 3.0). Those with untreated moderate-severe anxiety had 6.7% lower probability of VS (95% CI: -9.5, -3.9). Treated patients reporting moderate-severe anxiety had a 2.3% lower probability of VS than those with no anxiety (95% CI: -4.8, 0.3). In adjusted models, untreated moderate-to-severe anxiety remained associated with reduced VS among Black men (absolute difference: -3%; 95% CI: -7.5, 1.5), Black women (-2.9; -8.6, 2.7), and White men (-18.9; -28, -9.8).

Conclusion: Moderate-severe anxiety, especially when left untreated, may contribute to poor VS among people with HIV.

Figure. Percent of patients at each stage of the anxiety care continuum and differences in the prevalence of viral suppression in the Johns Hopkins HIV Clinical Cohort, 2014-2023
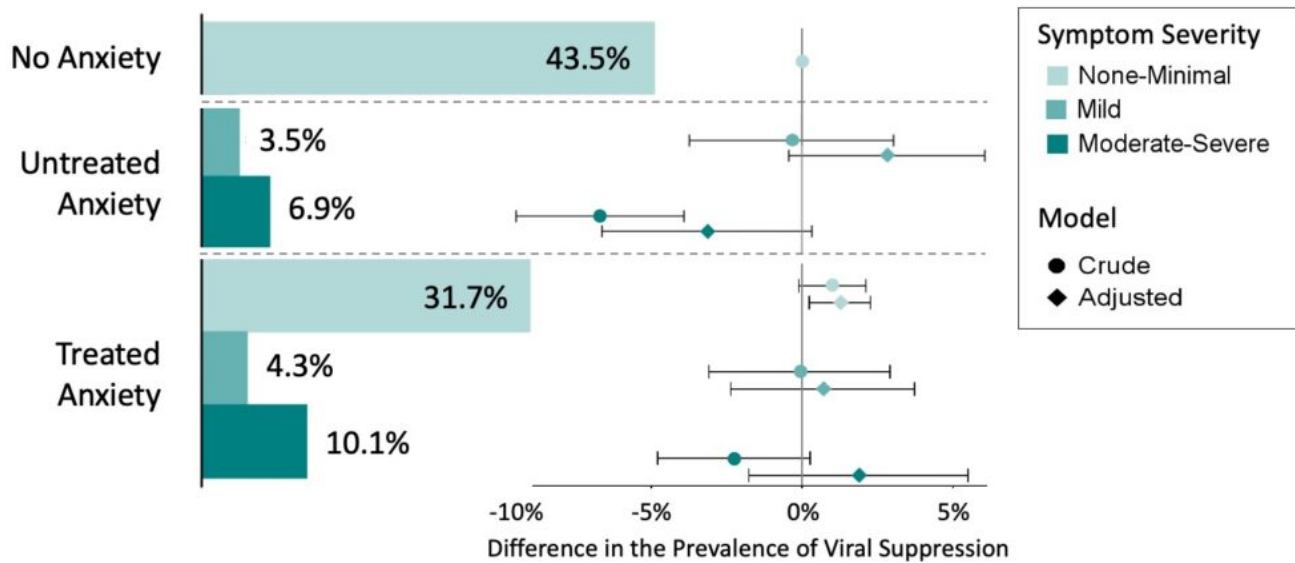
Understanding the relationship between depression and longitudinal HIV care continuum outcomes in a cohort of people entering HIV care in Cameroon Lindsey Filiatreau* Lindsey M. Filiatreau Peter Vanes Ebasone Anastase Dzudie Milton Wainberg Marcel Yotebieng Kathryn Anastos Rogers Ajeh Denis Nash Angela M. Parcesepe

Addressing mental health needs of people with HIV (PWH) has gained mounting traction as a strategy critical to ending the HIV epidemic. Yet, empirical evidence clarifying the relationship between depression and HIV care outcomes across the care continuum is scant. Multi-state methods can provide a holistic picture of how individuals engage and disengage in care over time and aid in understanding complex longitudinal exposure/outcome relationships.

From June 2019-March 2020 we enrolled PWH aged 21+ entering HIV care at 3 clinics in Cameroon. We conducted structured interviews to ascertain demographics and depression status (Patient Health Questionnaire-9 scores>9=probable depression) at enrollment and extracted participant clinical record data through January 1, 2022. We estimated time spent in six mutually exclusive and exhaustive HIV care states: linked to clinic; engaged at clinic, prescribed ART; disengaged from clinic; re-engaged at clinic; known death; known transfer out; and transitions between these states in the first 2 years following enrollment. Estimates were compared for those with vs. without (referent) probable depression using differences.

420 PWH contributed 825.4 person-years of follow-up. 20% (n=81) had probable depression at enrollment. A similar proportion of individuals with and without probable depression failed to return to care after their first visit (~10%). However, those with probable depression were less likely to be engaged in care at both years 1 and 2 [Figure; percent differences of 12.2% and 8.7%, respectively] and consistently demonstrated a higher hazard of transfer out compared to those without probable depression. Of those who disengaged from care, those with probable depression re-engaged later than others (re-engagement hazard peak: days 112 vs. 54).

Routine depression screening and sustained support for PWH with probable depression is warranted for PWH entering HIV care to improve population-level downstream treatment outcomes.
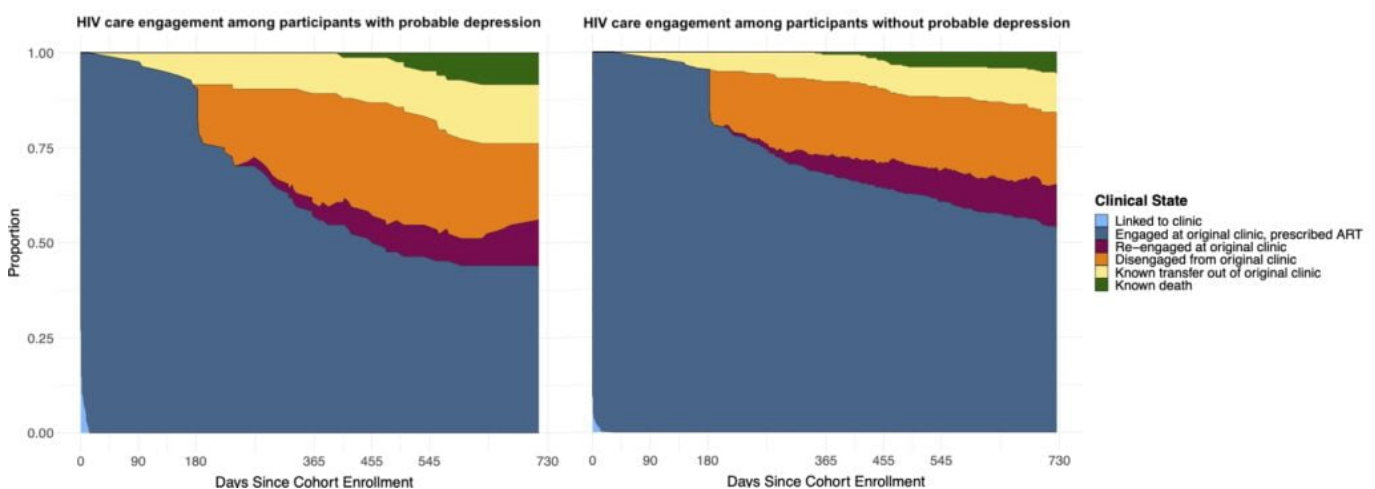
Latent class analysis of traumatic life experiences among people living with HIV in Florida.

Nanyangwe Siuluta* Nanyangwe Siuluta Karina Villlaba Catalina Lopez-Quintero Yancheng Li Yiyang Liu Robert L. Cook Nichole M. Scaglione

Background: Traumatic Life Experiences (TLE)-perceived events risking health, causing victim helplessness and fear—are more common among people with HIV(PWH) than the general US population. This study used latent class analysis (LCA) to identify unique LTE patterns and examined the consistency of LTE patterns across demographic subgroups in a sample of PWH.

Methods: From 2019-2022, the Florida Cohort examined individual, clinical, & community impacts on healthcare utilization and HIV outcomes in 495 PWH. Participants were 42% non-heterosexual men; 42% women; 59% aged 50+; & 43% Black. They self-reported LTE on questionnaires assessing sexual harassment (SH), unwanted sexual touch (UST), forced sex (FS), transactional sex, discrimination (D), physical attack (PAt), stalking (S), hate crimes, verbal (VAb), physical (PAb), & emotional (EAb) abuse. We used PROC LCA (SAS V9.4) to sequentially examine LCAs (2-5 classes); we added demographic covariates to the model that best fit the data.

Results: Model fit criteria (Entropy, AIC, BIC) indicated a four-class solution best fit the data. The Abuse & Discrimination class (41%) endorsed relatively high probabilities of VAb, EAb, PAb, PAt, & D. The Sexual Abuse Risk class (14%) reported high probabilities of S, SH, UST& FS in addition to VAb, EAb, & PAb. The Low-Risk class (35%) had consistently low probabilities of all LTEs; the High-Risk class (11%) had the highest probability of experiencing 9/12 LTEs. Subgroup analyses showed class consistency, but membership probabilities varied by sex, sexual orientation, race, & age – e.g. the largest proportion of non-heterosexual men (31%) were in the Abuse & Discrimination class, while the largest proportions of heterosexual men (50%) & women (34%) were in the Low-Risk class.   **Conclusion:** Findings highlight significant variability in LTE patterns. More work is needed to identify predictors of LTE class membership and to link LTE patterns to health outcomes in PWH.

Assessing the Impact of Population-Level Interventions on HIV Transmission Among Heterosexual African American/Black People: A Spatially Dynamic Agent-Based Modeling Study Shayla Nolen* Shayla Nolen Sam E. Bessey Katie B. Biello Bridgette M. Brawner Rice Akilah Dulin Chanelle J. Howe Brandon D. L. Marshall

Objectives: To assess the impact of population-level interventions on HIV transmission among heterosexual African American/Black people using a spatially dynamic, agent-based model.

Methods: We simulated a population of 130,565, hereby referred to as agents, representing the number of heterosexual African American/Black people who were living with diagnosed HIV or at risk for HIV in Philadelphia in 2019 in a spatially dynamic agent-based model. Agents in the model were assigned probabilities of engaging in unprotected sex with casual and main partners, spatially assortative mixing (i.e., the likelihood of selecting a sexual partner in an adjacent census tract [CT]), progression through the HIV care continuum (HCC), and incarceration based on their CT of residence and whether the CTs was more or less disadvantaged. We determined the CT's disadvantage status by creating a composite score that was dichotomized at the median. We tested the following interventions: opt-out testing, culturally congruent HCC interventions, criminal justice reform, and a combination of all the aforementioned interventions. For each intervention scenario, we compared the percentage reduction in new HIV diagnoses between 2019 and 2030 to the base case scenario (i.e., the current status quo).

Results: The relative percent reduction of the base case and all standalone interventions resulted in a 29-31% reduction. The combination intervention scenario resulted in a slightly larger relative decrease in new HIV diagnoses by 2030 at 34.2%.

Conclusion: Combinations of interventions that address structural factors that contribute to HIV transmission, such as incarceration and improved progression through the HCC, can make a more meaningful impact on reducing HIV transmission than interventions that solely address testing and treatment. However, the observed effects in this simulation study were small, suggesting that a high proportion of transmission may be due to other unmeasured structural factors.

Comparative effectiveness of extended release naltrexone and sublingual buprenorphine for treatment of opioid use disorder among Medicaid beneficiaries Rachael Ross* Rachael Ross Edward Nunes Mark Olfson Matisyahu Shulman Noa Krawczyk Elizabeth Stuart Kara Rudolph

Introduction: Extended release naltrexone (XR-NTX) and sublingual buprenorphine (SL-BUP) are medications for treatment of opioid use disorder. In contrast to methadone, XR-NTX and SL-BUP can be prescribed in any healthcare setting. There is limited real-world evidence to inform the choice between XR-NTX and SL-BUP. We compared their treatment effectiveness in a real-world population.

Methods: We created an active comparator, new user cohort using 2016-2019 Medicaid claims data from CA and NJ. We included adults who initiated XR-NTX or SL-BUP for OUD maintenance treatment and did not use any medication for OUD in the prior 90-days. We estimated comparative treatment effects of the medications on medication discontinuation and overdose, over 180 days (6 months) following initiation. We used a sequentially doubly robust estimator with nuisance models adjusted for baseline confounders estimated flexibly using SuperLearner.

Results: Our cohort included 1,755 XR-NTX and 9,886 SL-BUP patients. The figure presents the adjusted cumulative risk (as %) for medication discontinuation (top) and overdose (bottom). Patients were immune to discontinuation until day 60 after initiation of XR-NTX (injection duration + 31-day grace period) so initially SL-BUP discontinuation was higher, but by 180 days XR-NTX initiating patients were more likely than SL-BUP initiating patients to discontinue: 76% vs. 62%, respectively; RD 14% (95% CI 13, 16). There was minimal difference in the risk of overdose: 3.8% vs. 3.3%; RD 0.5% (95% CI -0.5, 1.5). Our results were robust to several sensitivity analyses.

Conclusions: Longer medication retention is important because risks of negative outcomes are elevated after discontinuation. Our results support selection of SL-BUP over XR-NTX. However, most patients discontinued medication by 6 months indicating that more effective tools are needed to improve treatment retention, particularly after XR-NTX initiation.

Figure. Cumulative risk (%) of discontinuation (top) and overdose (bottom)
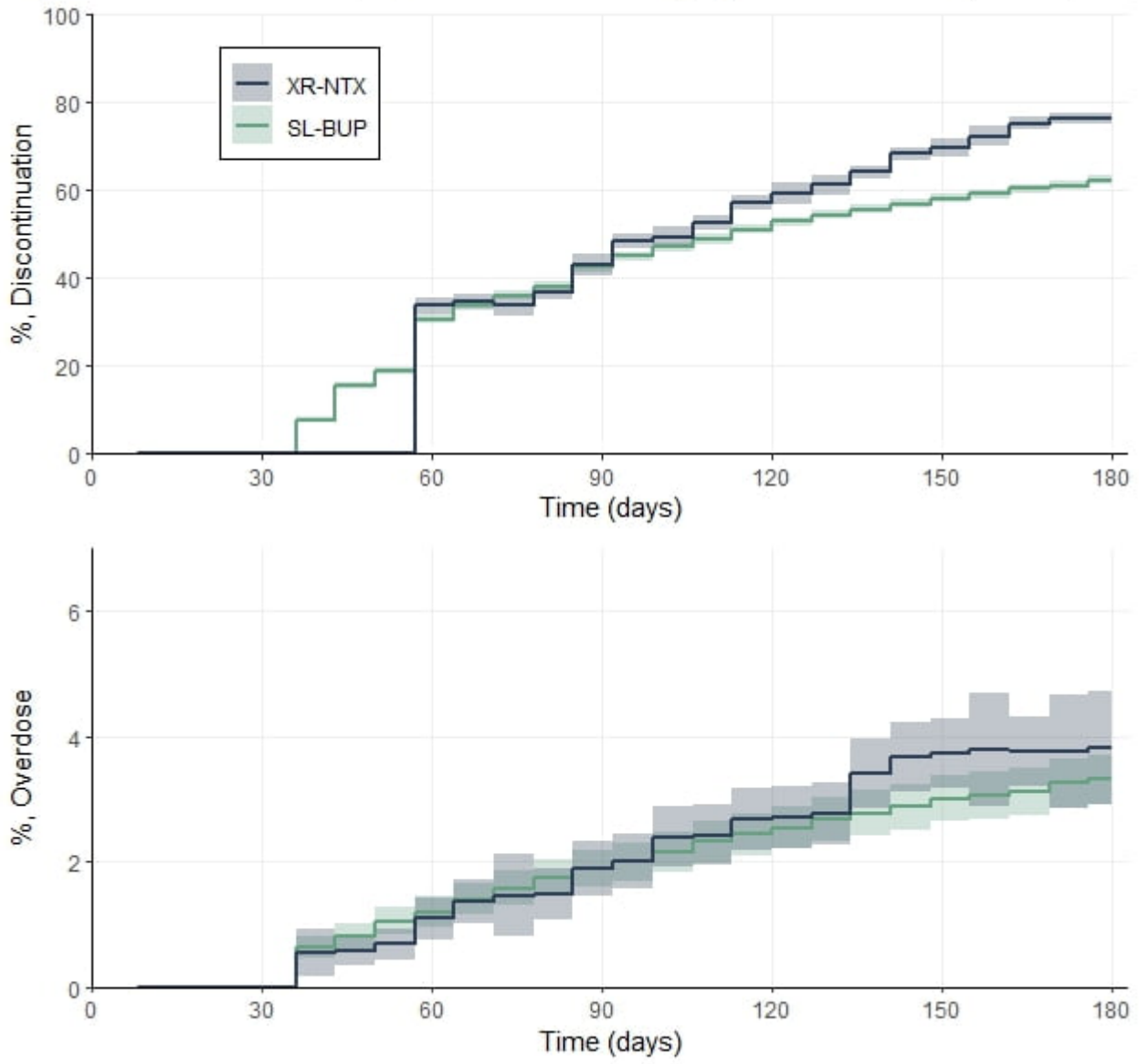
Treatment patterns of symptomatic therapies for Alzheimer's Disease and Related Dementias Huiwen Deng* Huiwen Deng Todd A. Lee Charles E. Gaber Kibum Kim Stephanie Y. Crawford Elizabeth A. Bayliss Xiaojuan Li

Currently approved symptomatic therapies for patients with Alzheimer's Disease and Related Dementias (ADRD) target cognitive and behavioral symptoms and may temporarily improve quality of life, yet their real-world treatment patterns remain underexplored. We identified senior ADRD patients (≥65 years) who newly initiated an acetylcholinesterase inhibitor (AChEIs: donepezil, rivastigmine, galantamine), memantine, or their combination from 2011 to 2019. Treatment patterns were assessed by summarizing initial therapy, treatment changes (switching or discontinuation), and retreatment following the first discontinuation during the 3 years following initiation. We assessed factors associated with switching or discontinuation of the initial therapy using subdistribution hazard model in which we controlled for patient demographics, clinical characteristics, and healthcare encounters. The analytic cohort included 68,434 AChEI, 14,038 memantine, and 4,711 dual therapy initiators. The median age was 82 years (IQR: 77, 87), and 62% were female. Donepezil accounted for the largest subset of the treatment initiators across the years (63% in 2011 to 73% in 2019). AChEI initiators had fewer comorbidities, similar frailty levels, and lower neuropsychiatric drug use at baseline compared to other initiators. Following initiation, 46% switched or discontinued their initial therapy within 6 months, with only 3% remaining on their initial therapy after 3 years. Dual therapy initiators had the highest switching (44%) and lowest discontinuation rates (30%), while donepezil initiators had the lowest switching (19%) but highest discontinuation rates (54%). Among those who discontinued treatment, 39% reinitiated treatment, with a median duration of 90 days to reinitiation (IQR: 62, 157). Elevated risk of switching was linked to younger age, while geographic location appeared to influence both switching and discontinuation. The results showed poor persistence to symptomatic therapy for ADRD.

Treatment Changes after Initiation
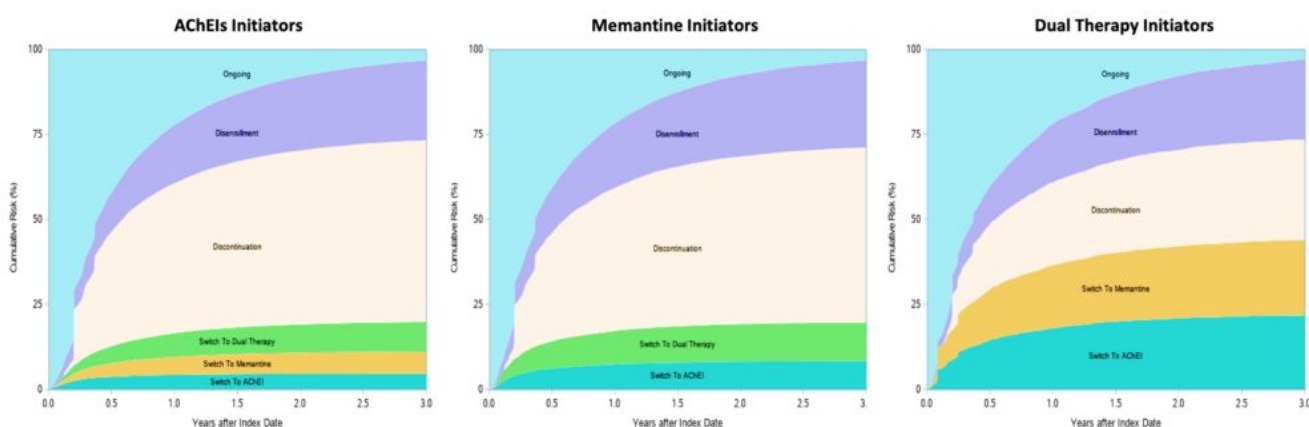
Illustrating the structures of bias from immortal time using directed acyclic graphs Guoyi Yang* Guoyi Yang Stephen Burgess C Mary Schooling

Background: Immortal time is a period of follow-up during which death or the study outcome cannot occur by design. Bias from immortal time has been increasingly recognized in epidemiologic studies. However, the fundamental causes and structures of bias from immortal time have not been explained systematically using a structural approach.

Methods: We use an example "Do Nobel Prize winners live longer than less recognized scientists?" for illustration. We illustrate how immortal time arises and present the structures of bias from immortal time using time-varying directed acyclic graphs (DAGs). We further explore the structures of bias with the exclusion of immortal time and with the presence of competing risks. We discuss how these structures are shared by different study designs in pharmacoepidemiology and provide solutions, where possible, to address the bias.

Results: We illustrate that immortal time arises from using postbaseline information to define exposure or eligibility. We use time-varying DAGs to explain the structures of bias from immortal time are confounding by survival until exposure allocation or selection bias from selecting on survival until eligibility. We explain that excluding immortal time from the follow-up does not fully address this confounding or selection bias, and that the presence of competing risks can worsen the bias. Bias from immortal time may be avoided by aligning time zero, exposure allocation and eligibility, and by excluding individuals with prior exposure.

Conclusions: Understanding bias from immortal time in terms of confounding or selection bias helps researchers identify and thereby avoid or ameliorate this bias.
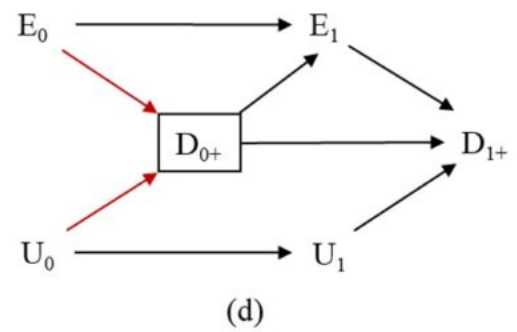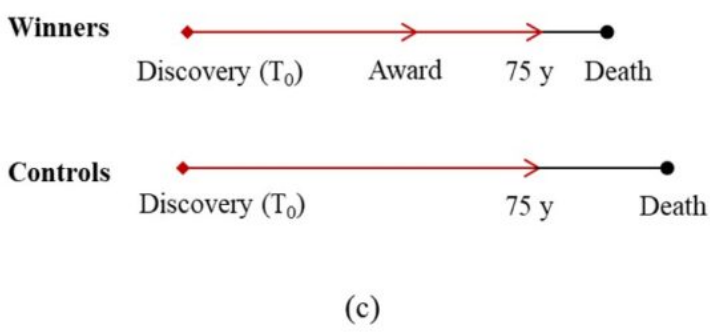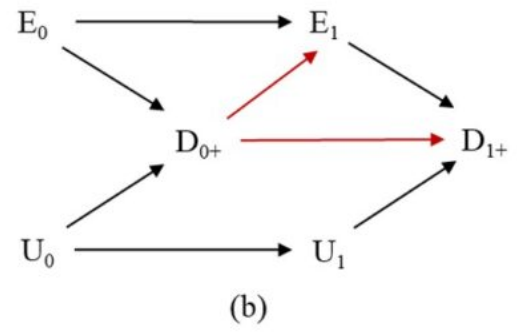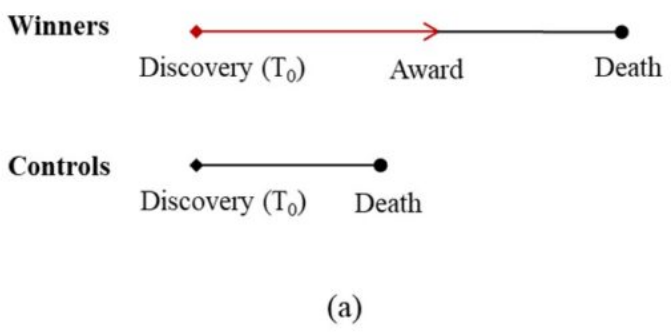
Association between rapid opioid dose tapering and polydrug overdose mortality among high-dose, long-term opioid therapy recipients in North Carolina between 2006-2018 Zoey Song* Zoey Song Bethany DiPrete Naoko Fulcher Vanessa Miller Pasangi Perera Brian Pence Shabbar I Ranapurwala

Chronic pain patients receiving high-dose, long-term opioid therapy (HDLTOT) and subsequently undergoing rapid dose tapering are likely to experience opioid withdrawal, use of illicit drugs, and opioid overdose that extends to polydrug overdose. Quantifying the association between rapid tapering and polydrug overdose can inform clinical practice and interventions. We constructed a retrospective cohort of 21,478 commercially insured North Carolina residents aged 18-64 who received HDLTOT (≥90 morphine milligram equivalent opioids for 90% of 90 consecutive days) before entering the cohort during 01/2006-09/2018. Time-varying rapid tapering (dose reduction >10% per week) or discontinuation, versus dose maintenance, increase, or gradual tapering of opioids were assessed monthly. Outcomes were polydrug overdose mortality from 1) any substance combination, 2) multiple opioids, and 3) opioids with other substance. Cumulative incidence and hazard ratios were estimated using inverse treatment and censoring probability-weighted marginal structural Fine-Gray models with follow-up time interaction. During the 4-year follow-up, we observed 69 overdose deaths from any substance combination, 27 from multiple opioids, and 23 from opioids with other substance. Polydrug overdose mortality hazard of any substance combination among the rapidly tapered was 1.58 [0.86-2.91] times that of people with stable tapering during the follow-up. Rapid tapering was not associated with overdose mortality of multiple opioids and opioids with other substance through 1 year and 1.5 years of follow-up, respectively (HR [95%CI]: 1.50 [0.46-4.87] and 1.29 [0.42-3.95]). However, the hazard ratio of overdose mortality during years 2-4 increased for multiple opioids (HR [95%CI]: 3.76 [0.85-16.51]). The increased polydrug overdose mortality during the later stage of follow-up among the rapidly tapered HDLTOT patients reflects the long-term safety and overall pain management concerns during opioid tapering.

Figure 1. Inverse probability of treatment and censoring weighted cumulative incidence (shaded 95%CI) of polydrug overdose mortality outcomes between rapid tapering or discontinuation vs. other dose reduction regime of HDLTOT in a statewide population within US during 2006-2018.
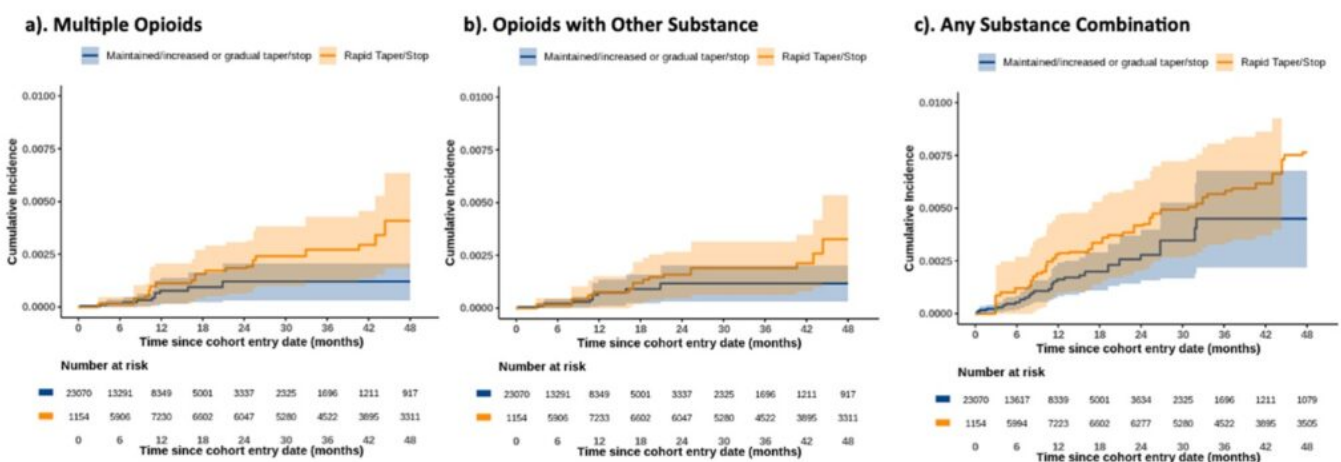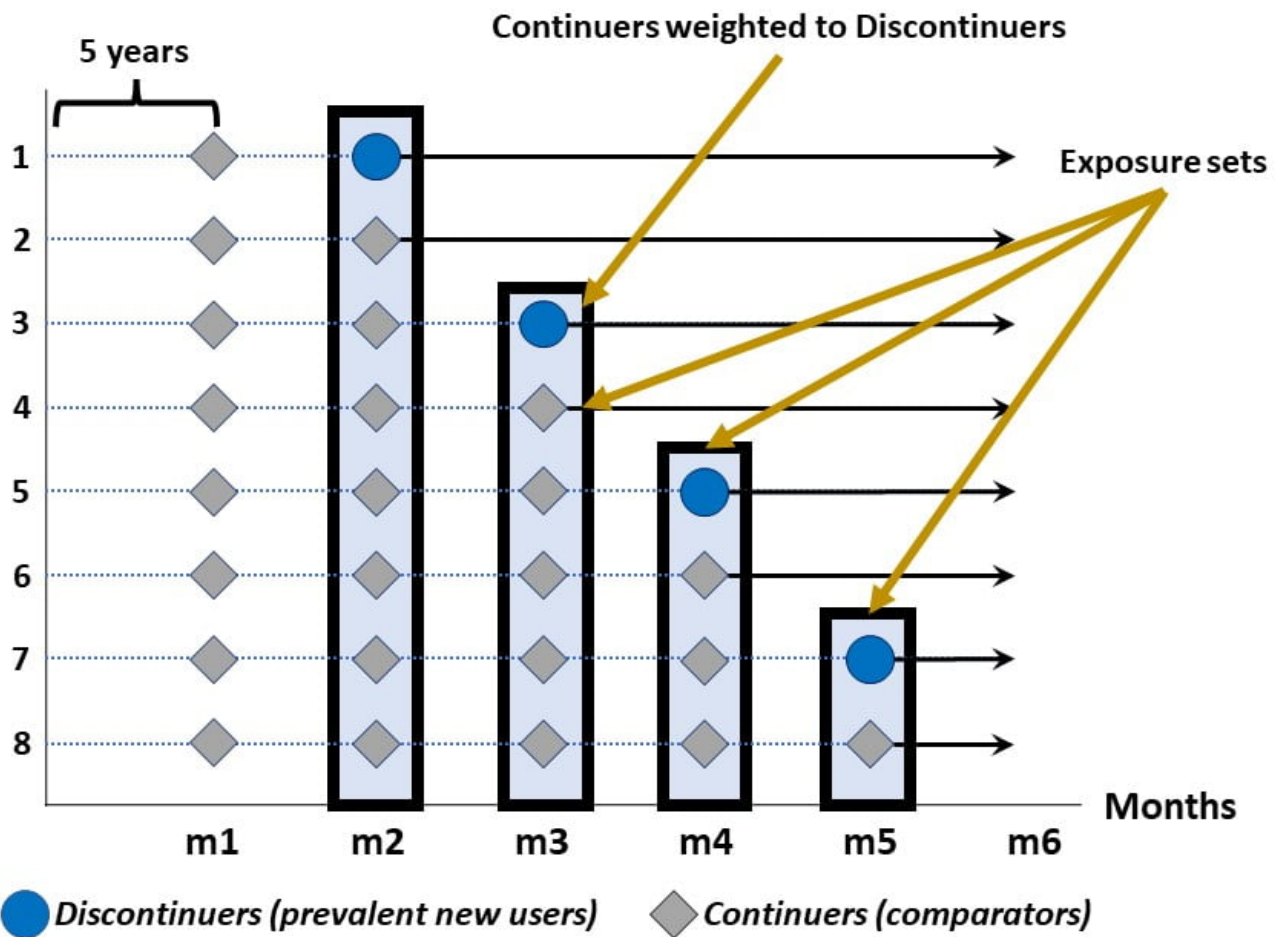
Adapting the prevalent new user study design to evaluate the effects of drug discontinuation: an example in statins and mortality Qoua Her* Qoua Her Alan Ellis Emilie Duchesneau Til Stürmer Jennifer Lund Viriginia Pate Michael Webster-Clark

Drug discontinuation studies often use causal contrasts to ask questions like: "what if everyone discontinued a drug immediately after some date" vs "what if no one ever discontinued drug?" Combining the prevalent new user (PNU) design and time-stratified odds weighting allows us to ask a different question: "what if the discontinuers had continued the drug rather than discontinued?"

We demonstrated this in a cohort of new statin users (i.e., no statin prescription in the previous year) with at least 5 years of subsequent continuous statin use (i.e., without a gap in statin use of >90 days) from a 20% random sample of Medicare fee-for-service beneficiaries. We adapted the PNU design to estimate the effect of statin discontinuation versus continuation on mortality among discontinuers, treating discontinuation like a switch to new treatment in the PNU design with continuing as the comparator. For each month after 5 years of use, we created exposure sets of discontinuers and continuers with equal duration of previous statin treatment and estimated a month-stratified propensity score for discontinuation (Figure 1). We calculated all-cause mortality rates, the rate difference (IRD), and the rate ratio (IRR) for discontinuers and the continuers with and without odds weights for the continuers. We estimated 95% CIs with the 2.5th and 97.5th percentiles from 150 bootstrap iterations.

We identified 113,109 statin initiators who continued for at least 5 years. Mortality rates per 100 person-years were 12.16 among discontinuers and 6.20 among continuers before applying odds weights. After weighing, the IRD was 3.06 (95% CI: 2.82, 3.43) per 100 person-years, and the IRR was 1.34 (1.30, 1.37).

While additional work (e.g., restriction to less-frail individuals) is necessary to avoid bias from the sick stopper effect, adapting the PNU design to drug discontinuation allows estimation of the treatment effect in a well-defined target population of clinical relevance.

Figure 1: The prevalent new-user study design was adapted to evaluate the effects of statin discontinuation on mortality among the discontinuers. Patients who *'discontinued'* statins were treated like switching to a new treatment and *'continued'* statins as the comparator. Monthly-stratified standardized mortality ratio weights were used to adjust for confounding.

Benchmarking an observational analysis against a randomized trial: an application to the effect of trastuzumab on the risk of disease-free survival in early curative breast cancer

Vanessa Voelskow* Vanessa Voelskow Xabier Garcia de Albeniz Anita Berglund Maria Feychting Tobias Kurth Anthony A. Matthews

Most published examples of benchmarking compare an observational study to a trial that estimates the effect of a treatment on the risk of death or another single outcome that is expected to be captured analogously in a trial and a routine clinical practice setting. This limits the scope of how we can use observational data to complement randomized trials.

We designed a target trial with a protocol as similar as possible to the B-31 and N9831 randomized trials, which estimated the effect of adjuvant trastuzumab plus chemotherapy compared with chemotherapy alone on the risk of disease-free survival and death from any cause in individuals with early human epidermal growth factor receptor 2 positive breast cancer in the curative setting. We then emulated the target trial using observational data from Swedish registries to understand if we can undertake an observational analysis that replicates the effect of trastuzumab not only on the risk of death, but also disease free survival. We applied inverse probability of treatment weighting, while cloning individuals who had data compatible with both treatment strategies at baseline and assigning each copy to one arm.

Our target trial emulation included 1578 women. We found a similar effect estimate after five years of follow-up (RR: 0.46, 95% CI: 0.33, 0.64) for the composite endpoint of disease-free survival as the two jointly analyzed B-31 and N9831 trials (HR: 0.48, 95% CI: 0.39, 0.59). The results after five years for death in our target trial emulation (RR: 0.33, 95% CI: 0.22, 0.49) would also lead to the same clinical decision as those from the randomized trials (HR: 0.67, 95% CI: 0.48, 0.93).

The results indicate that, with high-quality data, benchmarking observational analyses against trials can be extended to outcomes less severe than death, such as disease-free survival used in oncological studies with curative treatment intent.

Study Design

Treatment assignment in observational analyses – a practical application in the Swedish Primary Care Cardiovascular Database Anna Humphreys* Anna Humphreys Anthony Matthews Anita Berglund Jessica Young Bertil Lindahl Björn Wettermark Thomas Kahan Miguel Hernán

Introduction

In randomized trials, the intention-to-treat effect is the effect of assignment to a treatment strategy. When using observational data to emulate a target trial, estimating the intention-to-treat effect requires treatment strategy assignment to be defined. While the prescription of a treatment is a natural analog of treatment assignment, many databases only contain treatment dispensation data.

Objectives

We aimed to assess the implications of using prescription versus dispensation data to define treatment assignment in observational analyses by emulating two target trials that estimate the effect of Angiotensin Converting Enzyme Inhibitors (ACEI) and Angiotensin Receptor Blockers (ARB) versus Calcium Channel Blockers (CCB) on the five-year risk of cancer.

Methods

We used the Swedish Primary Care Cardiovascular Database (SPCCD), a database composed of electronic health records linked with national registers for more than 75,000 primary care patients with hypertension. SPCCD uniquely contains both prescription and dispensation data, and thus the first emulation used prescription as an analog for assignment, and the second used dispensation. The confounding structure differed between emulations, with the dispensing emulation also adjusting for education, birth country, income and medication history.

Results

In both the prescribing emulation and dispensing emulation, no difference was found between ACEI/ARB and CCB on the five-year risk of cancer (RR 0.92 (95% CI 0.78 – 1.10), and RR 1.00 (95%CI 0.80-1.21) respectively).

Conclusion

The use of prescription or dispensation data to define treatment assignment must be considered when interpreting effect estimates from observational analyses, as the effect of a treatment strategy may vary depending on how treatment is assigned and whether the differing adjustment variables are sufficient. While similar effect estimates were seen, there may be situations (eg treatments with acute effects) with greater implications.

Separable effects for adherence Kerollos Wanis* Kerollos Wanis Mats Stensrud Aaron Sarvet

Comparing different medications is complicated when adherence to these medications differs. We can overcome the adherence issue by assessing effectiveness under sustained use, as in the usual causal `per-protocol' estimand. However, when sustained use is challenging to satisfy in practice, the usefulness of this estimand can be limited. Here we propose a different class of estimands: separable effects for adherence. These estimands compare modified medications, holding fixed a component responsible for non-adherence. Under assumptions about treatment components' mechanisms of effect, the separable effects estimand can eliminate differences in adherence. These assumptions are amenable to interrogation by subject-matter experts and can be evaluated using causal graphs. We describe an algorithm for constructing causal graphs for separable effects, illustrate how these graphs can be used to reason about assumptions required for identification, and provide semi-parametric weighted estimators. We illustrate an application of the separable effects for adherence in simulated data based on a randomized trial in which investigators compare initiation of a thiazide diuretic or an angiotensin-converting enzyme inhibitor. The application considers a series of data generating mechanisms in order to give intuition for when separable effects assumptions will hold so that adherence is balanced.

Table 1: Properties of selected estimands that compare the effectiveness of pharmacologic treatments.

Estimand	Description	Natural adherence[a]	Testable[b]	Equivalent adherence[c]
'Intention-to-treat' effect	Comparison of risks under the natural adherence processes of the medications	✓	✓	✗
'Per-protocol' effect	Comparison of risks under interventions that enforce continuous adherence	✗	✓	✓
Principal stratum direct effect	Comparison of risks in the subgroup of the population who would continuously adhere under either medication	✓	✗	✓
Natural direct effect[d]	Comparison of risks under interventions that set adherence for each individual to its counterfactual value under one of the medications	✗	✗	✓
Randomized interventional analogue of the natural direct effect	Comparison of risks under the counterfactual distribution of adherence that would arise under one of the medications	✗	✓	✓
Stochastic adherence effect	Comparison of risks under interventions that randomly determine adherence according to an investigator-specified distribution	✗	✓	✓
Separable effect	Comparison of risks under the natural adherence processes of modified medications, holding fixed a component responsible for non-adherence	✓	✓	✓[e]

a Investigators consider interventions only on the initiated medication, rather than on adherence directly.
b Assumptions can be tested (in principle) by experiment.
c Medications are compared under equivalent adherence.
d Natural direct effects are not identified when there are time-varying confounders affected by prior exposure and mediator.
e The equivalent adherence expected under the interventions comprising the separable effects contrast does not follow by definition of the parameter but is rather contingent on assumptions, which may be encoded in causal DAGs.

Causal Inference

Combining information from trial participants and non-participants in registry-based trials

Camila Olarte Parra* Camila Olarte Parra Anthony Matthews Conor Macdonald Anita Berglund Issa J. Dahabreh

The strengths of randomized trials for estimating treatment effects are well understood, but trials often enroll selected populations and have high cost. These drawbacks can be overcome by designing trials nested in registries and using the registry infrastructure to collect information on both trial participants and non-participants. Here, we discuss the identifiability conditions that allow combining information from trial participants and non-participants in registry-based trials to estimate the effects of the randomized treatments, taking into account selection into the trial, assignment into treatment groups, adherence to the assigned treatment, and loss to follow up. We propose estimators that jointly use the randomized and observational data in registry-based trials under different identifiability conditions and we illustrate the use of the estimators using data from a major cardiovascular trial nested in a large national registry.

Association between Climatic Factors and Pregnancy Loss Stefania Papatheodorou* Stefania Papatheodorou Aashna Shah Veronica Wang Marc Weisskopf Petros Koutrakis Souzana Achilleos

Background: Ambient climatic factors have been linked to multiple adverse pregnancy outcomes. However, only a few studies examined exposure to climatic factors and the risk of pregnancy loss. This study aims to examine the effects of climatic factors on pregnancy loss in Nicosia, Cyprus, an area that is highly affected by climate change.
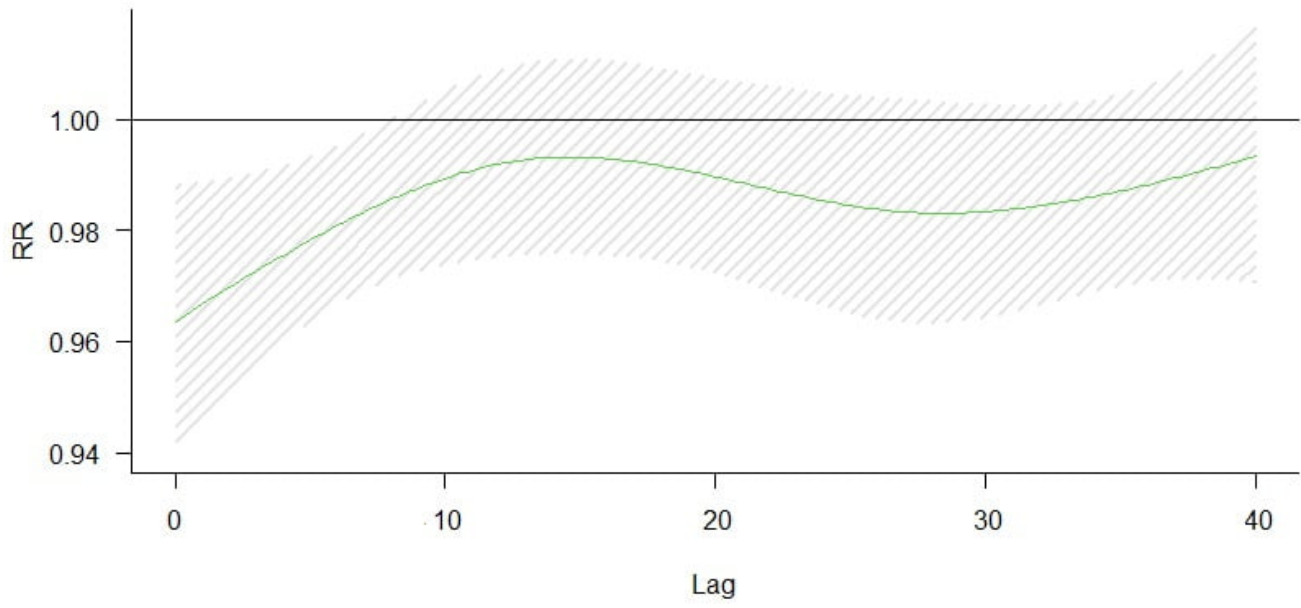
Methods: Birth registry data for Nicosia, Cyprus from 2014-2019, were linked with daily meteorological and traffic pollution data (minimum and maximum temperature, $^{\circ}C$; relative humidity, %; and NO2). Additional climactic variables (mean weekly temperature, standard deviation of the mean weekly temperature, heat index) were computed. We used a novel variation of time-series design and distributed lag models to explore the association between climatic factors and weekly live-birth identified conceptions (LBIC), to indirectly estimate pregnancy losses.

Results: In Nicosia (26,530 live births), an association between exposure to higher temperature and pregnancy loss was found between weeks 0-9, with the strongest association in weeks 0-1 weeks. Specifically, per 5 $^{\circ}C$ increase in mean temperature in week 0-1 we observed a lower rate of LBIC (Rate Ratio [RR]= 0.96 (95% confidence interval [CI]: 0.94 –0.98); the results for all other temperature-related and climatic exposures were similar. Furthermore, we found that temperature variability may have an impact in the later weeks of pregnancy. There is an association for weeks 20-35, with the strongest estimate in week 26 (RR= 0.93 (95% CI: 0.86 –0.99 per 5$^{\circ}C$ increase in the standard deviation of the mean temperature).

Conclusion: Using the weekly conceptions ending in a live birth, we analyzed the association between climatic factors and pregnancy loss. The results show that exposure to higher temperatures and humidity is associated with pregnancy loss very early in pregnancy while temperature variability may have an effect between weeks 20-35.

Association with 5 degrees increase in mean weekly temperature

Heat waves and preterm and early-term birth: effect modification by maternal- and area-level vulnerability factors
Amy Fitch* Amy Fitch Mengjiao Huang Matthew J. Strickland Andrew J. Newman Joshua L. Warren Howard H. Chang Lyndsey Darrow

Background: Extreme heat events are increasing in frequency and intensity and they disproportionately affect vulnerable populations. Previous research suggests that maternal exposure to extreme heat in the days before delivery is associated with preterm and early-term birth.

Methods: We examined possible effect modification of the relationship between acute heat wave exposure and two birth outcomes: preterm (<37 weeks) and early-term (37-38 weeks). Effect modifiers explored include area-level factors (e.g., social deprivation index (SDI)) and individual-level factors (e.g., maternal education). Live, singleton preterm or early-term births were identified from state vital records in eight states (CA, FL, GA, KS, NC, NJ, NV, OR) from 1990 to 2017. A novel, urban heat island-focused dataset was linked to births by zip code. Daily mean temperatures were used to identify heat waves. Heat waves were defined in multiple ways according to intensity and duration. We conducted time-stratified case-crossover (conditional logistic regression) analyses, pooling effect estimates across states using a fixed effects meta-analysis.

Results: Preliminary pooled results from three states (CA, NV, OR) suggested effect modification by SDI for early-term birth. For example, ORs (95% CI) for 4-consecutive days over the local 97.5th percentile mean temperature are 1.038 (1.024, 1.052) for high SDI and 1.014 (0.989, 1.039) for low SDI. There is no evidence of effect modification for preterm birth, OR 1.023 (0.999, 1.058) for high SDI and 1.025 (0.979, 1.073) for low SDI. These results are consistent with estimates for other heat wave definitions we explored. Results including the five additional states and other possible effect modifiers will be presented.

Conclusion: Preliminary results suggest that the effect of acute heat wave exposure on early-term birth is stronger in economically-disadvantaged communities.

A non-persistent endocrine disrupting chemical mixture is associated with increased odds of persistent nausea during pregnancy Brad Ryva* Brad Ryva Blair Wylie Antonia Calafat Susan Schantz Rita Strakovsky

Background: Pregnant women are exposed to many endocrine disrupting chemicals (EDCs) from consumer products. Pregnancy-related nausea is common, can persist past the first trimester, and has unclear, possibly hormonal etiology. Thus, we evaluated associations of an EDC biomarker mixture with nausea persistence.

Methods: Illinois women (n=433) reported nausea since conception or last study visit (yes/no) at median 13, 17, 23, 28, 34 weeks gestation and at delivery. We categorized women as never having nausea, or as having typical (ends by 17 weeks gestation), persistent (ends after 17 weeks gestation), or intermittent nausea. Women provided five urine samples across pregnancy, which we pooled and analyzed for 16 phthalate, three paraben, and six phenol biomarkers. We used quantile-based g computation to assess associations of an EDC mixture with nausea persistence overall and considered differences by fetal sex.

Results: Most women were of high socioeconomic status and had typical nausea (42%), followed by persistent nausea (25%) and irregular nausea (24%); 9% of women never developed nausea. Each 10% increase in the EDC mixture was associated with 27% higher odds of persistent nausea (95% Confidence Interval (CI): 0.97, 1.66), driven by di(isononyl) cyclohexane-1,2-dicarboxylate (ΣDiNCH), di-2-ethylhexyl phthalate (ΣDEHP), and ethylparaben. In women carrying males, each 10% increase in the EDC mixture was associated with 66% higher odds of persistent nausea (95% CI: 1.06, 2.61), driven by ethylparaben, ΣDiNCH, and di-isononyl phthalate (ΣDiNP). The EDC mixture was not associated with nausea persistence in women carrying females (Odds ratio (OR):1.08; 95% CI: 0.74, 1.58). We did not identify associations of the EDC mixture with never developing nausea or with having intermittent nausea.

Conclusion: Future studies should explore hormonal pathways responsible for these findings and investigate if decreasing EDC exposure can reduce nausea persistence in pregnancy.

Redlining in new york city: impacts on particulate matter exposure during pregnancy and birth outcomes Teresa Herrera* Teresa Herrera Akhgar Ghassabian Eunsil Seok Robin Ortiz Whitney Cowell Leonardo Trasande Sheryl Magzamen Eric Dwayne Brown Jr Anne Marie Stroustrup Ako A. Ako

Recent evidence suggests historical redlining policies have played a role in shaping the built environment and health outcomes of residents in urban areas. To date, only a handful of studies have examined redlining's association with air pollution and adverse birth outcomes in New York City (NYC). Additionally, no NYC-specific studies have examined the impact of redlining on birth weight.

Using a prospective cohort design, this study analyzed data from the National Institutes of Health (NIH) Environmental influences on Child Health Outcomes (ECHO) Program to investigate the extent to which maternal residence in a historically redlined neighborhood is associated with fine particulate matter (PM2.5) exposure during pregnancy at the residential address level using multivariable regression models. Additionally, we examined the extent to which maternal residence in a historically redlined neighborhood during pregnancy influenced birth weight z-score, preterm birth (PTB), and low birth weight (LBW).

Our air pollution model showed that having reported a residential address in a D graded census tract or an ungraded census tract was associated with increased PM2.5 exposure during pregnancy. We also found having reported a residential address in a D graded census tract or an ungraded census tract during pregnancy was associated with lower birth weight z-score. This association remained significant when controlling for individual and census-tract level race/ethnicity and income. When we controlled for PM2.5 in our secondary analyses assessing the relationship between redlining grade and birth outcome, our results did not change.

Our study supports the literature linking historical redlining to air pollution and birth outcomes. Our research warrants further investigation into the extent to which historical policies influence present-day environmental and health outcomes. This study contributes to our understanding of historical racism and perinatal health.

Effect of extreme heat exposure on the associations between weekly gestational exposure to fine particulate matter and preterm birth in a North Carolina birth cohort Alison K. Krajewski* Alison K. Krajewski Breanna Alman Ambarish Vaidyanathan Thomas J. Luben Kristen M. Rappazzo

Preterm birth (PTB;<37 weeks completed gestation) is associated with exposure to fine particulate matter (PM2.5). Recent studies suggest that extreme heat events (EHE) may further impact this association. We estimated the associations between PM2.5 and PTB, with different metrics for EHE. We examined the associations between gestational exposure to PM2.5 and PTB in a North Carolina birth cohort (N=552,567) from 2011-2015. Daily (24-hour average) PM2.5 concentrations from US Environmental Protection Agency's Fused Community Multiscale Air Quality Modelling System (fCMAQ) model were linked to a residential address at delivery, then averaged across each week of pregnancy, trimester, and entire pregnancy. A census tract indicator of EHE (maximum daily heat index above the 95th percentile for two consecutive days) was linked for the same time period. Modified Poisson regressions with robust errors were used to estimate risk differences (RDs) in PM2.5 per 10,000 births, adjusted for gestational parent race/ethnicity, age at delivery, Medicaid status, and rural-urban commuting area. Additional models included a dichotomous indicator of EHE (0 events, 1 or more events) as a co-exposure or an interaction term. The median PM2.5 concentration during pregnancy was 9.55 μg/m3, and PTB prevalence was 7.3%. The median number of EHE during pregnancy was 5 (range: 0-31). Overall, there were negative associations between PM2.5 and PTB, without adjustment for EHE (RDs ranged from -17 to -4), with adjustment for EHE (RDs ranged from -19 to 30), and with interaction (RDs ranged from -16 to -2). The strongest associations with EHE were in the third trimester, without PM2.5 [RD -226 (95% CI: -240, -212)], with PM2.5 [RD -282 (-297, -267)], and with interaction [-1022 (-1138, -906)]. Overall, we observed negative associations with gestational exposure to PM2.5 and PTB, with no evidence of interaction with EHE.

Aging

Adjustment of age for the association of neuroimaging biomarkers and cognition in a diverse cohort of older adults

Yi Lor* Yi Lor Alexander Ivan B. Posis Charles DeCarli Paola Gilsanz Elizabeth Rose Mayeda M. Maria Glymour Rachel A. Whitmer Kristen M. George Rachel L. Peterson

Introduction: Age and brain volumes are highly correlated, thus there are disciplinary disagreements on whether age-adjustment is appropriate in models estimating effects of brain volumes on late-life cognition. We examined how different age-adjustment approaches affect associations of MRI-based brain markers and cognitive change.

Methods: Using two harmonized older adult cohorts (Kaiser Healthy Aging and Diverse Life Experience, and Study of Healthy Aging in African Americans), we used linear mixed models to evaluate the associations of volumetric MRI brain regions of interest (ROI) with annual rate of change in executive function and verbal episodic memory over 3 waves (~16 months apart) using five age-adjustment approaches: 1) no adjustment, 2) residual age at MRI estimated from regression models on intracranial volume, within model adjustment for 3) age at baseline cognitive interview, 4) age at MRI scan, and 5) age at both baseline and MRI. All models adjusted for practice effects and interview mode.

Results: Of 484 participants (mean baseline age=74.5; SD=6.3, mean MRI age=87.7; SD=8.9), older age was associated with worse brain ROI volumes and lower baseline cognitive scores. Multiple ROI were associated with lower baseline cognition and faster rate of change. The ROI-cognition association was smaller in all age-adjusted models versus models without age adjustment (Figure 1). However, associations with cognitive change did not differ after age adjustment (Figure 1), regardless of adjustment approach. Model fit statistics (AIC, BIC, and log-likelihood) suggest that adjustment for both baseline age and age at MRI yield the best fit.

Discussion: Age adjustment altered the estimated association of MRI markers and baseline cognition but not cognitive change. Due to the relatively short follow-up time, age-adjustment may not have affected cognitive change. Studies that adjust for age may be underestimating the association of MRI brain markers with cognition.

Figure 1: Linear mixed model association of neuroimaging marker and baseline cognition and cognitive change with age adjustment approaches
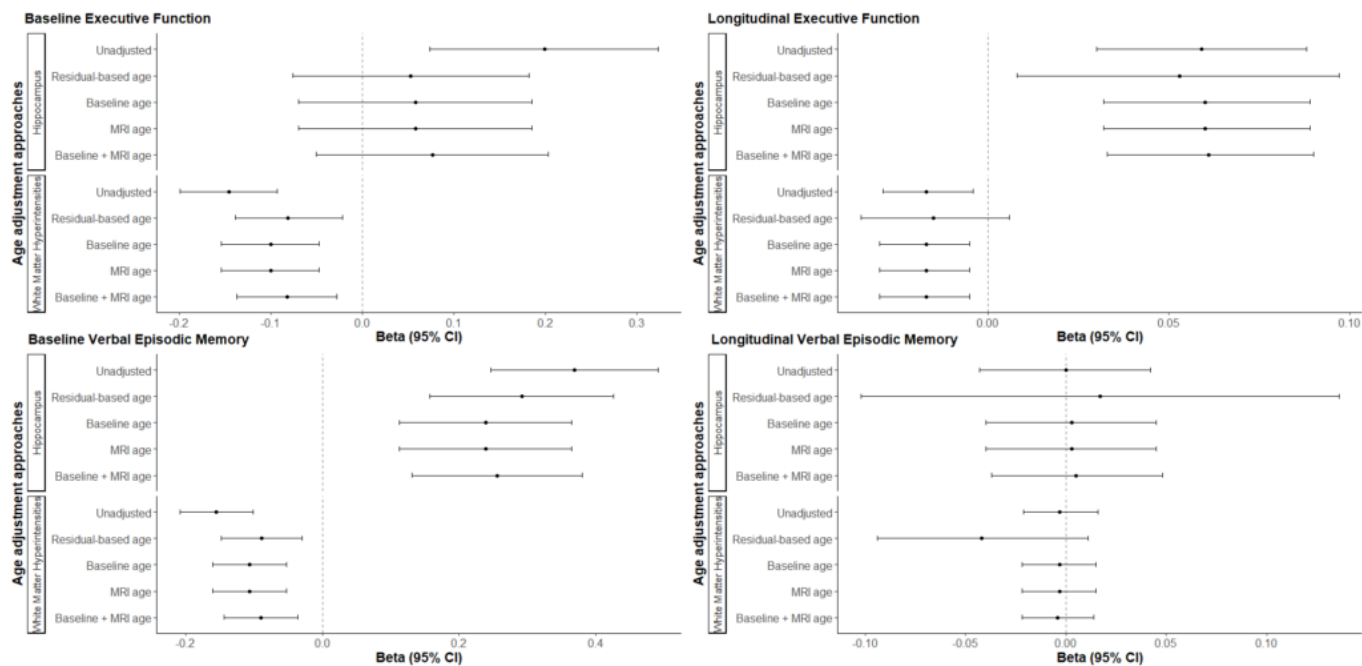
Estimated effect of APOE-ε4 genotype on risk of dementia over 13 years of follow-up in a diverse cohort of Asian and White older adults in California Yingyan Wu* Yingyan Wu L. Paloma Rojas-Saunero Yixuan Zhou Natalie Gradwohl Taylor M Mobley Willa D Brenowitz Thomas J Hoffmann Kacie D Deters Rachel A Whitmer Paola Gilsanz Gilbert C Gee Ron Brookmeyer Elizabeth Rose Mayeda

The APOE-ε4 allele is one of the most recognized risk factors for dementia in non-Latino Whites, but there is a reduced association found in Black and Hispanic groups and the evidence is limited for Asian American ethnic groups. Dementia incidence and the prevalence of APOE-ε4 carriership appear to be lower among Asian Americans than non-Latino Whites. This study aims to estimate the effect of the APOE-ε4 carriership on dementia incidence across Chinese, Japanese, Filipino, and non-Latino White older adults in Northern California. We followed 1,073 Chinese, 841 Japanese, 584 Filipino, and 42,802 non-Latino White members of the genotyped Genetic Epidemiology Research in Adult Health and Aging (GERA) cohort (mean age 70 at enrollment) via electronic health records from Kaiser Permanente Northern California from 2002-2020. APOE-ε2/ε4 carriers were excluded. We estimated the effect of APOE-ε4 genotype (carrier/non-carrier) on dementia incidence for each racial/ethnic group using adjusted average cumulative incidence curves from pooled logistic regression models including APOE-ε4, follow-up time (and an interaction term with APOE-ε4), age at baseline, and sex. Death was treated as a censoring event. Risk differences and risk ratios (RRs) at 13 years of follow-up are presented; 95% confidence intervals (CI) were obtained with bootstrapping. Prevalence of APOE-ε4 carriership was similar among Japanese (20.4%) and non-Latino Whites (22.6%) and slightly lower among Chinese (17.0%) and Filipino (13.2%) older adults. APOE-ε4 carriership was associated with higher dementia incidence in all racial/ethnic groups, with RRs (CI) ranging from 1.47 (0.79-2.54) among Filipinos to 1.91 (1.35-2.60) among Japanese. Patterns were similar on the absolute scale (Figure). Prevalence of APOE-ε4 carriership varied across racial/ethnic groups, but the association between APOE-ε4 carriership and dementia incidence was similar across groups on both the relative and absolute scales.

Risk Difference (%) and Risk Ratio at 13 years of follow up for the association between *APOE-ε4* and dementia

Aging
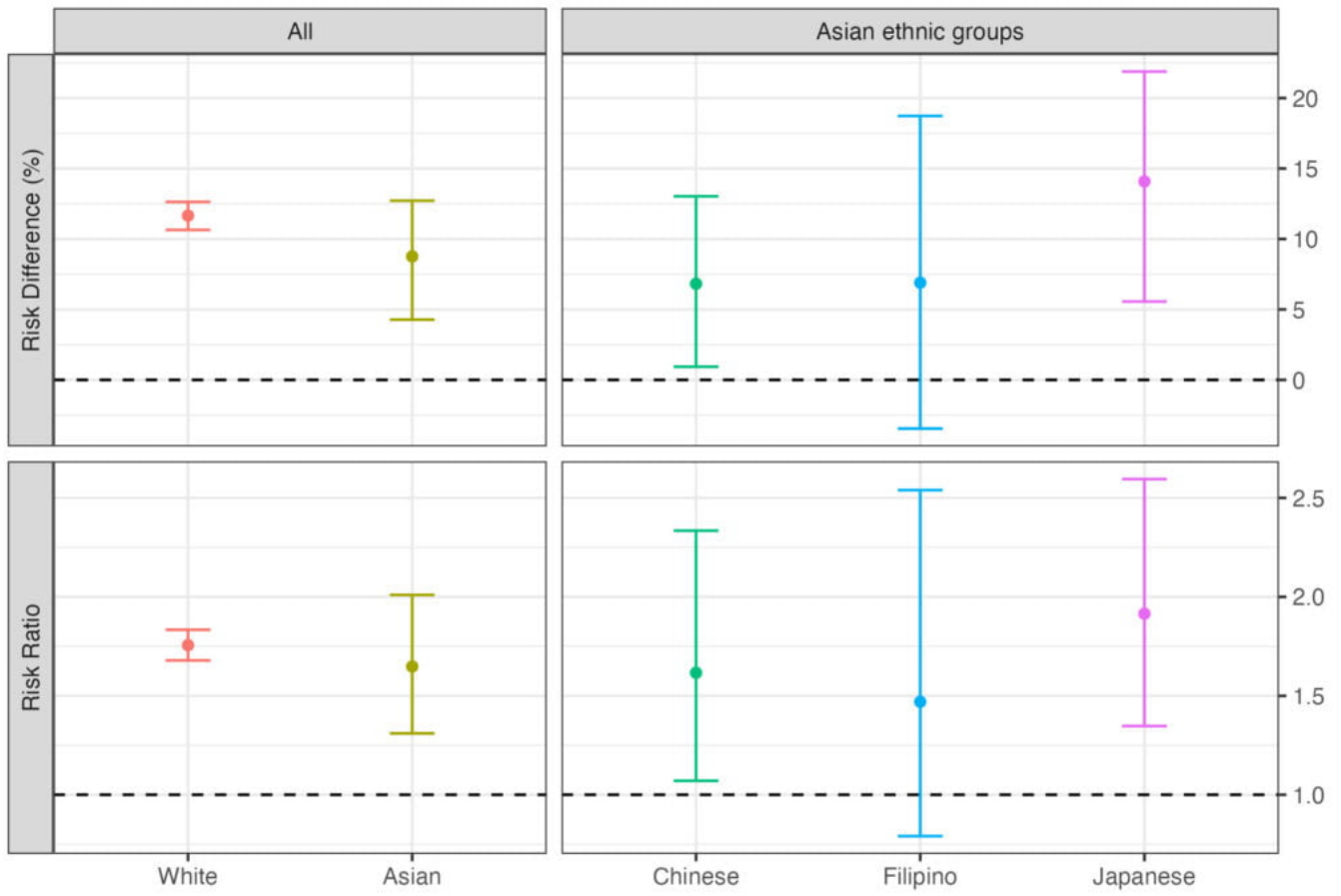
Association of Genetic Risk Score for Alzheimer's Disease With Late-Life Body Mass Index and Alcohol Use in All of Us Participants: Evaluating Reverse Causation Minhyuk Choi*

Minhyuk Choi Maria Glymour Scott Zimmerman

Background

Identifying the earliest age of physiologic or behavioral changes associated with Alzheimer's Disease (AD) is essential to guide prevention efforts and understand confounding in observational research. Changes in body mass index (BMI) or alcohol use may be early symptoms of AD but BMI and alcohol use may also influence AD risk. Using genetic risk of AD in a reverse Mendelian Randomization design establishes temporal order. We estimated the age at which differences in BMI and drinking behavior could first be detected comparing individuals with higher compared with lower genetic risk of AD.
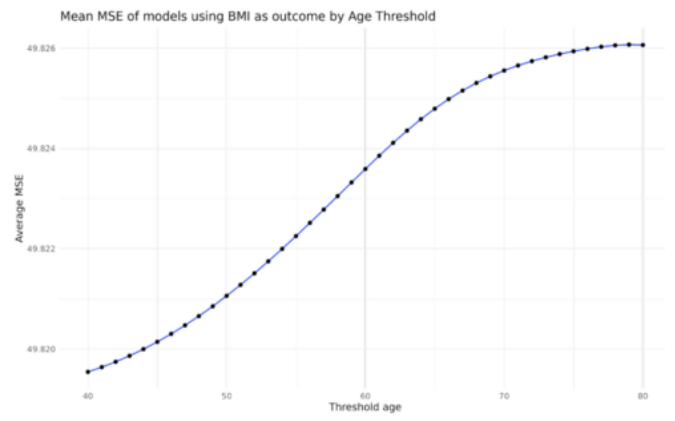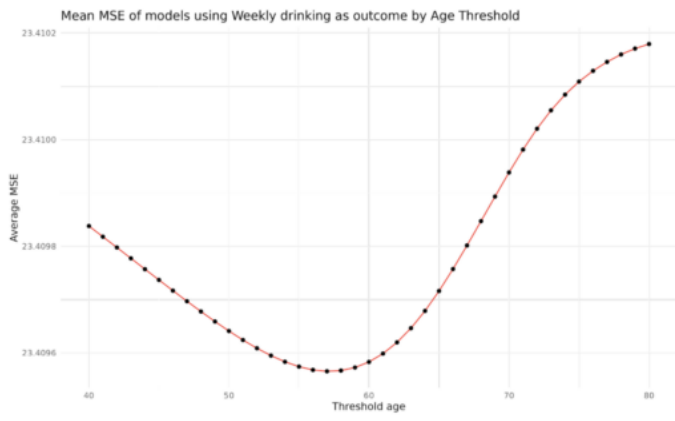
Methods

For All of Us cohort participants (N=160,740) who were dementia-free and aged 40+ at baseline, we calculated BMI with measured height and weight. Weekly drink count was self-reported at enrollment. An AD genetic risk score (AD-GRS) was calculated based on 23 single-nucleotide polymorphisms. We regressed weekly drinks on AD-GRS in linear models. We used linear mixed models to assess the age-specific association of AD-GRS with BMI, stratified by decade of age. We calculated the age at which AD-GRS began to be associated with differences in each outcome by comparing people with low to high AD-GRS using cross-validated sex- and ancestry-adjusted models.

Results

Average baseline age was 60.58 (SD=11.21). Alcohol use declined slightly with age (-0.018/year [95% CI -0.020, -0.155]), and this decline was roughly 17% faster for people with a 1 SD higher AD-GRS, but there was no clear age at which this association emerged. BMI declined slightly with age (-0.019 units/year [95% CI: -0.020, -0.018]) and this decline was roughly 35% faster for people with a 1-SD higher AD-GRS. This association was first detectable in people ages 50-60.

Conclusion

Our findings suggest that AD genes accelerate age-related weight loss starting in middle age and may also be associated with alcohol use reductions.

Mean MSE of models using Weekly drinking as outcome by Age Threshold



Mean MSE of models using BMI as outcome by Age Threshold

Applying a Causal Decomposition Approach to Quantify the Role of Education in Cohort Differences in Dementia Prevalence in the US Ruijia Chen* Ruijia Chen Rafeya Raquib Jingxuan Wang Sarah Ackley Jennifer Weuve warre046@umn.edu Maria Glymour Andrew C. Stokes

Introduction: While existing population health research suggests a decline in dementia prevalence in the United States, the explanations behind such trends remain unclear. This study applied a causal decomposition approach to quantify the role of education in birth cohort differences in dementia prevalence.

Method: We included participants from the 2000 to 2016 Health and Retirement Study (HRS) who were 70 years and older (N=17,710). We defined dementia status using an existing algorithm with similar sensitivity and specificity across racial/ethnic groups. We categorized participants into four birth cohorts: Asset and Health Dynamics Among the Oldest Old (AHEAD) <1924; Children of the Depression (CODA) 1924-1930; HRS 1931-1941; and War Babies (WB) 1942-1947. We applied a counterfactual causal decomposition approach that incorporates the age-period-cohort (APC) model with g-computation. We compared the observed prevalence of dementia in the natural course to a counterfactual scenario where all birth cohorts had the same distribution of education of the birth cohort with the lowest prevalence. Models adjusted for age, sex/gender, and race and ethnicity.

Result: Across the four cohorts, the WB 1942-47 cohort had the lowest prevalence of dementia compared with other cohorts, independent of age and period effects. In the counterfactual of all cohorts having the same distribution of education as the WB 1942-47 cohort, dementia prevalence would be 20.0% (95% CI: 15.3-25.3) lower for AHEAD, 15.0% (95% CI: 9.7-20.6) lower for CODA, and 7.5% (95% CI: 2.3-13.0) lower for HRS (see **Figure**).

Conclusion: We found marked declines in dementia prevalence across U.S. birth cohorts. Increases in educational attainment across cohorts may have substantially contributed to these declines.
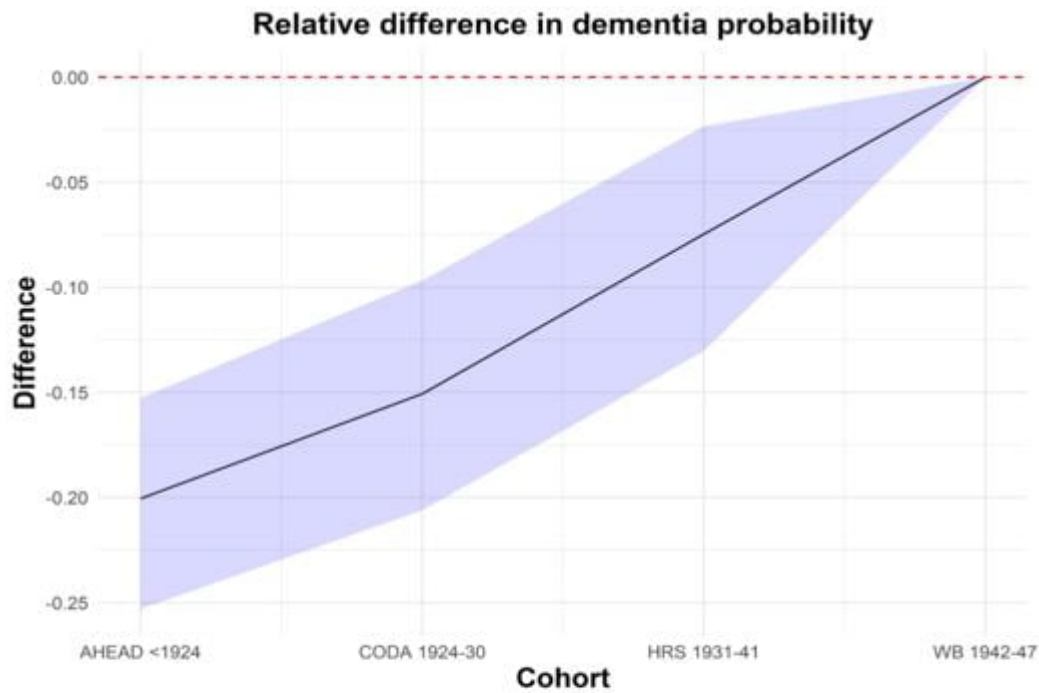
Figure. Relative difference (95% CI) between the counterfactual and natural course estimates of probability of dementia by birth cohort for education. Relative differences are calculated as (counterfactual/ natural course)-1. For example, -0.20 in the AHEAD cohort indicates that dementia prevalence in this cohort would be 20% lower if it has the same distribution of education as the WB cohort. Abbreviation: AHEAD <1924: Asset and Health Dynamics Among the Oldest Old <1924; CODA: Children of the Depression 1924-1930; HRS: Health and Retirement 1931-1941; WB: War Babies 1942-1947.

Social

20-year income volatility and cognitive function in NLSY79: a replication and extension of CARDIA findings Katrina L. Kezios* Katrina Kezios Calvin L. Colvin Leslie Grasset Catherine dP Duarte Anusha M. Vable M. Maria Glymour Adina Zeki Al Hazzouri

Life course financial circumstances may shape cognitive health and dementia risk. A 2019 study by Grasset et al. reported that income volatility in the CARDIA cohort over a 20-year period (1990-2010) in midlife was associated with worse cognitive function. However, CARDIA lacked a measure of early-life cognition, so reverse causation was a concern. Here, we replicate this study in the National Longitudinal Survey of Youth 1979 (NLSY79), a nationally representative sample nearly identical in age (23-35 to 43-55) to CARDIA participants during 1990-2010 and which includes an early-adulthood measure of cognition (via the Armed Forces Qualifications Test, administered in 1980). Income volatility was assessed as: standard deviation of the percent change in income and number of income drops >25% between ~biannual surveys from 1990-2010. Participants completed immediate and delayed 10-word recall, backwards counting, and serial 7 subtraction assessments during the survey at which they turned at least 48. Our sample (N=2,384) included those who completed all assessments in 2010 or later. Z-scored assessments were averaged to create a global cognition score and subdomain scores for memory and attention. Confounder adjusted linear models with bootstrapped 95% CIs were estimated for global cognition and each subdomain. While associations were smaller, conclusions were consistent with Grasset et al.: higher volatility and more income drops were associated with lower global cognition (e.g., β [95% CI] for 3+ vs 0 drops: -0.15 [-0.28, -0.02]). Early-adulthood cognition was a strong predictor of midlife cognition (ρ=0.39, p<0.001) and findings were stronger prior to its adjustment (e.g., β [95% CI] for 3+ vs 0 drops: -0.23 [-0.37, -0.11], which may partly explain the smaller coefficients in our study compared to Grasset et al. Overall, our findings add to a growing literature demonstrating the cognitive harms of life course financial hardship, including income volatility.

Identification conditions for the effect of treatment in the treated Catherine Wiener*
Catherine Wiener Stephen R. Cole

The average treatment effect (ATE) and the average treatment effect in the treated (ATT) are common estimands. Motivated by discrepancies in the ATE and ATT of tPA on in-hospital mortality in ischemic stroke patients, we describe identification conditions for the ATE and ATT, and conduct simulations to assess the validity of the ATE and ATT under varying settings.

The identification conditions for the ATE include causal consistency, exchangeability, and positivity. Exchangeability assumes that potential outcomes are independent of actual treatment. Positivity requires a nonzero probability of each treatment for each level of a confounder present in the data. To identify the ATT, we can (1) relax exchangeability and only require that the untreated potential outcomes are independent of actual treatment, and (2) relax positivity to the levels of confounders present in the treated.

For 5000 simulations, we sampled 6000 individuals from three hypothetical populations with varying prevalence of a confounder. We assigned treatment under two scenarios: complete positivity and partial positivity. We generated outcomes based on the confounder and a treatment effect risk ratio of 0.8 or 1.

Scenarios with complete positivity resulted in unbiased estimates of the ATE and ATT. Scenarios with partial positivity resulted in unbiased estimates of the ATT, but biased estimates of the ATE where the magnitude of the bias depended on the marginal prevalence of the confounder.

Our simulations reinforce that targeting the ATE when causal identifications are not met results in biased effect estimates. Our simulations also demonstrate that if partial identification conditions in a treatment group are met, the treatment effect in that group (or the ATT) can be consistently estimated, which allows epidemiologists to learn under a weaker set of assumptions

How to check the sequential positivity assumption without propensity scores? Arthur Chatton* Arthur Chatton Robert W Platt Michael Schomaker Miguel Angel Luque-Fernandez Mireille E Schnitzer

The positivity assumption, necessary for considering an association as causal, states that each individual could be theoretically treated or untreated based on their characteristics. A positivity violation occurs when the sample contains a subgroup of individuals with almost no treatment variability. To correctly estimate the causal effect, we must identify such individuals. This identification is complicated in longitudinal settings because positivity must be checked across all time points and generally relies on a large number of propensity score models, unlikely all correctly specified. The Positivity Regression Trees (PoRT) algorithm was recently suggested to check this assumption in cross-sectional settings without requiring assumptions about the modelling nor the data-generating process. It also provides a transparent way to identify the target population. We expand this method to longitudinal settings by considering the whole treatment regimen to identify the individuals and variables yielding a lack of positivity. We demonstrate the potential of this approach by reanalyzing a recent study investigating the effect of HIV antiretroviral therapy among children in South Africa with different levels of smoothing over the treatment histories and times.

Do some quantitative bias analyses overestimate the bias due to uncontrolled confounding?

Tsion A Armidie* Tsion Armidie Lindsay J Collin Richard F MacLehose Thomas P Ahern Timothy L Lash

In non-randomized studies aiming to answer causal questions, researchers estimate an exposure-outcome relationship, and confounding is a common concern. Adjustment for a minimally sufficient set of known and measured confounders will remove bias caused by those confounders; however, sometimes a confounder in the minimally sufficient set is unmeasured. Approaches exist to estimate the bias due to unmeasured confounding, including quantitative bias analysis (QBA). QBA assumes that the unmeasured confounder is independent of the measured controlled confounders. However, confounders are often correlated, so QBA to address unmeasured confounding would overstate the size of the bias in the presence of such correlation. This study uses an applied example to demonstrate how conventional bias analysis methods often overestimate the impact of unmeasured confounding.

This analysis used NHANES III (1988-1994) to examine the association between healthy eating index (HEI) and all-cause mortality (n=4457). A fully adjusted Cox regression model included tobacco use, sex, age, hypertension, BMI, education, and physical activity as the minimally sufficient adjustment set. Hazard ratios (HR) that would have been observed had one of hypertension, BMI, education, or physical activity been "unmeasured" were estimated by leaving them out of 5 separate Cox models. The strength of confounding was calculated by comparing the result with an unmeasured confounder with the fully adjusted estimate. We performed QBA for the "unmeasured" confounders, using the 'true' bias parameter estimates as given in NHANES.

The fully adjusted HR comparing Quintile 1 vs. 5 of HEI with all-cause mortality was 1.72 (95% CI 1.24 to 3.39). After treating hypertension, BMI, education, and physical activity as "unmeasured" confounders, little change in the HR was observed (1.72-1.88). The QBA bias-adjusted estimates ranged from 1.72 to 2.23.

Due to the correlation between covariates, the effect of bias due to treating confounders as unmeasured was negligible, but the bias analyses often suggested substantial bias. This applied example suggests that QBA is useful for evaluating unmeasured confounding but may overestimates the strength of bias when highly correlated variables have already been adjusted for.

Interventionalist interpretations of studies involving compound treatments Kerollos Wanis*
Kerollos Wanis Aaron Sarvet

When studying interventions, investigators will attempt to specify all their relevant characteristics. When a treatment has unspecified outcome relevant features, it has been referred to in the causal inference literature as a compound treatment. The study of compound treatments has been posed as a serious problem in causal inference research, due to violations of the "Stable Unit Treatment Value Assumption." But many treatments of interest are, in fact, compound treatments. This is true not only in observational research, but also in experimental studies. Investigators are unlikely to know all the outcome relevant features of an intervention to be studied. Indeed, the act of studying an intervention suggests some ignorance about its outcome causing mechanisms. And, even if known, were every intervention feature specified, the study might be obscure and of little practical relevance because the intervention would not reflect the natural flexibility of undergoing treatment in the real-world. We argue that causal effects of compound treatments are not only well-defined features of a study population, but might in fact be the effects most useful to decision makers in many scenarios. Inspired by the treatment decomposition that characterizes separable effect estimands, we reconsider compound treatments and the effects of interest when two such treatments are compared. This decomposition allows us to consider hypothetical interventions that modify the compound treatment. When the relevant features of a compound treatment are known and their values measured, data from observational or experimental studies can be used to study hypothetical modifications of compound treatments. When the outcome relevant features are not known, a separable effects decomposition can still allow investigators to study hypothetical modifications of compound treatments. We apply these methods to study the effect of donation after cardiac death on the survival of liver transplant recipients.

When measurement mediates the causal effect of interest Joy Z. Nakato* Joy Z. Nakato Brian Beesiga Janice Litunya Jaqui Mwango Kara Marson Judith A. Hahn Carol S. Camlin Diane V. Havlir Maya L. Petersen Moses R. Kamya Jane Kabami James Ayieko Gabriel Chamie Laura B. Balzer

In many studies, participants with measured outcomes differ meaningfully from participants with missing outcomes. A common approach to address missingness considers a hypothetical intervention to ensure complete measurement outcome. This approach fails when measurement mediates the causal effect of interest. Consider, for example, the OPAL study, a cluster randomized trial to compare bar-based recruitment strategies on uptake of HIV pre-exposure prophylaxis (PrEP) in rural Kenya and Uganda. Since starting PrEP is contingent on testing HIV-negative at a health clinic, clinic-based HIV testing is the key measurement variable. However, "intervening" to test all would block the indirect effect of the bar-based recruitment strategy (exposure) on PrEP uptake (outcome; Figure). To evaluate the total causal effect in such settings, we develop a general framework to define and identify a novel causal estimand, while still accounting for differential missingness. For the corresponding statistical estimand, we develop and apply a novel Two-Stage TMLE that also accounts for clustering and small sample sizes. Simulations demonstrate the practical performance of our approach as well as the limitations of more traditional approaches.
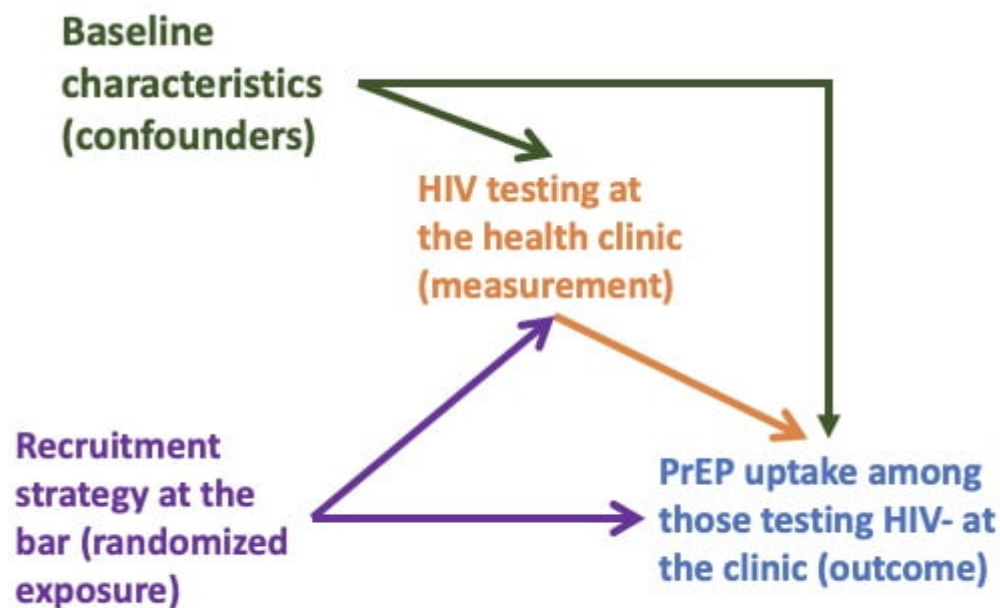
Figure: Simplified causal graph to illustrate how HIV testing is both a measurement indicator and mediator in the OPAL study.

Social

Workplace racial diversity, metalworking fluid exposure, and cardiovascular disease mortality among Black US autoworkers Hilary Colbeth* Hilary Colbeth Corinne Riddell Marilyn Thomas Sally Picciotto John Balmes
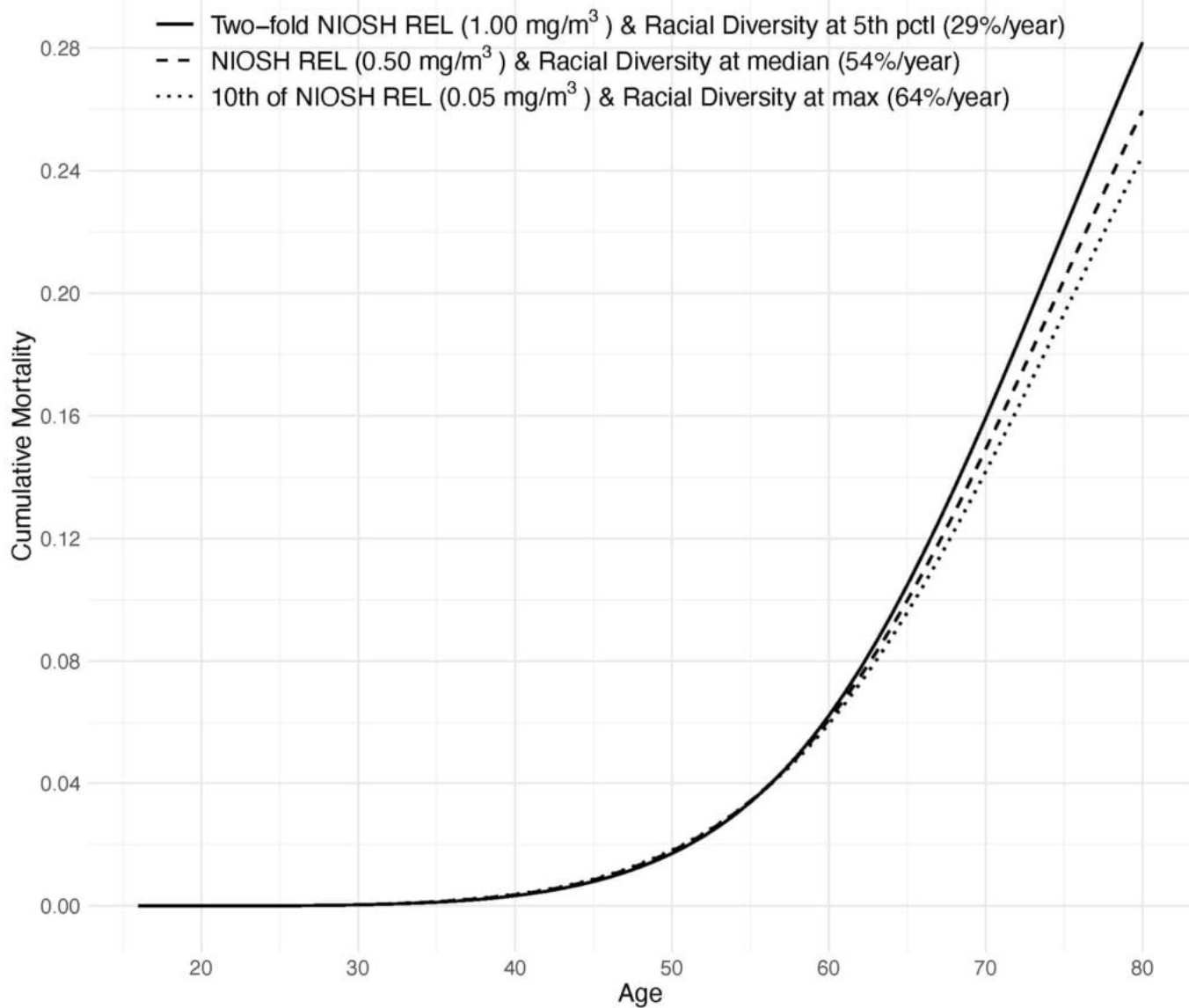
Objectives Factors promoting cardiovascular resilience among Black adults are not well understood. In particular, work as a social determinant of cardiovascular disease (CVD) and occupational exposures to particulate matter and other cardiovascular hazards remain understudied in Black working populations. Our objective was to assess the risk of CVD mortality among Black autoworkers from the United Autoworkers-General Motors cohort study under several hypothetical scenarios: increased exposure to workplace racial diversity, reduced metalworking fluid exposure, and both interventions together.

Methods We analyzed longitudinal data on 5,043 workers from the Detroit General Motors plant (follow-up 1941-2015), with 1,458 observed CVD deaths. We applied the parametric g-formula to assess risk under hypothetical scenarios with set values for plantwide racial diversity and selected exposure limits for metalworking fluid, separately and jointly.

Results We compared two hypothetical joint intervention scenarios: (1) plantwide racial diversity set to its median observed value (54% Black workers) and metalworking fluid at the National Institute for Occupational Safety and Health recommended exposure limit of 0.50 mg/m3 [moderate exposures] and, (2) racial diversity was set to its maximum observed value (64% Black workers) and the metalworking fluid limit was 0.05 mg/m3 [protective/low exposures]. At age 80, the CVD mortality risk difference per 1000 was 14.80 (95% confidence interval: 1.40, 27.00). These results were similar to those observed when increasing racial diversity alone.

Conclusions Our findings, based on Black autoworkers from an iconic cohort, reveal strong associations between CVD mortality and plantwide racial diversity and a more moderate relationship with MWF exposure. Our study demonstrates the importance of accounting for social conditions along with environmental exposures in occupational health effects research among historically racialized populations.

Association of oil spill related total hydrocarbon exposure with blood pressure and hypertension in the Gulf Long-term Follow-up Study Opal P. Patel* Opal Patel Jessie K. Edwards Anna M. Kucharska-Newton Eric A. Whitsel Braxton Jackson Lawrence S. Engel Dale P. Sandler

Background: Volatile organic compound and total hydrocarbon (THC) exposures are common following oil spills and are associated with risk of cardiovascular disease. In a study among Gulf Long-term Follow-up (GuLF) Study participants, THC exposure was associated with elevated risk of hypertension. However, that study did not evaluate individual constituents such as benzene, toluene, ethyl-benzene, xylene, and n-hexane (BTEX-H). Here we examine associations of BTEX-H exposures with blood pressure (BP) and hypertension.

Methods: Subjects comprised 6,813 Deepwater Horizon (DWH) oil spill workers who completed a GuLF Study home visit (2011 to 2013). A job-exposure matrix linked air measurement data to detailed participant DWH work histories to estimate cumulative exposures during oil spill response and clean-up work. Exposures to BTEX-H were assessed as quartiles, with the first quartile as the referent. Trained examiners took BP measurements during the home visit. Incident hypertension was defined as having elevated BP or newly diagnosed hypertension with new onset antihypertensive medication use since the spill. We estimated exposure effects on continuous BP using multivariable linear regression. We calculated prevalence ratios (PR) and 95% CIs for hypertension using modified Poisson regression. To assess the joint effect of the BTEX-H mixture, we used quantile g-computation.

Results: Among these participants, 79.3% were male, 52.9% were non-Hispanic white, and 34.7% were non-Hispanic black. Increasing quartiles of individual BTEX-H exposures exhibited exposure-response relationships for diastolic BP. The BTEX-H mixture was positively associated with both systolic (β=0.49; 95% CI: 0.15, 0.84) and diastolic BP (β=0.46; 95% CI: 0.21, 0.70). We observed non-monotonic increases in hypertension risk with increasing exposure to benzene, toluene, and hexane.

Conclusion: Higher exposures to BTEX-H were associated with modest elevations in hypertension risk and blood pressure.

Occupational

The association between combined exposure to lead and cadmium and gamma glutamyl transferase Shinhee Ye* Shinhee Ye Woojoo Lee Kyung-Eun Lee Sang Gil Lee Jung-Min Sung

Objectives: It is necessary to identify the association between combined exposure and workers' health. This study was carried out to examine the association between combined exposure to lead and cadmium and liver function tests (AST, ALT, and GGT).

Methods: This study utilized special health examination data for Korean workers exposed to harmful substances, data from the Korea National Health and Nutrition Examination Survey (KNHANES), and data from the National Health and Nutrition Examination Survey (NHANES). The health effects of single exposures were analyzed using generalized estimating equations (GEE) or multivariate linear regression. The health effects of combined exposures were analyzed using Bayesian kernel machine regression (BKMR). All models were adjusted for age, sex, company size (or family income), alcohol consumption habits, smoking status, and body mass index (BMI).

**Results:** In all analyses, an increase in GGT was consistently associated with an increase in combined exposures to lead and cadmium. In these analyses, the interaction between lead and cadmium was also consistently observed.

Conclusions: We suggest that workers exposed to both lead and cadmium should mitigate the exposure and need to undergo liver function tests in special health examinations.

Workplace wellness: contributions of long working hours and poor diet to cardiometabolic outcomes and mortality in U.S. workers Xiang Li* Xiang Li Jian Li Tong Xia Onyebuchi A. Arah Liwei Chen

Both long working hours (LWH) and poor diet contribute to cardiometabolic outcomes and mortality and have been rarely investigated as combined exposures. We examined the individual and joint associations of LWH and diet with cardiometabolic risk factors and mortality using a nationally representative sample of U.S. workers. We included 18,542 workers (aged 35-74 years) free of cardiovascular disease from National Health and Nutrition Examination Surveys (NHANES, 1999-2018), linked with the National Death Index to follow up on mortality status. Working hours were classified as <35, 35-40, 41-54, and ≥55 hours/week (i.e., LWH). Dietary quality was measured using the EAT-Lancet diet score assessed by two 24-hour dietary recalls and classified as high vs. low by the median score. The associations of LWH and dietary quality with cardiometabolic outcomes were estimated using logistic regression model (for obesity, hypertension, diabetes, hypercholesterolemia, or Framingham CVD risk score>20%) or Cox proportional hazard model (for all-cause, heart disease and CVD mortality), accounting for sampling strategies and confounders. Compared to working 35-40 hours/week, LWH was associated with higher odds of obesity (OR=1.19; 95% CI: 1.06-1.34) but not for other cardiometabolic outcomes. 1.13; 95% CI: 0.47-2.71among individuals with high Framingham CVD risk scores. Poor dietary quality was associated with higher odds of all cardiometabolic outcomes and CVD mortality in this study. Compared to workers without LWH and with high dietary quality, those with LWH and low dietary quality had the greatest odds of obesity (OR=1.60, 95% CI: 1.37-1.87), hypertension (OR=1.21, 95% CI: 1.00-1.46), and highest heart disease mortality (HR=1.81, 95% CI: 1.05-3.12). If plausibly causal with additional evidence, these findings suggest improving dietary quality among U.S. workers with LWH to mitigate cardiometabolic risks and mortality.
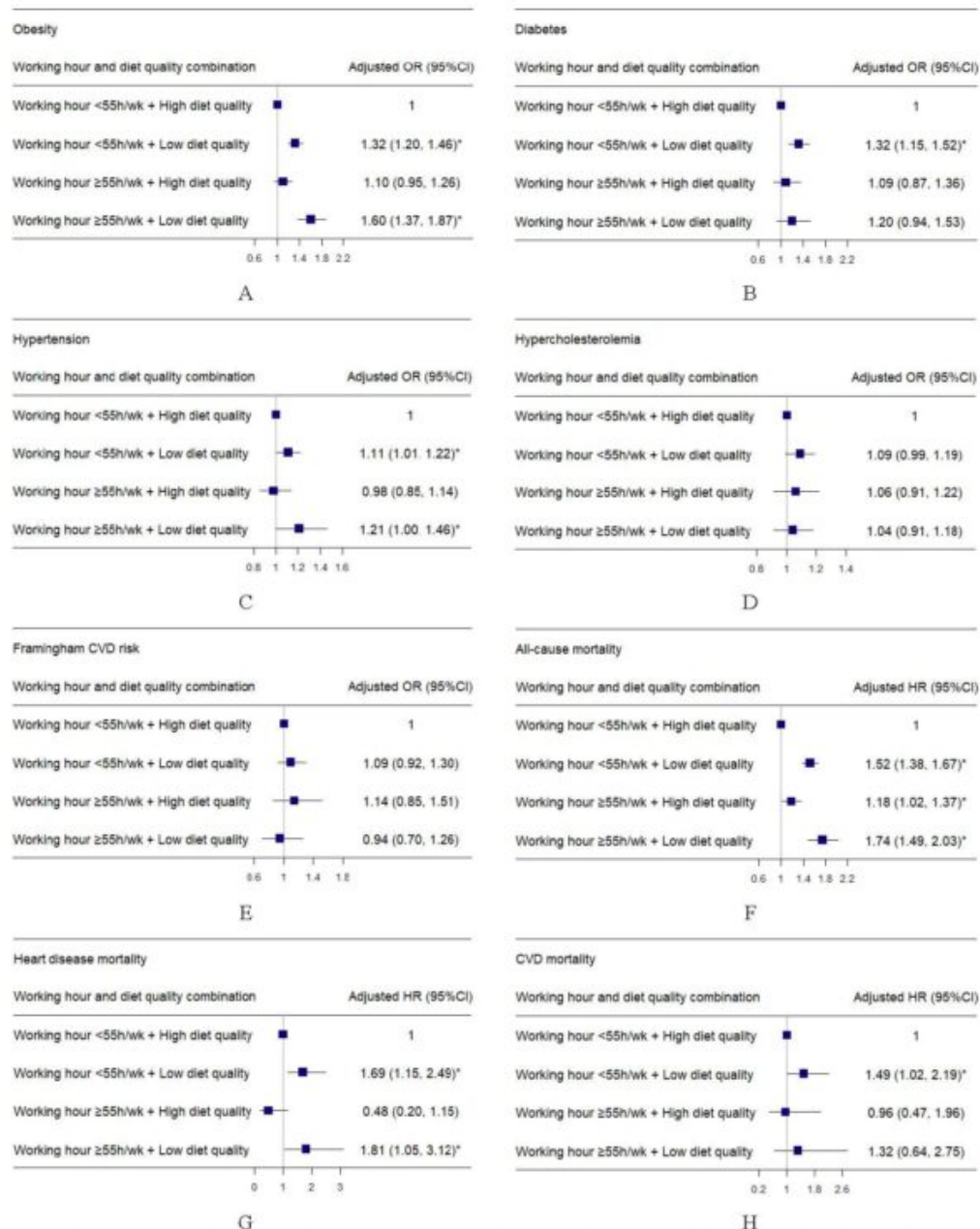
Figure1. Joint effect of long working hours and diet quality on cardiometabolic disease (A-E) and mortality (F-H) among all participants.

Abbreviation: CVD, cardiovascular disease; OR, odds ratio; HR, hazard ratio.

Obesity: body mass index ≥30kg/m².

Diabetes: previous diagnosis by a physician, or hemoglobin A1C≥6.5%, or fasting glucose ≥7 mmol/L, or 2H-OGTT≥11.1 mmol/L, or using any treatment.

Hypertension: previous diagnosis by a physician, or systolic blood pressure ≥ 130 mm Hg and/or diastolic blood pressure ≥ 80 mm Hg, or using any treatment.

Hypercholesterolemia: previous diagnosis by a physician, total cholesterol ≥ 200 mg/dL, or using any treatment.

Framingham CVD risk: high risk was defined as Framingham 10-year CVD risk score>20%.

High diet quality: EAT-Lancet diet score above median.

Results were weighted and adjusted for age, gender, race and ethnicity, annual income, education level, smoking, alcohol drinking, and leisure-time physical activity.

Self-reported chronic rhinosinusitis diagnoses and symptoms in WTC-exposed and non-WTC-exposed firefighters Ankura Singh* Ankura Singh Rachel Zeig-Owens Mayris P. Webber Alexandra Mueller David J. Prezant

Background

Studies conducted within World Trade Center (WTC)-exposed populations have shown that greater WTC exposure is associated with chronic rhinosinusitis (CRS) diagnoses and symptoms. We aimed to determine whether self-reported CRS diagnoses and related symptoms are elevated in WTC-exposed Fire Department of the City of New York (FDNY) firefighters when compared with non-WTC-exposed non-FDNY firefighters.

Methods

The study population included 9964 WTC-exposed and 2771 non-WTC-exposed firefighters who were actively employed on 9/11/01 and later completed a health survey. Participants indicated whether they had ever been diagnosed with CRS. Logistic regression analyses estimated the odds of self-reported CRS diagnoses in WTC-exposed vs non-WTC-exposed firefighters. Secondary analyses within the non-WTC-exposed group and a subset of WTC-exposed firefighters (N=7840) who completed the health survey during the same recent time period assessed associations between WTC exposure and current CRS-related symptoms. Models adjusted for age, race, smoking and BMI.

Results

More WTC-exposed firefighters (4681/9964, 47%) reported a CRS diagnosis than did non-WTC-exposed firefighters (544/2771, 20%; adjusted OR=3.25, 95% CI=2.92-3.61). Secondary analyses showed that WTC exposure was associated with CRS-related symptoms in the past 12 months, i.e. nasal/sinus congestion (OR=1.17, 95% CI=1.06-1.28), nose irritation (OR=1.48, 95% CI=1.24-1.76) and sinus pain/pressure (OR=1.41, 95% CI=1.26-1.59).

Conclusion

WTC exposure was associated with self-reported CRS diagnoses and recent CRS symptoms in firefighters. Elevated CRS in the WTC-exposed cohort could be a result of exposure to irritants at the WTC site. However, given the attenuated association between WTC exposure and recent CRS symptoms, the association between WTC-exposure and CRS diagnosis may be explained, in part, by enhanced surveillance and comprehensive healthcare provided to WTC-exposed firefighters via the WTC Health Program.

Odds of Self-Reported CRS and Current CRS Symptoms in World Trade Center (WTC)-exposed firefighters vs. non-WTC-exposed firefighters

	OR	LCL	UCL
Ever CRS	3.25	2.92	3.61
Current frequent headaches	1.15	0.98	1.34
Current sinus pain/pressure	1.41	1.26	1.59
Current nasal/sinus congestion	1.17	1.06	1.28
Current postnasal drip	1.03	0.93	1.13
Current nose irritation/soreness/burning	1.48	1.24	1.76
Current frequent nosebleeds	0.92	0.71	1.20

Odds Ratio
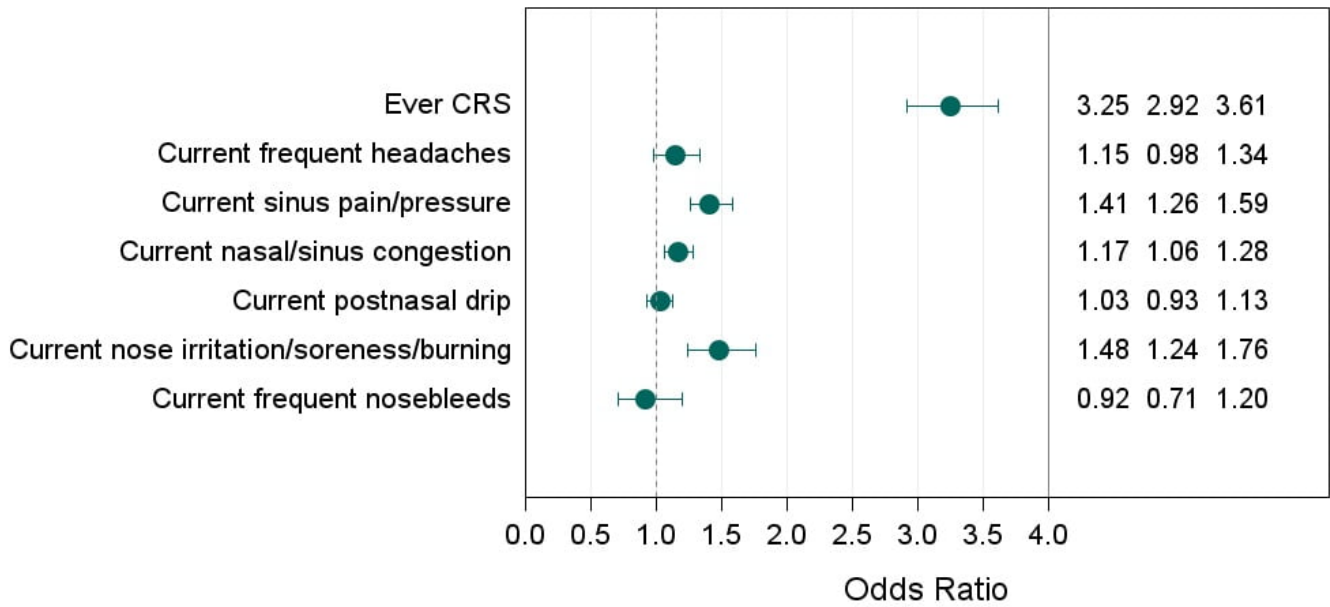
Generalization strategies for improving machine learning predictions: a multicentric analysis of neonatal mortality in low and middle-income countries Gabriel Silva* Gabriel Silva Alexandre Dias Porto Chiavegatto Filho

Neonatal mortality remains a critical concern, particularly in low- and middle-income countries. We developed a comprehensive evaluation of machine learning (ML) algorithms' performance in predicting neonatal mortality risk. Leveraging the dataset from the MNHR (Maternal and Neonatal Health Registry) – National Institutes of Health, contemplating a multicentric neonatal cohort of eight countries (Argentina, Bangladesh, Kenya, Democratic Republic of Congo, Pakistan, Guatemala, India, and Zambia), this study aimed to identify and compare effective training strategies to enhance the predictive performance of ML algorithms for multicentric neonatal data. We explored three distinct training frameworks: 1) a full algorithm for all participating countries, 2) country-specific algorithms trained locally, and 3) an approach using the largest country-specific training sample. We trained the algorithms using data from 2010 to 2016 and tested their predictive performance using data from 2017 to 2019. Five different ML algorithms (xgboost, lightgbm, catboost, adaboost and random forest) were trained with the five fundamental indicators recommended by the World Health Organization (WHO): maternal age, place of delivery, type of delivery, birth weight, and gestational age. The primary outcome was neonatal mortality, spanning from the first day of birth to the 42nd day after delivery. Our findings suggest that a generalized model, trained using collective data from all participating countries, demonstrated superior predictive performance, with an 0.811 AUC-ROC, 0.212 recall and 0.997 specificity. This study highlights the potential of using multi-country ML for improving neonatal health decisions in low- and middle-income countries, collaborating to pave the way for more globally-inclusive digital health strategies.

Big Data/Machine Learning/AI
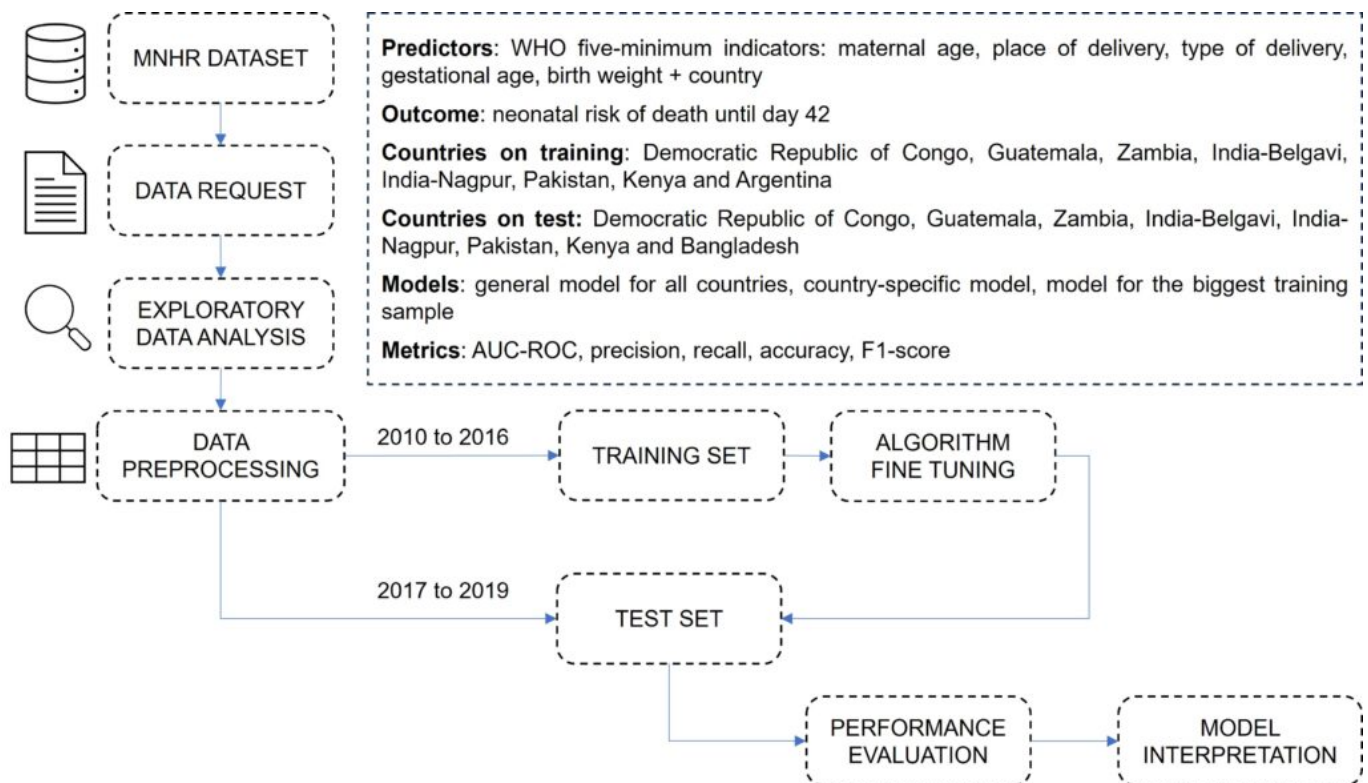
Machine Learning for Predicting Neonatal Prematurity in Seven Low- and Middle-Income Countries: Analysis of the Maternal Newborn Health Registry (MNHR) Pregnancy Outcomes Marianna Gerardo Hidalgo Santos Jorge Leite* Marianna Gerardo Hidalgo Santos Jorge Leite Gabriel Ferreira dos Santos Silva Fabiano Novaes Barcelos Carine Savalli Alexandre Chiavegatto Filho

Introduction: Preterm birth rates in developing nations contribute significantly to newborn mortality, largely attributed to preventable health conditions. Addressing this issue requires early intervention through health and public policies targeting high-risk pregnancies. Artificial Intelligence, specifically machine learning, has gained traction for predictive modeling in healthcare. The efficacy and generalizability of these algorithms hinge on leveraging routinely-collected data to identify pregnancies at risk for preterm birth.

Methods: We analyzed Global Network Maternal Newborn Health Registry (MNHR) data from 2017 to 2019 across seven low- and middle-income countries, encompassing 138,303 pregnancies and reporting term or preterm outcomes. Initially selecting 47 variables available at 20 weeks, we employed Boruta algorithm-based feature selection, identifying 19 variables for model training. Target encoding and z-score normalization were applied to qualitative and quantitative variables, respectively. Popular machine learning algorithms—XGBoost, Catboost, LightGBM, and Random Forest—were tested on a 30% test set.

Results: CatBoostClassifier yielded an Area Under the Curve (AUC)of 0.7599 (Sensitivity: 0.9882, Specificity: 0.1390). Site-specific analysis revealed superior performance of LGBMClassifier in site 2, the Democratic Republic of Congo (AUC = 0.7829, Sensitivity= 0.2385, Specificity= 0.9732) and site 8, Belagavi, India (AUC=0.7863, Sensitivity: 0.2412, Specificity: 0.9868). Key predictive variables included the number of antenatal visits, early enrollment for follow-up, and antenatal care in the first trimester.

Conclusion: Machine learning algorithms effectively predicted prematurity using 20-week pregnancy data from seven low- and middle-income countries. These tools can aid in identifying mothers at risk for premature delivery, especially in low-income regions. Further research should validate this methodology in diverse settings with similar routinely collected data.

Moderating role of socioeconomic status on the association between mass media exposure and the complete continuum of care utilization across South Asian countries Sohee Jung*
Sohee Jung Rockli Kim

Background: In low- and middle-income countries, mass media is an effective way to encourage women to continue to utilize maternal healthcare services by disseminating maternal health information. However, the role of socioeconomic status (SES) in the relationship between complete continuum of care (CoC) utilization in maternal healthcare services and mass media exposure in South Asia (SA) has not been sufficiently explored.

Method: Data from the Demographic and Health Surveys (2010-2022) across 11 SA countries were analyzed, including 218,435 women aged 15-49 who had births in the past five years. Women were considered exposed to mass media if they utilized at least one media (newspaper, radio, and television) more than once a week. Complete CoC utilization was defined if women had their first antenatal care (ANC) visit in the first trimester, had at least four or more ANC visits during pregnancy, gave birth with skilled birth attendants, and received at least one postnatal care after birth. Multilevel linear probability models were applied to examine whether SES characteristics (e.g., maternal education level, household wealth, and place of residence) moderate the relationship between mothers' media exposure and completion of CoC.

Results: Overall, 74.72% of women were identified as exposed to the mass media, and 43.80% utilized the complete CoC in maternal healthcare services. Mass media exposure was significantly associated with an increased probability of completing CoC (b=0.02; 95% CI=0.01,0.02) after adjusting for socioeconomic covariates. It was found that media exposure statistically increased the probability of completing CoC for women with higher education level compared to those with no education (b=0.03; 95% CI=0.01,0.05), those from higher quintiles compared to those from poorest quintile (b=0.05; 95% CI=0.03,0.08), and for those who were living in urban areas compared to those living in rural areas (b=0.02; 95% CI= 0.00,0.03).

Conclusion: Our findings indicate that SES moderates the effects of media exposure on increasing the probability of completing CoC in maternal health services. Therefore, tailored mass media campaigns should consider the lower SES groups to be able to receive relevant maternal healthcare information and complete CoC utilization.

Figure 1. Predicted percentage for interactions of mass media exposure and socioeconomic status on complete continuum of care utilization in maternal healthcare services in South Asia countries.

(A) Interaction of mass media and maternal education on the complete continuum of care utilization
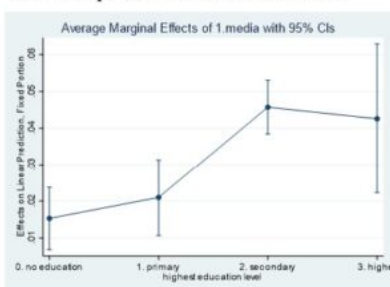
(B) Interaction of mass media and household wealth index on the complete continuum of care utilization
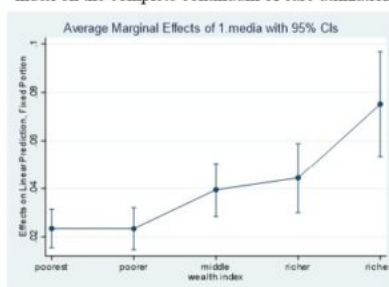
(C) Interaction of mass media and place of residence on the complete continuum of care utilization

Infectious Disease

Population-level tuberculosis burden attributable to incarceration and impacts of decarceral interventions in Latin America: a mathematical modeling study Yiran E Liu* Yiran Liu Yasmine Mabene Sergio Camelo Jeremy Goldhaber-Fiebert Julio Croda Jason R Andrews

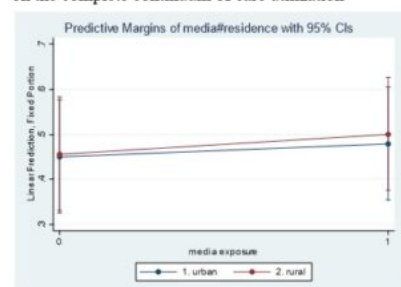Globally, tuberculosis (TB) incidence has declined by 8.7% since 2015, with 10.6 million cases in 2022. In contrast, Latin America has seen a 19% increase in TB incidence, highlighting the need to understand and address key TB drivers in the region, including incarceration. In Latin America, the prison population has quadrupled since 1990, and TB risk in prisons is 26 times higher than in the general population. In 2022, 9% of diagnosed TB cases in the region occurred in prisons. The true population attributable fraction (PAF) for incarceration is unknown but likely greater, due to under-diagnosis and to prison-acquired infections that progress and spread outside of prison. To assess the true role of incarceration as a TB driver, we developed and calibrated a compartmental transmission model for six diverse countries across Latin America: Argentina, Brazil, Colombia, El Salvador, Mexico, and Peru. We estimate that in 2019, the PAF for incarceration ranged from 6.4% (95% CrI; 4.0-9.8) in Mexico to 57.6% (51.1-63.2) in El Salvador. This corresponds to a range of absolute incident cases from 926 (623-1960) in Argentina to 31,837 (24,723-41,258) in Brazil. These estimates are commensurate with PAFs for other key TB risk factors like HIV and undernutrition. Looking forward, compared to a base-case scenario of stable incarceration rates, we find a substantial impact of decarceration on population TB incidence over a ten-year period **(Fig 1)**. For instance, in Brazil, a 50% decrease in entry rates, 50% increase in release rates, or both by 2034 could reduce population TB incidence by 13.1% (9.0-18.0), 13.2% (7.3-20.4), or 21.0% (13.8-29.1). Our findings reveal the outsized population TB burden attributable to incarceration in Latin America and the potential for decarceral interventions to re-ignite TB progress in the region.
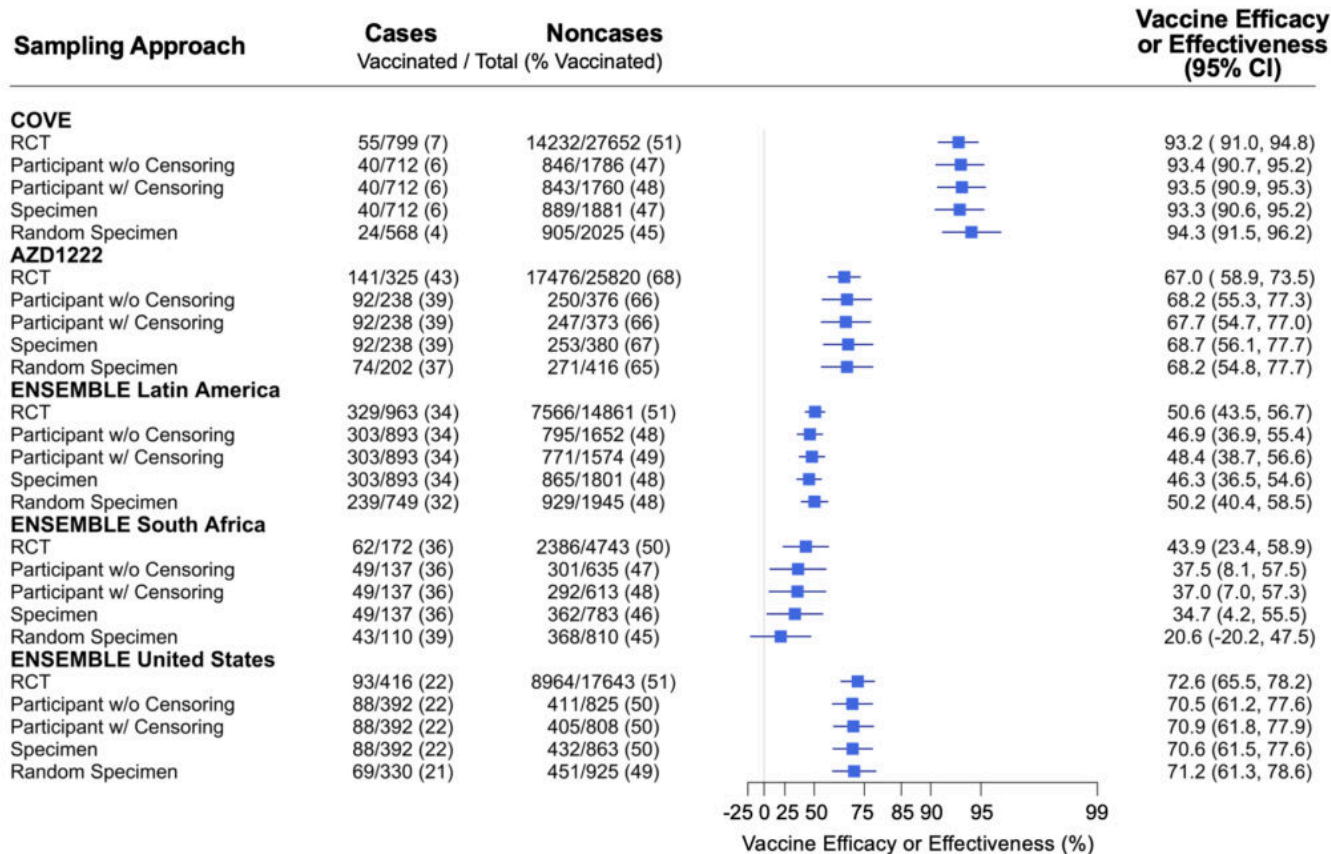
Fig 1. A) Incarceration prevalence under each scenario. B) Percent difference in population TB incidence in 2034 relative to stable scenario.

Study Design
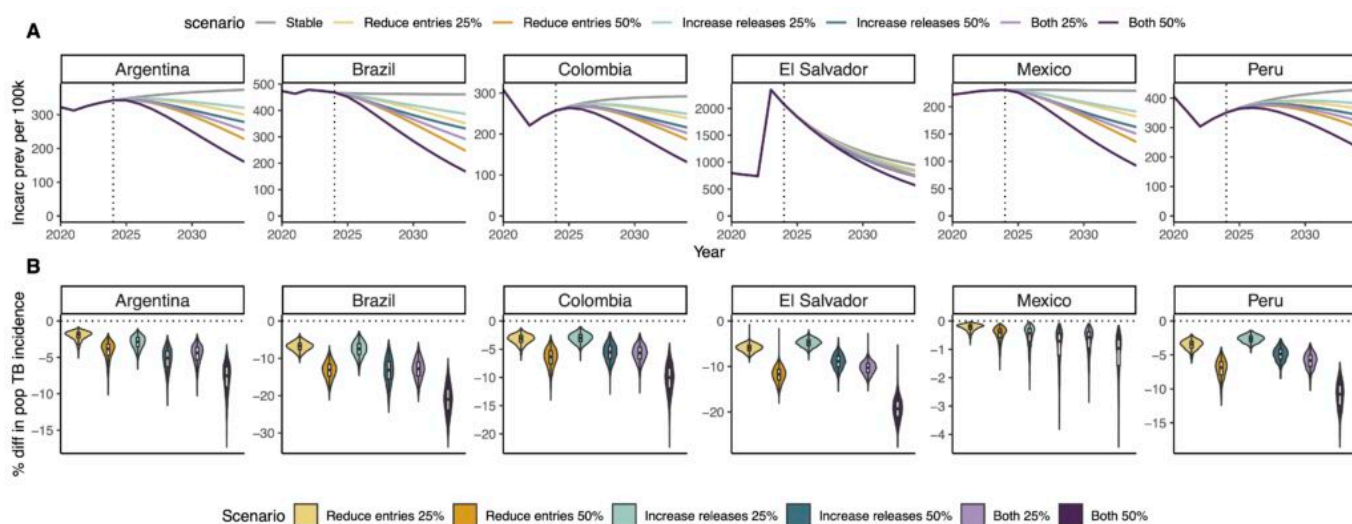
COVID-19 Vaccine Effectiveness: An Evaluation of the Test-Negative Design Using Randomized Placebo-Controlled Clinical Trials Leah I. B. Andrews* Leah Andrews M. Elizabeth Halloran Kathleen M. Neuzil Lars van der Laan Yunda Huang Jessica Andriesen Mayur Patel Heather Angier Leigh H. Fisher Holly Janes Kelsey Sumner Brendan Flannery Dean Follmann Peter B. Gilbert

During the COVID-19 pandemic, the United States government established the COVID-19 Prevention Network (CoVPN) and coordinated multiple phase 3 randomized, placebo-controlled vaccine efficacy trials. After regulatory authorization of the COVID-19 vaccines, the test-negative design (TND) was widely employed to estimate vaccine effectiveness in diverse populations and settings under real-world conditions. The TND is an observational study design that enrolls individuals with COVID-like symptoms who seek SARS-CoV-2 testing and compares vaccination status between cases who test positive vs. noncases who test negative. The TND reduces confounding by healthcare-seeking behavior, though other sources of confounding may remain. We assessed the conditions in which the TND reliably evaluates vaccine performance against virologically confirmed, symptomatic COVID-19 using CoVPN vaccine trial data from Moderna COVE, AstraZeneca/Oxford AZD1222, Janssen/Johnson & Johnson ENSEMBLE, Novavax PREVENT-19, and Sanofi/GSK VAT00008. We investigated the core TND assumption that vaccinated and unvaccinated healthcare-seeking populations have the same incidence of COVID-like symptoms caused by other pathogens besides SARS-CoV-2. We also constructed TND samples from the trial data according to four TND approaches and compared vaccine effectiveness estimators based on standard logistic regression vs. targeted maximum likelihood estimation under a semiparametric logistic regression model. In this randomized and blinded setting that is free of confounding, the core TND assumption was supported and TND vaccine effectiveness estimates were nearly identical to randomized, placebo-controlled vaccine efficacy estimates (three trials analyzed to date). Our study supports use of the resource-efficient TND for inferences on real-world COVID-19 vaccine effectiveness and presents a statistical method with robust confounding control, which is important when analyzing observational TND data.

Sampling Approach	Cases Vaccinated / Total (% Vaccinated)	Noncases Vaccinated / Total (% Vaccinated)		Vaccine Efficacy or Effectiveness (95% CI)
COVE				
RCT	55/799 (7)	14232/27652 (51)		93.2 (91.0, 94.8)
Participant w/o Censoring	40/712 (6)	846/1786 (47)		93.4 (90.7, 95.2)
Participant w/ Censoring	40/712 (6)	843/1760 (48)		93.5 (90.9, 95.3)
Specimen	40/712 (6)	889/1881 (47)		93.3 (90.6, 95.2)
Random Specimen	24/568 (4)	905/2025 (45)		94.3 (91.5, 96.2)
AZD1222				
RCT	141/325 (43)	17476/25820 (68)		67.0 (58.9, 73.5)
Participant w/o Censoring	92/238 (39)	250/376 (66)		68.2 (55.3, 77.3)
Participant w/ Censoring	92/238 (39)	247/373 (66)		67.7 (54.7, 77.0)
Specimen	92/238 (39)	253/380 (67)		68.7 (56.1, 77.7)
Random Specimen	74/202 (37)	271/416 (65)		68.2 (54.8, 77.7)
ENSEMBLE Latin America				
RCT	329/963 (34)	7566/14861 (51)		50.6 (43.5, 56.7)
Participant w/o Censoring	303/893 (34)	795/1652 (48)		46.9 (36.9, 55.4)
Participant w/ Censoring	303/893 (34)	771/1574 (49)		48.4 (38.7, 56.6)
Specimen	303/893 (34)	865/1801 (48)		46.3 (36.5, 54.6)
Random Specimen	239/749 (32)	929/1945 (48)		50.2 (40.4, 58.5)
ENSEMBLE South Africa				
RCT	62/172 (36)	2386/4743 (50)		43.9 (23.4, 58.9)
Participant w/o Censoring	49/137 (36)	301/635 (47)		37.5 (8.1, 57.5)
Participant w/ Censoring	49/137 (36)	292/613 (48)		37.0 (7.0, 57.3)
Specimen	49/137 (36)	362/783 (46)		34.7 (4.2, 55.5)
Random Specimen	43/110 (39)	368/810 (45)		20.6 (-20.2, 47.5)
ENSEMBLE United States				
RCT	93/416 (22)	8964/17643 (51)		72.6 (65.5, 78.2)
Participant w/o Censoring	88/392 (22)	411/825 (50)		70.5 (61.2, 77.6)
Participant w/ Censoring	88/392 (22)	405/808 (50)		70.9 (61.8, 77.9)
Specimen	88/392 (22)	432/863 (50)		70.6 (61.5, 77.6)
Random Specimen	69/330 (21)	451/925 (49)		71.2 (61.3, 78.6)

Vaccine Efficacy or Effectiveness (%): -25 0 25 50 75 85 90 95 99

Test-negative design sampling approaches are participant-based without censoring, participant-based with censoring, specimen-based, and random specimen-based.
COVE and AZD1222 randomized controlled trial (RCT) vaccine efficacy estimates are from the published final blinded phase RCT analyses.
ENSEMBLE RCT vaccine efficacy estimates were derived using an unadjusted Cox proportional hazards model since published RCT analyses were unavailable for all three regions.
Test-negative design vaccine effectiveness estimates were derived using a semiparametric logistic regression model.

Racial and ethnic disparities in excess deaths during the COVID-19 pandemic, March 2020 to December 2022 Anika T. Haque* Anika Haque Meredith S. Shiels Neal D. Freedman Amy Berrington de González

Background: The COVID-19 pandemic disproportionately impacted minoritized groups in the US. We estimated racial and ethnic disparities in excess deaths during COVID-19.

Methods: We obtained provisional death counts (2018-22) from death certificate data curated by the CDC; population estimates for the corresponding years were from the US Census Bureau. 2018-19 mortality rate data was used to generate expected death counts for 2020-22. Excess deaths were calculated by subtracting the expected deaths from the observed deaths from March 2020-December 2022. Rates were calculated by dividing excess deaths by the population count. Analyses were restricted to ≥35-year-olds, age-standardized to the 2019 population, stratified by race/ethnicity and year.

Results Compared to 2018-19 deaths, an estimated 462,300 excess deaths occurred between March and December 2020 (535,100 in 2021 and 306,900 in 2022). 75-76% of excess deaths were attributed to COVID-19 between 2020 and 2021, decreasing to 60% in 2022. Compared to White individuals (222.8 per 100,000), excess death rates between March 2020 and December 2022 were higher among Black (397.4), American Indian and Alaska Native (AI/AN) (467.5), Latino (347.8), and Native Hawaiian/Pacific Islander (NHPI) individuals (335.4); excess death rates for Asian Americans (151.7) were lower. Age-standardized non-COVID-19 excess deaths were 2-times higher in Black and AI/AN individuals than White individuals. Excess death disparities decreased over time; compared to White individuals, elevated excess death rates among Black (RRs=2.4, 1.8, 0.9 in 2020, 2021, and 2022, respectively) and Latino (RR=2.1, 1.7, and 0.7) individuals decreased in each subsequent year.

Conclusion: The COVID-19 pandemic had a substantial impact on US mortality, with excess deaths peaking in 2021. The findings highlight the disproportionate effect on Black, AI/AN, Latino, and NHPI communities. The racial and ethnic disparities in excess death rates declined over time.

COVID-19 Pandemic

Natural cause mortality inequities by immigration status among Asians and Pacific Islanders in California: March 2020 through February 2023 Ye Ji Kim* Ye Ji Kim Alicia R. Riley Josefina Flores Moraes Marie-Laure Charpignon Matthew V. Kiang Shelley DeVost Andrew C. Stokes Ruijia Chen Yea-Hung Chen Maria Glymour

Asian and Pacific Islanders (API) are the fastest growing population in the US. Yet, mortality inequities by subgroups remain unclear as this population is often treated as a monolith. Here, to inform future tailored pandemic responses, we quantify excess natural-cause mortality among API subgroups. We used individual-level death certificate data from the California Department of Public Health from Jan 2016 through Feb 2023. We restricted the analysis to California Asian residents (ages 25 and older) who died due to a natural cause to understand underlying health inequities. We classified decedents by age, country of birth, and immigration status (US-born citizens, documented foreign-born (FB), and undocumented FB persons based on their country of birth and no record of a plausible SSN sequence). The natural-cause excess deaths and relative risks were calculated for the time period Mar 2020 through Feb 2023, relative to the pre-pandemic period (Jan 2016 to Feb 2020), using dynamic harmonic regressions. The risk of natural-cause death among undocumented FB Asians almost doubled during the pandemic (RR (95% prediction interval)=1.9 (1.4, 3.1)), compared to a 20% increase among US-born Asian citizens (RR=1.2 (1.1, 1.3)) and documented FB Asians (RR=1.2 (1.1, 1.2)). Further, undocumented FB Asians who were more than 65 years old had nearly 3 times the risk of a natural cause death during than prior to the pandemic (RR=2.8 (1.8, 5.9)). In contrast, excess mortality was slightly higher among younger, US-born (RR=1.3(1.1, 1.6)) and documented FB Asians (RR=1.2 (1.2, 1.3)) than those over 65 (RR for US=1.2(1.1,1.2); RR for FB=1.1(1.0,1.5)). The COVID-19 pandemic had disparate impacts on natural-cause mortality among API populations, with especially harmful effects on undocumented FB individuals.

Applying machine learning to identify unrecognized COVID-19 deaths attributed to other causes of death in the United States Mathew V. Kiang* Mathew V. Kiang Dielle J. Lundberg Rafeya Raquib Benjamin Huynh Richard Li M. Maria Glymour Andrew C. Stokes

The true number of deaths caused by the SARS-CoV-2 virus in the US has been debated since the start of the pandemic. Excess mortality models are often used but cannot distinguish deaths due to SARS-CoV-2 infection versus other pandemic-related causes such as health care interruptions or social and economic impacts. We use a novel machine learning approach trained on individual death certificate data to differentiate deaths and produce refined estimates of COVID-19 mortality from 2020 to 2021. Leveraging variation in death certificate accuracy by place of death (i.e., COVID-19 deaths are more accurately reported in hospital settings due to widespread testing and national guidance), we fit six ML models across four covariate sets, which included individual, county, and pandemic characteristics. We tuned models and assessed performance using a train-validate-test split on the in-hospital deaths. The final model, XGBoost, had high out-of-sample performance (AUC ROC: .90; sensitivity: .80; specificity: .85). We used this model to predict COVID-19 mortality for out-of-hospital deaths and calculated adjusted reporting ratios (ARRs) for the number of predicted COVID-19 deaths compared to officially reported COVID-19 deaths. We estimated the actual number of COVID-19 deaths to be 31% higher than official reports (ARR: 1.31; 95% uncertainty interval [95% UI]: 1.30, 1.32). There was substantial variation between groups (Figure). For example, COVID-19 was underreported more frequently on death certificates recorded as Hispanic (1.44 [1.42, 1.45]) and on those recorded as male (1.35 [1.33, 1.38]). Major differences in ARR between counties and over time indicate how incomplete reporting of COVID-19 deaths could influence pandemic response. Our estimates of overall underreported COVID-19 deaths are consistent with unexplained excess mortality during the pandemic. Incorporating ML into the US death reporting system may provide more rapid, accurate, and complete mortality estimates.
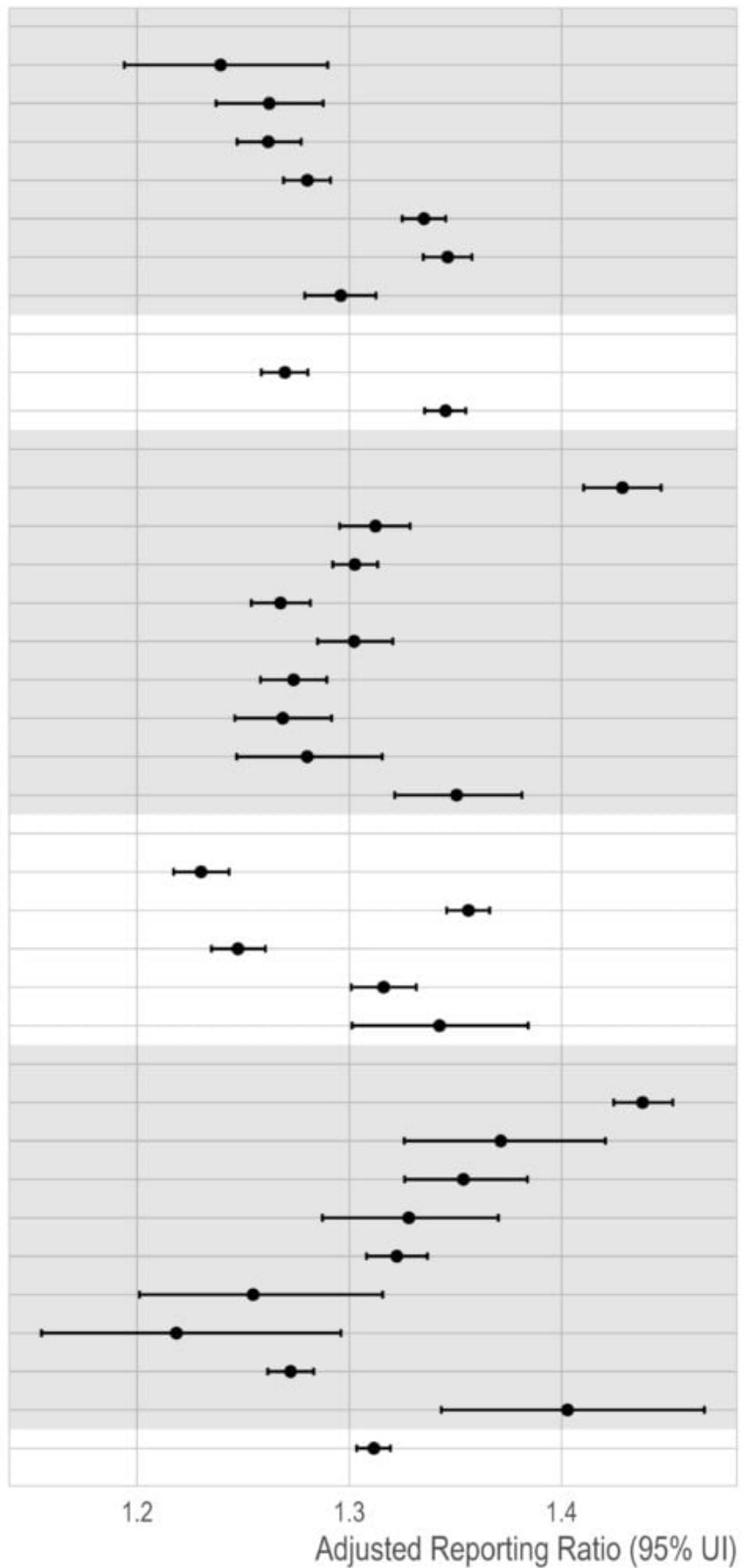
Floods and county-level mortality in the U.S.: A triply robust approach Lingzhi Chu* Lingzhi Chu Joshua L. Warren Erica Spatz Sarah Lowe Yuan Lu Xiaomei Ma Joseph S. Ross Harlan M. Krumholz Kai Chen

Background: With more frequent floods due to climate change and population expansion into high flood hazard areas, it is expected that flood-related human health burdens are increasing. However, current evidence on flood-related mortality is sparse. This study evaluated the medium- to long-term associations between floods and cause-specific mortalities over the entire contiguous U.S.

Methods: We stratified county-level monthly observations into treatment/control groups based on presence/absence of floods in a 12-month timespan. We used a triply robust approach: (1) regressing outcomes on covariates in the control group with inverse probability weighting; (2) estimating counterfactual outcomes in the treatment group had floods not occurred, using models fitted in (1); and (3) in the treatment group, comparing actual and counterfactual observations adjusting for confounders. Monthly death counts came from the CDC National Center for Health Statistics (2000-2020). We assessed average monthly counts of flood days over a lagged period (up to lag 0-11 months; e.g., the exposure at lag 0-7 months was the average monthly count of flood days over the current month and the past 7 months).

Results: Overall, there were 41,983,819 deaths. It was estimated that one flood day was associated with 9.3 [95% CI: 3.7, 15.0] excess all-cause deaths at lag 0-10 months (per 10,000,000 individuals), 3.4 [95% CI: 0.5, 6.3] excess deaths due to diseases of the circulatory system at lag 0-7 months, 2.9 [95% CI: 1.0, 4.7] excess deaths due to diseases of the respiratory system at lag 0-10 months, and 5.9 [95% CI: 3.6, 8.2] excess deaths due to external causes at lag 0-11 months.

Discussion: These findings suggest that floods are associated with excess county-level deaths. Further research is warranted, and a better understanding of the flood-health relationships will facilitate the allocation of healthcare resources in post-flood management.

Substance Use

A Crisis within a Crisis: Accelerating Racial Disparities in the US Overdose Epidemic Kumi Smith* Kumi Smith Colin Planalp Sarah Bennis Anotny Stately Jack Martin Ivan Nelson Pearl Evans

INTRODUCTION: More Americans died in 2021 from drug overdose than vehicle accidents or firearms combined. Mortality rates are climbing in all social groups, but the impact of recent system shocks—the COVID-19 pandemic, the fentanyl crisis—disproportionately affect racial and ethnic minoritized communities. Such shifts merit closer examination of race-specific mortality trends.

METHODS: We used the Centers for Disease Control and Prevention WONDER (Wide-Ranging Online Data for Epidemiologic Research) database to calculate age-adjusted opioid overdose mortality per 100,000 population by race and ethnicity from 1999 to 2022. We also explored trends in co-use of opioids with cocaine and methamphetamines, as well as state-specific Native/white and Black/white mortality rate differences.

RESULTS: Overdose deaths have increased 174% since 2009 when CDC first declared it an epidemic. Death disparities between Native and white (mortality rate difference [MRD], 28.7 deaths/100,000) and Black and white (MRD, 12.3 deaths/100,000) populations have reach an all-time high, while Asian and Hispanic/Latino rates remain below the national average. Native-white disparities are greatest in Minnesota (MRD, 237.4) and Black-white disparities are greatest in Washington DC (MRD, 106.8). Deaths from co-use are rising most rapidly in Native (opioids and methamphetamines) and Black (opioids and cocaine) Americans.

CONCLUSION: Recent accelerations in mortality across all groups predate the COVID-19 pandemic, implicating long-standing drivers of addiction and overdose. Black and Native overdose deaths in particular have reached crisis levels since the mid-2010's. Historic exclusion of these groups from access to medically prescribed opioids forced them to rely solely on an illicit drug supply increasingly contaminated with fentanyl. Future strategies to address these disparities must integrate their interrelated determinants including criminal/legal, socioeconomic, and stigma related factors.
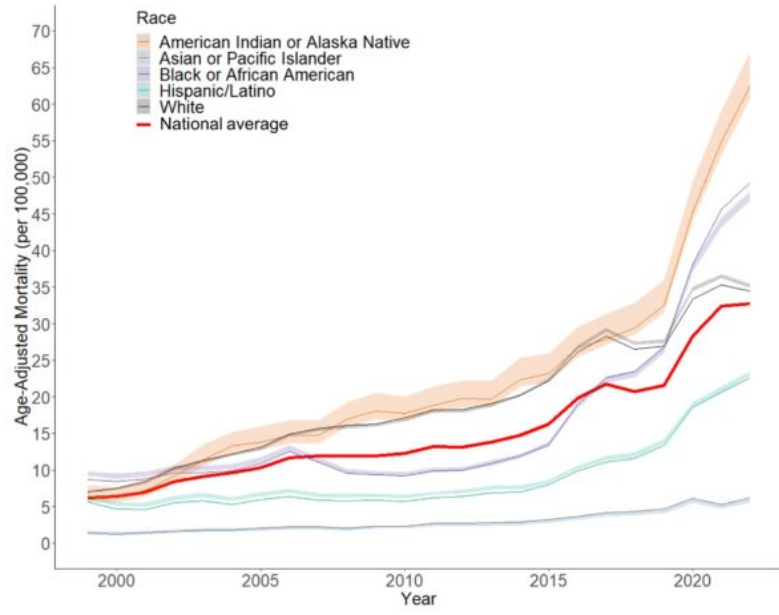
Adolescent worry typologies and associations with psychological distress, 1976-2021 Marco Thimm-Kaiser* Marco Thimm-Kaiser Noah T. Kreski Katherine M. Keyes

Adolescents' interactions with news, media, and the world around them have changed dramatically over the past decade. Psychological distress has increased in the same period. To examine whether patterns in adolescent concerns about societal challenges and their environment can explain recent increases in psychological distress after 2010, we conducted latent profile analyses of 121,471 12th grade students from annual cross-sectional Monitoring the Future surveys, 1976-2021, with ten ordinal items about reasons to worry (e.g., the economy, nuclear war) to identify adolescent "worry types." We then examined associations of worry typologies with loneliness and self-derogation before and after 2010 using logistic regressions adjusted for complex sampling and potential confounders. The results suggest four worry typologies: low worry, high worry, high urban problems worry (elevated worry about crime, drugs, poverty, race relations), high sustainability worry (elevated worry about pollution, energy shortages, etc.). Prior to 2010, high worry, urban problems worry, and sustainability worry, respectively, were associated with elevated adolescent loneliness (OR: 1.55 [1.45-1.67]; OR: 1.26 [1.18-1.35]; OR: 1.26 [1.17-1.37]) and with lower self-derogation (OR: 0.87 [0.81-0.94]; OR: 0.85 [0.79-0.92]; OR: 0.81 [0.74-0.88]). After 2010, all three worry typologies consistently predicted elevated levels of both loneliness (OR: 1.92 [1.69-2.19]; OR: 1.47 [1.30-1.66]; OR: 1.41 [1.22-1.63]) and self-derogation (OR: 1.38 [1.22-1.56]; OR: 1.15 [1.02-1.29]; OR: 1.25 [1.09-1.42]) and the observed associations were stronger than prior to 2010. In all cases, pre-to-post 2010 association changes were larger for females than for males, consistent with greater increases in psychological distress among female adolescents. In sum, adolescent worry typologies more strongly predicted adolescent psychological distress after 2010 and may in part explain recent increases.

Perinatal Cannabis Use Disorder and Risk of Disruptive Behavioral Disorders in Offspring: A Linked Data Cohort Abay Tadesse* Abay Tadesse Berihun Assefa Dachew Kim Betts Getinet Ayano Rosa Alati

Abstract

Background: In-utero exposure to cannabis might be linked to a higher risk of disruptive behavioural disorders (DBD), including conduct and oppositional disorders during childhood and adolescence. However, existing evidence relies on maternal self-reporting of cannabis use during pregnancy. To address this limitation, both the exposure (cannabis use disorder) and outcomes of interest (DBD) were validated using diagnostic tools, specifically the International Classification of Diseases-Australian Modification (ICD-10-AM) classification system.

Objective: This study aimed to examine the associations between prenatal cannabis use disorder (CUD) and DBD in offspring using a large-scale cohort study.

Methods: This population-based cohort study was conducted by participating 222,534 mother-offspring pairs using linked data derived from health data registries in New South Wales (NSW), Australia. The data were sourced from the Perinatal Data Collection (PDC), covering all live birth cohorts from January 2003 to December 2005. This dataset was linked to the NSW Admitted Patient Data Collection (APDC) and Ambulatory Mental Health Data collections (AMB-MH) using unique identifications for mothers and offspring. The exposure variable (CUD) and the occurrence of DBD in offspring, the primary outcomes of interest, were identified through the ICD-10-AM criteria (coded as F12.0-F12.9 and F91.0-F91.9, respectively). Associations were examined using Generalized Linear Models (GLMs) with a binomial family regression model to estimate relative risks. Additionally, gender-specific sensitivity analyses were carried out.

Results: After adjusting for pertinent confounding factors, we observed a five-fold rise in the risk of disruptive behavioural disorders in children exposed to prenatal CUD [RR = 4.87 (95% CI 3.43 – 6.93)] compared to non-exposed offspring. In our stratified analyses, a significant gender difference was observed; female offspring has a slightly higher risk of DBD than their male counterparts [RR = 5.20 (95% CI 2.80, 9.60) versus RR = 5.01 (95% CI 3.26, 7.69)].

Conclusion: This study shows that maternal prenatal CUD is linked to a higher risk of DBD in offspring, with a stronger risk in female offspring. Further research is needed to understand these gender-specific effects and the relationship between maternal CUD and DBD risk in children.

Mental Health

Suicide Among Veteran Cancer Survivors: Rates and Methods, 2010-2020 Julie Kittel* Julie Kittel Alexandra Schneider Elissa Kolva Lindsey Monteith Claire Hoffmire

Of Veterans Health Administration (VHA)-using veterans who died by suicide in 2021, 39% had no known mental health (MH) or substance use diagnosis. While suicide rates among VHA-using veterans with MH diagnoses have declined, rates among those with no MH diagnosis increased 12% from 2001-2021. Future research on the role of physical health conditions, such as cancer, in suicide prevention is necessary to develop targeted intervention strategies. We compared suicide rates among VHA-using veterans: (1) with a cancer history other than non-melanoma skin cancer (n=439,667), and (2) an age and sex frequency matched cohort randomly selected from all VHA-using veterans between 2010-2020 with no history of cancer. The non-cancer group were assigned an index date from a VHA visit in the same month and year as the diagnosis date of the matched cancer patient. Medical, administrative and mortality data were obtained. Suicide rates were calculated overall and by time period (2010-2015, 2016-2020) and stratified by age. Cox proportional hazard models were fit to compare cancer and non-cancer groups. Frequencies and proportions of suicide methods were calculated by cancer history and age. History of cancer was associated with a 37% increased hazard of suicide after adjusting for MH and demographic characteristics (HR=1.37; 95% CI: 1.24, 1.50). Suicide rates were especially elevated among those 85 years of age and older. Of cancer survivors who died by suicide, 79.4% (95% CI: 76.6, 82.0) used a firearm, compared to 72.3% (95% CI: 69.2, 75.2) with no cancer history. Firearm use was more prevalent in cancer survivors ages 70-84 (89.9%; 95% CI: 86.4, 92.8). Veteran cancer survivors are at increased risk for suicide and are more likely to use firearms as their suicide method. This risk is especially pronounced in older veterans. These findings can directly inform suicide risk assessment in this population. Future research should identify risk and protective factors in this population.

Association between Maintenance Dose of Mood Stabilizer and Relapse Risk in Patients with Incident Bipolar Disorder in Korea: A Nationwide, Register-based Cohort Study

Sunghyuk Kang* Sunghyuk Kang Sun Jae Jung

Background: It is recommended to treat the maintenance phase of bipolar disorder with the minimal effective dose of mood stabilizers, but evidence on a quantitative dosing strategy is lacking. We aimed to estimate the association between relative maintenance doses of mood stabilizers compared to the dose during the first admission and the risk of relapse in patients with incident bipolar disorder.

Methods: This retrospective cohort study included patients with incident bipolar disorder between 2002 and 2020, identified from the National Health Information Database of South Korea. Patients who were hospitalized for incident bipolar disorder and used mood stabilizers ≥0.1 defined daily doses during the first admission were included. After discharge from the first admission, relative maintenance doses of mood stabilizers were calculated using the dose during the first admission, representing dose in acute phase, as the denominator. Relapse was defined as rehospitalization for mood disorders (ICD-10; F30–39). The hazard ratio (HR) of relapse was estimated using extended Cox regression, with time-varying exposure of relative mood stabilizer dose.

Results: Out of 10,542 patients (mean age=37.0 years; 51.2% women) admitted for incident bipolar disorder, 50.4% relapsed. The risk of relapse did not vary with a relative maintenance dose of mood stabilizers >60%, but for doses lower than that, the risk of relapse increased as the dose was reduced (reference=80–100%; 0–20%, HR=1.66 [95% CI: 1.39–1.99]; 20–40%, 1.29 [1.13–1.47]; 40–60%, 1.22 [1.08–1.38]; 60–80%, 1.05 [0.93–1.19]; >100%, 1.07 [0.94–1.22]).

Conclusion: Among patients with incident bipolar disorder, the risk of relapse was elevated with a substantial reduction in maintenance doses of mood stabilizers compared to the acute dose. Physicians should consider prescribing sufficient mood stabilizer doses to prevent relapse in patients with bipolar disorder.

Mental Health

Persistence of psychological distress from adolescence through mid-life in the United States: results from Monitoring the Future Katherine Keyes* Katherine Keyes Victoria Joseph Justin Jager Mark Olfson Megan Patrick

Background: Depression, loneliness and other psychological distress symptoms are common in the US. While symptoms are known to be highly prevalent, data from outside the US suggest that prospective assessments generate substantially higher estimates of cumulative lifetime risk than retrospective assessments; such data have not been produced for the US. Here we use national data with repeated assessment of psychological distress to provide lifetime cumulative risk estimates for the US.

Methods: Monitoring the Future includes 6,993 individuals followed from age 18 (in 1976-1978) to age 60 (in 2018-2020), with ~4 assessments (range 1-12). Psychological distress included three subscales: loneliness (2 items), self-derogation (4 items), and low self-esteem (4 items); a total score was dichotomized based on 75th percentile for each subscale. We estimated the cumulative risk of 1+ period with high psychological distress among those with 2+ follow-ups, and prospective prediction from age 18 to 60 using logistic regression.

Results: Among those followed to 60 with 2+ follow-ups, 63.6% had at least 1 period of high psychological distress (males: 61.5%; females: 65.7%). A total of 39.9% had 1 period; 16.0% had 2 periods; and 7.7% had 3+ periods of high psychological distress. Most risk accumulation occurred during early adulthood; 52.4% had a period of high psychological distress by age 24. Those with high loneliness at age 18 had 2.42 times the risk of high loneliness at age 60 (95% confidence interval 2.01-2.90); those with low self-esteem at age 18 had 4.27 times the risk of low self-esteem at age 60 (95% confidence interval 3.57-5.09).

Conclusion: By age 60, most US adults will experience at least 1 period of high psychological distress, and the majority of risk accumulates early in adulthood. Adolescent distress prospectively predicts later life distress, thus intervention and prevention efforts in adolescence are critical for addressing late life mental health problems.

Associations between Residential Proximity to Oil and Gas Development and Risk of Hypertensive Disorders of Pregnancy in a North American Preconception Cohort Study

Mary Willis* Mary Willis Fintan Mooney Martha Koenig Erin Campbell Nicole Deziel Amelia Wesselink Samantha Parker Lauren Wise

Background: The oil and gas industry continues to expand rapidly around the world. Pollution from oil and gas development includes reproductive toxicants at levels that may harm pregnant people. Although many studies find that closer residential proximity to oil and gas development is associated with worse birth outcomes, only one study to date has examined pregnancy complications, a key driver of maternal-infant health.

Methods: Using data from Pregnancy Study Online (PRESTO, an Internet-based prospective preconception cohort study in the U.S and Canada), we examined associations between residential proximity to active oil and gas development in the preconception period and risk of hypertensive disorders of pregnancy (gestational hypertension, pre-eclampsia). We calculated the distance between a participant's geocoded address and the nearest active oil or gas development site. Among participants whose pregnancy progressed beyond 20 weeks' gestation, we obtained self-reported and birth certificate data on diagnosis of gestational hypertension and pre-eclampsia over follow-up. We implemented log-binomial regression models to estimate risk ratios (RRs) and 95% CIs, adjusting for preconception covariates (age, parity, body mass index, and smoking).

Results: Among 6,352 pregnant participants, 12.8% (n=813) resided within 5 km of active oil or gas development. Residence within 5 km of active oil or gas development was associated with gestational hypertension (RR=1.35, 95% CI: 1.12, 1.63) and preeclampsia (RR=1.50, 95% CI: 0.95, 2.37), compared with residence ≥20 km away from active oil and gas development. The magnitude of associations dissipated for participants who resided at farther buffer distances (e.g., 5-10 km, 10-15 km, 15-20 km).

Conclusion: Our preliminary results suggest that close residential proximity to oil and gas development during the preconception period is associated with higher risk of hypertensive disorders during pregnancy.

Cardiovascular

Urinary metal mixtures and incident cardiovascular disease and all-cause mortality in an ethnically diverse population of adults: evidence from the Multi-Ethnic Study of Atherosclerosis (MESA) Irene Martinez-Morata* Irene Martinez-Morata Kathrin Schilling Ronald A. Glabonjat Arce Domingo-Relloso Melanie Mayer Katlyn McGraw Tiffany Sanchez Joel Kaufman Dhananjay Vaidya Miranda R. Jones Michael P. Bancks Daichi Shimbo R.Graham Barr Wendy Post Linda Valeri Steven Shea Ana Navas-Acien

Background: Environmental metals are increasingly recognized as risk factors for cardiovascular disease (CVD) and mortality, yet prospective studies assessing the impact of metal mixtures, which are more likely to mimic real-life exposures, are limited. We assessed prospective associations of two multi-metal panels measured in urine with incident CVD and mortality in a population of adults from the Multi-Ethnic Study of Atherosclerosis (MESA).

Methods: A total of 6,599 participants (mean age 62.1 years, 53% female, 39% non-Hispanic white, 27% non-Hispanic Black, 22% Hispanic/Latino, 12% Chinese) with urinary metals available at baseline (2000-2001) were followed through December 2019. A multi-element panel of n=15 metals were measured. Six metals (cadmium, tungsten, uranium, cobalt, copper, and zinc) were selected as priority following previous evidence. Progressively adjusted Cox proportional hazards models with an Elastic-Net penalty were used to estimate the hazard ratio (HR) and 10-year survival probability of incident CVD (fatal and non-fatal) and all-cause mortality per one interquartile range (IQR) difference in baseline urinary metals. The levels of i) the six priority metals, and ii) all metals available (n=15) were included in the Elastic-Net constraint as the mixtures. Sociodemographic, behavioral, and clinical covariates were forced into the models as potential confounders.

Results: Over 17.7 years median follow-up, 1,162 participants developed CVD and 1,844 died. All the priority metals were selected by the Elastic-Net. In the models adjusted by sociodemographic, behavioral, and clinical factors, the HR (95%CI) and 10 year-survival probability difference per one IQR increase in the priority metals mixture were, respectively 1.29 (1.11, 1.56), -1.1% (-2.0, -0.5) for incident CVD; and 1.66 (1.47, 1.91), -2.0% (-2.6, -1.5) for all-cause mortality. For the n=15 metals models, the covariate-adjusted HR and 10 year-survival probability difference were 1.27 (1.07, 1.59), -1.0% (-1.9, -0.3) for incident CVD; and 1.39 (1.19, 1.62), -1.3% (-1.9, -0.7) for mortality, respectively.

Conclusion: This large epidemiological study in US adults indicate that higher urinary metal levels, when analyzed as a mixture, are associated with increased risk of incident CVD and all-cause mortality.

Utility of Framingham Stroke Risk Profile for predicting stroke among United States Veterans Serena Houghton* Serena Houghton Timothy Treu Daniel C. Posner Laura Tarko Vasileios-Arsenios Lioutas David R. Gagnon Peter W.F. Wilson Kelly Cho Hugo J. Aparicio

Background: The Framingham Stroke Risk Profile (FSRP) is a validated clinical tool to predict an individual's risk of stroke and is used in research to assess the incremental utility of novel risk factors. We examined use of the FSRP model among a diverse cohort of US Veterans within the Veterans Health Administration (VHA).

Methods: We included Veterans aged ≥45 years with no prior transient ischemic attack or stroke (N=6,362,405; 96% male) with a primary care visit, blood pressure, and cholesterol measure from 2007-2017 (mean age, y:66.0 [male]; 57.6 [female]). Veterans were followed for stroke up to 10 years (mean:7.3 y) from the blood pressure date, censored at the first of death, last visit date, or end of 2019. Stroke was defined as the first inpatient ICD 9 or 10 diagnosis code (ischemic or hemorrhagic) in the VHA electronic health record, Centers for Medicare and Medicaid Services, or primary cause in the National Death Index for fatal stroke. We examined discrimination (C-statistic [C]) and calibration (Observed/Expected [O/E]) of the FSRP within the VHA for 10-year predicted stroke risk using Cox models stratified by sex and race/ethnicity.

Results: There were 260,286 (4.3%) incident strokes among males and 6,507 (2.5%) among females. The FSRP showed weaker discrimination in males (C:0.67, 95%CI:0.63-0.70) compared to females (C:0.76, 95% CI:0.70-0.80). Discrimination was higher in Asian Veterans compared to other racial/ethnic groups. The FSRP overestimated 10-year stroke risk in Veterans overall (O/E:0.65 male; 0.92 female) and in most race/ethnicity subgroups; however, it underestimated risk in Black women (O:2.8%; E:1.5%).

Conclusion: In a large, diverse cohort of Veterans, the ability to predict stroke using the FSRP varied by sex, race, and ethnicity. Consideration of these factors, as well as recalibration and the addition of Veteran-specific risk factors (e.g., combat history, traumatic brain injury) may improve the model's predictive ability.

Figure 1. Calibration (A) and discrimination (B) of the 2018 Framingham Stroke Risk Prediction model in the Veterans Health Administration

Abbreviations: AI/AN = American Indian/ Alaska Native, NH/PI = Native Hawaiian/ Pacific Islander
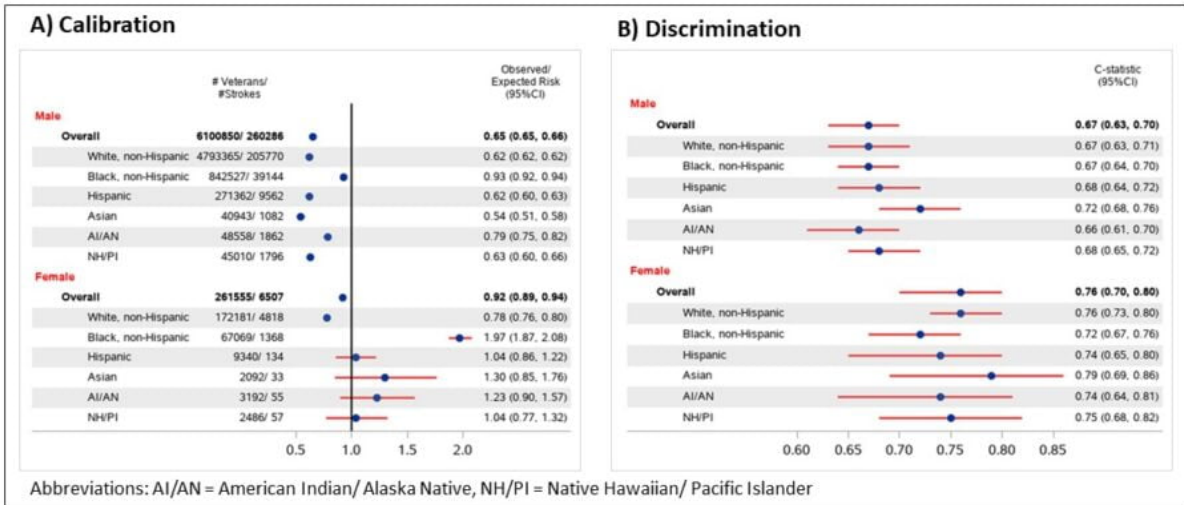
Cardiovascular

Additional Moderate Temperature Days Increases Risk of Cardiovascular Emergency Room Visits Across Climate Regions in the US Erin Liedtke* Erin Liedtke Melanie Sona Kelly Jones Shannon Zenk

Rising US temperatures are concerning, yet the impact of moderate temperatures (<37°C) on cardiovascular (CV) health is largely overlooked. As the frequency of moderate temperature days increases, it may be critical that interventions aiming to address heat exposure go into effect at lower temperatures. To the best of our knowledge there has been no investigation that examines the impact of moderate temperatures on cardiovascular emergency room (ER) visits across regions. This study aims to explore the association between exposure to additional days at moderate temperatures and the risk of CV-related ER visits during the hottest months of the year in 3 different climate regions in the US. Using gridded daily weather data, monthly counts of days with highs ranging from 27°C to 37°C between June and September were identified. Poisson regression models were run with ER CV data (N=3,727,219) from the Healthcare Cost Utilization Project in Arizona (AZ), Georgia (GA), North Carolina (NC), and New York (NY) to examine the impact of additional moderate temperature days on ER visit risk. All states demonstrated an increased cardiovascular ER visit risk for additional days above 27°C: AZ (RR 1.28, 95% CI 1.26-1.30), GA (RR 1.21, 95% CI 1.20-1.21), NC (RR 1.14, 95% CI 1.13-1.15), and NY (RR 1.11, 95% CI 1.13-1.14). Our findings also reveal regional differences in risk associated with heat. In different states, additional days at different temperatures reflect a similar risk, notably in NY (33°C, RR 1.38, 95% CI 1.36-1.39) and GA (37°C, RR 1.38, 95% CI 1.31-1.45). Our analysis indicates that moderate temperatures significantly increase the risk of cardiovascular ER visits, demonstrating the importance of designing interventions aimed at mitigating the risks posed by moderate temperatures. Geographical variability in risk underscores the need for region-specific strategies to address cardiovascular health risks associated with moderate temperatures.

Cumulative exposure to risk factors and subsequent cardiovascular disease events: The Jackson Heart Study Rishi Parikh* Rishi Parikh Paul Muntner Shakia Hardy Mario Sims Yuan-I Min Kendra Sims Alexis Reeves Yongmei Li Michelle Odden

Background: Cumulative exposure to risk factor levels may capture additional future CVD risk independent of a single measure later in life. We examined the association between cumulative exposure to systolic blood pressure (SBP), low-density lipoprotein cholesterol (LDL-C), and fasting plasma glucose (FPG) with CVD events among African-American participants in the Jackson Heart Study (JHS).

Methods: We included all JHS participants with SBP, LDL-C, and FPG measurements at Exams 1 (2000-2004) and 3 (2009-2013) who were alive at 8 years of follow-up after Exam 1. We calculated 8-year cumulative exposures as the area under the trajectory of each risk factor using all available measurements from Exams 1, 2, and 3. Adjudicated coronary heart disease (CHD), stroke, and heart failure (HF) events after 8 years were evaluated as outcomes in separate models. We used conditional Cox regression models for recurrent events, with 8-year cumulative exposures of risk factors, values of the risk factor at 8 years after Exam 1, and covariates at Exam 1 as independent variables. Models were conducted separately for each risk factor, and exposures were standardized for comparability.

Results: Among 3,188 eligible JHS participants, mean age was 54 years, and 64% were women. Over a median follow-up of 6.2 years, there were 88 CHD, 78 stroke, and 519 HF events. Cumulative exposures to SBP and LDL-C were associated with more CHD events after adjustment for covariates and the 8-year value, with cumulative exposure to LDL-C having the strongest association [adjusted hazard ratios (aHR) per SD: 1.79 (95% CI: 1.13, 2.86)] (**Table)**. Cumulative exposure to SBP and FPG were associated with HF events after adjustment [aHR: 1.10 (95% CI: 1.02, 1.18) and 1.08 (95% CI: 1.00, 1.15), respectively]. Estimates of cumulative and 8-year values of all 3 risk factors were in the harmful direction for stroke events, but only the 8-year values were robustly associated with stroke.

Conclusions: Cumulative exposure to risk factors provides additional information on CVD risk compared with single measurements later in life. CVD risk stratification methods in African American adults should consider long-term risk factor levels when assessing CVD risk.

Table. Associations between 8-year cumulative exposure to risk factor levels, 8-year values of risk factors, and CVD events among 3188 Jackson Heart Study participants.

Risk factor	Exposure term in model	Standard deviation	Adjusted* Hazard ratio (95% CI) per standard deviation of exposure		
			CHD (N=88)	HF (N=519)	Stroke (N=78)
Systolic blood pressure	Cumulative exposure, mmHg-years	139	1.18 (0.98, 1.42)	1.10 (1.02, 1.18)	1.13 (0.91, 1.40)
	8-year value, mmHg	19	1.00 (0.83, 1.20)	0.94 (0.87, 1.02)	1.28 (1.05, 1.56)
LDL cholesterol	Cumulative exposure, mg/dL-years	309	1.79 (1.13, 2.86)	0.90 (0.70, 1.16)	1.31 (0.75, 2.27)
	8-year value, mg/dL	37	1.33 (1.10, 1.62)	0.98 (0.89, 1.08)	1.72 (1.39, 2.13)
Fasting plasma glucose	Cumulative exposure, mg/dL-years	261	1.05 (0.88, 1.26)	1.08 (1.00, 1.15)	1.16 (0.99, 1.36)
	8-year value, mg/dL	31	0.98 (0.79, 1.21)	1.07 (0.99, 1.15)	1.24 (1.04, 1.48)

*Covariates include: Age, sex, income, education, current smoker, alcohol use, height-to-weight ratio, HDL cholesterol, total cholesterol, triglycerides, estimated glomerular filtration rate, CVD history, diabetes, anti-hypertensive medication use, diabetic therapy, statin use, diuretic use

Beyond race and income: the role of contextual deprivation in air pollution and cardiovascular disease Jiajun Luo* Jiajun Luo Zhihao Jin Briseis Aschebrook-Kilfoy
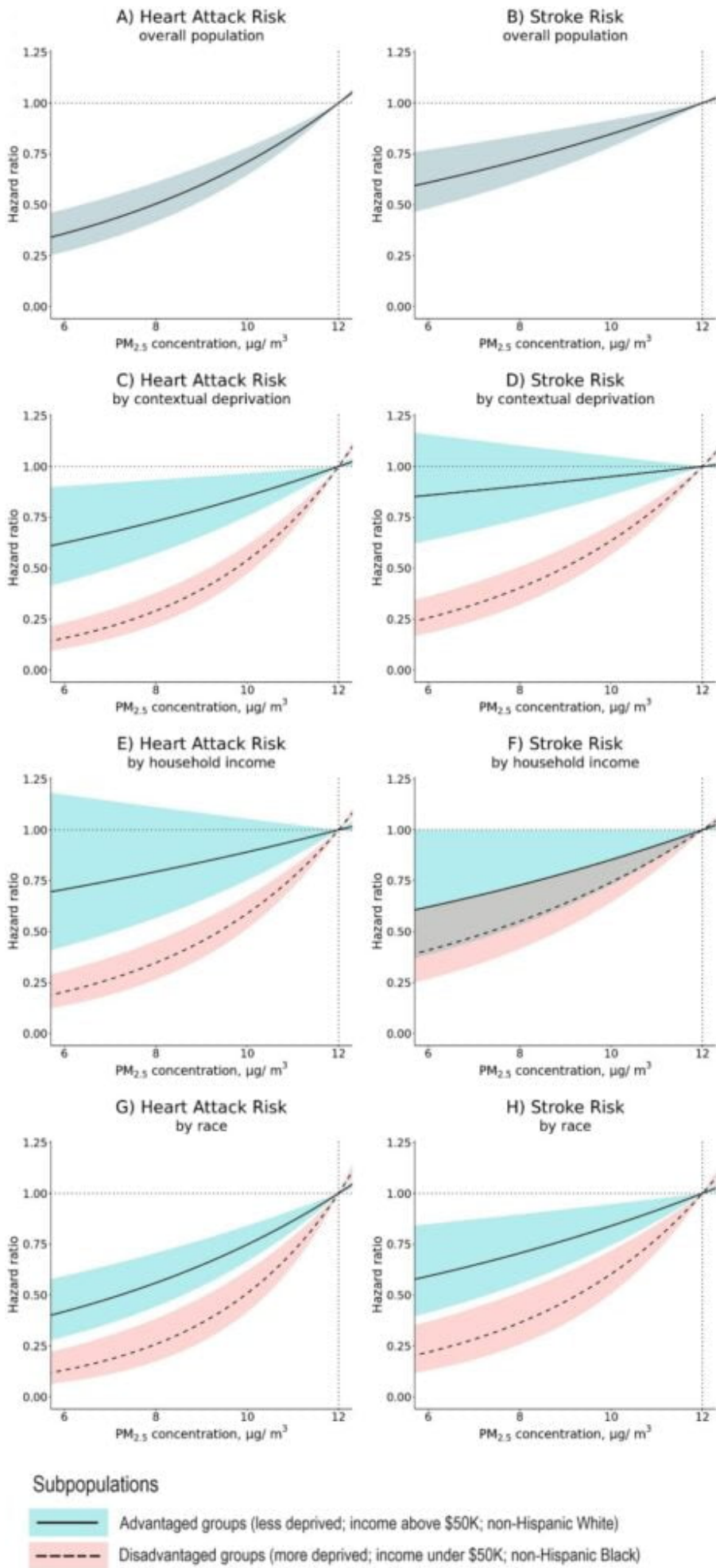
Background: Socioeconomically disadvantaged groups are more influenced by fine particulate matter (PM2.5). Previous research primarily examined individual-level socioeconomic factors, but contextual deprivation is usually ignored.

Objective: To assess disparities in PM2.5 exposure effects among subpopulations defined by different socioeconomic characteristics

Method: Data from over 210,000 participants in the All of Us Research Program (up to February 2023) were used to estimate hazard ratios (HRs) and exposure-response curves for PM2.5 exposure and heart attack or stroke incidents. Subpopulations were categorized by contextual deprivation (less/more deprived), household income (above/below $50K), and race/ethnicity (non-Hispanic White/Black). Ratio of hazard ratios (RHRs) measured disparities among these groups.

Results: Lower PM2.5 levels correlated with reduced heart attack and stroke risks across all participants. However, disadvantaged groups (more deprived, income under $50K, non-Hispanic Black) showed greater benefits from reduced PM2.5 levels. The disparities were most pronounced in groups defined by contextual deprivation. For instance, reducing PM2.5 from 12 to 6 µg/m3, the HR (95% confidence interval) for stroke was 0.86 (0.64-1.16) in the less deprived vs. 0.26 (0.18-0.36) in the more deprived; 0.62 (0.39-1.00) in the over $50K vs. 0.41 (0.27-0.63) in the under $50K; 0.59 (0.41-0.85) in non-Hispanic Whites vs. 0.22 (0.13-0.37) in non-Hispanic Blacks. The RHR was highest for contextual deprivation (3.35 [2.13-5.27]), compared to income (1.52 [0.79-2.92]) and race (2.70 [1.40-5.22]).

Conclusion: While individual race and income remain undeniably crucial for the unequal impacts of PM2.5, our findings suggest that contextual deprivation is a more robust socioeconomic characteristic modifying the effect of PM2.5 exposure.

A) Heart Attack Risk
overall population

B) Stroke Risk
overall population

C) Heart Attack Risk
by contextual deprivation

D) Stroke Risk
by contextual deprivation

E) Heart Attack Risk
by household income

F) Stroke Risk
by household income

G) Heart Attack Risk
by race

H) Stroke Risk
by race

Subpopulations

Advantaged groups (less deprived; income above $50K; non-Hispanic White)

Disadvantaged groups (more deprived; income under $50K; non-Hispanic Black)

Trends in heavy episodic drinking in Canada by gender and socioeconomic position from 2000-2021: an age-period-cohort analysis Alessandra Andreacchi* Alessandra Andreacchi Erin Hobin Arjumand Siddiqi Brendan Smith

Background:

Age, period, and birth cohort (APC) modelling is vital for epidemiological surveillance, providing insights into changes in alcohol use over time. Exploring variation in APC models for alcohol use across sociodemographic groups helps contextualize the causes of temporal changes. This study examined APC trends in heavy episodic drinking (HED) in Canada by gender and socioeconomic position.

Methods:

An APC analysis of repeated cross-sectional data from the Canadian Community Health Surveys (2000-2021) was conducted using hierarchical cross-classified random effects logistic regression. HED, defined as binge drinking ≥monthly in the past 12 months, was examined in relation to gender and socioeconomic position measured by household income and education.

Results:

Population-level trends showed steeper HED decreases in adolescent (aged 12-17) and young adult (aged 18-29) men than women and increases in middle adult (aged 30-64) women. Gender-specific APC models revealed strong age and birth cohort effects. HED peaked in young adulthood and decreased with age. HED was greatest in the 1980-1989 cohort but decreased in the most recent 1990-2009 cohort, particularly in men. Higher household incomes demonstrated a positive gradient for HED across age, period, and cohort, while trends varied by education. Compared to lower education groups, people with ≥ a bachelor's degree had the lowest HED in middle adulthood. HED among people with ≥ a bachelor's degree was low in earlier cohorts, converging with other education groups in recent cohorts due to a greater HED increase, particularly in women.

Conclusion:

The gender gap in HED is converging in Canada; recent cohorts of young men are reducing HED, while high-risk cohorts of women are entering middle adulthood with increased HED linked to higher education. Gender and socioeconomic position should be considered in research to contextualize trends and in alcohol policies to assess potential differential reductions in HED.

Substance Use

Applying intersectional approaches to studying the trajectories of adolescent alcohol and cannabis use: A combination of intersectional multilevel analysis of individual heterogeneity and discriminatory accuracy (MAIHDA) and group-based trajectory modeling (GBTM) methods with application to youth in first time contact with the legal system Yu (Seashore) Li* Yu(Seashore) Li Johanna B. Folk Chase Anderson Michelle V. Porche Marina Tolou-Shams Brandon D.L. Marshall

Background: Longitudinal analyses applying intersectional theories to the study of developmental alcohol and cannabis use trajectories among youth are lacking.

Methods: We used intersectional multilevel analysis of individual heterogeneity and discriminatory accuracy (MAIHDA) and group-based trajectory modeling (GBTM) to examine the relationship between eight intersectional strata defined by racial/ethnic & sexual minority identities and joint trajectories of self-reported, past 4-month alcohol use and cannabis use among justice-involved youth. Participants were recruited following their first ever contact with a family court system in a Northeastern state and followed prospectively for 24 months; assessments were completed every 4 months.

Results: Participants were 397 youth in first time contact with the legal system (30.2% sexual minority, 10.8% Black, 42.3% Latinx, 15.1% other/multi-racial, 31.7% White). Trajectory modeling identified four distinct trajectories of alcohol use: consistently low (43%), early initiators (12%), decreasing use (27%), and consistently high use (18%); see Figure 1A. Similarly, we found four trajectories of longitudinal cannabis use: consistently low (45%), early initiators (8%), decreasing use (20%), and consistently high cannabis use (27%); see Figure 1B. In MAIHDA models, we found a significant main effect for sexual minority status: sexual minority youth were more likely to be assigned to the consistently high alcohol and cannabis use trajectories compared to heterosexual youth. However, we did not observe substantial variation attributable to the intersectional strata defined by sexual minority status and race/ethnicity.

Conclusion: This research demonstrates the feasibility of combining MAIHDA and GBTM approaches to study the intersectional predictors of longitudinal substance use.

Figure 1a. Group-based trajectories of self-reported past 4 month alcohol use among first-time offending, justice-involved youth
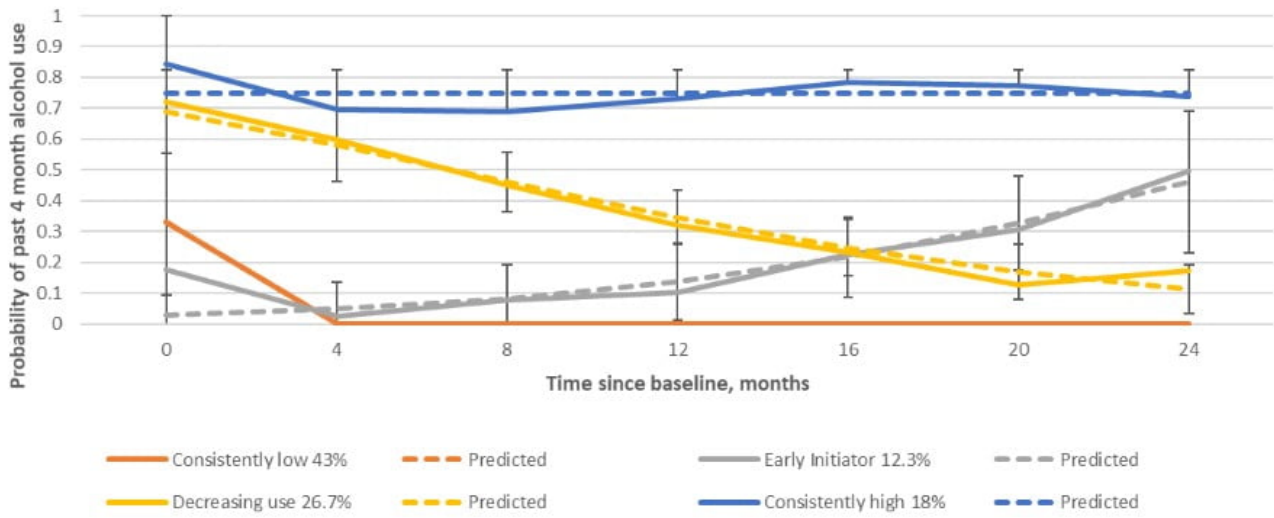
Figure 1b. Group-based trajectories of self-reported past 4 month cannabis use among first-time offending, justice-involved youth
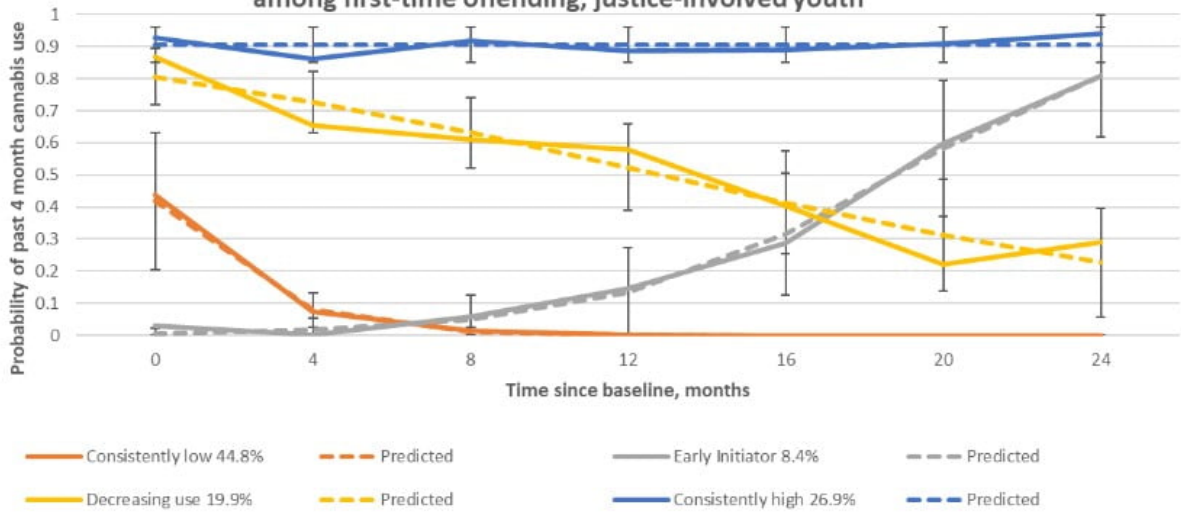
Tracking spatiotemporal trends in the public stigmatization of opioid use on social media

Anna Nguyen* Anna Nguyen Shashanka Subrahmanya Russ Altman Johannes Eichstaedt Mathew Kiang

Background: Stigma around opioid use is a fundamental hinderance to effectively addressing the US opioid overdose crisis. Public stigma affects community support for local public health responses, such as safe injection sites or syringe exchange programs. However, surveying public opinion in real-time is difficult. Here, we applied natural language processing techniques to social media data to gain insight into the evolving dynamics of stigma and public perceptions about opioid use.

Methods: We queried posts made after January 1, 2015 from the r/SanFrancisco, r/Philadelphia, r/Chicago, and r/Atlanta subreddits that contained at least one mention of opioids or overdose. We estimated sentiment in these conversations over time using the National Research Council Canada (NRC) Emotion Lexicon. We modeled 100 topics across all forums using Latent Dirichlet Allocation and estimated their frequencies over time using locally estimated scatterplot smoothing (LOESS).

Results: We extracted 833 posts and 27,309 comments across all forums. Opioid-related posts were most prevalent between 2017-19 in r/Philadelphia, while in r/SanFrancisco there have been more recent increases in 2022 and 2023. Topics around harm reduction, policing, and mental health emerged from the combined text, with distinct regional trends in topic frequency and sentiment. Notably, discussions around safe injection sites were consistent over time in r/Atlanta, gradually increased in r/Chicago, peaked between 2020-21 in r/SanFrancisco, and spiked in 2022-23 in r/Philadelphia. Positive sentiment around safe injection sites was highest in r/Atlanta, but increased over time in r/Chicago.

Conclusions: Language analyses provided insights on the evolving stigmatization of opioid use, revealing complex spatiotemporal patterns in prevalent topics and the sentiments surrounding them. This work can be used to guide targeted interventions and communication strategies as the opioid overdose epidemic continues to evolve.

Frequencies of Select Topics Extracted from Regional Subreddits
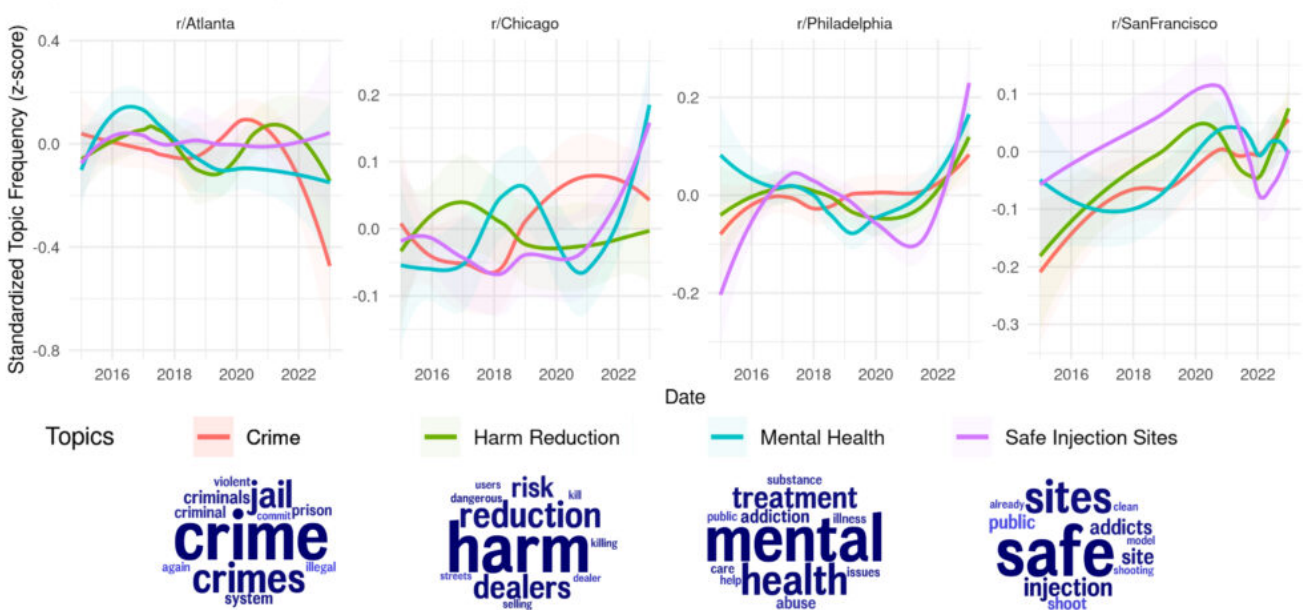
Engagement in substance use disorder treatment after an emergency department visit among persons at high risk of opioid overdose: A prediction analysis Fiona Bhondoekhan*

Fiona Bhondoekhan Yu Li Laura C. Chambers Francesca L. Beaudoin Benjamin D. Hallowell Linda Mahoney Mackenzie M. Daly Jamieson Goulet Brandon D.L. Marshall

Background: Predictors of substance use disorder (SUD) treatment engagement after opioid-related emergency department (ED) visits are uncertain. We sought to identify predictors of treatment engagement to inform linkage services in the ED setting.

Methods: This analysis used data from a randomized trial comparing the effectiveness of certified peer recovery specialist (CPRS) and licensed clinical social worker (LCSW) linkage services for ED patients at risk of opioid overdose in Rhode Island (2018-2021). Potential predictors were obtained from a baseline questionnaire. SUD treatment engagement within 90 days of ED discharge was obtained from administrative data linkage. Classification and regression tree (CART) models identified predictors of treatment engagement by linkage service. Model performance was assessed using predictive accuracy, sensitivity, specificity, and positive/negative predictive value.

Results: Of 648 participants (CPRS=323, LCSW=325), 350 (54%) were aged 31-50 years, 206 (32%) were male, and 278 (43%) engaged in SUD treatment within 90 days (CPRS=44%, LCSW=42%). In the CPRS service, predictors of treatment engagement were stable housing, no history of treatment barriers, history of treatment/recovery services, no prior bipolar disorder diagnosis, no prescription drug use in last 6 months, and current unhealthy alcohol use. In the LCSW service, predictors were having health insurance, no overdose in last 12 months, not currently in pain, and no prior mental illness treatment or anxiety disorder diagnosis. CART analyses had low predictive accuracy (CPRS=61%, LCSW=55%, Table 1), suggesting these measures had minimal utility for predicting treatment engagement.

Conclusion: For ED patients at risk of opioid overdose, measured characteristics did not adequately predict SUD treatment engagement following an ED visit involving CPRS or LCSW services. It remains important to offer behavioral/social support services to ED patients at risk of opioid overdose.

Table 1. Model performance of CART analysis separately for participants who received LCWS and CPRS linkage services in the ED.

	CPRS (n = 323)	LCSW (n = 325)
Sensitivity, %	65.7%	58.3%
Specificity, %	55.2%	42.9%
Positive predictive value, %	63.9%	77.8%
Negative predictive value, %	57.1%	23.1%
Predictive accuracy, %	60.9%	54.8%

STATE-SPECIFIC E-CIGARETTE USE AMONG US YOUTH BY SEXUAL ORIENTATION, 2019-2021 YOUTH RISK BEHAVIOR SURVEY Mohammad Ebrahimi Kalan* Mohammad Ebrahimi Kalan Ateeqa iJAZ Archana Vardhan Omolayo Joy Anjorin Lisa L Lindley Rima Nakkash

Introduction: Evidence indicates higher rates of electronic cigarette (e-cigarette) use among lesbian, gay, bisexual, and transgender (LGBT) youth compared to their cisgender heterosexual peers, which is a significant concern in the US. In this nationally representative sample of US youth, we aimed to explore the state-specific weighted prevalence of e-cigarette use among LGBT youth and how it differs from their cisgender heterosexual peers.

Methods: A pooled analysis was conducted using data from the 2019 and 2021 Youth Risk Behavior Survey. Overall, 37 US states collected data from high school students (grades 9-12; N= 271,614) on sexual identities (LGBT, n= 40848) and cisgender heterosexual (n= 230,766). The weighted prevalence of current (past 30-day) use of e-cigarettes by US states was reported. A multivariable regression model was performed to examine the association between sexual identity and vaping e-cigarettes controlling for potential confounders including demographics (i.e., age, sex, race/ethnicity, and school grade), current cigarette use, and other tobacco products use. Weighted adjusted odds ratios (AOR) and corresponding 95% confidence intervals (95%CIs) were reported. Data for the state of California was collected only for the 2019 YRBS.
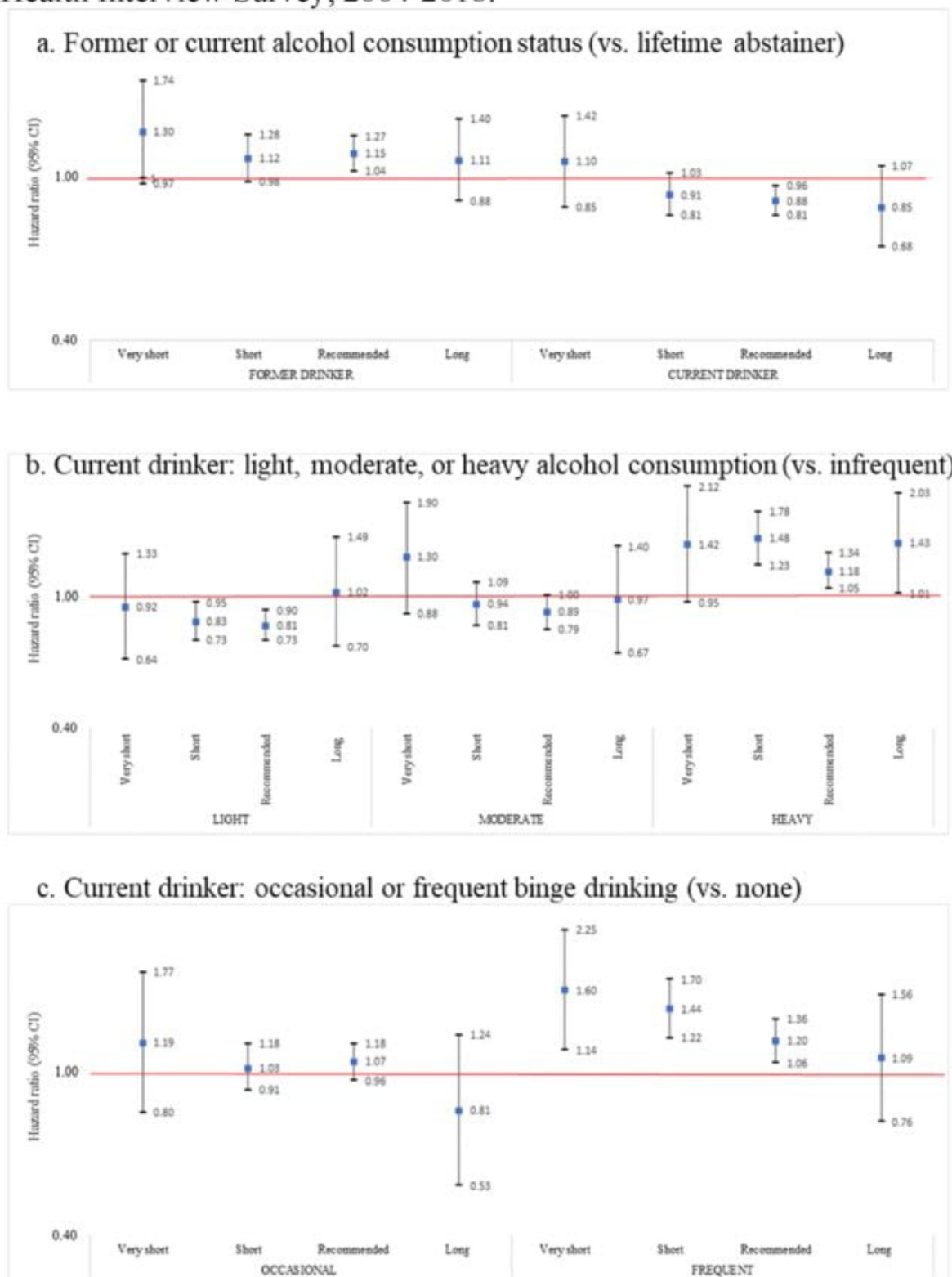
Results: In 2019-21, current e-cigarette vaping was higher among US LGBT than cisgender heterosexual youths (28 vs 19%; p<.001). The weighted prevalence of current vaping was predominant among LGBT (vs. cisgender heterosexual) in several US states including West Virginia (41% vs. 30%; p=.02), North Carolina (40% vs. 29%; p<.0001), New Mexico (39% vs. 28%; p<.0001), Ohio (39% vs. 18%;p=.0013), North Dakota (35% vs. 26%;p=.0014), and Kentucky (34% vs.17%;p<.0001). The lowest prevalence of current vaping among LGBT (vs. cisgender heterosexual) youth was in Alabama (19% vs. 20%; p= 0.25) and California (19% vs.18%;p=.933). The multivariable regression model showed that compared to cisgender heterosexual peers, US LGBT youth were at greater risk of vaping (AOR= 1.37;95%CI:1.01-1.86; p<.001) in 2019-21, after accounting for the aforementioned confounders.

Conclusions: This nationally representative study adds to the existing literature that e-cigarette use among LGBT youth is prevalent in the US, with a wide spectrum within US states. National and state-level vaping prevention strategies should consider sexual identities in designing, developing, and implementing targeted tailored vaping prevention and cessation programs.

The behavioral correlates alcohol consumption and sleep duration in relation to all-cause mortality risk among a nationally representative sample of US adults Erline E Martinez-Miller* Erline Martinez-Miller Frankie LaPorte Symielle A. Gaston Chandra L. Jackson

Alcohol use and short sleep are correlated and independently linked to mortality; joint alcohol-sleep contributions to mortality are unclear and may vary by sociodemographic characteristics. Evidence could, for instance, inform sleep targets to reduce alcohol-related risk. We used pooled, self-reported National Health Interview Survey data (2004-2018) linked to the National Death Index (2004-2019). Alcohol use categories were: lifetime abstainer, former drinker, current drinker, and for current drinkers: consumption (infrequent, light, moderate, heavy) and binging (none, occasional, frequent). Sleep duration was very short (<5 hours/night), short (<7), recommended (7-9), and long (>9). We estimated joint sleep-alcohol associations with mortality risk overall (Figure[F]1) and by sex/gender, race/ethnicity, and age in adjusted Cox proportional hazard models. Among 188,255,360 US adults, median age was 41 (IQR: 29-52) years, 51% were female, 65% were non-Hispanic White (NHW), 68% were current drinkers, and 7,244,235 (4%) died. Current drinkers reported 11% heavy drinking and 10% frequent binging. For 31%, sleep duration was short. For those with recommended sleep, mortality risk was higher for former drinkers (HR: 1.15 [1.04, 1.27]) and lower for current (0.88 [0.81, 0.96]) compared to lifetime abstainers (F1a). Among those with short and recommended sleep, light vs. infrequent drinking was associated with lower risk (0.83 [0.73-0.95]) while heavy drinking was associated with higher (1.48 [1.23-1.78]; F1b). For those with short sleep, compared to non-bingers, frequent bingers had higher risk (1.44 [1.22, 1.70]); occasional drinkers did not (F1c). For moderate drinkers with recommended sleep, NHWs had lower risk (0.82 [0.72, 0.94]) and NH Black adults had higher (1.30 [0.99, 1.71]). For those aged ≥35 years, frequent vs. non-bingers with short sleep had higher risk, while those <35 did not. Behavioral correlates and sociodemographic characteristics shape mortality risk.

Figure 1. Adjusted* hazard ratios (95% confidence intervals) for mortality risk by three measures of alcohol consumption within sleep duration categories: National Health Interview Survey, 2004-2018.


a. Former or current alcohol consumption status (vs. lifetime abstainer)

b. Current drinker: light, moderate, or heavy alcohol consumption (vs. infrequent)

c. Current drinker: occasional or frequent binge drinking (vs. none)

Abbreviations: CI, confidence interval.
*Models adjusted for age, sex, race/ethnicity, marital status, educational attainment, poverty status, health status, body mass index, smoking status, physical activity, survey year (3-year increments), and alcohol intake*sleep duration.

State-level changes in probation and parole rates and Black / White disparities in the 21st century
Hedwig Lee* Brenda Bustos David Rigby Ruth Wygle Joan Casey Alison Gemmill Allison Stolte Ralph Catalano Tim Bruckner Hedwig Lee

Although public health has increasingly studied the collateral consequences of prison and jail incarceration, we know little about the health consequences of other forms of criminal legal system contact and supervision, including probation and parole. Understanding spatial and racial-ethnic variation in probation and parole across US states can provide new insights into how carceral supervision impacts population health and health disparities. However, information on state-level probation and parole have not been adequately described. Using data from the Bureau of Justice Statistics and the US Census for the years 2001 and 2018, we provide a novel description of state-year variation in the rates of parole and probation supervision and the racial (Black-White) disparities in these rates. At the national level from 2001 to 2018, the probation population decreased and the racial composition of the probation population remained steady (roughly 30% Black and 55% White). However, there was broad state-level variation in Black and White probation population over time. In all but five states, the Black-White gap in probation rates declined between 2001 and 2018. Similarly, the Black-White gap in parole rates has declined in all but seven states since 2001. The parole population was 41.9% Black and 35.5% White in 2001, but 33.5% Black and 42.8% White in 2018.The shrinking Black-White gaps might indicate preferential provision of probation and parole favoring White people, while disproportionately retaining Black people in prison and jail. The potential population health implications of these race-specific changes over time warrant further investigation.

Figure 1. Parole and Probation Rates, by Race (2001-2018), in all US states. Each state contains a unique time plot.
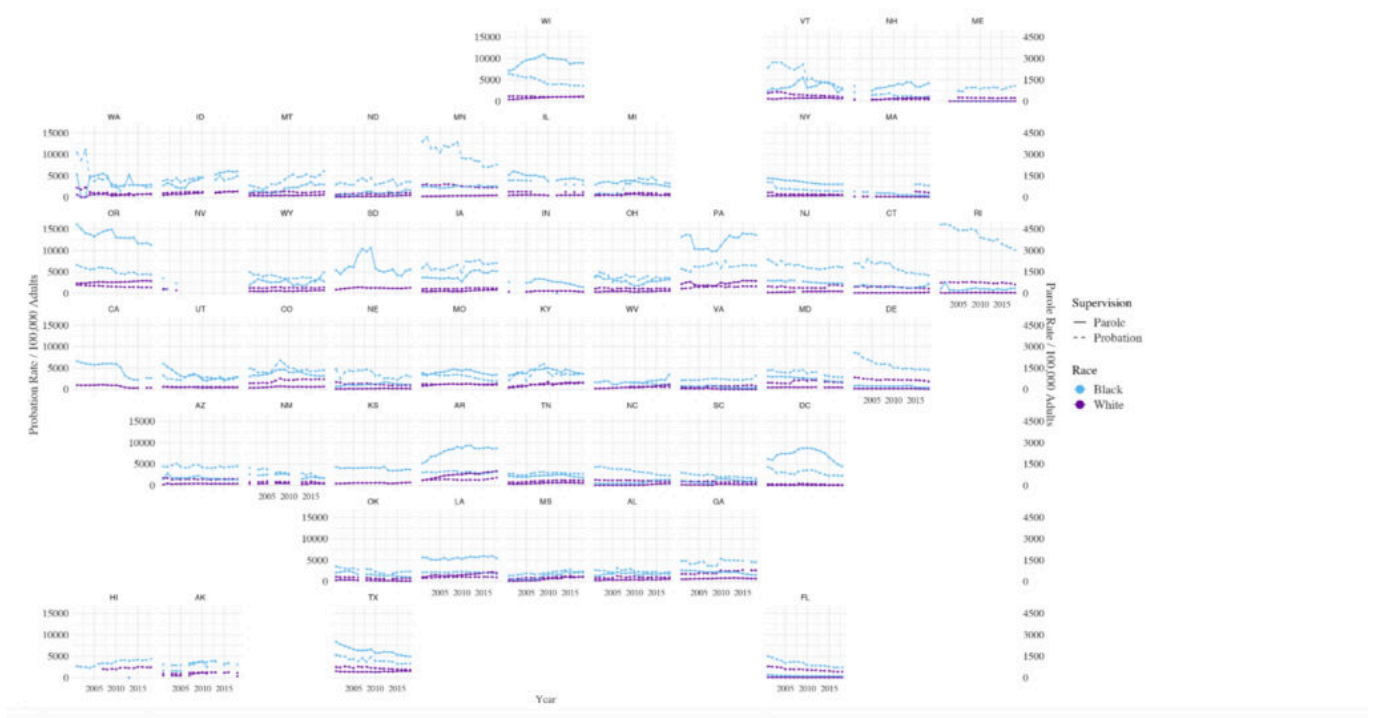
Early-life exposure to punitive school discipline is associated with adverse cognitive aging outcomes in early adulthood: Findings from the National Longitudinal Study of Adolescent to Adult Health (Add Health) Catherine Duarte* Catherine Duarte Jillian Hebert Tanisha Hill-Jarrett Anusha Vable

Exclusionary school discipline practices – like suspension or expulsion – are a mechanism of structural racism that disproportionately shape the experiences of minoritized children in US schools and may have implications for their health. An emerging literature links inequitable punitive school discipline exposure to racial inequity in midlife cognitive aging and later life dementia risk, however little work has evaluated if proposed pathways from punitive school discipline to dementia begin to diverge earlier in the lifecourse. In National Longitudinal Study of Adolescent to Adult Health (Add Health) cohort data (N=3,442), we use linear mixed effects models with bootstrapped confidence intervals (500 iterations) to evaluate if exclusionary discipline (3-levels: no discipline, ever suspended, ever expelled) in Grades 7-12 is associated with cognition (z-scored memory, attention, composite cognitive measure) in early adulthood (ages 24-32 years), adjusting for sociodemographic, childhood socioeconomic status, and childhood cognition indicators. In descriptive analyses, Black (22% of sample, but 31% of suspended and 44% of expelled) and Native/Indigenous participants (1% of sample, but 1.4% of suspended and 1.8% of expelled) bore a disproportionate burden of punitive school discipline in early life. In adjusted models, compared to no punitive discipline, both suspension (: -0.13, 95%CI: -0.21, -0.05) and expulsion (: -0.19, 95%CI: -0.32, -0.05) were associated with lower memory z-scores. There was no association between punitive school discipline and attention or the composite cognitive measure. Consistent with lifecourse epidemiology models, results suggest exposure to punitive discipline in secondary school may shape aging-related cognitive function in early adulthood, with implications for racial inequity in later life dementia risk.

Social

Public health consequences of the mass criminalization of adolescence: Does school discipline mediate the relationship between community policing and adolescent psychiatric hospitalization? Seth Prins* Seth Prins Megan Marziali Erin Annunziato Krish Bhatt

Background. The school-to-prison pipeline describes a set of policies and practices that discipline and punish adolescents rather than provide support for their underlying educational and developmental needs. Over 10 million students in the US attend schools with police but no counselor, nurse, psychologist, or social worker. Since the 1990s, suspensions and expulsions have doubled, and school-based arrests have increased 300-500%. The school-to-prison pipeline parallels wider trends in policing and punishment, in which schools' surrounding communities experienced rises in aggressive policing. Yet, the pathway from community policing to school discipline to adolescent mental health outcomes remains underexplored.

Methods. To determine whether this pathway exists in New York City, we aggregated (by Zip Code Tabulation Area and month) policing incidents from New York City Open Data, school discipline incidents from the Civil Rights Data Collection, and adolescent psychiatric hospitalizations from New York's Statewide Planning and Research Cooperative System (SPARCS), from 2006 – 2014. We employed the parametric mediational g-formula approach to estimate randomized analogues of natural direct (rNDE) and indirect effects (rNIE) for various hypothetical interventions to reduce school discipline, in the presence of exposure-induced mediator-outcome confounding, a potential issue in this setting. Confounders of exposure-outcome, exposure-mediator, and -mediator-outcome relationships included zip-code-level measures of poverty, unemployment, educational attainment, percentage of residents self-identifying as Black, percentage of the population below 24 years of age, and mean distance to inpatient hospital services.

Preliminary results. A total of 11,900,192 policing incidents, 225,682 school discipline incidents, and 2,118,481 person-days of hospitalization were aggregated to 19,440 ZCTA-months. After adjusting for neighborhood-level sociodemographic characteristic, an increase in one policing incident per 1,000 residents was associated with a 0.3% increase in the rate of youth psychiatric hospitalization time (IRR 1.003 [1.001 – 1.005]). Results from the mediation analysis are forthcoming.

Conclusions. If we find that school discipline mediates the relationship between policing and adolescent psychiatric hospitalizations at the zip code level, our study will be among the first to demonstrate a concrete pathway from the mass criminalization of adolescence and adolescent mental health. The study will bolster efforts to modify school discipline policies to reduce adolescent criminalization and improve adolescent mental health.

Social

The effect of Section 8 voucher receipt in the Moving to Opportunity Study on perceived racial/ethnic discrimination in Black and Hispanic adolescents Anna Krasnova* Anna Krasnova Dustin T. Duncan Jeremy Kane Kara Rudolph

Background: Section 8 vouchers help low-income families relocate to lower-poverty neighborhoods, but they could also alter school and neighborhood racial/ethnic composition, increasing exposure to perceived racial/ethnic discrimination, which can be harmful to adolescent mental health. We estimated the extent to which voucher receipt affected risk of perceived discrimination in different contexts among adolescents and tested for effect heterogeneity across voucher types, cities, and sexes.

Methods: We selected non-Hispanic Black and Hispanic adolescents (mean age=10.1; SD=0.1) residing in Boston, Chicago, New York, or Los Angeles, with at least one non-missing perceived racial/ethnic discrimination outcome at school, neighborhood, shop, or by police from the Moving to Opportunity (MTO)(n=2200). MTO randomized low-income families to a low poverty voucher (LPV), traditional voucher (TRV), or control group. We utilized the doubly robust adaptive least absolute shrinkage and selection operator to select effect modifiers (self-reported sex and city) in each voucher comparison group and discrimination setting. We estimated the effect of voucher receipt at baseline (1994-1998) on perceived discrimination in 2001-2002, stratifying by the previously identified effect modifiers, and using multiple imputation to address covariate missingness.

Results: Compared to no voucher, on average across cities, LPV receipt reduced the risk of perceived discrimination by police among boys (RD: -0.05; 95% CI: -0.11, 0). In Los Angeles, LPV receipt and TRV receipt, respectively, reduced the risk of perceived school (RD: -0.11; 95% CI: -0.18, -0.03), and neighborhood discrimination (RD: -0.06; 95% CI: -0.11, -0.02).

Conclusion: Offering vouchers to families in low-poverty neighborhoods may lower risk of perceived police, neighborhood, and school discrimination and its harmful effect on adolescent mental health. (U.S. Census Bureau authorization, CBDRB-FY24-CES018-005).

Prenatal exposure to race-based stressors and cardiovascular health: The Bogalusa Heart Study
Emily Harville* Emily Harville Maya David Patrizia Maria Santos Lydia Bazzano

Prenatal stress has been associated with cardiovascular health in offspring, and race-based stress may be particularly damaging. Bogalusa, Louisiana was a hotspot of the Civil Rights Movement and reactionary violence in the 1960s, while the Bogalusa Heart Study, a seminal study in childhood cardiovascular health, began in 1973. We aimed to examine whether cardiometabolic risk levels differed in children who were in utero during peak times of violence. We categorized time as "Bloody Bogalusa" (June-July 1965), early tensions (May 1964-May 1965), later tensions (August 1965-August 1966), and prior to (January 1960 to April 1964), and after this period (August 1966-December 1969). Mean levels of each cardiometabolic marker were examined by time period, stratified by race, with control for age, sex, and secular trend. Birthweight and gestational age were also examined. The study population was one-third Black (n=1277, 33.8%) and two-thirds white (n=2498, 66.2%). Mean age at study visit was 8.6 years. Sixty-two were born during the Bloody Bogalusa period, 437 in the period directly before, and 359 in the period directly after. The outcomes that most closely conformed to the hypothesis were glucose and gestational age: glucose levels were highest among Black children born during the Bloody Bogalusa period (beta=64.12 compared to the earliest period, p<0.01), and gestational age was lower for Black participants born during this time (beta=-1.29 weeks, p=0.05), while no difference was seen for white participants (p for interaction < 0.01 for both). However, for glucose, this is based on a very small number of births. In utero exposure was not associated with other outcomes. Effects of these prenatal exposures were insufficiently large to be clearly demonstrated in a sample of this size. Future studies will need to examine more detailed social and biological measures to identify which aspects of these events were relevant to health.

Medical mistrust and COVID-19 vaccine attitudes and behavior: Findings from a population-based cohort study in Michigan Soomin Ryu* Soomin Ryu Akash Patel Kristi L. Allgood Delvon T. Mattingly Jana L. Hirschtick Robert Orellana Nancy L. Fleischer

Background: Uptake of COVID-19 vaccines has stalled in the U.S. Some studies suggest that medical mistrust may be a barrier, but evidence is limited due to cross-sectional designs or convenience sampling.

Methods: We examined associations of self-reported measures of medical mistrust with COVID-19 vaccine attitudes at baseline and uptake of vaccination at follow-up using a population-based sample of adults in Michigan with PCR-confirmed SARS-CoV-2 infection between March 2020 and May 2022. We summed ratings for three items of the Medical Mistrust Index (MMI) to measure trust in healthcare providers. For vaccine attitudes, we averaged ratings for two items on importance of getting the COVID-19 vaccine. We defined vaccination uptake as ever receiving at least one dose of a COVID-19 vaccine. We conducted (1) linear regression models to examine cross-sectional associations between MMI and vaccine attitudes (n=3,863), (2) modified Poisson regression with robust standard errors to estimate prospective associations between MMI and vaccination status (n=3,502), and (3) effect-modification and stratified analysis by race and ethnicity.

Results: The mean MMI score was 1.89 (range: 1−4), where a higher score indicated a higher level of medical mistrust. The mean vaccine attitudes score was 3.45 (range: 1−5), with a higher score indicating a higher level of positive vaccine attitudes. At follow-up, the prevalence of receiving a COVID-19 vaccine was 77.5%. Higher MMI was associated with less positive vaccine attitudes at baseline (b= −0.63, SE= 0.036), and lower COVID-19 vaccine uptake at follow-up (aPR: 0.85, 95% CI: 0.82–0.88). Interestingly, these associations were more pronounced among non-Hispanic White individuals than among racial and ethnic minoritized individuals.

Conclusions: Understanding drivers of medical mistrust may help rebuild public trust in healthcare systems needed to promote vaccine uptake and improve public health.

The prospective associations of Long Covid with incident cardiovascular, respiratory, and metabolic diseases: Results from a population-based cohort study in Michigan Luis Zavala-Arciniega* Luis Zavala-Arciniega Lynda Lisabeth Robert C Orellana Nancy L Fleischer

Aim: To evaluate the prospective association of Long COVID (LC) with the incidence of cardiovascular, respiratory, and metabolic outcomes among adults.

Methods: We used data from the Michigan COVID-19 Recovery Surveillance Study, a population-based longitudinal study of adults with PCR-confirmed SARS-CoV-2 infection from March 2020 through May 2022 in Michigan. We included adults who responded to the baseline survey (median 5.3 months post-onset) and the first follow-up survey (median 21.9 months post-onset) and were free of the outcome at baseline. We categorized LC into three categories (never LC, recovered from LC, and current LC). We evaluated four self-reported incident outcomes: 1) hypertension (n=2,693), 2) heart rate or heart rhythm issues (n=3,426), 3) diabetes mellitus (n=3,374), and 4) asthma (n=3,201). We conducted modified Poisson regression to examine each prospective exposure-outcome association separately, controlling for baseline covariates age, sex, race and ethnicity, income, current smoking, body mass index, preexisting conditions, survey mode (telephone, online), and pandemic phase.

Results: In adjusted models, the incidence of hypertension, heart rate or heart rhythm issues, and asthma were all higher among adults who reported current LC compared to those who never reported LC (hypertension: RR=1.71 CI 95% 1.21, 2.43; heart rate and heart rhythm: RR=1.98 CI 95% 1.17-3.34; asthma: RR=3.13 CI 95% 1.92-5.07). However, current LC was not associated with a higher incidence of diabetes (RR=1.49, CI 95% 0.83-2.70). Interestingly, compared to never reporting LC, recovering from LC was not associated with any of the outcome measures.

Conclusion: These results suggest that experiencing persistent LC increases the risk of cardiovascular and respiratory diseases among adults. Our findings show the need to implement health policies to prevent onset of LC and improve health care for people experiencing LC.
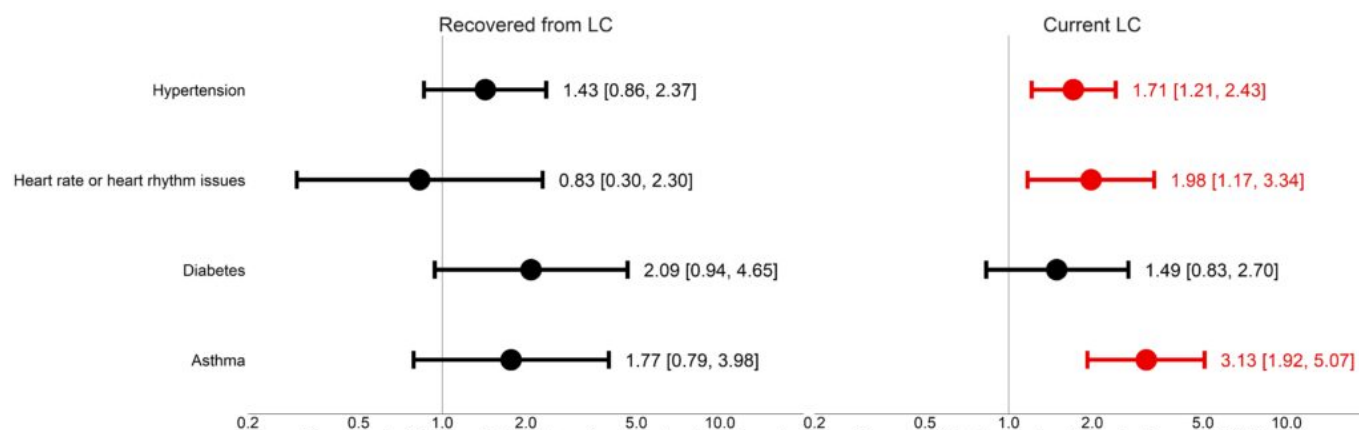

Figure 1. Incidence of Hypertension, heart rate or heart rhythm issues, diabetes and asthma by Long COVID status
Incidence Rate Ratio (IRR) [95% CI] Observations N = 2,693-3,426
Models adjusted by age, sex, race and ethnicity, income, pre-existing conditions, body mass index, smoking status, survey mode and pandemic phase

Evaluating Age-Based Transmission Dynamics of COVID-19 in Household Settings William Lyon* William Lyon Bridget Kruszka Ryan Murphy

Background: In this study, we aim to better understand the dynamics of household transmission of COVID-19, with a focus on age-specific transmission patterns within household clusters. Improved understanding of general household risk may inform public health recommendations in the future.

Methods: Using data from California's CalCONNECT contact tracing platform, a retrospective cohort study was conducted from June 2020 to June 2021 of COVID-19 households clusters. Possible transmission events in household clusters were identified when the serial interval of the household index case and a secondary case was 14 days or fewer. The index case was defined as earliest laboratory confirmed SARS-CoV-2 infection in the household. Odds ratios were calculated using a logistic regression model, adjusted for sociodemographic covariates at both individual and household levels. The resulting contrasts were visually displayed in a heatmap, scaled by probability.

Results: A total of 291,768 household contacts from 116,584 households with a COVID-19 index case were analyzed. Compared to the reference group of households with index cases aged 40-60 years, higher risk of transmission was found in households with index cases aged 0-5 (OR=1.08, 95%CI=1.03-1.13), 6-10 (OR=1.11, 95%CI=1.03-1.13), and 11-13 (OR=1.13, 95%CI= 1.07-1.18). Lower risk was noted for ages 14-18 (OR=0.93, 95%CI=0.90-0.95), 19-25 (OR=0.84, 95%CI=0.82-0.87), and 26-39 (OR=0.96, 95%CI=0.94-0.98). No significant risk difference was observed in households with index cases aged 65+ (OR=1.00, 95%CI=0.97-1.04). The interaction between the index and household contact age groups, particularly trends among young children and older adults, is visually detailed in heatmap format(see figure).

Conclusion: Younger COVID-19 index cases were associated with higher risk of transmission among household contacts. These results suggest an importance of age-based strategies in public health mitigation efforts against the spread of COVID-19.

Probabilistic Age Interaction Heatmap: Trends of COVID-19 Contact Infection Risk within 14 Days of Index Case (Derived from Adjusted Regression Model)
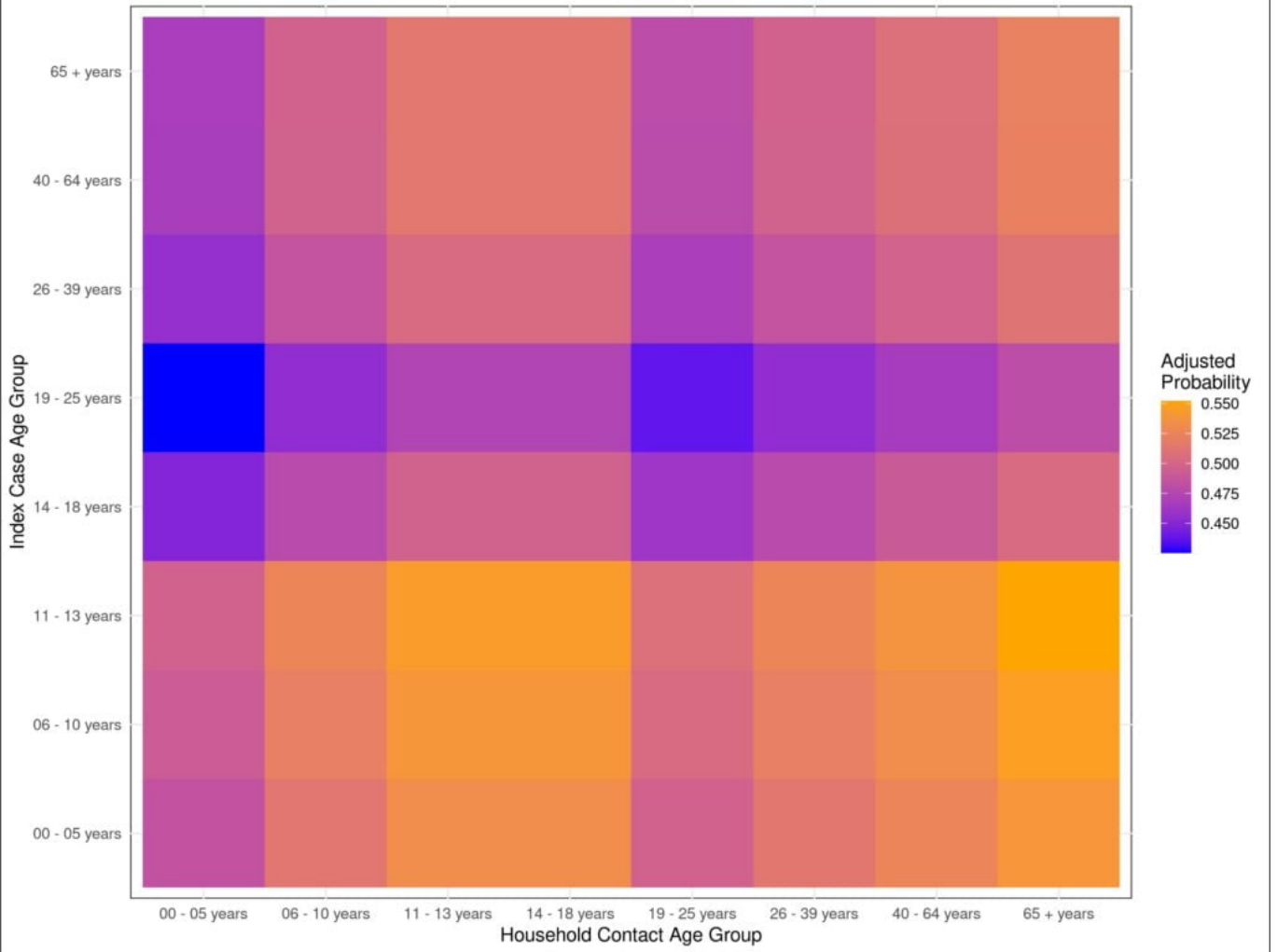
Is BMI Status Prior to SARS-CoV-2 Infection Associated with Post-acute Sequelae of SARS-Cov-2 Infection? Findings from 172,136 Pediatric Individuals in the RECOVER Initiative

TING ZHOU* TING ZHOU Bingyu Zhang Dazheng Zhang Qiong Wu Michael J. Becich Saul B. Blecker Jiajie Chen Nymisha Chilukuri Haitao Chu Elizabeth A. Chrischilles Leonor Corsino Carol R. Geary Susan Kim David M. Liebovitz Yiwen Lu Chongliang Luo Hiroki Morizono Abu SM. Mosa Nathan M. Pajor Suchitra Rao Srinivasan Suresh Yacob G. Tedla Leah Vance Utset David A. Williams Caren Mangarelli Ravi Jhaveri Christopher B. Forrest Yong Chen

BACKGROUND The role of elevated body mass index (BMI) as a modifiable risk factor for post-acute sequelae of SARS-CoV-2 infection (PASC) among the pediatric population is not rigorously investigate. We aim to quantify the association between BMI status prior to SARS-CoV-2 infection and the risk of PASC among the pediatric population.

METHODS In this retrospective cohort study spanning from March 1, 2020, to May 31, 2023, using data from 26 children's hospitals and health institutions in the US, a total of 172,136 individuals aged 5 to 21 years who were diagnosed with SARS-CoV-2 infection were followed up through 179 days. We used both ICD-10 code U09.9 for post-COVID-19 condition, unspecified and potential computable PASC phenotypes as the PASC outcomes and examined their incident occurrences among the pediatric population within 28 to 179 days following the initial SARS-CoV-2 infection. BMI status prior to SARS-Cov-2 infection (healthy weight, overweight, obesity, and severe obesity) was assessed within 18 months prior to SARS-CoV-2 infection and the latest measure was selected if there were multiple measures. Among participants with SARS-CoV-2 infection, we estimated a relative risk (RR) for the association between BMI status and PASC using Poisson regression and modified Poisson regression adjusting for sociodemographic and clinical factors, i.e., age, sex, race and ethnicity, predominant variant, healthcare utilization metrics prior to cohort entry, the Pediatric Medical Complexity Algorithm (PMCA) index, and severity of acute phase COVID-19. We performed sensitivity analyses to validate our findings by accounting for the time of BMI status assessment, release date of the U09.9 ICD-10 code, time of taking serology testing, severity of the acute phase of COVID-19, COVID-19 vaccination status, type of health insurance, diabetes as a comorbidity, and use of weight loss drugs.

RESULTS Among 172,136 participants with SARS-CoV-2 infection, the median age of BMI status assessment was 12.8 years, the median age of cohort entry was 13.2 years, and the median time from BMI status assessment to COVID-19 infection was 4.1 months. Among all participants, 90,187 (52.4%) were female, 87,275 (50.7%) were non-Hispanic White, 42,982 (25.0%) were Hispanic, 33,065 (19.2%) were Non-Hispanic Black, 8,814 (5.1%) were Asian American/Pacific Islander, and 85,613 (49.7%) had obesity or severe obesity. A total of 1,385 (0.8%) participants were identified as having PASC with a U09.9 diagnosis code, and 74,317 (43.2%) had at least one incident occurrence of the potential PASC phenotypes during the follow-up period. Compared with participants with a healthy weight, those who had overweight, obesity, and severe obesity had 4.0% (RR, 1.040; 95% CI, 0.861-1.255), 25.2% (RR, 1.252; 95% CI, 1.062-1.477) and 40.8% (RR, 1.408; 95% CI, 1.241-1.598) higher risk of PASC when identified using U09.9, respectively. For potential PASC phenotypes, the RRs of any occurrence in the categories of overweight, obesity, and severe obesity compared to the healthy BMI category were 1.030 (95% CI, 0.982-1.080), 1.108 (95% CI, 1.064-1.109), and 1.174 (95% CI, 1.138-1.213), while the corresponding estimates of total occurrence were 1.053 (95% CI, 1.000-1.109), 1.137 (95% CI, 1.088-1.188), and 1.182 (95% CI, 1.142-1.223), respectively. Results were comparable in the sensitivity analyses.

CONCLUSIONS In this large, retrospective pediatric cohort study, overweight, obesity, and severe obesity was associated with a higher risk of PASC in a dose-dependent manner. Future research endeavors should expand the spectrum of PASC outcomes by incorporating newly elucidated PASC phenotypes.

Vaccine effectiveness estimates from a test negative design without controlling for prior infection underestimate true vaccine effectiveness Ryan Wiegand* Ryan Wiegand Bruce Fireman Morgan Najdowski Mark Tenforde Ruth Link-Gelles Jill Ferdinands

Test negative designs (TNDs) are frequently used to assess vaccine effectiveness (VE). For COVID-19 vaccines, differences in infection-induced protection between vaccinated and unvaccinated individuals may confound the association between vaccination and outcomes but ascertaining infection history can be challenging, especially for capturing asymptomatic or paucisymptomatic infections. Failure to account for infection history may bias VE estimates. We simulated individual-level SARS-CoV-2 infection and COVID-19 mRNA vaccination histories from January 19, 2020, to May 13, 2023. Simulated vaccination rollouts and TNDs were used to calculate VE against infection and against severe disease. VE was calculated from logistic regression models as (1-OR)*100%. Models were either unadjusted for infection history (uncontrolled) or were adjusted for the months since last infection and number of prior infections (controlled). Bias was assessed in estimates of VE from controlled as well as uncontrolled models compared to VE calculated without infection-induced protection. Uncontrolled models typically underestimated VE more than controlled models (Figure). For vaccination in the last 3 months, mean bias for protection against infection was -4.8 percentage points (pp) (95% CI -5.7, -3.9) for uncontrolled analyses and -3.0 pp (CI -3.9, -2.0) for controlled analyses, and mean bias for protection against severe disease was -4.0 pp (CI -5.5, -2.4) for uncontrolled and -2.4 pp (CI -4.0, -0.7) for controlled. When VE approaches zero, such as when vaccine-induced protection has waned, failure to account for infection history may result in a VE estimate below zero, e.g., in uncontrolled analyses, VE against infection 5-11 months since vaccination was -2.4% (CI -2.7, -2.0). VE estimates from TNDs without prior infection information tended to underestimate VE, in most scenarios by less than 8 percentage points.
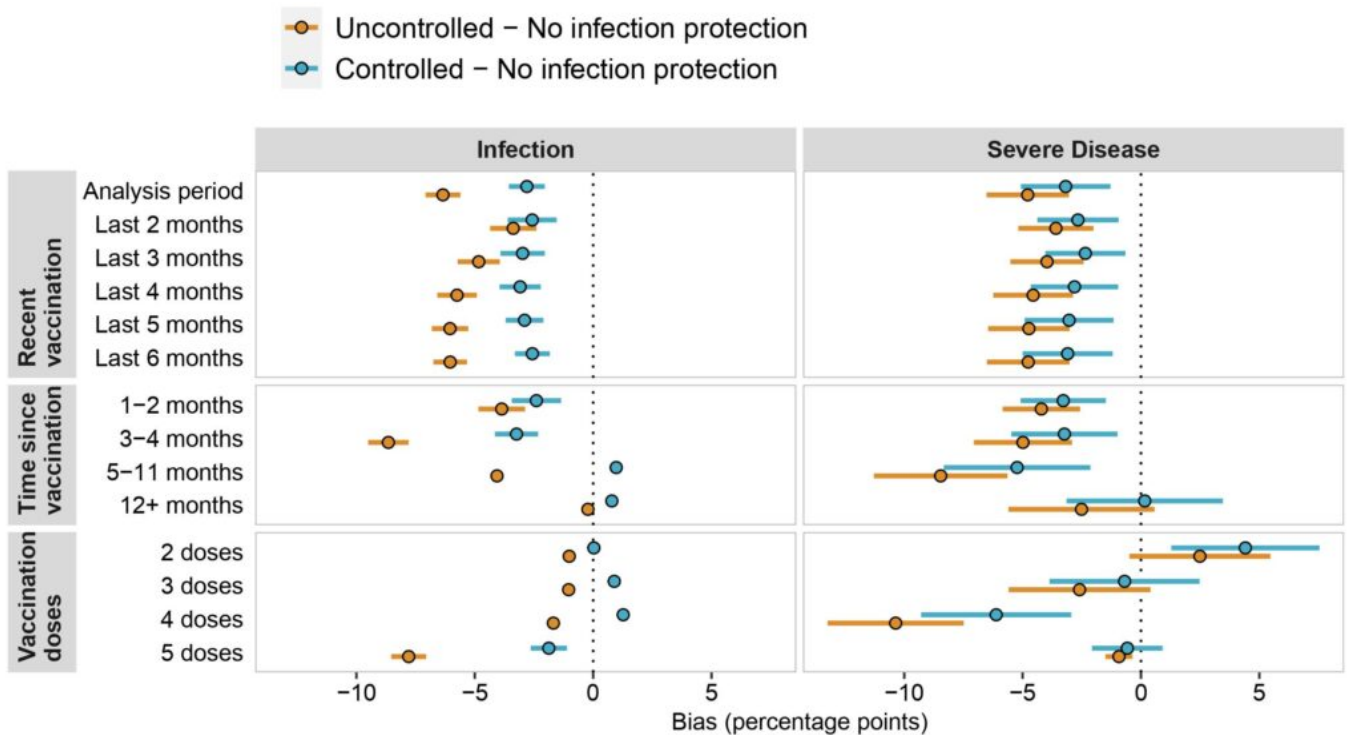
Uncovering Patterns in Overdose Deaths: An Analysis of 'Spikes' in Massachusetts Fatal Overdose Data, 2017-2022 Hannah Lee* Hannah Lee Lee Erin Stringfellow Huiru Dong Mohammad Jalali

Research Objective: Two overdose-related trends have emerged in recent years both nationally and in Massachusetts. First, fatal overdoses increasingly involve stimulants like methamphetamine and cocaine. Second, racial disparities are increasing, with the rate of overdoses among Black and/or Hispanic populations now exceeding that of Whites in recent years. There is some speculation that these growing deaths, especially among Black people, are due to contamination of cocaine with fentanyl, which could result from sudden changes in the drug supply. At the same time, first responders often report that periods of calm are followed by a sudden rise in overdoses, which could also point to exogenous supply shocks. In this exploratory analysis, we assessed whether spikes were associated with differences in the drugs involved in deaths or in the race and ethnicity of the people who were dying.

Study Design: To identify spikes in overdose deaths, we used a peak detection algorithm, leveraging z-scores, which is characterized by its robustness, adaptability through lag, threshold-based signaling for significant deviations, and the influence parameter governing the impact of new signals on the calculation of moving mean and standard deviation. Spikes were defined conservatively as deaths exceeding 2.5 rolling standard deviations above the 30-day rolling average. Then, we analyzed the distribution of race and drugs involved on days identified as spikes and those not identified as such. We categorized drugs involved in deaths as: opioid without fentanyl; fentanyl without stimulants; non-cocaine psychostimulants with and without fentanyl; cocaine with and without fentanyl; and both non-cocaine psychostimulants and cocaine.

Population Studied: The study population consisted of 9,990 individuals recorded in Massachusetts' vital statistics data from 2017-2022 who had experienced a fatal overdose incident. Among these individuals, the median age was 42, 72.2% were males, and 69.2% were White.

Principal Findings: On average, the number of daily deaths in Massachusetts ranged from 4.2 in 2017 to 5.2 in 2022. There was an average of 11.7 spikes in overdose deaths per year. After aggregating the counts of overdose deaths for spike and non-spike days separately throughout the years, we did not find any differences across races (p-value = 0.963) and types of drugs involved (p-value = 0.780) among total overdose deaths in spike days compared to non-spike days. The same results were found when considering each year separately.

Conclusions: Our results suggest that certain days in Massachusetts witnessed a higher number of overdose deaths than anticipated solely based on individual-level variations, potentially attributed to factors influencing people who use drugs as a whole. However, the lack of identified relationships between spike days and drug involvement or the race and ethnicity of the people who died of overdose suggest that significant supply shocks might not be contributing to the growing involvement of stimulants in overdose deaths or to growing racial disparities. We note limitations in our current analysis (primarily, low levels of granularity) that could be leading to false negative conclusions.

Implications for Policy or Practice: Given that the current analysis does not point to an obvious difference in the race and ethnicity of those who are dying on spike days, or in the drugs involved,

there may be continuous underlying trends that are more explanatory regarding racial disparities and stimulant involvement. These should be investigated as rigorously as the current narrative around drug contamination.

Non-fatal overdose and naloxone possession prevalence among adults experiencing homeless; Results from the California Statewide Study of People Experiencing Homelessness Ryan D. Assaf* Ryan D. Assaf Meghan D. Morris Margot Kushel

Overdose is the leading cause of death among people experiencing homelessness (PEH), but little is known about non-fatal overdose and overdose prevention efforts in this population. There are over 181,000 PEH nightly in California, representing 28% of those experiencing homelessness and half of those experiencing unsheltered homelessness in the US. Using cross-sectional data from a representative sample of PEH in California, we estimated non-fatal overdose and naloxone possession prevalence, overall and by substance use behaviors. We weighted participant (n=3,200) responses to represent the statewide adult PEH population and calculated weighted distributions for prevalence estimates. The median age was 46 years (IQR 35.9, 55.8), two-thirds were cisgender men (67.3%) with similar distributions of White (27.9%), Latinx (26.4%), and Black and African American (26.3%). Lifetime and recent (during current homelessness episode) non-fatal overdose prevalence was 19.6% and 10.0%, respectively **(Figure 1)**; of those with lifetime non-fatal overdose, half (52.4%) experienced a non-fatal overdose during their current episode of homelessness. Of those with a recent non-fatal overdose experience, 34.6% reported any meth/amphetamine and opioid use in the last 6 months, 21.4% reported any meth use only, and 15.7% reported any meth, opioids, and cocaine/crack cocaine use; 35.1% of those with a recent non-fatal overdose reported injecting substances in the last 6 months. One-quarter (24.9%) possessed naloxone; 43.4% of those with lifetime non-fatal overdose possessed naloxone, 56.7% of those with a recent non-fatal overdose did, and 20.3% who never had a non-fatal overdose did. Non-fatal overdose is prevalent among PEH and concentrated in those who used more than one illicit substance, who used meth only, and who did not inject drugs. There is a need to increase overdose prevention in PEH. Increasing naloxone possession could reduce the risk of fatal overdose.

Figure 1: Prevalence of non-fatal overdose and naloxone possession among adults experiencing homelessness in California, 2021-2022
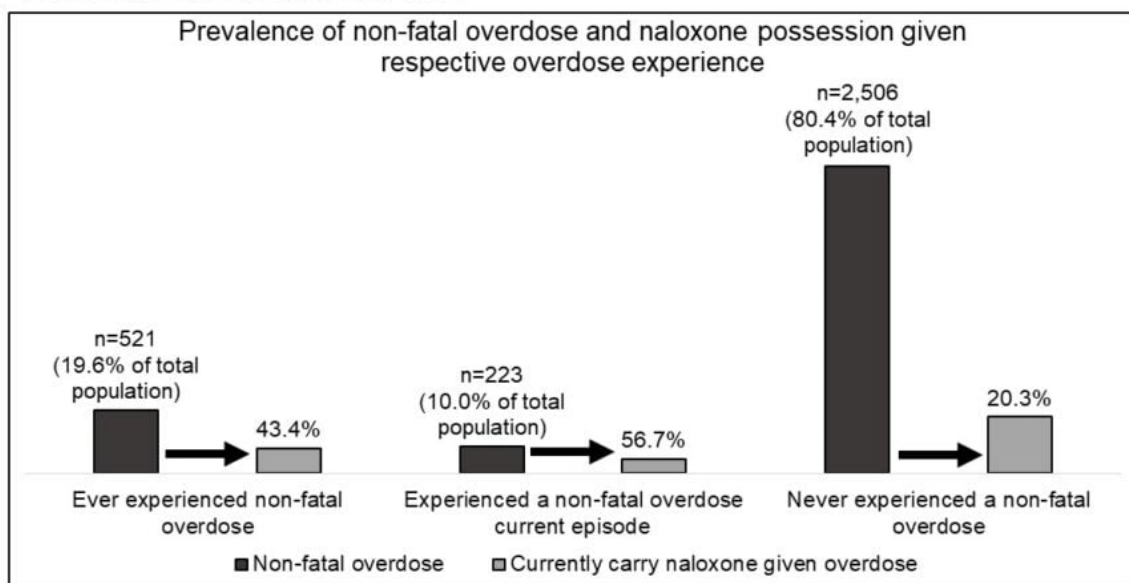
aPercent is a weighted percent of the sample to represent the adult population of people experiencing homelessness in California

Frequency of supervised consumption service use and acute care utilization in people who inject drugs Ayden Scheim* Ayden Scheim Zachary Bouck Zoë R. Greenwald Vicki Ling Shaun Hopkins Matt Johnson Ahmed Bayoumi Tara Gomes Dan Werb

Background: Supervised consumption service (SCS) use among people who inject drugs may reduce acute care utilization; however, prior studies have been limited by self-reported data and dichotomous exposures.

Methods: We conducted a prospective cohort study using linked questionnaire and health administrative data among people who inject drugs in Toronto, Canada (2018–2020). Baseline SCS use frequency was defined by a participant's self-reported proportion of injections performed at an SCS over the past six months: "all/most" (≥75%), "some" (26–74%), "few" (1–25%), or "none" (0%). Outcomes measured over the following six months included: emergency department (ED) visits; hospitalizations; ED visits or hospitalizations for opioid-related overdose; and hospitalizations for injection-related infections. The relative effects of varying SCS use levels on study outcomes were estimated using inverse-probability-weighted negative binomial regression models.

Results: Of 467 participants, 25.5%, 30.4%, 28.7%, and 15.4% respectively reported "all/most", "some", "few", and "none" levels of SCS use at baseline. SCS use frequency was not associated with ED visits, hospitalizations, or hospitalizations for injection-related infections. Participants reporting "some" SCS use had a higher rate of ED visits or hospitalizations for opioid-related overdose (versus "few"; rate ratio=2.30, 95% confidence interval=1.15–4.61).

Conclusions: In this first SCS evaluation linking client surveys to comprehensive health administrative data, SCS use had little impact on objectively measured acute care utilization, which was high overall. Results highlight the importance of disaggregating heterogeneous SCS use patterns and considering (non)comparability of SCS user and non-user groups.

Evaluating the predictive performance of administrative data sources to forecast overdose deaths at the neighborhood level with machine learning in Rhode Island John Halifax* John Halifax Bennett Allen William Goedel Benjamin Hallowell Maxwell Krieger Alex Skinner Magdalena Cerdá Brandon Marshall Daniel Neill Jennifer Ahern
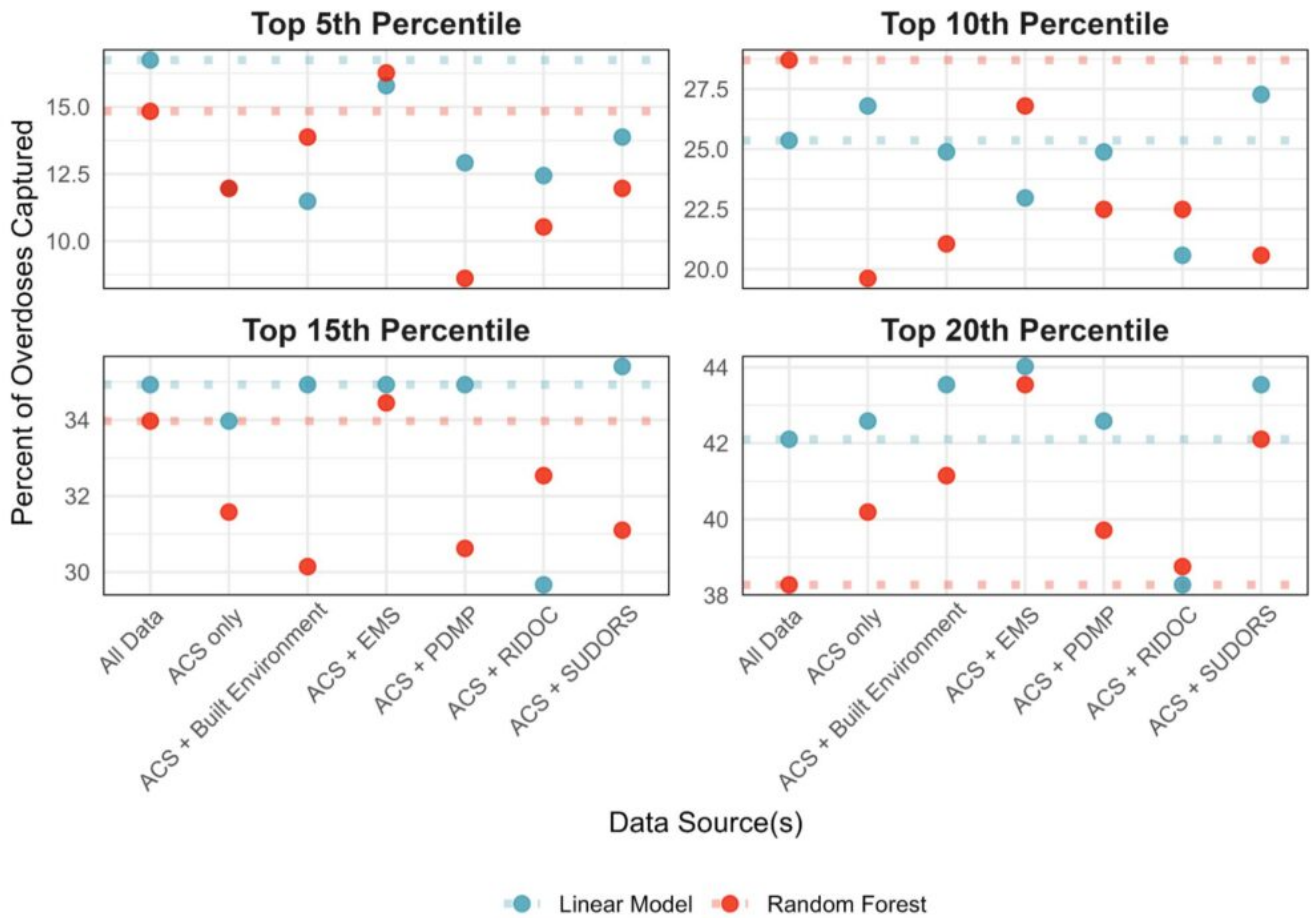
Street-based harm reduction efforts (including mobile outreach) to people who use drugs is a practical and cost-effective delivery model for overdose prevention. The PROVIDENT trial in Rhode Island evaluates the effectiveness of machine learning (ML) predictive analytics to forecast overdoses and prioritize neighborhoods for mobile outreach. Rhode Island is uniquely positioned to adopt this approach due to its robust overdose surveillance system. In other jurisdictions, fewer data sources may be readily available.

To provide a template for other settings where data availability may be limited, we evaluate the predictive performance of seven combinations of data sources across two ML models. Public American Community Survey (ACS) data was used as the starting set, with other sources across five domains (built environment, emergency medical services [EMS] non-fatal overdose response, prescription drug monitoring program [PDMP], carceral release, and historical fatal overdose data) appended separately. A seventh dataset merged all six data sources. The two prediction approaches were linear regressions and random forests embedded in a nested cross-validation design. The primary outcome was continuous fatal overdose at the census block group (CBG) level, which was used to calculate the proportion of statewide overdoses captured by CBGs in top percentiles by predicted fatal overdose.

Preliminary results indicate that ACS and EMS data together frequently outperformed or at least neared models trained on all data sources. Both modeling approaches performed well, with linear regressions generally outperforming random forests. Findings suggest that neighborhood-level fatal overdose prediction is feasible using ACS data combined with only one other public health data source, establishing an accessible template. Initial results demonstrate that jurisdictions may be able to leverage existing data to accurately predict area-level overdose to guide targeted overdose prevention.

Figure 1. *Proportion of statewide overdoses in Rhode Island between July-December 2021 captured in the top 5%, 10%, 15%, and 20% of CBGs by predicted overdose. Performance by linear models is shown in blue, and performance by random forest models are shown in red. Dashed lines indicate the performance of the models trained on all data sources*

CBG, Census block group. ACS, American Community Survey data. EMS, Emergency medical service runs for nonfatal overdose data. PDMP, Prescription drug monitoring program data. RIDOC, Rhode Island Department of Corrections prisoner release data. SUDORS, State Unintentional Drug Overdose Reporting System prior six-month fatal overdose count data.

Substance Use

Spatial Epidemiology of Nonfatal Overdose in a Community-Based Cohort of Marginalized Women in Vancouver, British Columbia (2014-2022) Shira Goldenberg* Shira Goldenberg Esteban Valencia Ofer Amram Kate Shannon Charlie Zhou Kathleen Deering

Given limited data regarding the spatial epidemiology of overdose among women amid the current overdose crisis, we evaluated the spatial epidemiology of nonfatal overdose in a cohort of marginalized women, including (a) potential changes in spatial clustering over time, and (b) the association between residential proximity to spatial overdose clusters and recent nonfatal overdose over 8-years. Baseline and follow-up questionnaire data were from a merged community-based cohort of marginalized women who use drugs in Vancouver, Canada (09/2014-08/2022). Kernel density estimation and hotspot analysis were used to describe the spatial distribution and clustering of overdose; bivariate and multivariable logistic regression with generalized estimating equations (GEE) modeled the association between residential proximity to spatial overdose clusters (assessed as living in or within 250, 500, or 750m of an overdose cluster) and recent (last 6 months) nonfatal overdose. Over the 8-year study, among 650 participants (3497 observations) the period-prevalence of recent nonfatal overdose was 36.0%. Annual prevalence of nonfatal overdose increased over the study, from 6.7% in 2014-15 to 14.3% in 2021-2022. 44.5% (n=289) of participants resided within an overdose cluster at least once during the study. Most overdoses occurred in Vancouver's downtown and downtown eastside/Strathcona neighborhoods (78.7%). The highest-density clusters were in the downtown eastside/Strathcona, where clusters became larger and more dispersed from 2016-onwards. Multivariable GEE analysis indicated that residential proximity to overdose clusters was associated with higher odds of recent nonfatal overdose. Marginalized women face a high and rising burden of nonfatal overdose, which is influenced by the spatial 'risk environments' in which they reside. Scale-up of geographically tailored overdose prevention services, harm reduction, and safe housing for marginalized women are critically needed.

Figure 1. Multivariable GEE logistic regression models of the association between residential proximity to neighborhoods characterized by high density of overdose and recent nonfatal overdose among marginalized women in Vancouver, BC, 2014 - 2022
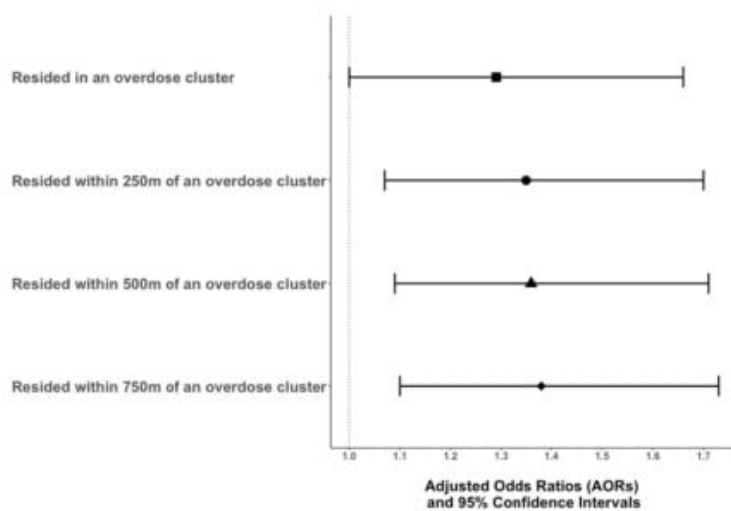
NOTE: Models adjusted for minoritized sexual orientation, racialization, lifetime mental health diagnosis, unstable housing, and whether an interview was conducted prior to or during the COVID-19 public health emergency (April 2020-onwards)

A call for guidance on when using multiple imputation to predict missing race and ethnicity data is ethical Arshya Gurbani* Arshya Gurbani Karen Nielsen Kevin Maloney Jalyane Arias

The case for disaggregated and complete race and ethnicity data is clear: it is necessary to measure disparity in order to address it. Yet, despite guidance on the necessity of collecting data on race and ethnicity, large gaps remain in administrative healthcare and national data sets. Multiple imputation (MI) has gained popularity as an approach to avoiding biases in the presence of missing data. Some argue that the cost of collecting accurate race data at study onset may be more burdensome than the risks of imputation, while others contend that intentional representation in studies and greater standardization of how race and ethnicity data are collected are a more sustainable route. Implementation guidance for MI focuses on the validity and sensitivity of specific MI methods. However, there remain critical gaps to assure the ethical adoption of imputation methods and evaluating the consequences of their use. Ethical guidance is important to determine whether imputation is appropriate and in the subsequent dissemination of results. There is little guidance available from the government, funders, or academia on how to handle missing race/ethnicity data when conducting imputation. Compelling guidance from the Urban Institute calls for impact assessments of the decision to impute, community representation throughout the data life cycle, clearer informed consent policies for subsequent use of secondary and missing data, and thresholds of acceptable benefit/burden considerations. This call for guidance should be amplified from within academia as well-it's a conversation that should be had by epidemiologists and statisticians in conjunction with ethicists. This paper explores the extent of missing race data in large secondary health data sets, identifies gaps in established methods for imputing data, and makes a case the need for both ethical and statistical guidance both while analyzing and while communicating results of analyses involving imputed race data.

Privacy-preserving record linkage in community settings: merging EMR & HMIS data
Paulina Kaiser* Paulina Kaiser Zoe Herrera Carson Mowrer Jonathan Ratliff Cory Hackstedt Barbara Hanley Mark Edwards

The difficulty of merging siloed datasets, especially datasets that include identifiable information, is a major barrier in epidemiologic research. Privacy-preserving record linkage (PPRL) allows investigators to match individuals across datasets using cryptographically hashed information instead of direct identifiers. We used this technique to explore how characteristics of homelessness were associated with health status and healthcare utilization in a three-county suburban region in Oregon. We merged electronic medical records data from a regional healthcare system with data from the local HUD-designated community action agency's Homeless Management Information System (HMIS). The EMR dataset included measures of healthcare utilization (urgent care visits, ED visits, and hospitalizations) and total costs for members of Oregon's Medicaid program. The HMIS dataset included assessments of social history and vulnerability. We merged on a hashed ID created from first name, last name, and date of birth, resulting in a total of 775 individuals matched across datasets at a similarity threshold of 0.85. Individuals in the merged dataset were 58% male and 88% white. Compared to individuals with a low vulnerability index score, those with high vulnerability were more likely to have two or more ED visits in 2022 (48% vs 36%) and were more likely have two or more urgent care visits (11% vs 6%). Individuals defined as chronically homeless were more likely to have multiple ED visits (43% vs 29%) and multiple hospitalizations (9% vs 3%) compared to the non-chronically homeless. Additional analyses are planned, including multiple regression models. PPRL offers a practical, low-cost way to overcome barriers to merging HIPAA-protected identifying information across siloed datasets. This technique is feasible in community-based settings and has potential to inform targeted interventions to improve population health outcomes.

Deriving residential histories for population health research: An example from the Sister Study Patrick Ringwald* Patrick Ringwald Diane Ng David Stinchcomb Deborah Bookwalter Aimee D'Aloisio Jennifer Ish Dale Sandler Alexandra White

Background: Epidemiologic studies of cancer etiology are increasingly focused on the impact of environmental exposures over the life course. Obtaining complete and accurate residential histories for study participants, however, is often costly or impractical. **Purpose:** To apply a method for deriving residential histories in the Sister Study cohort to assess residential mobility from 1980 through enrollment (2003-2009). **Methods:** We submitted a file with participant names and identifiers (e.g., DOB, baseline address) for the full cohort of 50,884 women (ages 35-74 years) to a commercial data vendor (LexisNexis) for address linkage. The returned addresses were combined with existing self-reported addresses and geocoded to build a comprehensive residential history. Addresses outside of the 1980-2009 period were excluded; further, we linked the USPS Residential Delivery Indicator to identify and exclude businesses. The cleaned dataset was then processed with free, open-source SAS programs developed by Westat which use an algorithm to match and combine common addresses and to resolve overlaps/gaps between dates. Modifications were made to prioritize participant's self-reported addresses. **Results:** LexisNexis returned at least one address for 93.5% of the cohort. Those older than 64 at enrollment were less likely to be matched compared to the younger women. On average, we received 8 addresses per person for the years of interest. We excluded 15,414 businesses (4% of addresses returned). Based on the available data, we derived complete residential histories covering 1980 through enrollment for 40% of participants with improved results over time (74% starting in 1985; 96% starting in 1990). **Conclusion:** We have demonstrated a practical approach to assessing residential mobility in a large, national prospective study by sourcing commercial address data, using an open-source algorithm, and integrating with self-reported residence data to generate plausible residential histories.

Methods/Statistics

Towards a methodology for community-based spatial epidemiology: Lessons from the collection, geocoding, and analysis of unstructured location data within a community-based research setting Esteban J. Valencia* Esteban J. Valencia Kathleen Deering Shira Goldenberg Kate Shannon Hoaxuan Zhou Ofer Amram

Background

Spatial epidemiology within community-based research can uniquely advance knowledge on the social ecology of health for marginalized peoples, particularly within micro-level environments. Yet spatial methods require precise, structured location data. For community-based researchers using self-report tools that collect unstructured location data, there is no standard approach for data collection and geocoding. To address this, we review the collection, geocoding, and analysis of unstructured location data from community-based research with marginalized women. We further synthesize these processes into a framework for collecting and geocoding unstructured location data.

Methods

We draw on two community-based cohort studies of a) sex-workers and b) women living with HIV, from Vancouver, Canada (2010-2023). Location data were elicited using self-report, and include: place of residence, overdose events, healthcare access sites (e.g., HIV care), and experiences of violence. We detail an approach to parse and geocode unstructured location data and evaluate the quality of resultant coordinates. We used these data to create variables representing novel integrations of socio-structural and spatial components.

Results

Median participant age was 35 years, 38% were Indigenous, and 66% were women of color. Over 13 years, 981 participants contributed 89207 location data points, 81% of which were successfully geocoded. Almost half of all coordinates corresponded to one of 300 distinct sites in Vancouver. Data were used to create socio-structural variables, such as residential proximity to spatiotemporal clusters of non-fatal overdose or experiences of gender-based violence.

Discussion

For community-based researchers who rely on self-report tools, we provide a unique methodological framework demonstrating how the collection of unstructured location data can be used to understand intersections between spatial epidemiology and the social ecology of health for marginalized peoples.

Identifying Equity Focus Areas within the City of Milwaukee: A Multivariate Geo-Spatial Index Integration Approach for Strategic Interventions Sivani Manchu* Feras Rizeq Sivani Manchu

This report presents a comprehensive geospatial analysis aimed at establishing an Equity Focus Area within the city of Milwaukee. The analysis integrates three crucial indices: The Milwaukee Childhood Opportunity Index (MCOI), the Milwaukee Asset Index (MAI), and Milwaukee Health Department Outcome Vulnerability Index (MHDOVI). By leveraging these indices, the study aims to identify areas within Milwaukee that require targeted interventions to promote equity and enhance the overall quality of life for its residents.

The MCOI assesses the quality of opportunities available to children in different neighborhoods, encompassing education, healthcare, safety, economic and social support. The MAI evaluates the distribution of essential resources and amenities, reflecting economic disparities and accessibility to critical services. The MHDOVI identifies and addresses health disparities by quantifying and assessing the vulnerability of different populations to health risks and challenges.

The analysis encompasses data collection, data integration, spatial analysis, index computation, and equity focus area identification. By applying geospatial techniques to these indices, the study unveils patterns of inequity across Milwaukee's landscape. These findings facilitate the identification of areas in need of strategic investments and interventions, ensuring that resources are allocated to areas with the highest potential for positive impact.

These insights are invaluable for policymakers, urban planners, and community advocates striving to cultivate a more equitable city. By synthesizing multidimensional data, this analysis fosters a holistic understanding of disparities, enabling evidence-based decisions to be made in the pursuit of a fairer and more inclusive Milwaukee. As cities worldwide grapple with issues of equity, this report serves as a model for utilizing geospatial analysis and index integration to drive positive change and create lasting impact within urban communities.

Big Data/Machine Learning/AI

Personalised dynamic prediction in dialysis using a novel super learning framework Arthur Chatton* Arthur Chatton Michèle Bally Renée Lévesque Ivana Malenica Robert W Platt Mireille E Schnitzer

Obtaining continuously updated predictions is a major challenge for personalized medicine. In end-stage kidney diseases, a major cause of morbidity and mortality worldwide, dialysis is the standard therapy. However, achieving high blood-filtered volumes time after time and across patient populations requires clinical skills and readily accessible information and data. Nephrologists and nurses must continually re-assess multiple parameters refreshed with each HDF session and consider time-varying clinical status changes, which is daunting in busy dialysis centres.

Dynamic prediction models provide predicted outcome values that can be updated over time for an individual as new measurements become available. Previous approaches to prediction were mainly based on parametric models, but there is a current trend towards using more flexible machine learning approaches. Ensemble methods leverage combinations of parametric regressions and machine learning approaches into one final prediction.

We extend an ensemble method called super learner for (i) dynamically predicting a repeated continuous outcome and (ii) optimizing the prediction for the patients the clinician faces up by combining approaches trained on the personal history of the patient or on an external (i.e., "historical") cohort. We also propose a new way to validate such personalized prediction models. We illustrate its performance by predicting the convection volume of patients undergoing hemodiafiltration, a specific dialysis technique, in Montréal, Canada.

The personalized dynamic super learner outperformed its candidate learners with respect to median absolute error, calibration-in-the-large, discrimination, and net benefit. We finally discuss the choices and challenges underlying its use and implementation.

Symptoms of depression and anxiety and use of generative artificial intelligence, the metaverse, and social media and among U.S. adults Catherine Ettman* Catherine Ettman Alice Y. Fan Ross Hatton Haiyang Yang Salma M. Abdalla Sandro Galea

Advances in digital technologies such as generative artificial intelligence (AI), the metaverse, and social media are transforming society. There is growing concern about the link between digital technologies and mental health, but few studies have explored whether mental health is associated with use of newer digital technologies, such as ChatGPT and the metaverse, among the general adult population. Using data from the COVID-19 and Life Stressors Impact on Mental Health and Well-Being (CLIMB) study, a nationally representative, probability-based sample of U.S. adults collected in March-April 2023 (N=2,479), we explored the relation between positive screen for generalized anxiety disorder (GAD-7 ≥ 10) or depression (PHQ-9 ≥ 10), demographic characteristics, and financial assets with the use of generative artificial intelligence (AI), metaverse, and social media. We used multivariable logistic regressions to estimate the odds of having ever used generative-AI such as ChatGPT, having ever used the metaverse, and using social media for more than 3 hours per day (which was the median number of daily use among responders), adjusting for mental health and demographic characteristics. Survey weights aligned the sample with the U.S. adult population according to the Current Population Survey. Persons who screened positive for anxiety or depression were more likely to report having ever used the metaverse and using social media for 3 or more hours a day but were not more likely to report having ever used generative-AI. Persons with positive screen for depression or anxiety are more likely to use the metaverse and use social media for more than 3 hours per day, suggesting that these platforms may each be used to engage persons with poor mental health. These findings highlight different associations between mental health and digital technology use, potentially paving the way for targeted mental health guardrails to ensure that potential adverse impacts of digital technologies are mitigated.

Causal Inference

A Comparison of Causal Forests and the DR-Learner for Estimating Conditional Average Treatment Effects Qi Zhang* Qi Zhang Ya-Hui Yu Ashley Naimi

Conditional average treatment effects (CATEs) hold great promise for precision medicine, particularly in settings where effect modification is likely. Theoretical work has developed methods to estimate CATEs, including the double-robust (DR) learner and the causal forest algorithm. Here, we conduct a simulation study comparing the finite sample properties of the DR learner and the causal forest algorithm. We explore performance in a range of scenarios with a binary effect modifier and when a set of conditioning variables are included with varying degrees of effect modifiers present. Scenarios explored different effect parametrizations, sample sizes, proportions of modifying to non-modifying variables, and number of confounding variables. For all analyses, we used 10-fold cross fitting, and linear projection approach to identify pre-specified modifiers. Our preliminary results suggest that both the causal forest and the DR learner have good 95% confidence interval coverage in most settings. However, the DR learner outperformed the causal forest in coverage (93% vs. 88%) under the scenarios of strong treatment effect but low heterogeneity. We also found that the best linear projections may not always reliably identify pre-specified effect modifiers when either method is used, especially in small sample sizes (with a successful identification of 53% at best scenario). This will provide practical insights to guide method selection for estimating CATEs in empirical research.

Simulations to improve the rigor & reproducibility of real-data applications Nerissa Nance*
Nerissa Nance Maya Petersen Mark van der Laan Laura Balzer

The Roadmap for Causal Inference outlines a systematic approach to our research endeavors: define the effect of interest, evaluate needed assumptions, conduct statistical estimation, and carefully interpret results. At the estimation step, it is essential that the estimation algorithm be carefully pre-specified to optimize its expected performance for the specific real-data application. Simulations that realistically reflect the application, including key characteristics such as strong confounding and rare or missing outcomes, can help us gain a better understanding of an estimator's performance and achieve this goal. We illustrate this with two examples, using the Causal Roadmap and realistic simulations to inform estimation selection and full specification of the Statistical Analysis Plan. First, in an observational longitudinal study, outcome-blind simulations are used to inform nuisance parameter estimation and variance estimation for longitudinal targeted maximum likelihood estimation (TMLE). Second, in a cluster-randomized control trial with missing outcomes, exposure-blind simulations are used to ensure control for type-I error in Two-Stage TMLE. In both examples, realistic simulations empower us to pre-specify an estimator that is expected to have strong finite sample performance and also yield quality-controlled computing code for the actual analysis. Together, this process helps to improve the rigor and reproducibility of our research.

Leveraging natural language processing to identify housing and income insecurity concepts from clinical notes of patients with opioid-related disorders Shivani Mehta* Shivani Mehta Hyelee Kim Matthew S. Pantell Tasce Bongiovanni James D. Harrison William Brown, III

Introduction: Electronic health records (EHRs) contain structured data elements for capturing social determinants/drivers of health (SDOH), such as Z codes (International Classification of Disease codes for social risk factors). Z codes are underutilized, potentially underestimating SDOHs' impact on opioid-related disorders (ORDs). Natural Language Processing (NLP) offers efficiency in identifying SDOH-related information from patient clinical notes. **Objective**: Use NLP to identify concepts of housing and income insecurity from clinical notes of patients with ORDs. **Methods**: The sample includes 2,846 adult patients (≥18 years) with ORDs in University of California, San Francisco Health outpatient encounters (January 1, 2018 – December 31, 2019). cTAKES (Clinical Text Analysis & Knowledge Extraction System) extracts housing and income insecurity concepts from patient clinical notes using the Unified Medical Language System (UMLS) dictionary. We used Systemized Nomenclature of Medicine – Clinical Terms codes to map UMLS concept unique identifier codes for a broader capture. Validation involved manual assessment by two independent reviewers. **Results**: For housing insecurity, cTAKES flagged 7,216 clinical notes associated with 834 unique patients (29.3%), and 333 patients (11.7%) had an Z code for housing insecurity (Z59.0, Z59.1, Z59.8). For income insecurity, cTAKES flagged 487 clinical notes associated with 273 unique patients (9.6%). Only 7 unique patients (0.25%) had a Z code for financial problems (Z59.5, Z59.6, Z59.7, Z59.86). cTAKES has 91% sensitivity, 100% specificity for housing insecurity, and 77% sensitivity, 99.5% specificity for income insecurity. **Conclusion**: This study underscores the inadequacy of relying solely on structured data elements for comprehensive SDOH data. The advanced text processing capabilities of NLP tools like cTAKES prove crucial in identifying meaningful SDOH information from clinical narratives.

Behavior

Evaluating Efficacy and Adherence in Sensor-Based Technologies for Enhancing Children's Physical Activity with the Virtual Fitness Buddy Ecosystem Tzu-Chun Chu* Tzu-Chun Chu Allan Tate Catherine Ball Joshua Baldwin Kyle Johnsen Michael Schmidt Neila Grimsley Sun joo Ahn

Modern digital technologies enable personalized, socially supportive, and cost-effective health interventions for children, potentially surpassing traditional methods. This study assessed the efficacy of the tablet-based Virtual Fitness Buddy (VFB) ecosystem on enhancing physical activity (PA).

A randomized control trial at three YMCA sites assigned participating families to an intervention with a tablet featuring a virtual dog for setting and sharing PA goals, or a control group with a regular tablet for syncing Fitbits. All children received Fitbits to track PA levels and sedentary behavior (SB). Hierarchical linear mixed models with random intercepts (site, child/parent) and slopes (observation day) evaluated the VFB ecosystem's effect on PA and SB. Treatment-on-treated analyses measured adherence across four domains: goal achievement, review intervals, Fitbit usage, and virtual pet engagement. Latent profile analysis of these domains identified two distinct participant classes of overall intervention adherence.

The study comprised 17 control and 24 treatment families (41 adults, 41 children), with 16 in high adherence. Predominantly boys with a median age of 9, treatment groups were balanced demographically. No significant changes were observed in light/moderate activity or sedentary time between groups, but the treatment group had a 9.5-minute (95% CL: -11.42, -7.28) reduction in vigorous activity. High-adherence children in the treatment group, with more goal achievements, frequent reviews, longer Fitbit wear, and engaging play, showed an 11-minute (95% CL: 4.01, 18.41) increase in moderate physical activity compared to low-adherence peers.

The study emphasizes the need for holistic adherence assessments in digital interventions like the VFB ecosystem for boosting children's physical activity in real-world, non-lab settings. The promise of digital interventions as a scalable behavioral intervention solution relies on user adherence to ecosystem features.

The Associations of Positive and Adverse Childhood Experiences with Disordered Eating Behaviors among College Students Cynthia Yoon* Cynthia Yoon

Background: Children undergo positive, neutral, or adverse experiences. Although positive and adverse childhood experiences are individually associated with disordered eating behaviors, a limited body of research has comprehensively examined the entire spectrum of childhood experiences in relation to disordered eating behaviors.

Purpose: To examine the extent to which childhood experiences are associated with disordered eating behaviors among college students.

Methods: Data were derived from a cross-sectional study of college students (N=1491; 59.0% women, Mage 20.4±3.3yrs in 2022-2023). Positive and adverse childhood experiences were self-reported and categorized into four groups: low positive and low adverse experiences; high positive but low adverse experiences; low positive but high adverse experiences; and high positive and high adverse experiences. Six disordered eating behaviors (e.g., binge eating) were self-reported and dichotomized. Logistic regressions examined associations between childhood experiences and disordered eating behaviors.

Results: Participants with high positive but low adverse experiences had 4.4 to 8.3 percent point lower predicted probability (PP) of disordered eating behaviors while participants with low positive but high adverse experiences had 1.6 to 14.3 percent point higher PP of disordered eating behaviors than those with low positive and adverse childhood experiences (PP range= 30.6%, 95% CI=22.5-38.6 to PP=53.5%, 95% CI= 44.8-62.2%) after adjustment for sociodemographic variables.

Conclusion: Childhood experiences were associated with disordered eating behaviors but differed by the type and extent of experiences and disordered eating behaviors. Public health efforts should promote positive experiences and prevent adverse experiences during childhood to mitigate the risk of engagement in disordered eating behaviors during college.

Behavior

Perceived Stress as a Mediator in the Relationship Between Daily Movement Behaviors and Psychological Distress in College Students During COVID-19
Marcus Vinicius Nascimento-Ferreira* Marcus Vinicius Nascimento-Ferreira Maria Isabela Alves de Almeida Silva Ana Clara Arrais Rosa Marina Lira da Silva Armando Rodrigues de Alencar Santos Luiz Fernando de Oliveira Barbosa Shirley Cunha Feuerstein Kliver Antonio Marin Maira Tristão Parra Erika da Silva Maciel Ethan T. Hunt Augusto César F. De Moraes

Objective: To investigate the mediating effect of perceived stress on the association between 24-hour movement behavior (physical activity, sedentary behavior, and sleep) and psychological distress in college students during the COVID-19 pandemic.

Methodology: This study is a part of the 24-hour movement behavior and metabolic syndrome (24h-MESYN) cohort study. We examined 195 college students from Imperatriz, MA, Brazil (Gini Index: 0.56). Most participants (68.7%) were female, 44.6% aged 21-25, 65.8% studied health sciences, and 24.5% were in early semesters. We assessed physical activity, sedentary behavior, and sleep using the International Physical Activity Questionnaire-Short Form, South American Youth Cardiovascular and Environmental Sedentary Behavior Questionnaire, and Pittsburgh Sleep Quality Index. Perceived stress and psychological distress were measured with the Perceived Stress Scale and Brief Symptom Inventory. We considered the following confounding variables: biological sex, age, ethnicity, maternal education, degree program, shift, time, enrolled classes, and daily study hours. Our analysis applied structural equation modeling with bootstrapping.

Results: We identified a negative association between perceived stress and both physical activity (β: -0.012 [CI95%: -0.025 to -0.002]) and a positive association with psychological distress (β: 1.088 [CI95%: 0.910 to 1.273]). A significant total effect (β: -0.022 [CI95%: -0.038 to -0.006]) and indirect effect (β: -0.014 [CI95%: -0.027 to -0.001]) were observed, while the direct effect (β: -0.008 [CI95%: -0.024 to 0.006]) was not significant. Mediation accounted for 60.2% of the total effect. No mediated effects were found for sedentary behavior or sleep duration.

Conclusion: Perceived stress played a mediating role in linking physical activity to psychological distress. These findings highlight the potential effect of managing physical activity levels on perceived stress and offer insights into promising strategies for alleviating psychological distress.

Exploring Life Satisfaction as a Mediator between Perceived Stress and Eating Behavior in College Students During COVID-19 Marcus Vinicius Nascimento-Ferreira* Marcus Vinicius Nascimento-Ferreira Barbara Saldanha Lima Millena Vaz De Carvalho Jacqueline Fernandes de Sá Xavier Marcia Ferreira Sales Antonio Gibran de Almeida Cardoso Rhavenna Thais Silva Oliveira Shirley Cunha Feuerstein Kliver Antonio Marin Fernando Rodrigues Peixoto Quaresma Ladislau Ribeiro Nascimento Gabriela Berg Augusto César F. de Moraes

Objective: To investigate the mediating effect of satisfaction with life on the association between perceived stress and eating behavior in college students during the COVID-19 pandemic.

Methods: This research is part of the 24-hour movement behavior (physical activity, screen time, and sleep) and metabolic syndrome (24h-MESYN) study. The sample was 195 college students from a low-income region from Brazil (Imperatriz, MA; Gini Index of 0.56), composed of 68.7% females, 44.6% aged between 21 to 25 years; 65.8% enrolled in a health sciences degree; 24.5% enrolled in the 1st to 3rd semester. We assessed perceived stress, satisfaction with life, and eating behavior using the Satisfaction with Life Scale, Dutch Eating Behavior Questionnaire, and Perceived Stress Scale. We assessed external, restrained, and emotional eating scores as outcomes. The potential confounders were biological sex, age, ethnicity, maternal education, degree program, shift, time, number of classes enrolled, and daily study hours. We performed structural equation modeling with bootstrapping procedures.

Results: Perceived stress was negatively associated with satisfaction with life (β: -0.355 [CI95%: -0.460 to -0.251]), and satisfaction with life was negatively associated with external eating (β: -0.018 [CI95%: -0.033 to -0.004]). A significant positive total effect was found (β: 0.019 [CI95%: 0.010 to 0.029]), with both indirect (β: 0.006 [CI95%: 0.001 to 0.012]) and direct effects (β: 0.013 [CI95%: 0.002 to 0.023]) statistically significant. Mediation explained 33.9% of the total effect. No mediated effects were observed for restrained eating or emotional eating.

Conclusion: Satisfaction with life seems to mediate the association between perceived stress and external eating. The findings suggest that satisfaction with life could be a protective mechanism in stressful life events experienced during the COVID-19 pandemic.

Investigating the association between physical activity and epigenetic aging using structured life course modelling in the Health and Retirement Study Farah Ammous* Farah Ammous Jessica Faul Colter Mitchell

Regular physical activity is an effective lifestyle intervention for promoting wellbeing and healthy aging. One pathway by which exercise can shape biological processes is through epigenetic modifications. Investigating how and when exercise influences epigenetic processes offers promising avenues for tailored interventions. Using data from a representative sample of participants aged 56 years and older from the Health and Retirement Study, we investigated the association between physical exercise (Biennial follow-up from 2004–2016 for a total of seven waves) and epigenetic aging (2016). We defined exercise as moderate ($\geq$ 2 per week) or vigorous intensity ($\geq$ 1 per week) and used three epigenetic aging measures (GrimAA, PhenoAA, and pace of aging (PACE)). We applied weighted linear regression for cross-sectional associations in 2016 (N=3542) and a modified structured life-course modelling approach (SLCMA), testing three life-course hypotheses: accumulation, recency, and sensitive periods (N=2483). In 2016, participants who engaged in exercise were younger (69 vs. 71 years) and had a healthier cardiometabolic risk profile. After adjusting for age, sex, race/ethnicity, education, body mass index, diabetes, heart disease, stroke, total cholesterol, high density lipoprotein, and blood pressure, exercise was associated with decreased epigenetic aging (Beta = -1.0 years (95%CI: -0.7– -1.4) for GrimAA, -1.4 years (95%CI: -0.8 – -2.0) for PhenoAA and -0.03 (95%CI: -0.02 – -0.04) for PACE). For the three measures, SLCMA models selected the recency hypothesis, which considers an exposure cumulatively but inversely weighted by the length of time passed since it occurred. Our study shows that exercise is associated with slower epigenetic aging after adjusting for socioeconomic and cardiometabolic measures. Over a 12-year follow-up, reported exercise closest to the time of epigenetic aging assessment appears to have a stronger effect on aging compared to earlier exercise.

Behavior

The Associations of Partner Cyber Abuse with Disordered Eating Behaviors and Intuitive Eating among College Students Cynthia Yoon* Cynthia Yoon

Background: Abuse encompasses sexual, physical, emotional, and cyber abuse. While the associations of sexual, physical, and emotional abuse with eating behaviors are well established, the relationships between cyber abuse and eating behaviors remain unclear.

Purpose: To examine associations of cyber abuse with intuitive eating and disordered eating behaviors among college students.

Methods: Data were derived from a cross-sectional study of college students (N=1493; 58.9% women, Mage 20.4±3.3yrs in 2022-2023). Partner Cyber Abuse (e.g., partner changed my password which limited my access to bank accounts) was assessed with the Partner Cyber-Abuse Questionnaire. Intuitive eating was assessed with the Intuitive Eating Scale-2. Six disordered eating behaviors (e.g., overeating and binge eating) were assessed with the Questionnaire on Eating and Weight Patterns-5. Linear regressions and Modified Poisson regressions were used to examine associations of partner cyber abuse with intuitive eating and disordered eating behaviors, respectively.

Results: Cyber abuse was cumulatively associated with lower intuitive eating scores and greater prevalence of all disordered eating behaviors except for binge eating (p for trend < .04). Among the nine cyber abuse items, "partner changed my password which limited my access to bank accounts" emerged as a factor associated with both lower intuitive eating scores (β=-6.93, 95% CI= -11.77, -2.08) and a heightened prevalence of disordered eating behaviors (aPR range= 1.28-2.48) after adjustment for sociodemographic variables.

Conclusion: Partner cyber abuse was cumulatively and individually associated with eating behaviors. **To enhance eating behaviors,** cyber abuse should be addressed, and the underlying mechanism of such associations should be explored.

Voice, Swallowing, Speech, and Language Problems in the United States Pediatric Population: The 2022 National Health Interview Survey (NHIS) Howard J. Hoffman* Howard J. Hoffman Chuan-Ming Li May S. Chiu Stephen M. Tasko Mabel L. Rice

Communication is essential to early child development, yet many speech and language disorders go untreated. Increasing the proportion of children who receive treatment is a US public health priority included in Healthy People 2030. A Voice, Speech and Language (VSL) Supplement was included in the 2022 National Health Interview Survey (NHIS), the principal source of information on the health of the US civilian noninstitutionalized population. A nationally representative sample (n= 6,125), representing 60.7 million children aged 3-17 years, is analyzed. Parents reported on their children's communication disorders (CD) of voice, swallowing, speech, or language, including the duration, severity, changes in past year, and healthcare visits for evaluation/treatment. An estimated five million children had CD lasting one week or longer during the last 12 months, a prevalence of 8.3% (12.6%, 6.6%, 5.9% by age groups, 3-7, 8-12, and 13-17 years). Males had a higher CD prevalence, 9.5% [95% confidence interval (CI): 8.4%-10.8%], compared to females, 7.1% [95% CI: 6.1%-8.2%]. Speech disorder prevalence was 5.9%, language, 3.6%, voice, 1.6%, and swallowing, 0.8%. CD prevalence increased significantly with decreasing parental education and household income. Health conditions associated with CD were poorer general health, early developmental delay, learning disability, sensory impairment (vision, hearing, and motor), anxiety or depression, and asthma. The proportion receiving healthcare last year was 49.1% for moderate and 74.3% for worse problems. Diagnosis with COVID-19 was not associated with increased CD, but likely led to fewer healthcare visits during the pandemic. Healthcare providers included speech-language pathologists, early intervention specialists, and occupational/physical therapists. VSL problems can be more severe when accompanied by other disorders, however, many manifest as idiopathic. When left untreated, VSL problems may have serious lifelong consequences.

The Role of Vemp as a Marker in the Progression of HTLV-1- Associated Myelopathy Tiago Almeida de Oliveira* Tiago Oliveira Juliana Augusta Nunes da Cruz Denise Utsch Gonçalves Júlia Fonseca de Morais Caporali Nathália de Castro Botini Rausse Tatiana Rocha Silva Ana Lúcia Borges Starling César Daniel Alves Caldeira Tiago Almeida de Oliveira Ludimila Labanca

Myelopathy (HAM) associated with human T-cell lymphotropic virus type 1 (HTLV-1) is a chronic inflammation of the spinal cord that leads to impairment of posture and gait. The diagnosis of HAM is usually delayed. To evaluate the role of galvanic vestibular evoked myogenic potential (G-VEMP) as a marker of progression to HAM in individuals followed for 10 years. This longitudinal study was carried out between 2012 and 2022 and was approved by the Research Ethics Committee (number: 2898825). All 21 HTLV-1-infected participants were submitted to a clinical, neurological and G-VEMP examination in 2012(T1), 2017(T2), and 2022(T3). Galvanic stimuli were applied bilaterally to the mastoid processes and VEMP was recorded from the gastrocnemius muscle. The latency and amplitude of the short-latency (SL) and medium-latency (ML) responses and the progression of individuals from asymptomatic carrier to possible-HAM and HAM were investigated. Data were compared using the Friedman and multiple linear regression. It was considered significant $p < 0.05$. Twenty-one individuals were included, with a mean age of 61 years at T1 and 13 (62%) women. There was an increase in the latency of the SL and ML response over the 10-year follow-up ($p < 0.001$). The SL and ML wave amplitude decreased ($p < 0,001$). The percentage of altered VEMP at T1 was 33%, T2 was 43% and T3 was 52%. All individuals with altered VEMP at T1 developed possible-HAM or HAM during follow-up. The diagnostic accuracy of G-VEMP was 90,48%, sensitivity 78%, and specificity 100%. Using multiple linear regression analysis, the effect of CL is statistically significant and positive (beta = 1.02, 95% CI (0.23, 1.81), $t(28) = 2.66$, $p = 0.013$; standard beta = 0.52, 95% CI (0.12, 0.92)). The Friedman test followed by Dunn showed that the VEMP signal is significantly different between T1 and T3.

Neurology

Prevalence and Risk Factors of Communication Disorders in the United States Adult Population: The 2022 National Health Interview Survey (NHIS) Chuan-Ming Li* Chuan-Ming Li Howard J. Hoffman May S. Chiu Stephen M. Tasko Mabel L. Rice

The purposes of this study are to estimate the prevalence of communication disorders (CD) in US adults and to identify associated risk factors. The cost of lost or degraded employment opportunities due to CD has been estimated as 1.5% of the Gross National Product, or about $400 billion in 2023. A Voice, Speech, and Language Supplement was included in the 2022 NHIS, a nationally representative survey of the US population. The sample adults (n= 27,651, 18+ years) reported voice, swallowing, speech, and language disorders, along with age at onset, duration, severity, and healthcare visits for evaluation/treatment. Logistic regression was used to estimate associations between CD and risk factors. Models were adjusted for age, sex, race/ethnicity, education, income, geographic location, body mass index, and general health status. The prevalence of those with CD lasting 1+ week during the last 12 months was 10.7% out of 260.5 million (M) US adults. The prevalence of voice disorders was 5.8% (14.2 M), swallowing disorders 3.5% (8.5 M), speech disorders 3.4% (8.3 M), and language disorders 1.9% (4.5 M). Of these affected individuals, 9.8% sought evaluation/treatment services from speech-language pathologists, doctors, or other healthcare professionals. Professional services for rehabilitation led to improved function for 48% and improved personal/social quality of life for 54%. Risk factors associated with increased CD included ever having had a stroke, arthritis, anxiety disorder, depression, chronic fatigue syndrome, asthma, a weakened immune system, hearing difficulty, difficulty remembering or concentrating, prescription medications in the past 12 months for anxiety, depression, and other emotional or concentration difficulties. Voice, swallowing, speech, and language disorders are common among adults. To improve outcomes, we must increase awareness, access, and utilization of effective rehabilitation programs, which can significantly improve quality of life.

Associations of the COVID-19 pandemic and pandemic-related exposures with cognitive function in women: A prospective cohort study

Siwen Wang* Siwen Wang Anthony Menor Lori B Chibnik Jae H Kang Chirag Vyas Deborah Blacker Laura D. Kubzansky Karestan C Koenen Andrea L Roberts

Background The COVID-19 pandemic involved factors possibly associated with cognitive decline, such as bereavement and SARS-CoV-2 infection. We examined the associations of the COVID-19 pandemic and pandemic-related exposures with change in cognitive function among middle-aged women.

Methods We included 20,660 female participants from the Nurses' Health Study II, aged 51–70 years, who had completed one or more cognitive assessments (Oct 2014–Sep 2022). Cognitive function was measured using the Cogstate Brief Battery, a self-administered online battery. Participants completed assessments every 6–12 months, contributing 53,534 assessments in total. Of these, 9,249 assessments (17%) were performed after the beginning of the pandemic (on Mar 1, 2020, or thereafter). 15,091 women had only pre-pandemic and 378 women had only post-pandemic assessments. We calculated a psychomotor speed and attention composite score, a learning and working memory composite score, and a global score. We fit weighted multivariable-adjusted generalized estimating equation models to examine the differences as well as the rate of cognitive change pre- and post-pandemic.

Results The mean (SD) age at first cognitive assessment was 62.8 (4.9) years, and at the start of the pandemic it was 66.4 (4.6) years. After adjustment for age at assessment, educational attainment of participants and their parents, cognitive test practice effects, and comorbidities (e.g., diabetes, hypertension), we did not observe a difference in cognitive function comparing assessments taken after the pandemic vs. before (β [95% CI], psychomotor speed and attention: -0.01 SD [-0.04, 0.02]; learning and working memory: -0.01 SD [-0.04, 0.02]; global score: -0.01 SD [-0.03, 0.01]). SARS-CoV-2 infection, post-COVID-19 conditions (e.g., long COVID), and death of loved ones were not associated with rate of cognitive change. Rates of pre- and post-pandemic cognitive decline did not differ significantly across strata of comorbidities (e.g., hypertension, diabetes, depression).

Conclusions The COVID-19 pandemic and COVID-19-related events were not associated with cognitive decline in this large cohort of older women with up to 2.5 years of follow-up after pandemic onset. Future studies with more diverse study populations are required to confirm our findings.
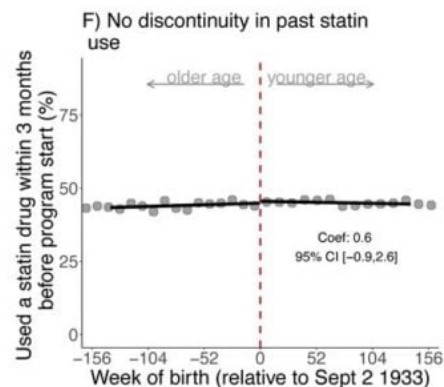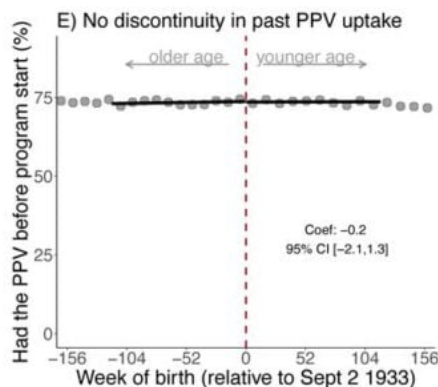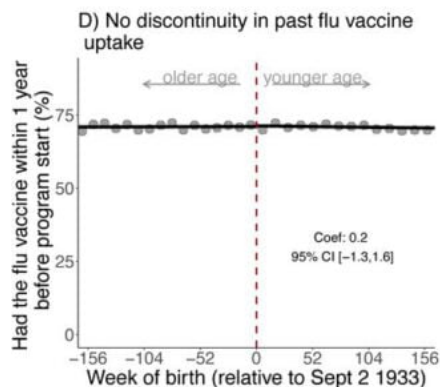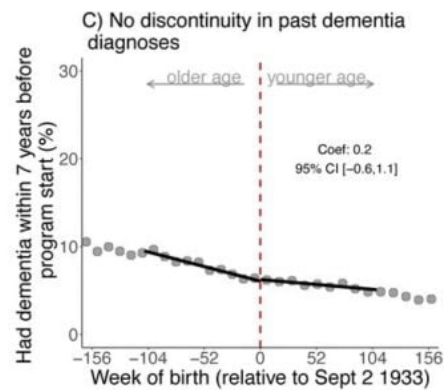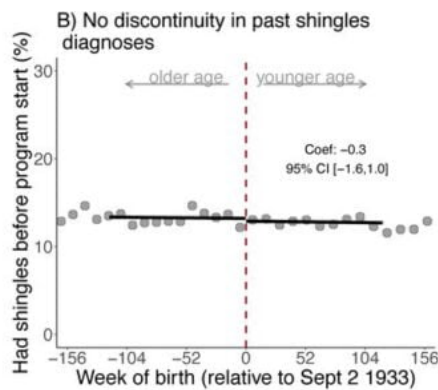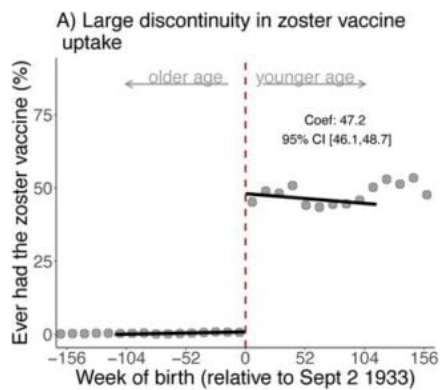
Causal evidence that herpes zoster vaccination prevents or delays a proportion of dementia cases: A natural experiment in Wales Felix Michalik* Pascal Geldsetzer Markus Eyting Min Xie Simon Heß

Aims: To determine the causal effect of herpes zoster (HZ) vaccination on new diagnoses of dementia.

Methods: In the UK, eligibility for the HZ vaccine (Zostavax) was determined based on an individual's exact date of birth. Those born before September-2-1933 were ineligible (and remained ineligible for life), while those born on or after September-2-1933 were eligible. This natural experiment likely provides causal, as opposed to correlational, evidence because there is no plausible reason why adults born just one week apart should differ systematically from each other. We used a regression discontinuity design in Welsh country-wide data on primary and secondary care encounters, and death certificates. The outcome was a new dementia diagnosis as recorded in any of these data sources.

Result: We included 282,541 individuals born between September-1-1925 and August-31-1941. The percentage who received the HZ vaccine increased from 0.01% among those one week too old to be eligible, to 47.2% among those one week younger. Receiving the vaccine reduced the probability of a new dementia diagnosis over seven years by 3.5 percentage points (95% CI: 0.6–7.1, p=0.019), corresponding to a 22.4% relative decrease. To support causality, we show that i) there were no differences in pre-existing conditions or uptake of other preventive interventions across the date-of-birth eligibility cutoff; ii) the HZ vaccine had no effects on any other common causes of morbidity and mortality; and iii) no other interventions used the same date-of-birth eligibility cutoff.

Conclusions: Our findings suggest that HZ vaccination slows or prevents the natural history of dementia. Unlike existing studies in this field, this analysis provides causal evidence because individuals who differ in age by just one week are likely exchangeable with each other on both observed and unobserved characteristics, except for a large difference in the probability of receiving the HZ vaccine.

A) Large discontinuity in zoster vaccine uptake

Coef: 47.2
95% CI [46.1,48.7]

B) No discontinuity in past shingles diagnoses

Coef: −0.3
95% CI [−1.6,1.0]

C) No discontinuity in past dementia diagnoses

Coef: 0.2
95% CI [−0.6,1.1]

D) No discontinuity in past flu vaccine uptake

Coef: 0.2
95% CI [−1.3,1.6]

E) No discontinuity in past PPV uptake

Coef: −0.2
95% CI [−2.1,1.3]

F) No discontinuity in past statin use

Coef: 0.6
95% CI [−0.9,2.6]

LATEBREAKER

Aging

Sustained poverty from early adulthood through midlife and cognitive function Calvin Colvin* Calvin Colvin Katrina Kezios M. Maria Glymour Adina Zeki Al Hazzouri

Prior studies suggest that low income is associated with poorer cognition in mid and late life. Less is known about effects of sustained poverty from early adulthood through midlife on cognition. We used data from 2,631 National Longitudinal Study of Youth 1979 (NLSY79) cohort members to examine the association of sustained poverty over 20 years (1990-2010) with midlife cognitive function. We included NLSY79 cohort members who had ³3 income measures during the exposure period (mean age in 1990: 27 years) and a midlife cognitive assessment between 2010 and 2016 (mean age at assessment: 48 years). We defined sustained poverty by the proportion of family incomes below 200% of the Federal Poverty Line. Participants' midlife cognition was assessed via a modified version of the Telephone Interview for Cognitive Status (TICS-m). We grouped individual TICS-m assessments together based on cognitive domains (memory or attention), and averaged Z-scores across domains to create a global measure of cognition. Earlier-life (i.e., young-adulthood) cognition was assessed by the Armed Forces Qualification Test (AFQT) in 1980. In linear regression models adjusted for confounders, explanatory health factors, and AFQT percentile score, participants who were always in poverty had worse memory (Z-score, -0.28 [95% CI: -0.44, -0.11]), attention (Z-score, -0.25 [95% CI: -0.46, -0.06]), and global cognition (Z-score, -0.35 [95% CI: -0.51, -0.19]) compared to those never in poverty. Similar findings were seen for participants experiencing periodic poverty. The coefficients for sustained poverty are consistent in magnitude with the cognitive benefit prior work has suggested one receives with 5 additional years of education. In conclusion, we found that sustained poverty from early adulthood through midlife predicted worse midlife cognitive function, even accounting for young adult cognition. Long-term exposure to poverty may be an important determinant of midlife cognitive health.

Comparative safety of antidepressants on motor-vehicle crash risk among older adults with depression: a sequential target trial emulation Marzan A. Khan* Marzan Khan Nina R. Joyce Melissa R. Pfeiffer Seth A. Margolis Brian R. Ott Allison E. Curry Melissa R. Riester Andrew R. Zullo

Background: Selective serotonin reuptake inhibitors (SSRIs), atypical antidepressants (AAs), and tricyclic antidepressants (TCAs) are often prescribed for depression, but might increase the risk of motor-vehicle crash (MVC) in older adults through sedation, dizziness, and blurred vision.

Objective: Estimate the effect of initiating AAs and TCAs versus SSRIs on 1-year risk of MVC.

Methods: We emulated a sequence of 470 target trials each consecutive week from January 6, 2008 through January 1, 2017 using a novel linkage of Medicare fee-for-service health insurance claims and New Jersey police-reported MVCs and drivers' licensing data**.** Eligible patients aged ≥ 66 years with depression were included in one or more target trials; thus person-trials were the unit of analysis. Using stabilized inverse probability of treatment and censoring weighted estimators to account for potential confounding and selection bias, we estimated cumulative incidence curves and risk ratios (RRs). We computed weights using pooled logistic regression models involving up to 67 demographic, comorbidity, medication, and healthcare utilization covariates. Percentile bootstrapped 95% confidence limits (CLs) were estimated.

Results: In the intention-to-treat (ITT) estimand, there were 31 MVCs among 644 TCA-treated person-trials, 65 among 2,130 AA-treated person-trials, and 380 among 10,260 SSRI-treated person-trials. In the per-protocol (PP) estimand there were 28 and 199 MVCs among AA and SSRI-treated person-trials, respectively. The adjusted ITT and PP RRs comparing 1) AA to SSRI were 0.97 (95% CLs 0.68, 1.46) and 0.94 (95% CLs 0.49, 1.35) respectively and 2) TCA to SSRI were 1.02 (95% CLs 0.57, 1.86) and 0.93 (95% CLs 0.29, 1.89) respectively.

Conclusion: We observed similar risks of MVC between the TCA, AA, and SSRI treatment strategies. MVC risk should not be a major concern when clinicians select between these antidepressants to treat depression among older adults.

Aging

The association of midlife obesity and BMI with cognitive change in a diverse cohort of individuals 80+ Claire Meunier* Claire Meunier Paola Gilsanz Joseph Roscoe Maria M. Corrada Kristen M. George M. Maria Glymour Elizabeth Rose Mayeda Alexander Ivan B. Posis Brandon Gavett Rachel Whitmer

Midlife obesity elevates dementia risk, yet little is known regarding its effects on short term cognitive change in those who survived to age 80. We pooled data for participants aged 80+ from LifeAfter90, Kaiser Healthy Aging and Diverse Life Experiences Study, and Study of Healthy Aging in African Americans (n=671; 33% White, 12% Latino, 17% Asian, 35% Black) to examine the association between midlife obesity and cognitive decline (executive function (EF), verbal episodic (VEM), scores standardized to baseline sample). First clinical measure of body mass index (BMI;kg/m2) at ages 40-60 was categorized as normal (18.5-24.9), overweight (25-29.9), and obese (30). Linear models and linear mixed models with random intercepts/slopes adjusted for age of BMI, age at first clinical assessment, gender, race, education, visit mode, and practice effects analyzed the association between midlife obesity and cognition. Participants' mean age at BMI assessment was 44.6±4.3 years, mean age at first cognitive assessment was 88.5±5.3 years; 9% obese and 31% overweight, with a mean of 2.7±1.7 visits over 1.4±1.2 years. Midlife BMI categories were not associated with baseline EF (compared to normal BMI: obesity β(95%CI)=-0.07(-0.30,0.15); overweight β=-0.01(-0.15,0.12)) or annual decline (obesity β=-0.03(-0.05,0.10); overweight β=-0.03(-0.06,0.02); Figure 1). Obesity was associated with lower baseline VEM (obesity β=-0.25(-0.49,-0.02)), though overweight did not significantly differ from normal BMI (β=-0.12(-0.26,0.01)). BMI was not associated with VEM decline (obesity β=-0.04(-0.04,0.07); overweight β=-0.01(-0.06,0.15); Figure 1). When modeled linearly, BMI was not associated with decline in EF (β<0.01(>-0.01,0.01)) or VEM (β<0.01(>-0.01,0.01)). In a diverse cohort of individuals aged 80+, midlife obesity was not associated with faster cognitive decline. While midlife obesity is a risk factor for dementia it may not be associated with short term cognitive changes after age 80.

Figure 1: Predicted cognitive decline in executive function and verbal episodic memory by midlife BMI category

Aging
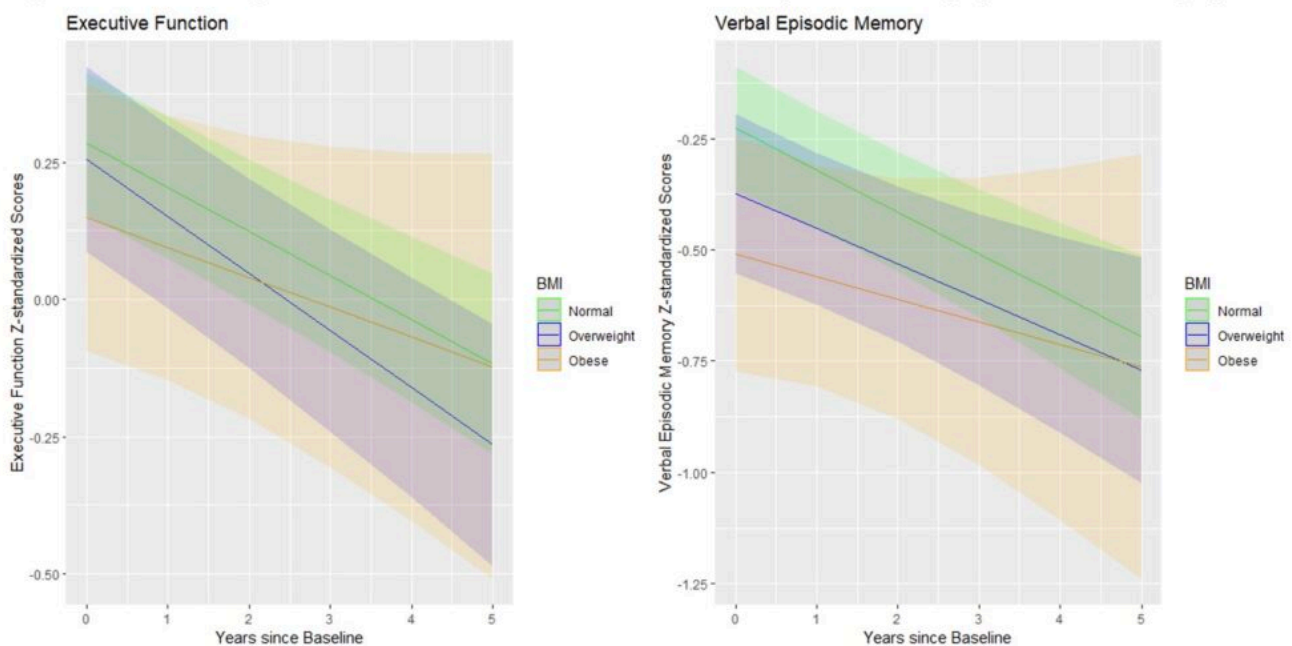
Associations of four types of pollen with dementia related emergency departments in the Midwestern United States 2006-2013
Peter S. Larson* Peter S. Larson Allison L Steiner Robert Melendez Marie S. O'Neill Carina J. Gronlund

Climate change is increasing the length of intensity of seasonal patterns of various species of aeroallergenic pollens.
Pollens of many types have been shown to exacerbate symptoms of allergic rhinitis and asthma, both of which have been associated with
cognitive decline and dementia in older adults. However, the patterns of association between specific pollen exposure and dementia related
events are unknown. This research uses a database of dementia related emergency department visits among Medicare recipients age 65+ (N= 5.1
million visits) in 30 counties each in Michigan, Ohio and Pennsylvania and a prognostic, model based raster of four types of pollens,
deciduous broadleaf, evergreen, grass and ragweed, to test associations of pollen exposure with dementia related episodes.
We regressed daily ED visit counts by ZIP Code Tabulation Area (ZCTA) on cumulative seasonal pollen concentration counts for
each evergreen, deciduous broadleaf, grass and ragweed pollen class including confounders for precipitation and temperature. We used
Poisson regression models with daily population-at-risk offsets within a distributed-lag-non-linear models and a 21-lag-day exposure history.
We found that 21 day cumulative exposure to >90th percentile of deciduous broadleaf pollen was positively associated with increases in dementia
related ED visits (risk ratio 1.13 95% confidence interval (1.08, 1.18)). Sensitivity to deciduous broadleaf pollens, which appear
in late Winter/early Spring, should be considered as an important risk factor for dementia related episodes.

Diet and Health Behaviors Associated with Osteoarthritis Knee Pain During the COVID-19 Pandemic: The Multicenter Osteoarthritis Study (MOST) Morgan Wolff* Morgan Wolff Sarah Nash Cora Lewis Michael Nevitt David Felson Tuhina Neogi James Torner

Objectives: To understand changes in diet and health behaviors and investigate associations of pain increase with changes in behaviors among a group of older adults with or at risk for osteoarthritis during the COVID-19 pandemic.

Methods: We conducted a cross-sectional mailed survey in the summer of 2022 among participants of the Multicenter Osteoarthritis Study (MOST) following another survey that investigated COVID-19 infection, vaccination, and pain increase during the COVID-19 pandemic. This follow-up survey examined how diet and health behaviors (snacking, sitting down, perceived support to eat healthy, etc.) changed during the COVID-19 pandemic. We analyzed knee pain increase from the first survey as a function of demographic and behavioral factors using the Chi-squared tests to investigate if diet and health behaviors had an association with pain development or progression.

Results: We mailed 555 surveys, and 502 were returned (90.5%). In univariate analyses, self-reported changes in diet and health behaviors were significantly associated with pain increase. These variables include frequency of eating a healthy and balanced diet, frequency of snacking, and time spent sitting down. These variables also significantly differed between demographic characteristics, especially gender.

Discussion: Among MOST participants, there were significant changes within self-reported diet and health behaviors, with especially evident differences by gender. Increased knee pain during the COVID-19 pandemic was significantly associated with these changes in behaviors (light PA, eating a healthy diet, using weight loss products, and skipping meals).

Aging

The Association between Caregiving Patterns and the Burdens and Benefits of Caregiving

Talha Ali* Talha Ali Gail McAvay Joan Monin Thomas M Gill

BACKGROUND: Several studies have documented the burdens of caregiving in family and other unpaid caregivers of older adults. Little is known about the benefits of caregiving among these helpers. Using a previous typology of care types, we examine whether caregivers providing different types of care report different levels of burdens and benefits.

METHODS: Using data from the 2015 and 2017 rounds of the National Health and Aging Trends Study (1423 care recipients) and the National Study of Caregiving (2146 caregivers), we assess caregiving burden in the domains of financial, emotional, and physical difficulties and caregiving benefits, including increased confidence, ability to deal with difficult situations, and closeness to the care recipient.

RESULTS: Results of the logistic regression models show that caregivers in care types that provide more hours of care and help with mobility, self-care, and household tasks are more likely to experience physical burden. Yet, they are also more likely to report that caregiving increased their ability to deal with difficult situations.

CONCLUSIONS: The type of care provided, defined in terms of caregiving intensity, regularity, and specific activities, has distinct implications for caregiving-related burdens and benefits. Findings suggest that physicians should periodically assess the type of care provided to their patients to gauge anticipated burdens or benefits caregivers might experience and their implications for the care recipient's health. Findings also have implications for caregiving interventions, which should identify coping strategies that not only reduce caregiving-associated burdens but also increase caregiving-associated benefits for caregivers.

Aging

Incarceration and Performance on Immediate and Delayed Verbal Recall Tests: Results from National Longitudinal Study of Adolescent to Adult Health – Parent Study Alexander Testa* Alexander Testa

Objective: This study aimed to investigate the cognitive functioning of formerly incarcerated older adults compared to their never-incarcerated counterparts, focusing on immediate and delayed verbal recall.

Methods: Data are from 2,003 respondents who participated in the National Longitudinal Study of Adolescent to Adult Health – Parent Study (AHPS) (ages 47-82; mean age 62). AHPS participants were AHPS word recall memory exercises to the parent respondent from the Rey Auditory-Verbal administered Learning Test, including (a) 90-second (immediate or short-term verbal memory), (b) 60-second recall tests (delayed or long-term verbal memory), and (c) combined word recall on the 90- and 60-second tests

Results: Adjusting for control variables, respondents who reported prior incarceration had a lower rate of verbal recall on the combined word recall (Incidence risk ratio [IRR] = .915, 95% Confidence Interval [CI] = .840, .997) and immediate word recall (IRR = .902, 95% CI = .817, .996). When restricting the sample to respondents over age 60, prior incarceration was associated with lower combined word recall (IRR = .847, 95% CI = .752, .954), immediate word recall (IRR = .857, 95% CI = .762, .963), and delayed word recall (IRR = .834, 95% CI = .713, .974).

Discussion: This study underscores the adverse impact of prior incarceration on cognitive functioning in the older adult population, emphasizing the need for targeted interventions and support for formerly incarcerated older adults. The results reinforce the importance of addressing the long-term consequences of incarceration, especially as individuals enter older adulthood.

Aging

Causal effects of body composition on lifespan: Mendelian randomization analysis Zhu Liduzi Jiesisibieke* Zhu Liduzi Jiesisibieke Zhu Liduzi Jiesisibieke C Mary Schooling

Background: Observational studies examining the relation of body composition with lifespan are inconsistent. We conducted a Mendelian Randomization (MR) study to assess effects of key features of body composition on lifespan in men and women.

Methods: We conducted a MR study using inverse variance weighting to investigate the impact of measures of body composition (fat mass, fat-free mass, body fat percentage, waist circumference, appendicular lean mass, and grip strength) on lifespan we also adjusted fat-free mass and appendicular lean mass for potential confounding by fat mass, and assessed mediation by waist circumference. Sensitivity analyses included the weighted median and MR-Egger methods.

Results: In univariable MR, genetically predicted fat mass (per standard deviation higher) decreased men's lifespan by 2.69 years (95% confidence interval [CI] -3.14 to -2.23) and women's by 2.48 years (95% CI -3.04 to -1.93), with similar findings for body fat percentage and waist circumference. Appendicular lean mass and grip strength were positively associated with lifespan in men, but not women. In multivariable MR, after adjusting for confounding by fat mas, fat-free mass was also beneficial for men. The effect of BMI on lifespan was largely mediated by waist circumference.

Conclusion: Our study reinforces the benefit of lower fat mass, and less central obesity for both men and women and provides additional evidence highlighting the role of body composition rather than relying solely on BMI, with possibly a greater role of lean or fat-free mass in men. Waist circumference is a key target of intervention for men and women.

Descriptive epidemiology of New York City older adult patients with multiple chronic conditions Sarah Conderino* Sarah Conderino John Dodson Yuchen Meng Mark G. Weiner Catherine Rabin Wilson Jacobs Parampreet Bakshi Melissa Lee Jenny Uguru Lorna E. Thorpe

Background: Co-occurrence of multiple chronic conditions (MCCs) is a significant public health concern among older adults, with differential burden by race/ethnicity and sex. Our objective was to characterize comorbidity profiles and cardiometabolic risk factor trajectories among older adults with MCCs in New York City (NYC) using an intersectionality approach.

Methods: Electronic health record (EHR) data were obtained from the INSIGHT Clinical Research Network. The study population included NYC residents aged 50 or older with MCCs with at least one ambulatory visit in the six months before COVID-19 pandemic onset (9/7/2019–3/6/2020). We descriptively characterized comorbidity profiles and assessed the cardiometabolic risk factors of blood pressure, cholesterol, A1C, and weight by the intersection of sex and race/ethnicity.

Results: There were 367,901 older adults with MCCs in the INSIGHT sample. Comorbidity profiles were heterogeneous (Figure 1), but the most common profile across sex-and-race/ethnicity groups was co-occurring hypertension and hyperlipidemia (6% alone, 59% in combination with other conditions). Burden of these two conditions differed across groups, with highest hypertension prevalence among Black females (87.3%) and males (87.4%) and highest hyperlipidemia prevalence among Asian (78.9%) and white males (79.0%). Cardiometabolic risk factors also differed significantly, with highest systolic blood pressure among Black females (mean=134.8mmHg) and males (mean=134.8mmHg) and lowest obesity among Asian females (16.5%) and males (15.7%). Across all race/ethnicity groups, females had a higher average LDL cholesterol than males.

Conclusions: Significant disparities were observed in comorbidity burden and cardiometabolic risk factors, which may reflect underlying systems of power and discrimination, such as health care access. Public health interventions are needed to prevent chronic disease onset and improve disease management among minoritized populations.

Figure 1. Comorbidity Profiles among NYC Residents Aged 50 and Older with Multiple Chronic Conditions Receiving Care at NYC INSIGHT Facilities, September 2019-March 2020

Aging
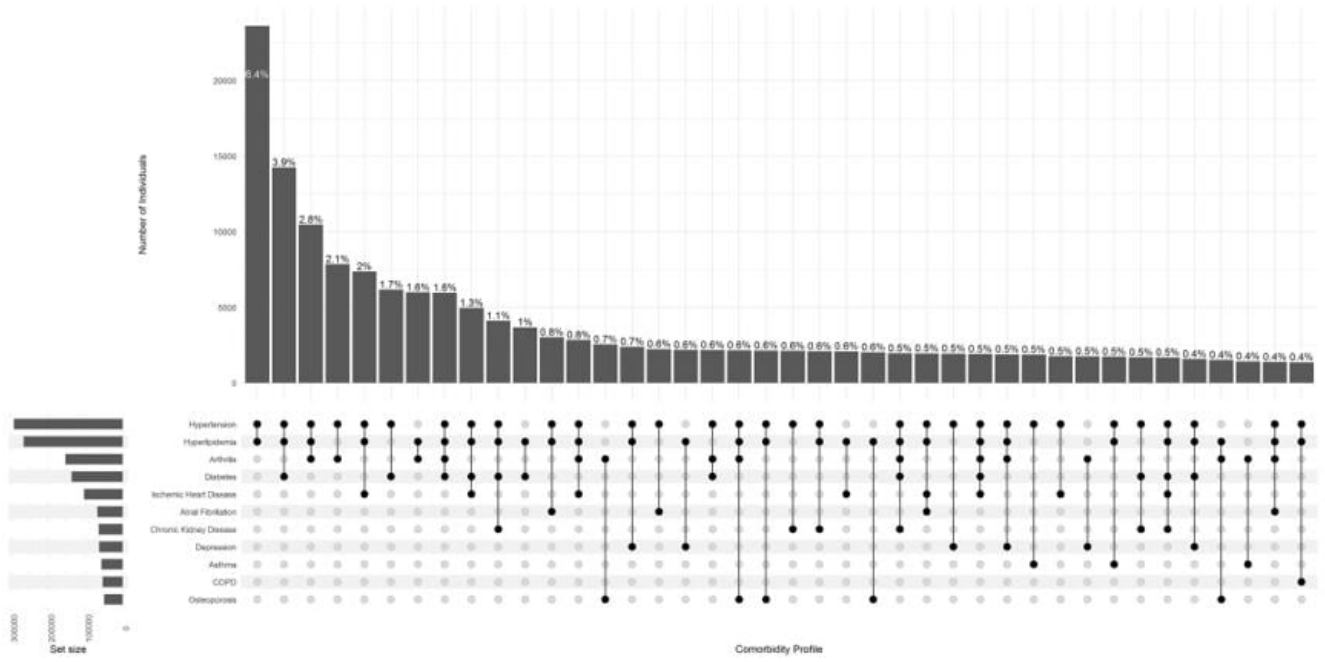
Life Course Educational Trajectories and Persistent Infections in Young Adulthood Jennifer Momkus* Jennifer Momkus Kathleen Mullan Harris Y. Claire Yang Chantel Martin Jessie K. Edwards Allison E. Aiello
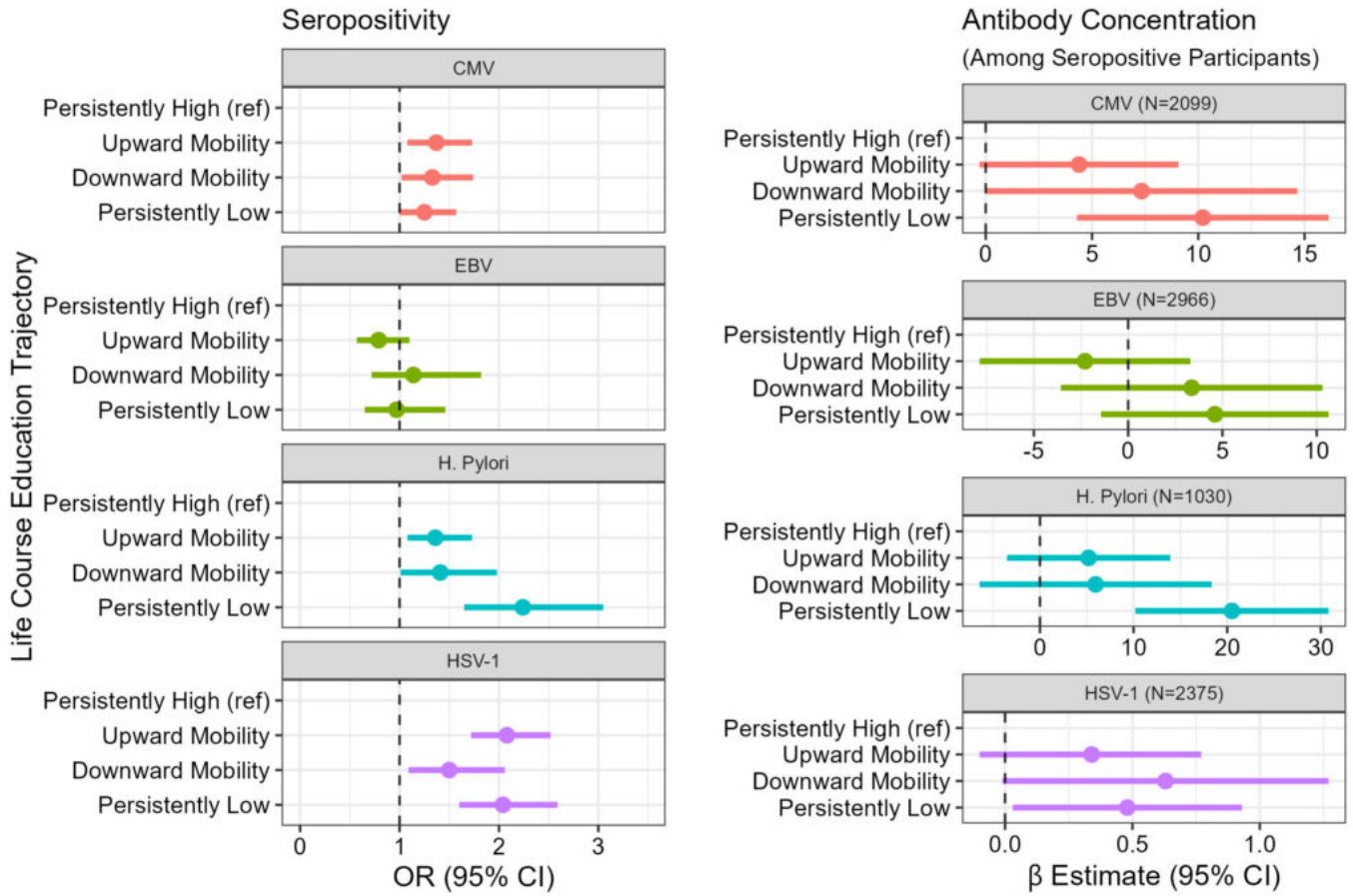
Background: Persistent infections including cytomegalovirus (CMV), herpes simplex virus type 1 (HSV-1), Epstein-Barr Virus (EBV), and Helicobacter pylori (H. Pylori) may accelerate aging and alter immunity across the life course. Educational trajectories may strongly shape the risk of exposures and responses to these infections.

Methods: We analyzed data from Waves I and IV of the National Longitudinal Study of Adolescent to Adult Health (Add Health). Using parental education from Wave I and participant education from Wave IV, we created a life course education trajectory measure wherein a high school degree or less was considered low. The resulting four trajectories included low-low (persistently low), low-high (upward mobility), high-low (downward mobility), and high-high (persistently high). We tested Wave IV blood spots for HSV-1, EBV, CMV, and H. Pylori IgG antibodies. Logistic regression models were used to calculate odds ratios (OR) for associations between intergenerational education and infection seropositivity, adjusting for age, sex, immigrant generation, and race/ethnicity. For those who were seropositive, linear regression was used to estimate the average differences in antibody concentration, adjusting for the same covariates. Survey weights were incorporated in all analyses.

Results: Associations varied by infection and trajectory type. For example, the ORs for HSV-1 seropositivity were similar for the upward mobility (OR=2.08, 95%CI: 1.72, 2.52) and persistently low education trajectories (OR=2.04, 95%CI: 1.60, 2.59), but weaker for the downward mobility trajectory (OR=1.50, 95%CI: 1.09, 2.06). The persistently low education trajectory (i.e. low-low) was the only category significantly associated with increased antibody concentrations for CMV (β=10.2 U/mL, 95%CI: 4.3, 16.1), HSV-1 (β=0.48 U/mL, 95%CI: 0.03, 0.93), and H. Pylori (β=20.5 U/mL, 95%CI: 10.2, 30.8).

Conclusions: Low education is linked to elevated odds of persistent infection and poorer immune response to infection, with differential effects based on the life course trajectory and the infection type. Understanding the temporal dynamics underlying these associations, particularly the timing and length of exposure, is essential for addressing health disparities across the life course.

Association Between Life Course Education Trajectory and Persistent Infections
Add Health Wave IV, N=4573

Seropositivity

CMV
EBV
H. Pylori
HSV-1

Antibody Concentration
(Among Seropositive Participants)

CMV (N=2099)
EBV (N=2966)
H. Pylori (N=1030)
HSV-1 (N=2375)

Life Course Education Trajectory

Persistently High (ref)
Upward Mobility
Downward Mobility
Persistently Low

OR (95% CI)

β Estimate (95% CI)

adjusted for age, sex, immigrant status, and race/ethnicity

Aging

State-level effect of Medicaid expansion on Alzheimer's disease and related dementias mortality Jenna Rajczyk* Jeffrey Wing Jenna Rajczyk Julie Strominger Parvati Singh

Introduction: With the rapid aging of the US population, the prevalence of dementia is projected to double. The enactment of the Affordable Care Act's Medicaid expansion may have created opportunities for dementia detection and classification. We examine whether and to what extent Medicaid expansion influenced potential reporting of dementia as the underlying cause of death.

Methods: State-level Alzheimer's disease and related dementias (ADRD) mortality data for persons 65 years and older were downloaded from CDC WONDER for 2000-2019. ADRD was classified as ICD-10 codes: F01, F03, and G30. Staggered difference-in-difference analysis was used to estimate the ADRD mortality rate pre- and post-Medicaid expansion. An overall average treatment effect for the treated (ATT) was estimated along with dynamic event study analysis to gauge the temporal effect window post-Medicaid expansion. As a sensitivity analysis, results were compared to all-cause and cardiovascular disease (CVD) mortality.

Results: A total of 29 out of 50 states expanded Medicaid by 2019. Post expansion, ADRD mortality increased by 9.02 per 100,000 people (95% CI: 1.81, 16.23). The change in mortality was most pronounced two years post expansion, gradually increasing each year (two-years post ATT: 10.02; 95% CI: 3.51, 16.52; five-years post ATT: 13.58; 95% CI: 2.82, 24.34; Figure). This trend was not observed across the same period for CVD mortality (ATT: 0.80; 95% CI: -12.42, 14.02) and the post-expansion difference observed for all-cause mortality lacked precision compared to dementia mortality (ATT: 7.43; 95% CI: -23.12, 37.98).

Conclusions: ADRD mortality increased following state-level Medicaid expansion, but this increase was not observed similarly for CVD mortality nor all-cause mortality. The lag between expansion and the increase in mortality may arise from increased detection through Medicaid supported care and being listed or correctly identified as the underlying cause of death.

State-level average treatment effect for the treated (ATT) for years post-Medicaid expansion (treatment) on (A) Alzheimer's disease and related dementias, (B) all-cause, and (C) cardiovascular mortality (underlying cause of death per 100,000 persons 65 years and older) across the US, 2000-2019.
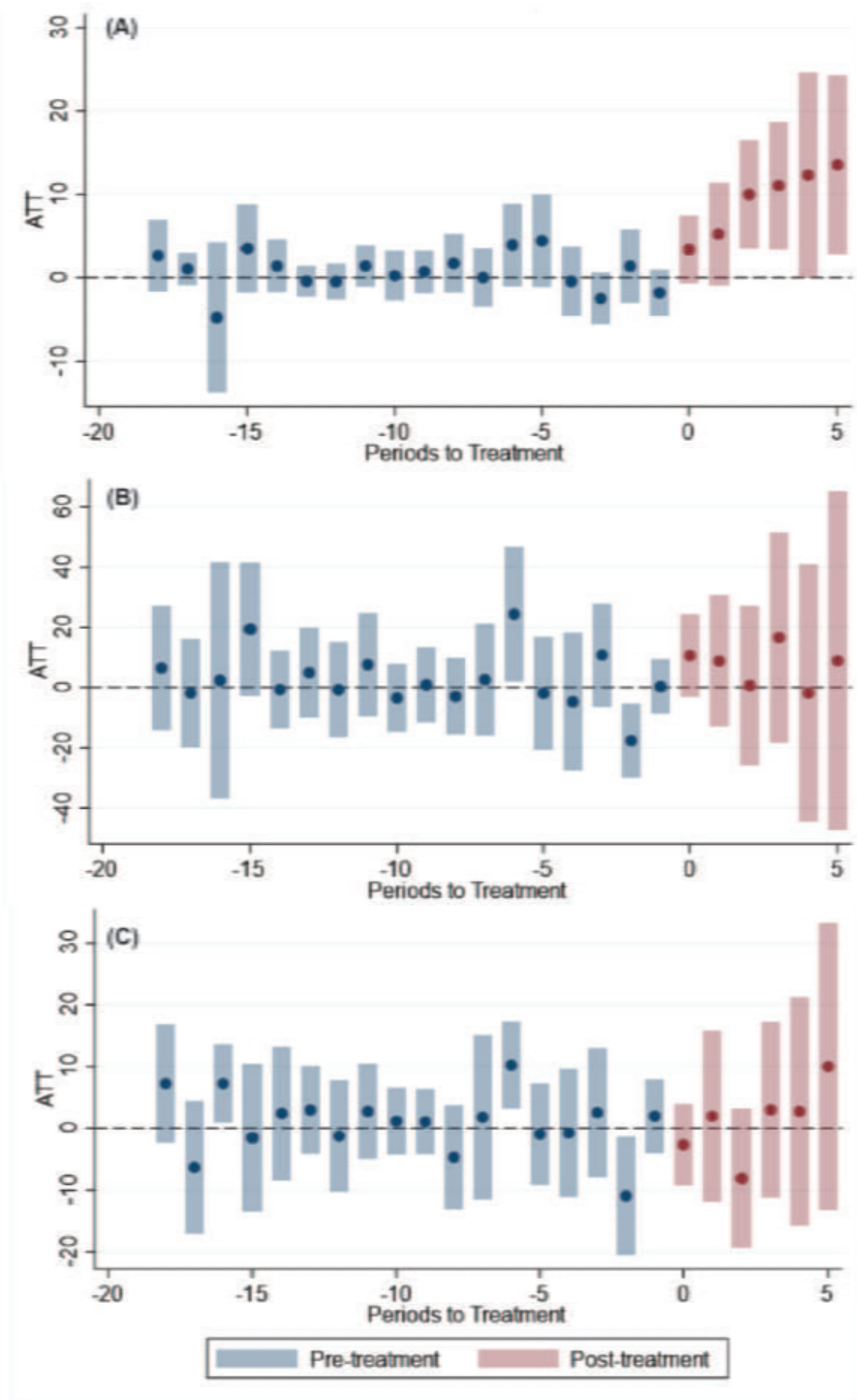
Assessing the effects of COVID-19 related disruptions on disability in a diverse cohort of older adults Joseph Fong* Joseph Fong L. Paloma Rojas-Saunero Ryo Ikesu Paola Gilsanz Rachel A. Whitmer M. Maria Glymour Elizabeth Rose Mayeda
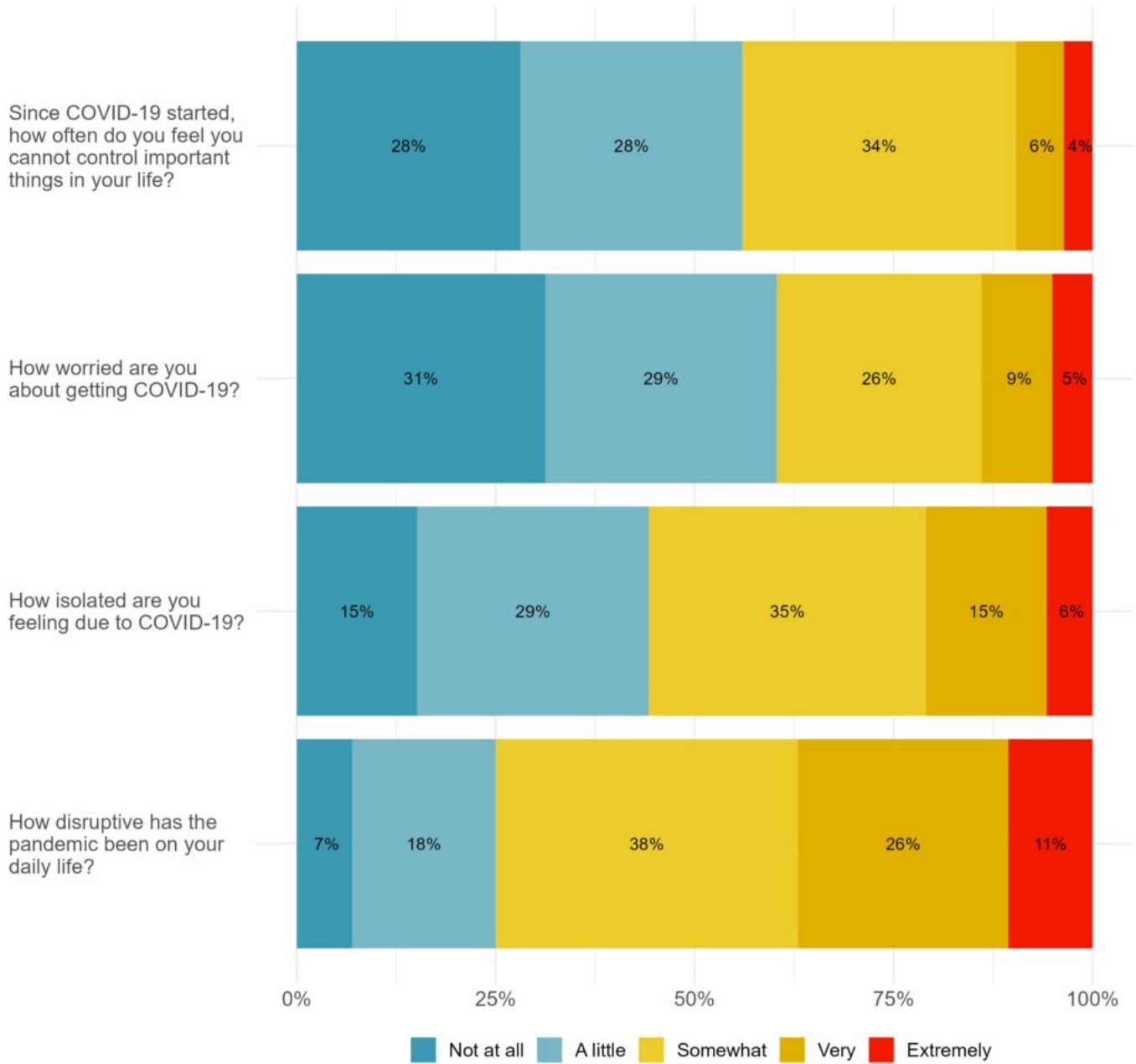
Background: The COVID-19 pandemic has had far-reaching effects in the US, disrupting health and social systems. Some studies have reported COVID-19 disruptions were associated with disability in older adults, but there are significant gaps in evaluating health effects of COVID-19 disruptions in racially/ethnically-diverse older adults.

Methods: Data are from the Kaiser Healthy and Diverse Life Experiences (KHANDLE) study, a cohort of long-term Kaiser Permanente Northern California members aged 65+ at recruitment in 2017. COVID-19 disruption (social and personal) was calculated as the mean of 4 Likert questions (1 never – 5 extremely) from the COVID-19 Impact Survey score collected from Nov 2020 to Jun 2021. Outcome was probability of disability (>=1 functional limitation out of 12 domains) assessed between 2017-2023. We used generalized estimating equations with robust standard errors to estimate prevalence ratios (PR) for the association of COVID-19 disruption and probability of disability; covariates included sex, race/ethnicity (Asian, Black, Latino, and White), parental education, income range, income worries, childhood socioeconomic status, subjective social status, baseline age, years in study, and interview mode for outcome assessment (phone vs. face-to-face) .

Results: The analytic sample included 416 participants; mean age = 74.7 years (SD = 6.1), mean follow-up time was 4.0 years (SD = 1.3). 72% reported at least one functional limitation. Mean COVID-19 disruption score was 2.6 (SD = 0.8) (Figure 1). One-unit higher COVID-19 disruption score was associated with higher probability of disability (PR = 1.10 [95% CI: 1.06, 1.13]).

Conclusion: Higher COVID-19 disruption was associated with higher probability of disability. Next steps include estimating effects of COVID-19 disruption on change in probability of disability over time.

Figure 1: COVID-19 Questionnaire Items*

Since COVID-19 started, how often do you feel you cannot control important things in your life?
28% | 28% | 34% | 6% | 4%

How worried are you about getting COVID-19?
31% | 29% | 26% | 9% | 5%

How isolated are you feeling due to COVID-19?
15% | 29% | 35% | 15% | 6%

How disruptive has the pandemic been on your daily life?
7% | 18% | 38% | 26% | 11%

0%   25%   50%   75%   100%

Not at all | A little | Somewhat | Very | Extremely

*From the National Alzheimer's Coordinating Center (NACC)

Understanding the variations in oral health issues and access to dental care among Canadian adults across age groups, household income, and self-rated oral health status: a descriptive analysis using the CLSA Chau* Chau Huynh Annie Sun Amy Hsu Serena Chen Shehreen Hossain Therese Chan Heidi Sveistrup

Background and Objectives: Oral health is integral to overall quality of life and physical well-being. Despite the evidence on the cumulative effects of poor oral health, access to dental care remains inequitable among equity-deserving groups. Considering the roll-out of the Canadian Dental Benefit plan in 2024, we sought to examine trends in dental health status, prevalence of dental issues, and access to services by age and household income.
Methods: We conducted descriptive analyses using prospective cohort data from the Canadian Longitudinal Study of Aging at baseline (2011-2015) and three-year follow-up (2015-2018). T-tests and chi-squared tests were used to examine differences in access to care and dental issues by age (under and over 65 years), household income (<50k, 50-100k, >100k), oral health status (poor, fair, good, very good, excellent), and changes in oral health status between baseline and at the three-year follow-up.
Results: Our study comprised 44,817 Canadian adults. Respondents with a household income of <$50k had the lowest self-rated oral status of 'fair' and 'poor' and had a higher proportion of dental issues (0.5-25%), e.g., swelling, dry mouth, tooth decay, compared to all other income groups (p<.0001). Most participants in the low-income category did not have any dental insurance (54.0% in those under 65 years; 69.8% in those over 65 years), while most participants in the higher income categories had private dental insurance (71.2% in those under 65 years; 50.2% in those over 65 years). Persons under 65 years with a lower income experienced the largest increase (11.5%) in other oral health issues between baseline and follow-up and had the fewest annual dental visits (p<.0001).
Conclusion: Barriers to accessing preventative care and treatment increases the risk of adverse oral health outcomes and chronic morbidities. Reframing policies to meet the needs of vulnerable groups are critical to quality of life and reducing healthcare costs.

Behavior

Sex-Specific Associations of Cigarettes, E-cigarettes and Dual Use with Premature Atherosclerotic Cardiovascular Disease Olatokunbo Osibogun* Olatokunbo Osibogun Ememgini Elo-Eghosa

Background: Premature atherosclerotic cardiovascular disease (ASCVD) is increasing in young adults (<55 years), posing challenges to future health and productivity. While research suggests a higher risk in females who smoke cigarettes compared to males, sex differences in the impact of cigarette and e-cigarette use patterns on premature ASCVD are limited. This study investigated these sex-specific associations using data from a population-based sample.

Methods: Using data from 480,317 adults (ages 18-54; ~50% female) in the 2020-2022 Behavioral Risk Factor Surveillance System, logistic regression models were used to assess the associations between cigarette and e-cigarette use patterns and self-reported premature ASCVD, stratified by sex.

Results: In females, former dual (adjusted odds ratio: 1.38 [95% CI: 1.05, 1.81]), current exclusive cigarette (1.54 [1.19, 2.00]), current cigarette/former e-cigarette (1.39 [1.11, 1.76]), and current dual (2.20 [1.50, 3.23]) use were positively associated with premature ASCVD compared to never use. Conversely, former exclusive e-cigarette, current exclusive e-cigarette, former exclusive cigarette, and former cigarette/current e-cigarette use showed no significant association.In males, former exclusive cigarette (1.40 [1.11, 1.76]), former dual (1.60 [1.24, 2.07]), current exclusive cigarette (1.81 [1.40, 2.33]), current cigarette/former e-cigarette (1.99 [1.52, 2.53]), and current dual (2.18 [1.56, 3.06]) use were positively associated with premature ASCVD. Former exclusive e-cigarette use showed a negative association, while current exclusive e-cigarette and former cigarette/current e-cigarette use showed no significant association.

Conclusion: Both sexes showed higher odds of premature ASCVD for dual and exclusive cigarette use. Although the cross-sectional design limits causal inferences, the findings suggest comprehensive tobacco cessation programs tailored to diverse use patterns are needed to reduce premature ASCVD.

Behavior

Medical expenditure attributable to short sleep in China: Empirical results based on the 2018 China Family Panel Studies Xiaoyu Li* Xiaoyu Li Xumeng Yan Fang Han Ichiro Kawachi

Background

Short sleep is associated with increased morbidity risks and therefore can induce substantial medical costs. This study estimates the total and out-of-pocket amount of medical expenditure attributable to short sleep among Chinese adults.

Methods

Using a 2018 nationally representative Chinese dataset, we employed two-part regression models to examine the associations between short sleep (<6h, 6-7h vs >7h) and annual total or out-of-pocket medical expenses. Counterfactual estimations were used to estimate individual and population medical cost due to short sleep.

Results

The mean age of participants was 46.6 years (SD = 16.7), with 50.1% of them being male. Among 29118 participants, 2,037 (7.0%) slept less than 6 hours, 8,457 (29.0%) slept 6 to 7 hours, and 18624 (64.0%) slept more than 7 hours per day. Those sleeping <6 hours had higher odds of medical expenditure (OR = 1.28, 95% CI: 1.14, 1.43), and when they did, they spent 1,438.05 CNY (95% CI: 991.23, 1884.87) more than those sleeping > 7 hours. The corresponding estimates for out-of-pocket medical expenditure were 1.27 (95% CI: 1.14, 1.42) and 905.16 CNY (95% CI: 632.46, 1177.86). Short sleep (< 6 h) accounted for 3.25% of the expected total medical expenditure and 3.20% of the expected out-of-pocket medical expenditure for an average person. The share of medical spending due to short sleep is higher in groups who were female, divorced/widowed, poorly educated, living in rural residential areas, and working on farming jobs. In 2018, China's total medical expenditure attributable to short sleep (< 6 h) was estimated to be 106.31 billion CNY (16.36 billion USD), of which 65.78 billion CNY (10.12 billion USD) was out-of-pocket (61.88%).

Conclusion

Short sleep was associated with increased medical expenses in China. Promoting adequate sleep can potentially mitigate healthcare costs, especially for vulnerable populations.

Machine Learning for Predicting Cardiovascular Health in South American Pediatric Population. Tiago Almeida de Oliveira* Mateus Silva Rocha Tiago Almeida de Oliveira Marcus Vinicius Nascimento-Ferreira Alexandre Chiavegatto Filho Augusto Cesar Ferreira De Moraes

This study aimed to develop cardiovascular health (CVH) prediction models for South American children and adolescents, incorporating a range of extrinsic and intrinsic factors. We analyzed data from the South American Youth/Child Cardiovascular and Environmental (SAYCARE) Study, an observational multicenter feasibility study, focused on individuals aged 3-18 years in five different South American cities. Of the initial 475 participants, those with incomplete data on dietary intake, physical activity, nicotine exposure, sleep health, body mass index, blood lipids, fasting glucose, blood pressure, or missing covariate data were excluded. The models considered sociodemographic, maternal, environmental, and behavioral factors, including nutritional status. CVH was categorized as low (Class 1 – prevalence 0.56), moderate (Class 2 – prevalence 0.24) or high (Class 3 – prevalence 0.20). The study employed a 70/30 split for training and testing the algorithms. This approach provided a comprehensive analysis of CVH predictors in this demographic. Exploratory analysis, employing Spearman and biserial correlation, addressed multicollinearity concerns (dropping variables with a correlation >0.90). Z-score was used for feature standardization, and one-hot encoding was applied to categorial features. After preprocessing and data cleaning, the sample size was comprised of 297 observations. A six-class model comparison was undertaken using popular algorithms for tabular data (XGBoost, KNN, LightGBM, SVM, Logistic Regression Multinomial, and Random Forest) and different multinomial strategies (One vs One, One vs Rest, Multiclass). The chosen model, Random Forest, exhibited superior performance, and after refinement and validation through 5-fold cross-validation using Grid Search, the Multiclass model was selected. It achieved an area under the ROC curve of 0.88 in the test set, with strong predictive capabilities across CVH categories (Class 1: 0.85, Class 2: 0.79, Class 3: 0.99).

Big Data/Machine Learning/AI

Evaluation of the Oversampling Method for Balancing Pediatric Chest Radiograph Dataset in Classification Using Convolutional Neural Network VGG-16 Tiago Almeida de Oliveira*
Tiago Almeida de Oliveira Giullber Valentim da Silva Roberta Moreira Wichmann Crysttian Arantes Paixão Luciana de Queiroz Leal Gomes

X-ray images are widely used in medical diagnosis, particularly for detecting pneumonia. This study utilizes a Convolutional Neural Network (CNN), specifically the VGG-16 architecture, to classify pediatric chest tomography images for pneumonia presence. The research addresses data imbalance using oversampling with data augmentation and employs transfer learning with pre-trained CNN weights to enhance training efficiency and performance. The dataset used comprises pediatric chest radiographs for pneumonia diagnosis, categorized into two classes: Pneumonia (4273 images) and Normal (1583 images). Prior to analysis, data augmentation techniques were applied, including random cropping, resizing, and adjustments in brightness and contrast. This process involved randomly selecting 845 images from the Normal class, equivalent to approximately 62.63% of the original images, to generate an additional 2526 images. Comparative analyses on imbalanced and balanced datasets showed an initial accuracy of 93.26%, with precision values of 0.94 for Pneumonia and 0.83 for Normal. After applying data augmentation for balance, accuracy improved to 94.23%, with recall metrics rising to 0.92 for Normal and 0.96 for Pneumonia. Evaluation included a confusion matrix for metrics like Precision, Recall, F1-score, and Accuracy. Graphical evaluation methods, such as the ROC curve and Precision-Recall graph, were also employed. The computational analysis was executed in Python 3.10.9, utilizing libraries like Tensorflow for transfer learning and Scikit-learn for metric calculations. Notably, the model trained on the balanced dataset demonstrated a slight enhancement, as indicated by an AUC of 0.94 in the ROC curve, compared to the model trained on the imbalanced dataset, which obtained an AUC value of 0.92. The study highlights VGG-16 CNN's effective use in achieving strong classification results with minimal training. Data augmentation improves model performance, emphasizing the potential of advanced imaging and deep learning for accurate pediatric pneumonia detection and broader healthcare diagnostics.

Using Natural Language Processing On Clinical Text For Health Outcomes Research: Challenges And Future Advances Abayomi Adegunlehin* Abayomi Adegunlehin
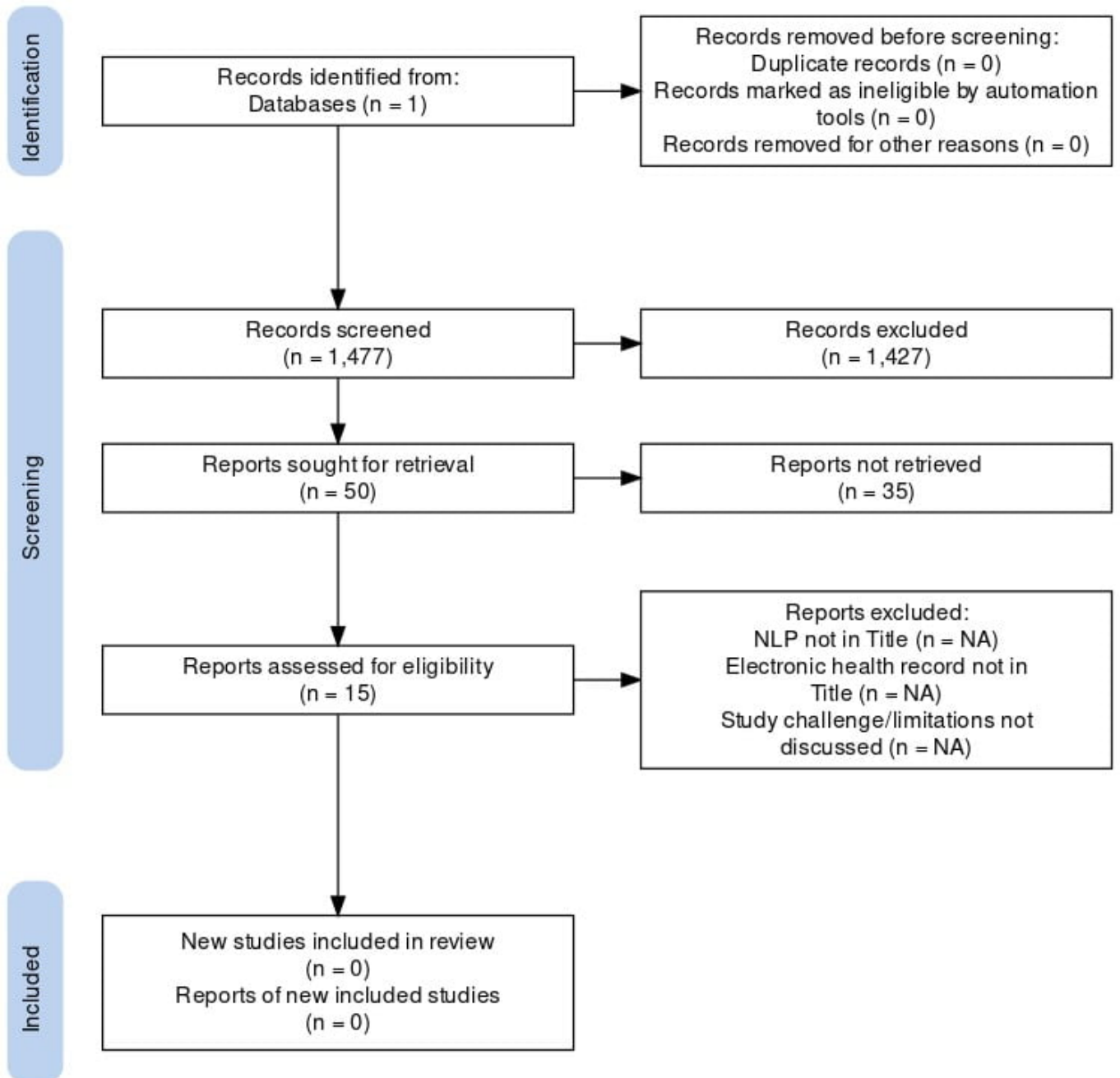
As clinical data become increasingly available in healthcare, machine learning (ML) has revolutionized many areas, like early intervention for disease progression and comorbidities, clinical predictions, clinical natural language processing, and so on. Despite the immense feats and possibilities of applying ML techniques in the medical field, its impact remains limited. This gap stems from persistent challenges hindering the possibilities of clinical natural language processing (NLP) in healthcare research and patient health outcomes.

Therefore, this annotated bibliography seeks to provide future researchers with an understanding of these common challenges to guide their research. When these challenges are known beforehand and handled, clinical NLP's possibilities in improving health outcomes will significantly increase.

To achieve the goal of this research, this annotated bibliography systematically identified and analyzed critical challenges within the past decade's research, drawing from the PubMed Medline Database. The systematic review yielded 15 articles using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The range of clinical topics identified in these articles are radiology, cancer, Joint Arthroplasty, Drug Overdose, Opioid, ischemia, Disorder normalization, HIV Risk Assessment, Pneumonia, Aortic Stenosis, Axial Spondyloarthritis, Atrial Fibrillation, and Liver Disease.

This review study identified critical challenges in patient healthcare outcomes research and provided valuable recommendations for future research endeavors. Among the challenges identified are data quality limitations, model validation issues, data standardization, addressing model bias, and ethical concerns surrounding bias and patient privacy. Adopting these recommendations in future patient healthcare outcomes research will lead to more robust, accurate, and equitable research outcomes. This, in turn, will contribute to enhanced healthcare decision-making, improved patient care, and, ultimately, better health outcomes for individuals and communities.

Identification of new studies via databases and registers

Identification

Records identified from:
Databases (n = 1)

Records removed before screening:
Duplicate records (n = 0)
Records marked as ineligible by automation tools (n = 0)
Records removed for other reasons (n = 0)

Screening

Records screened
(n = 1,477)

Records excluded
(n = 1,427)

Reports sought for retrieval
(n = 50)

Reports not retrieved
(n = 35)

Reports assessed for eligibility
(n = 15)

Reports excluded:
NLP not in Title (n = NA)
Electronic health record not in Title (n = NA)
Study challenge/limitations not discussed (n = NA)

Included

New studies included in review
(n = 0)
Reports of new included studies
(n = 0)

Big Data/Machine Learning/AI

Exploring Unsupervised Machine Learning for psychometric properties assessment: a 24-hour movement behavior questionnaire validity Shirley Cunha Feuerstein* Shirley Cunha Feuerstein Lorrane Cristine Conceição da Silva Helen Ferreira de Brito Souza Evellyn Ravena da Silva Gomes Letícia Ribeiro Borges Kliver Antonio Marin Francisco Winter Figueiredo Luis Gracia-Marco Heraclito Barbosa de Carvalho Augusto César Ferreira de Moraes Marcus Vinícius Nascimento-Ferreira

Objective: To test the structure solution of an online 24-hour movement behavior questionnaire (24h-MBQ) in college students by unsupervised machine learning.

Methods: We invited 195 college students (68.7% females; 44.6% aged 21 to 25 years; 65.8% majoring in the undergraduate degree courses in health sciences; and 24.5% were in early semesters). We developed a questionnaire with 19 items extracted from previously validated tools, composed by physical activity (6-item), sedentary behavior (10-item) and sleep duration (3-item). We employed the exploratory factor analysis with Varimax rotation. We extracted the factors based on the Kaiser criterion, with eigenvalues greater than 1 necessary for factor retention. Additionally, we carried out unsupervised machine learning, determining cluster numbers via the Calinski/Harabasz index. We retrieved these values based on the number of factors observed in the exploratory factors analysis. After identifying the clusters, we applied the k-median method to create them. Differences among clusters were assessed using Kruskal-Wallis test with Dunn's post hoc test.

Results: In the exploratory factor analysis, we identified seven factors where the explained variance was 66.80%. We identified three clusters using unsupervised machine learning and this structure was able to distinguish differences in physical activity (physically active vs. long sleeper, p = 0.02), sedentary behavior (all cluster comparison, p < 0.001), and sleep time duration (all cluster comparison, p < 0.001).

Conclusion: The 24h-MBQ has structure solution able to identify differences among clusters related to physical activity, sedentary behavior, and sleep duration. Employing machine learning to generate hierarchical clusters shows potential as a method for assessing the structural solution in psychometric assessments in epidemiological research.

Keywords: Physical Activity; Sedentary behavior; sleep duration; subjective tool.

Machine learning to predict long-term post-stroke cognitive decline in a Brazilian stroke cohort (EMMA study)

Carine Savalli* Carine Savalli Alessandra Baccaro Maria C Escalante-Rojas Marianna G H S J Leite Isabela M Benseñor Paulo A Lotufo Yuan-Pang Wang Alessandra C Goulart Alexandre Chiavegatto Filho

Following a stroke, cognitive decline is a common long-term disability that affects patients. To advise on preventive and intervention strategies, it is necessary to assess the risk of progressive cognitive decline in patients during the initial stages. This study aimed to evaluate the cognitive status of stroke patients from a Brazilian community-based cohort (EMMA study) in the sub-acute phase of stroke (1–3 months), in a follow-up assessment at 6 months (n=100), 1-year (n=103), and 2-years (n=57). The Modified Telephone Interview for Cognitive Status (TICS-M), which has been validated in Brazil, was used to assess cognitive status. Two outcomes were analyzed for each follow-up: an absolute decrease in the TICS-M score or a decrease of at least 10% from baseline. The machine learning algorithm XGBoost was trained using various variables collected at baseline, including demographics, comorbidities, clinical and laboratory variables. After hyperparameter tuning, we evaluated the predictive performance of each model in a repeated 5-fold cross-validation, using the area under the ROC curve (AUC) as the primary metric. The highest level of performance was achieved in predicting a decrease of at least 10% in TICS-M score within one year after the stroke. When considering the outcome of any absolute decrease in the TICS-M score, we found AUC values of 0.60 (SD=0.09), 0.53 (SD=0.12), and 0.40 (SD=0.21), for the 6-month, 1-year, and 2-years follow-up periods, respectively. When considering the decrease of at least 10% in TICS-M, we found an AUC of 0.59 (SD=0.13), 0.66 (SD=0.12), and 0.53 (SD=0.19) for the 6-month, 1-year, and 2-years follow-up, respectively. According to this post-stroke cognitive decline model based only on routine clinical variables, the TICS-M tool presented a low to moderate performance for screening any change in cognition status. Future studies should incorporate other relevant variables and train other machine learning algorithms.

CIPHER: A Key Resource for Evaluating Emerging Phenotypes Vidisha Tanukonda* Vidisha Tanukonda Ashley Galloway Monika Maripuri Yuk-Lam Ho Francesca Fontin Jeffrey Gosian Michael Murray Rahul Sangar Edward Zielinski Joanne Sordillo Katherine P Liao Tianxi Cai Sumitra Muralidhar Jacqueline Honerlaw Kelly Cho Tiffany Sim

Electronic health records (EHR) based phenotypes represent clinical conditions or characteristics derived from information contained within health systems, enabling reuse of EHR data for research and healthcare operations. Thus, developing phenotypes with high accuracy is critical for quality of data analytics and utilization. The Department of Veterans Affairs has developed CIPHER (Centralized Interactive Phenomics Resource), a growing public knowledgebase comprised of over 5000 computable phenotype definitions and data visualization tools, for research acceleration.

CIPHER is uniquely structured to provide information about the portability of a phenotype across healthcare systems. For example, ICD-10 code U09.9 (Post COVID-19 condition, unspecified) introduced in 2021, is used to identify patients with Long COVID. A recent manuscript provided one of the first assessments of the accuracy of the code at three healthcare systems. In January 2024, this nascent phenotype definition and its validation metrics were added to CIPHER (Figure 1A), making them widely available. CIPHER's integrative platform allows for entry of an array of metrics, allowing users to easily compare the performance and quickly evaluate the definition's applicability. For instance, the wide range in PPV for U09.9 across health systems (23.2% to 62.4%) shows that the value of the code varies by site in its ability to accurately classify Long COVID cases (Figure 1B).

The CIPHER metadata standard ensures information needed to replicate a phenotype algorithm is available to users and provides critical information about phenotype portability or limitations. Definitions such as the Long COVID phenotype can be replicated across additional cohorts, and if validated, the resulting performance metrics can be deposited in the knowledgebase. CIPHER's novel approach positions it as an immeasurable resource for evaluating emerging phenotypes and presents the framework to standardize existing definitions.

## 1A: CIPHER Webpage

Long COVID-19

Validation

Description of Validation

COVID positive patients were identified for chart review. Among this cohort we sampled patients based on two approaches i) with a U09.9 code and ii) without a U09.9 code but with a new onset PASC related ICD code, which allows us to assess the performance of the U09.9 code. To operationalize the long COVID definition based on health agency guidelines, we grouped symptoms into a "core" cluster of 11 commonly reported symptoms among long COVID patients and an extended cluster, that captured all other symptoms by disease domain. (Maripuri et al 2023). Patients having at least 2 symptoms persisting for >=60 days that were new onset after their COVID infection, with at least one symptom in the core cluster, were labeled as having long COVID per chart review.

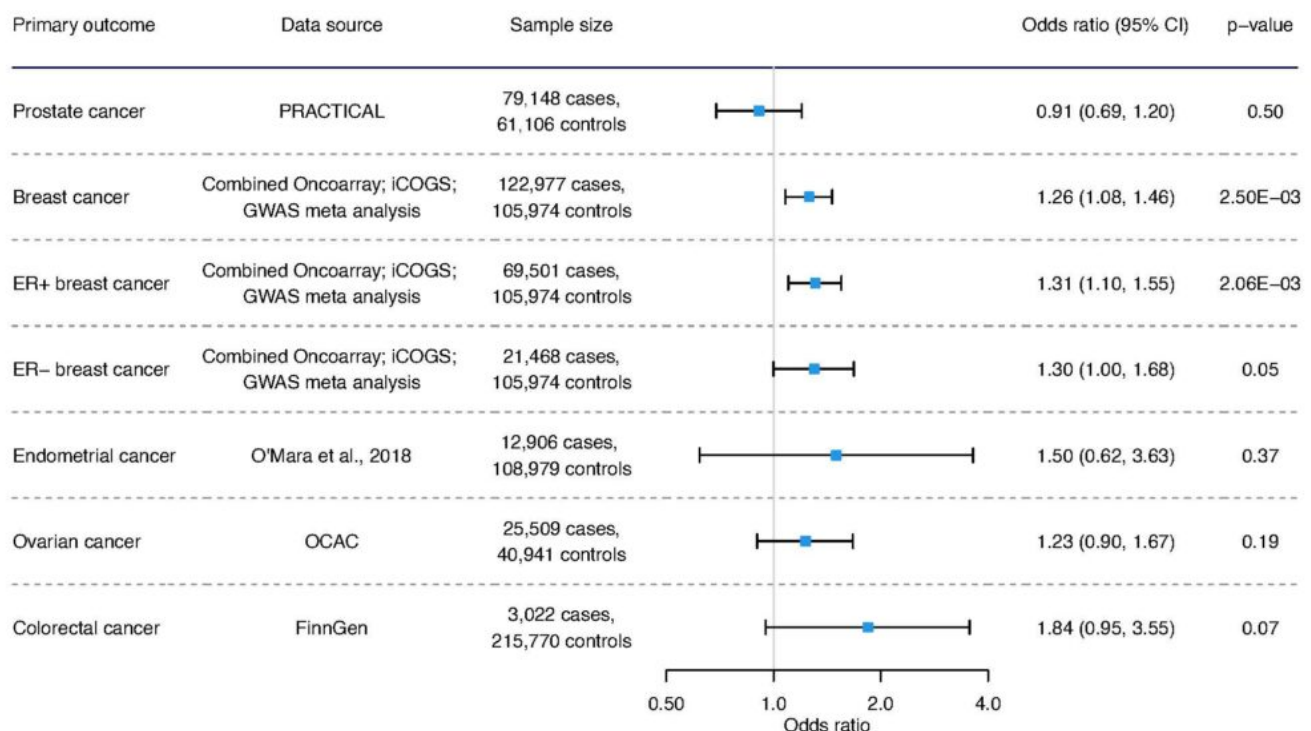| Performance Metric |
| --- |
| Sensitivity |
| Specificity |
| Negative Predictive Value (NPV) |
| Positive Predictive Value (PPV) |
| Area Under the ROC Curve (AUC) |
| Kappa |
| Weighted Sensitivity |

1B: Validation Metrics
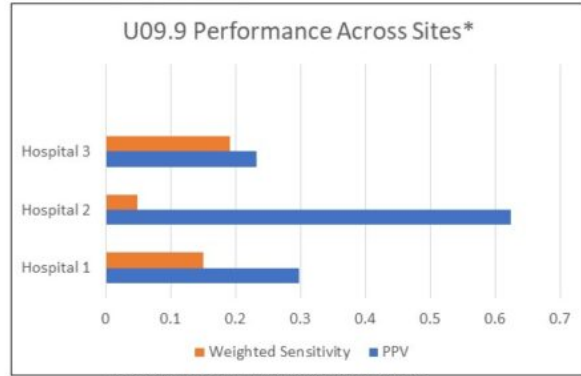
*Bar graph is not included on the CIPHER website

Using genetics to assess the role of acetate in ischemic heart disease, diabetes, and sex hormone-related cancers: a Mendelian randomization study Jie Zhao* Jie Zhao

Acetate, a short chain fatty acid, has attracted increasing attention with dual reputation, a potential benefit on cardiovascular health whilst concern on cancer, especially sex hormone-related cancers. These effects have been rarely examined in humans. To fill in this research gap, we used Mendelian randomization to minimize confounding and test causal relationship. Specifically, we used genetic variants strongly (p<5×10-8) and independently (r2<0.001) associated with acetate, and applying to large genome-wide association studies of ischemic heart disease (IHD) (up to 154,373 cases), diabetes (109,731 cases), and five sex hormone-related cancers (prostate, breast, endometrial, ovarian and colorectal cancer, 8,679 to 122,977 cases). Several methods, including penalized inverse variance weighting (pIVW), IVW, weighted median and weighed mode were used in the analysis. This study shows acetate is related to lower risk of IHD (odds ratio (OR) 0.61 per SD increase in acetate, 95% confidence interval (CI) 0.39 to 0.98) but higher risk of breast cancer (OR 1.26, 95% CI 1.08 to 1.46), robust to different sensitivity analyses. Acetate or factors affecting the activity of acetate may serve as potential targets for IHD and breast cancer, with implications for new drug development.

Primary outcome	Data source	Sample size		Odds ratio (95% CI)	p-value
Prostate cancer	PRACTICAL	79,148 cases, 61,106 controls		0.91 (0.69, 1.20)	0.50
Breast cancer	Combined Oncoarray; iCOGS; GWAS meta analysis	122,977 cases, 105,974 controls		1.26 (1.08, 1.46)	2.50E−03
ER+ breast cancer	Combined Oncoarray; iCOGS; GWAS meta analysis	69,501 cases, 105,974 controls		1.31 (1.10, 1.55)	2.06E−03
ER− breast cancer	Combined Oncoarray; iCOGS; GWAS meta analysis	21,468 cases, 105,974 controls		1.30 (1.00, 1.68)	0.05
Endometrial cancer	O'Mara et al., 2018	12,906 cases, 108,979 controls		1.50 (0.62, 3.63)	0.37
Ovarian cancer	OCAC	25,509 cases, 40,941 controls		1.23 (0.90, 1.67)	0.19
Colorectal cancer	FinnGen	3,022 cases, 215,770 controls		1.84 (0.95, 3.55)	0.07

LATEBREAKER

Cancer

Body Mass Index is Positively Associated with Overall Cancer Risk Among College Students in the United States: Results from the National College Health Assessment Shenghui Wu*
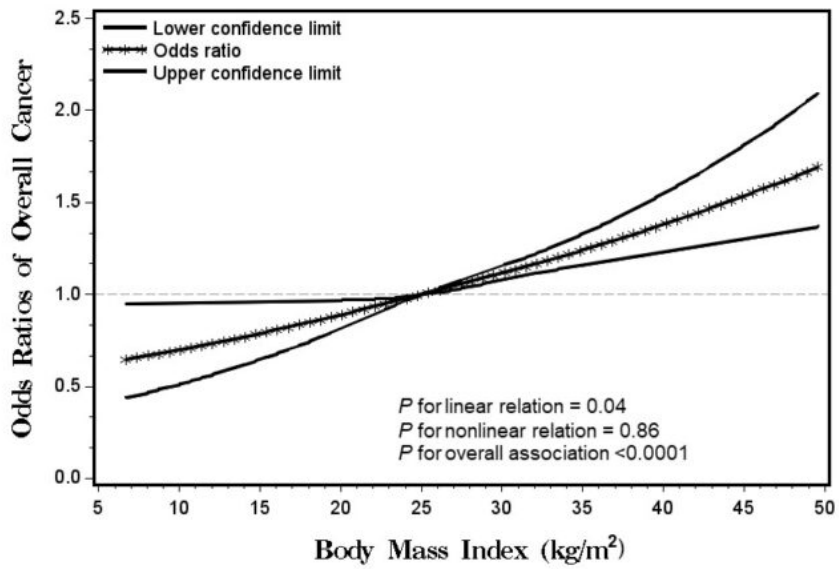Shenghui Wu Martie Thompson Richard W. Christiana Adam Hege Jennifer Schroeder Tyson

Background: To understand the dose-response relation between body mass index (BMI) and cancer, as well as the associations between overweight/obesity and overall cancer risk in US college students, we conducted the first epidemiologic study to examine these associations using data from the American College Health Association-National College Health Assessment (ACHA-NCHA).

Method: The ACHA-NCHA provided self-reported data on demographic information, physical activity, BMI, smoking status, and overall cancer during 2019-2022 (n=275,185; 0.08% cancer cases). A cubic spline model and logistic regression analyses were used to evaluate associations between BMI and cancer risk adjusting for covariates.

Result: The cubic spline observed that BMI (kg/m2) was positively associated with the odds of overall cancer risk after adjusting for age, sex, race, ethnicity, education level, physical activity, and smoking status (P for linear relation=0.02 and P for overall association<0.0001); a one kg/m2 increase in BMI was associated with a 1% increased overall cancer risk. Multivariable-adjusted logistic regression analyses showed that overweight (30>BMI≥25 kg/m2)) [odds ratio (OR): 1.20 (95% confidence interval (CI): 1.08-1.34)], and obesity (BMI≥30 kg/m2) [1.48 (1.32-1.65)] were positively associated with cancer risk.

Conclusion: BMI, especially overweight/obesity, may be positively associated with overall cancer among college students in the US. To reduce cancer risks, targeted interventions to keep healthy weight among college students are warranted.

Figure 1. Smoothed Plot for Odds Ratios (ORs) of the Overall Cancer Risk According to Body Mass Index (BMI) (kg/m^2). The ORs were estimated by using the restricted cubic-spline logistic regression models with knots placed at the 5th, 50th, and 95th percentiles of BMI. The model was adjusted for age, sex, race, ethnicity, education, physical activity, and smoking status.
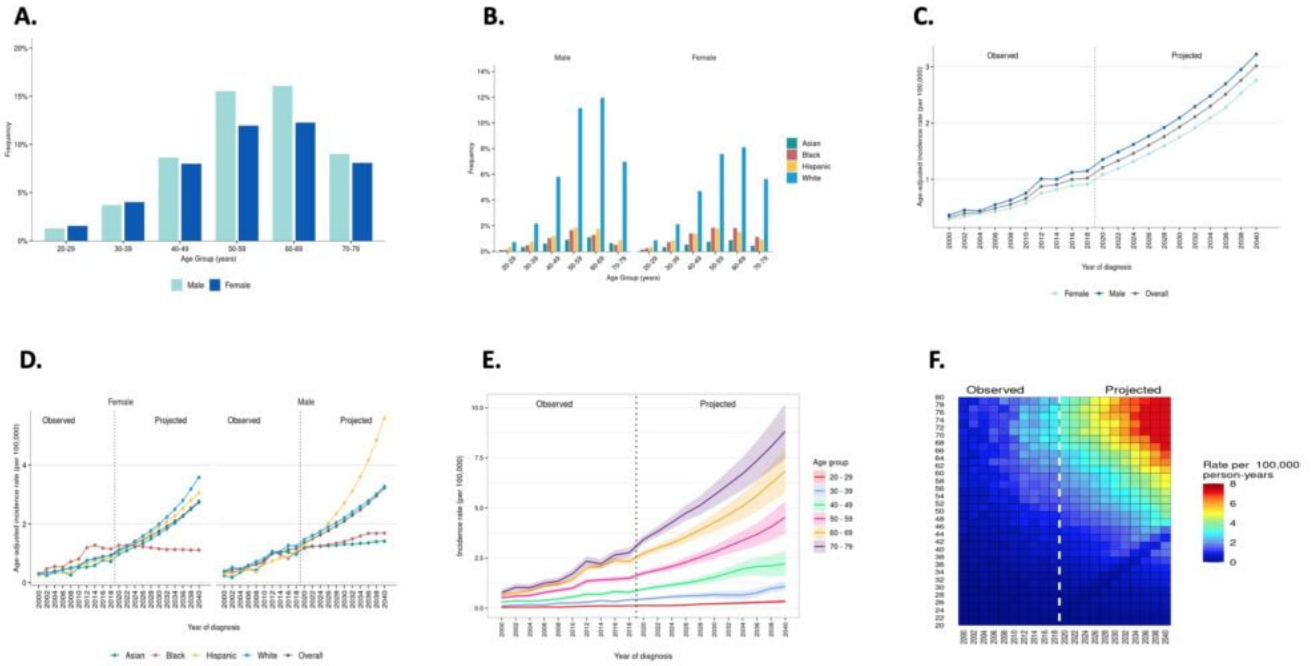
Pancreatic Neuroendocrine Tumors: Projecting Future Incidence in the United States up to 2040 Ganesh K. Giri* Samuel Antwi Ganesh K. Giri Miko A. Wieczorek Sophia G. Blumenfeld Dave O. Hodge Thorvardur R. Halfdanarson

Background: Pancreatic neuroendocrine tumor (pNET) is an orphan, rare malignancy accounting for about 2% of all pancreatic cancers. The incidence of pNET has been rising in the U. S. over the past few decades with a shift towards more early-stage diagnoses, but the etiology of this cancer is poorly understood. Because of insufficient data on pNETs, quantitative projection of future trends could inform strategies for risk prevention to help reduce incidence of this frequently fatal cancer.

Methods: We analyzed population data from the Surveillance Epidemiology and End Results Program (SEER 21) among individuals ages 20 to 79 years who were diagnosed with pNET between the years 2000 and 2019 (n=14,284). Age-period-cohort (APC) models were used to estimate changes in pNET incidence rates in both the observed period (2000-2019) and the projection period (2020-2040). Stratified analyses were performed by sex and ethnicity. All analyses were standardized to the 2010 U.S. population.

Results: Age-standardized pNET incidence rate increased each year, with per 100,000 person-years incidence rate of 0.32 in 2000 to 1.21 in 2019 to 3.02 in 2040. Overall, pNET incidence rates rose from 0.66 per 100,000 in the observed period to 2.00 per 100,000 in the projection period. Incidence rates were higher in men than women. Among women, pNET incidence rates are projected to be highest in non-Hispanic Whites, followed by Hispanics, and Asians, and expected to decrease in non-Hispanic Black women. Among men, incidence rates are expected to be highest in Hispanics, followed by non-Hispanic Whites, non-Hispanic Blacks, and expected to decline in Asian men.

Conclusion: Although pNETs have long been an orphan cancer, incidence rates increased in nearly all sexes and ethnicities in the observed period and are expected to continue to rise in most groups up to 2024, except for non-Hispanic Black women and Asian men. This study provides evidence of projected increases in pNET incidence in several population subgroups, especially Hispanics, non-Hispanic Whites, and non-Hispanic Black men, underscoring the need for vigilance in screening for pNET in these groups.

Figure 1. Incidence of pancreatic neuroendocrine tumors (pNETs) in the United States among individuals between the ages 20-79 years who were diagnosed from 2000 to 2019, with projections up to 2040. Panel **A** shows participants distribution in the observed data by age and sex. Panel **B** shows participants distribution by age, sex, and ethnicity. Panel **C** shows trends in pNET incidence overall, and by sex for the observed and projection periods. Panel **D** shows observed and projected trends in pNET incidence by sex and ethnicity. Panel **E** shows pNET incidence trends by age and panel **F** shows expected increase in pNET incidence at older ages starting from about 2027 to 2040.

LATEBREAKER

Cancer

Is there an association between Christian Religious Affiliation and Likelihood to Adhere to Recommended Cervical Cancer Screening Guidelines? Brittany Krenek* Brittany Krenek Idara Akpan Rohit Balasundaram Erika Thompson Justin Luningham

Purpose: Cervical cancer remains a United States (US) public health concern. The United States Preventative Services Task Force (USPSTF) recommends cervical cancer screenings (CCS) for individuals aged 21-65 –year-olds with a cervix; 74.2% adhere. Social and cultural-religious factors influence CCS adherence; however, little is known about adherence across Christian denominations. This study explored associations between CCS adherence and religious denomination affiliation, controlling for sociodemographic. Method: Women with a cervix 21-49 years old (n = 4561) were surveyed for USPSTF CCS adherence from the National Survey of Family Growth (2017-2019). Likelihood of adherence by Christian denomination vs. no religious affiliation was examined with weighted multivariable logistic regression, controlling for race/ethnicity, education, and age. Results: Overall, 56.3% of participants adhered. Adherence rates across Christian denominations were 65.8% among Black Protestants, 59.0% among Mainline Protestants, 53.2% among Catholics, 49.6% among Evangelical Protestants, 49.3% among other Religion, and 58.7% for no religious affiliation. Compared to no religious affiliation, evangelical Protestants and non-Christian religions had lower odds of adherence (OR=0.80, 95%CI [0.66, 0.98] and OR=0.67, 95%CI [0.52,0.86], respectively). Non-Hispanic Black women were more likely to adhere than non-Hispanic White women (OR = 1.96, CI [1.52, 2.53]). Women aged 30 or older were less likely to adhere than 21–29-year-olds (OR = 0.19, CI [0.16, 0.22]). No significant association was found between adherence and educational level. Conclusion: An association between adhering to CCS guidelines and religious denomination, accounting for sociodemographic, was indicated. Evangelic Protestants or non-Christian religions were less likely to adhere. Additional studies should further evaluate associations and advise culturally tailored campaigns to reduce CCS stigmas and increase overall adherence.

Pre-diagnostic Symptom Related Healthcare Utilization in Ovarian Cancer Patients: Insights from Latent Class Analysis Akalya Villenthi* Akalya Villenthi May Kuo Dawn Michelle Ritzwoller Sharon Peacock Hinton Stephanie B Wheeler Christopher Baggett Victoria L Bae-Jump Caroline A Thompson

Ovarian cancer (OCa) is the 6th leading cause of cancer-related mortality in U.S. women due to frequent late stage at diagnosis. While there is no recommended screening test, a better understanding of the pre-diagnostic symptom burden could provide evidence about how to improve earlier diagnosis. We used Latent Class Analysis (LCA) a statistical method to identify subgroups in high dimensional data, from analyzing symptom-related pre-diagnostic healthcare utilization (HCU) in a population-based sample of OCa patients residing in North Carolina. Adult OCa patients diagnosed 2009-2019 with 12+ months pre-diagnostic continuous insurance enrollment were identified from a linkage of statewide cancer registry and multiple-payer claims. We classified potential OCa symptoms using ICD codes and identified the provider type visited for the earliest symptom-related HCU. The LCA model included sociodemographic variables, comorbidity scores, OCa symptoms, and earliest provider type visited. We used logistic regression to estimate the relationship between class and stage at diagnosis. The study population included 2147 OCa patients who had symptom related pre-diagnostic HCU,64% were diagnosed with late-stage tumors, and 16% presented to the emergency department (ED). Among black patients (13%), 70% were late stage, and 24% presented to the ED. LCA identified two classes, **Class 1 (N = 1165, 54%):** younger women with primarily abdomen-specific symptoms and lower comorbidity scores who more often presented to primary care, and **Class 2 (N = 982, 46%)**: older women with higher non-specific symptom burden and multiple comorbidities who more often presented to the ED. Notably, **73%** of Black patients and 64% of lower income patients belong to Class 2 (vs. **42%** white and 34% highest income). Class 2 patients had **90%** higher odds of late-stage OCa**(OR:1.9; 95% CI:1.6-2.3)**. Our findings provide valuable insights for tailoring healthcare interventions aimed at enhancing the early detection of OCa.

LATEBREAKER

Cancer

Extremely Low-Frequency Magnetic Fields and Radiofrequency and the Risk of Childhood Central Nervous System Tumors in Mexico City Juan Manuel Mejia-Arangure* Juan Manuel Mejia-Arangure Victor Correa-Correa Juan C. Núñez-Enríquez Aurora Medina-Sanson

The central nervous system tumors (CNSt) are the second most common cancer in children and represent an important contributor to mortality in this age group. Their etiology remains largely unknown, however previous reports indicate that exposure to extremely low frequency magnetic fields (ELF-MF) and radiofrequency (RF) may be related to the risk of developing CNSt. Mexico City has a high frequency exposure to high levels of ELF-MF, however the RF exposure in the population is not known. Hence, we aim to investigate the association between ELF-MF and RF exposure and the risk of developing CNSt.

A case-control study in Mexico City from 2017 to 2022, where residential 24-hour ELF-MF measurements were obtained and the time of RF exposure was calculated for 200 patients with CNSt and 793 controls under 16 years of age. For ELF-MF exposure <0.1 µT was used to define the reference group. For RF exposure, we estimated the total exposure time in cell phone calls and the total time of use of electronic devices with and without internet use; exposure strata were grouped by quartiles, considering the lower quartile (<20000 minutes) as the reference group. Logistic regressions were implemented in R and SPSS.

ELF-MF exposure at ≥ 0.3 µT was observed in 11.6 % of our population. An increased risk of developing CNSt associated with high ELF-MF exposure (≥ 0.4 µT), aOR 2.64 95% CI 1.22-5.51. Cell phone use showed no differences between cases and controls. The use of electronic tablet for prolonged periods (>20000 min) with and without internet was associated with increased risk of developing CNSt, with an aOR of 2.46 (95% CI 1.02-5.64) and 6.17 (95% CI 1.49-30.51), respectively.

In the present study, the proportion of children exposed to ≥ 0.3 µT in Mexico City was high compared to those reported worldwide. Our results indicate that exposure to high levels of ELF-MF and prolonged use of electronic tablet with or without internet may be associated with increased risk of developing CNSt.

Cancer

Establishing a linked, pooled, longitudinal electronic health record (EHR) cohort to study racial/ethnic disparities in hepatocellular carcinoma (HCC) surveillance Enyao Zhang* Enyao Zhang Caroline A. Thompson Mindy Hebert-Derouen Alison Canchola Aly Cortella Pushkar Inamdar Janet Chu Sixiang Nie Mai Vu Ma Somsouk Michele Tana Anna Rubinsky Iona Cheng Mi-Ok Kim Mark Segal Chanda Ho Yihe G. Daida Su-Ying Liang Hashem El-Serag Scarlett Gomez Salma Shariff-Marco

Hepatocellular carcinoma (HCC) is a major contributor of cancer deaths in the U.S. Yet, uptake of guideline-recommended surveillance is low among those at higher risk of developing HCC, particularly in racial/ethnic minoritized groups. Surveillance underuse highlights a complex mix of patient, provider, healthcare system, and neighborhood level factors. Despite known racial/ethnic disparities in guideline surveillance, in-depth analysis identifying specific contributory factors is limited. We established a novel real world data resource to identify contributors to racial/ethnic disparities in HCC surveillance among a geographically and racially/ethnically diverse high-risk cohort. The study combined electronic health record (EHR) data from Sutter Health and Kaiser Permanente, with particularly robust representation of Hispanic and disaggregated Asian American groups, linked with state cancer registry data and neighborhood data. We included individuals from 2000-2017 with an in-person encounter, no prior liver cancer, and with clinical indication of cirrhosis, chronic hepatitis B or C, or a high Fib-4 score (indicating advanced liver fibrosis). Surveillance, defined as biannual ultrasounds, was measured by ever/never surveilled and time up to date with surveillance. Multivariable models will assess surveillance adherence disparities across racial/ethnic groups. Of the 73,048 high-risk patients identified (12,728 in Kaiser Permanente and 60,320 in Sutter Health), approximately 90% had cirrhosis, hepatitis B or C. Most were born between 1945-1965, with a balanced sex ratio and diverse racial/ethnic composition, including 21% Asian American, 8% Hispanic, and 5% Black. Utilizing detailed EHR data, this study creates a diverse cohort, differing from prior HCC surveillance research that relied on administrative and cancer registry data. Results will provide for a better understanding of racial/ethnic disparities and suggest multilevel factors for adherence improvements.

Association between Dual Eligibility and Diagnosis of Distant Stage of Colorectal Cancer (CRC) Among Low-Income Individuals in Urban Areas: An Analysis of SEER-Medicare Claims Data Saif Al Amin* Saif Al Amin Eman Metwally Sharon Peacock Hinton Caroline A. Thompson

Colorectal cancer (CRC) is a major health concern in the United States, with elevated mortality rates and pronounced disparities, particularly among low-income, urban populations. Older adults who are dually eligible Medicare-Medicaid beneficiaries are a particularly vulnerable demographic. Limited research has examined CRC outcomes in this population, especially late stage at diagnosis, which is strongly associated with poor survival. We examined the association of dual eligibility and CRC stage at diagnosis among low-income urban residents in the United States, and whether this association varied by race. We analyzed Surveillance, Epidemiology, and End Results linked Medicare data for individuals aged >65, living in low-income urban areas and diagnosed with primary invasive CRC between 2008-2017, who had 12 months pre-diagnostic continuous enrollment in Medicare (A/B, fee for service). To estimate the association between dual eligibility and late-stage CRC, we used a log-binomial regression model additionally adjusted for age, frailty, and comorbidities. A simple quantitative bias analysis was used to address potential confounding due to nursing home residency status. The analysis included 22,193 patients, 89% were non-Hispanic white, 54% were female, 59% had high frailty scores (>0.15), 92% were dual-eligible and 20% were diagnosed at distant stage. The estimated prevalence ratio (PR) of 1.11 (95% CI: 1.04-1.22) indicates a slightly higher adjusted prevalence of distant-stage CRC among duals compared to their non-dual counterparts. The QBA yielded an upward corrected PR of 1.14. No modification of this association was found by patient race. Despite being eligible for additional medical coverage, our study reveals that dually eligible populations are still at risk for poor CRC outcomes. These insights may be useful for shaping effective strategies and interventions to reduce the impact of CRC outcomes in vulnerable populations.

Cancer

Association Between Pre-diagnostic Cigarette Smoking and Colorectal Cancer Survival by Molecular Subtypes and Age-onset Status. Herve* Herve Fossou Zacharie Eric Bakwa Lolema II Amanda I. Phipps

Background: Colorectal cancer (CRC) is the third most common malignancy in US adults, and approximately 36% of those diagnosed die within 5 years of diagnosis. Smoking, an established risk factor for CRC, is suggestively associated with poorer CRC survival. However, it is unclear if this association varies by molecular subtypes or age at diagnosis.

Methods: Using data from two complementary study populations: the Colon Cancer Family Registry and the Advanced Colorectal Cancer of Serrated Subtype, we assessed the association of smoking history with CRC survival, overall and across CRC case groups. Tumor markers were tested in centralized laboratories, including microsatellite instability status (MSI), BRAF and KRAS somatic mutation status, and CpG island methylator (CIMP) status. Combinations of these tumor markers were used to classify participants into several etiologically distinct subsets. Information on age at diagnosis was available from cancer registry records. We used Cox regression analyses to describe associations of smoking with CRC survival overall and within groups defined by age at diagnosis and molecular subtypes.

Results: Among 4,901 participants in this study, 1,378 died due to CRC during study follow-up (average follow-up period = 13.6 years). Those who reported having ever smoked were more likely to die from CRC than never-smokers (HR=1.27; 95% CI:1.13-1.42); this association persisted after multivariable adjustment (HR=1.21; 95% CI:1.06-1.38). In analyses stratified by age at diagnosis, the observed association with smoking was limited to individuals with later-onset CRC (HR= 1.26 1.06-1.50). In analyses stratified by tumor molecular subtypes, smoking was similarly associated with survival for most subtypes, although this association was only statistically significant among participants with tumors that were CIMP-low or negative, MSI-low or MSS, BRAF and KRAS wildtype (HR=1.23 1.03-1.47).

Conclusion: Cigarette smoking is associated with poorer survival after CRC diagnosis, particularly for individuals diagnosed with CRC at later ages.

Cancer

Working conditions, sleep, and the risk of lung cancer Bernadette van der Linden* Bernadette van der Linden Drinbardha Elshani Arnaud Chiolero Stéphane Cullati

BACKGROUND Lung cancer is important in the working-age population in terms of incidence. Within a life course and eco-social perspective, smoking has been identified as a major cause, but the effects of other factors, including of occupation, are currently not well known. Work occupies large parts of life and working conditions might be a cause of cancer through its impact on stress or sleep disturbances causing suppressed immune function and melatonin dysregulation. Our aim was therefore to assess the effects of working conditions and sleep on lung cancer.

METHODS Data from the UK Biobank were used, a large-scale cohort study including half a million people between 40 and 69 years old at baseline and living in the UK. Incident cancer diagnoses were verified through the linkage with cancer registries. Logistic regression was used to estimate the association of working conditions and sleep with lung cancer risk, adjusted for potential confounders. Further analyses, including of the mediating effect of sleep on the relationship between working conditions and cancer, are ongoing and will be presented.

RESULTS 3923 lung cancers were diagnosed during 15 years of follow-up. Preliminary analyses showed that individuals who worked between 16-30 hours a week and who worked in jobs that never or rarely involved heavy manual or physical work had a lower risk of lung cancer (odds ratio (OR) = 0.78, 95% CI 0.62, 0.98; OR = 0,75, 95% CI 0.59, 0.95, respectively). A longer (OR = 1.64, 95% CI 1.04, 2.59) as well as a shorter (OR = 1.15, 95% CI 1.01, 1.31) than recommended sleep duration and having an evening chronotype (OR = 1.38, 95% CI 1.10, 1.72) were associated with a higher risk of lung cancer.

CONCLUSION Working conditions and sleep characteristics are associated with lung cancer risks. It is important to further understand and study the potential mechanisms behind these associations to help identify occupations and populations at higher risk as well as intervention targets.

Cancer risk, all-cause mortality, and graft failure/retransplantation with belatacept use among kidney transplant recipients in the United States Shyfuddin Ahmed* Shyfuddin Ahmed Karena Volesky-Avellaneda Kelly J Yu Jon Snyder Judy R Rees Fiona Zwald Ajay Israni Charles F Lynch Baozhen Qiao Christopher D Blosser Ruth M. Pfeiffer Eric A. Engels

Kidney transplant recipients (KTRs) have elevated cancer risk due to use of immunosuppressive medications. Belatacept (BEL), a less nephrotoxic CTLA4 agonist, was introduced for maintenance immunosuppression in 2011, but is contraindicated in EBV-seronegative KTRs due to risk of posttransplant lymphoproliferative disorder (PTLD). Evidence on cancer risk and other outcomes with BEL is limited.

We used linked US transplant and cancer registry data on KTRs treated with BEL (n=1,705) or tacrolimus (TAC, n=42,756). KTRs were followed from transplant until earliest of first cancer diagnosis, death, or graft failure/retransplantation (GF/RT) during 2011-19. We fit multivariable Cox regression models to compare cancer incidence between BEL and TAC users. We also assessed risk of basal cell carcinoma (BCC), skin squamous cell carcinoma (SCC), PTLD, death and GF/RT using the US transplant registry data (2,715 BEL, 68,626 TAC users).

Overall cancer incidence was 11.66 and 11.55 per 1000 person-years in BEL and TAC users, respectively. We did not find increased risk with BEL use for cancer overall (hazard ratio [HR] 1.03, 95%CI 0.78-1.36) and 11 individual cancer types, or death (1.10, 0.98-1.24) (see Table). BEL was associated with increased risk of stomach cancer (HR 4.73, 95%CI 1.30-17.18) and colorectal cancer (2.87, 1.16-7.07), based on small numbers (Table). BEL was not associated with risk of SCC, BCC, PTLD, or mortality overall and was associated with decreased risk of GF/RT (HR 0.88, 95%CI 0.76-1.02). Notably, BEL was associated with increased all-cause mortality in EBV-seronegative KTRs (HR 1.92, 95% 1.21-3.04).

This large study provides reassurance that BEL does not increase overall cancer risk compared to TAC among KTRs. The findings for stomach and colorectal cancers require further study. We observed a benefit in terms of GF/RT overall but an adverse association of BEL with death in EBV-seronegative KTRs, for whom this medication is contraindicated.

Table: Distribution and risk of the outcomes associated with belatacept use in kidney transplant recipients

Outcomes	Belatacept	Tacrolimus	Belatacept vs. tacrolimus	
	Incidence/1000 PY (n)	Incidence/1000 PY (n)	Unadjusted HR (95% CI)	Adjusted HR (95% CI)
Any cancer*	11.66 (53)	11.55 (1497)	1.02 (0.78-1.35)	1.03 (0.78-1.36)
Stomach	0.66 (3)	0.18 (23)	**3.73 (1.12-12.42)**	**4.73 (1.30-17.18)**
Colorectum	1.32 (6)	0.42 (54)	**3.31 (1.42-7.72)**	**2.87 (1.16-7.07)**
Pancreas	0.22 (1)	0.33 (43)	0.68 (0.09-4.93)	0.78 (0.10-5.90)
Lung	0.88 (4)	1.09 (141)	0.86 (0.32-2.32)	0.91 (0.33-2.51)
Melanoma	0.66 (3)	0.52 (68)	1.32 (0.42-4.20)	1.25 (0.38-4.15)
Breast (female only)	1.14 (2)	1.38 (70)	0.81 (0.20-3.32)	0.87 (0.21-3.69)
Ovary (female only)	0.57 (1)	0.26 (13)	2.13 (0.28-16.29)	2.03 (0.24-17.28)
Bladder	0.66 (3)	0.31 (40)	2.10 (0.65-6.78)	2.10 (0.61-7.21)
Kidney	1.32 (6)	1.85 (240)	0.70 (0.31-1.57)	0.63 (0.28-1.45)
Thyroid	0.66 (3)	0.46 (59)	1.43 (0.45-4.55)	1.37 (0.41-4.55)
Non-Hodgkin lymphoma	1.10 (5)	1.30 (169)	0.84 (0.34-2.03)	0.90 (0.36-2.25)
Myeloma	0.44 (2)	0.23 (30)	1.92 (0.46-8.06)	1.48 (0.33-6.57)
Kaposi sarcoma	0.44 (2)	0.18 (23)	2.39 (0.56-10.17)	2.29 (0.49-10.63)
Miscellaneous	2.64 (12)	2.09 (271)	1.30 (0.73-2.32)	1.44 (0.79-2.61)
Squamous cell carcinoma**	5.33 (59)	5.59 (1758)	0.96 (0.74-1.25)	0.87 (0.67-1.13)
Non-Hispanic White	10.28 (56)	11.18 (1654)	0.92 (0.71-1.20)	0.84 (0.64-1.10)
Basal cell carcinoma**	3.60 (40)	3.75 (1183)	0.96 (0.70-1.31)	0.84 (0.61-1.16)
Non-Hispanic White	6.92 (38)	7.56 (1128)	0.91 (0.66-1.25)	0.82 (0.59-1.13)
PTLD**	1.61 (18)	1.47 (467)	1.08 (0.67-1.73)	1.22 (0.76-1.98)
EBV seropositive at baseline	1.50 (16)	1.02 (253)	1.47 (0.89-2.44)	1.59 (0.94-2.67)
EBV seronegative at baseline	2.27 (1)	4.20 (167)	0.49 (0.07-3.46)	0.50 (0.07-3.56)
Death**	26.47 (295)	22.58 (7157)	**1.21 (1.08-1.36)**	1.10 (0.98-1.24)
EBV seropositive at baseline	25.69 (273)	23.18 (5700)	**1.14 (1.01-1.28)**	1.06 (0.93-1.20)
EBV seronegative at baseline	43.38 (19)	17.82 (709)	**2.69 (1.71-4.25)**	**1.92 (1.21-3.04)**
Graft failure/ retransplantation**	17.14 (191)	20.81 (6596)	**0.83 (0.72-0.96)**	0.88 (0.76-1.02)
EBV seropositive at baseline	16.84 (179)	20.62 (5072)	**0.82 (0.71-0.96)**	**0.86 (0.73-0.99)**
EBV seronegative at baseline	25.11 (11)	20.91 (832)	1.23 (0.68-2.24)	1.38 (0.76-2.51)

Bolded results indicate statistical significance (p<0.05).

Abbreviations: CI Confidence interval; EBV Epstein-Barr virus; HR Hazard ratio; Post-transplant lymphoproliferative disorders; PY Person-year

Adjusted for age (3 categories: <40 Years, 40-59 Years, ≥60 Years), transplant year (continuous), induction therapy with polyclonal antibody, induction therapy with IL2 antagonist, induction therapy with corticosteroid, and maintenance therapy with corticosteroid

* Outcomes were ascertained from the linked US transplant and cancer registry data (belatacept N=1,705, tacrolimus N=42,669,).

** Outcomes were ascertained from the US transplant registry (belatacept N=2,715, tacrolimus N=68,626).

Rural-Urban Differences in the Age-Adjusted Pediatric Cancer Mortality in the United States Josiane Kabayundo* Josiane Kabayundo Reitumetse Setai Emma Hymel Krishtee Napit Abraham Mengist Don Coulter Jenna Allison Shinobu Watanabe-Galloway Kendra Ratnapradipa

Introduction: While there is evidence of decreasing pediatric cancer mortality rates in the United States, limited studies exist on rural-urban disparities of pediatric cancer mortality; in addition, there is a knowledge gap in understanding whether these disparities differ by race. This study aimed to: **(**1) examine rural-urban differences in age-adjusted pediatric cancer mortality rate during the period 2016-2020 in the United States; (2) examine the moderating effect of race on the impact of rurality on pediatric cancer mortality (3) determine the time trend of pediatric cancer mortality rate between 2000 and 2020. **Methods:** The Surveillance, Epidemiology, and End Results (SEER) 12 data (2000-2020) were used to estimate the age-adjusted mortality rates (per 1,000,000 population) among children aged 0-19. The primary exposure variable was rurality. Rural-urban continuum Codes (RUCC) were used to classify rural and urban areas. SEER*Stat was used to calculate age-adjusted pediatric cancer mortality rates using the U.S. 2000 standard population and Tiwari modifications. Rural-urban pediatric cancer mortality rate comparisons were made for all cancers combined. Stratified analysis was conducted to test the moderation effect of race on the relationship between rurality and pediatric cancer mortality rates. Joint point analysis was used to estimate the annual percent changes (APCs) in mortality rates by rurality and racial/ethnic status. **Results:** Overall, there was no significant difference in age-adjusted mortality rates between rural and urban areas. When stratified by race, among Blacks, the mortality rate was lower in rural compared to urban areas (11.2 vs. 26.6 per 100,000), and among Americans Indians, the rate was higher in rural compared to urban areas (33.4 vs. 12.2 per 100,000). The mortality rates decreased between 2000 and 2020 (APC=-1.84, P<0.05). Both rural and urban areas have experienced a significant pediatric cancer mortality decline, however, urban areas experienced a steeper decline, with an APC of -1.86% compared to -1.57% in rural areas. Among different racial groups, Whites show a significant decline (APC of -2.01%) from 2000-2020, compared to Blacks (APC=-1.51%). **Conclusion:** Despite the decrease in mortality rates in both urban and rural areas, there are still geographic and racial disparities. Targeted interventions that address mortality rates among pediatric cancer patients should be developed.

Cancer

Disparities by Race, Ethnicity, and Socioeconomic Status in Survival among a Community-based Sample of Young Women with Metastatic Breast Cancer in the United States Jennifer Wang* Jennifer Wang Andrea Betts Caitlin Murphy

Background: Breast cancer is the most commonly diagnosed cancer in young women. We examined differences in survival by race/ethnicity and socioeconomic status (SES) among young women diagnosed with metastatic breast cancer (mBC) in community-based settings.

Methods: Young women (age 18-49 years) diagnosed with de novo or recurrent mBC between 2013 and 2021 were identified from the Flatiron Health electronic health record database, comprising 280 community-based cancer clinics in the U.S. Survival was compared by race/ethnicity and census-tract level SES, overall and by clinical subtype (HR+/HER2-, HER2+, triple negative [TN]). Cox proportional hazards models were used to examine associations with all-cause mortality, adjusting for age and year at diagnosis, clinical subtype, and practice type (community, academic).

Results: We identified 3,204 young women diagnosed with mBC (57.3% non-Hispanic White [NHW], 15.9% non-Hispanic Black [NHB], 13.0% Hispanic, 3.6% non-Hispanic Asian or Pacific Islander, 10.1% non-Hispanic Other). Most women had HR+/HER2- mBC, and a higher proportion of NHB and Hispanic vs. NHW women had TN mBC. Median survival was 47 months (95% CI: 44, 50) and differed by race/ethnicity and SES. For example, NHB women (34 months, 95% CI: 30, 38) had worse survival compared to NHW women (47 months, 95% CI: 42, 52), and women in the highest (59 months, 95% CI: 52, 72) vs. lowest quintile (40 months, 95% CI: 34, 49) of SES had better survival. In adjusted analysis, race/ethnicity was associated with mortality but not SES. For example, NHB women had 1.11 (95% CI: 0.96, 1.30) times increased risk compared to NHW women. This pattern persisted for women with HR+/HER2- but not HER2+ or TN mBC.

Discussion: There were no differences by race/ethnicity and SES in survival of young women with TN mBC, suggesting this subtype is not inherently more aggressive in young Black and Hispanic women. By contrast, disparities persisted for young women with HR+/HER2- mBC.

Cancer

Childhood cancers in relation to maternal depression and use of antidepressants Julia Heck*

Julia Heck Yu-Hsuan Chuang Ya-Hui Hu Onyebuchi A. Arah Beate Ritz Pei-Chen Lee

Background: Depression is one of the most common mood disorders in the general population, including in pregnant women. Severe maternal stress, such as bereavement, has been associated with increased childhood risks of non-Hodgkin lymphoma and hepatic and testicular cancers. Also, pregnancy intake of antidepressants was previously linked to child's neuroblastoma. This study examined whether maternal depression and use of antidepressants could be related to pediatric cancers.

Methods: This cohort study included all children born in Taiwan from 2004-2014 (N=1,995,184). We linked the Taiwan Maternal and Child Health Database, the Cancer Registry, and the Taiwan National Health Insurance database, including the Pharmaceutical Register. From these sources, we obtained depression diagnoses (using International Classification of Disease-9 coding) and antidepressant pharmaceutical use [via Anatomical Therapeutic Chemical (ATC) codes]. We used Cox proportional-hazard regressions to quantify the joint associations of maternal depression before or during pregnancy and the filling of antidepressant prescriptions (from 9 months before pregnancy until birth) with childhood cancers.

Results: Depression and/or antidepressant prescription use were related to a possible increase in retinoblastoma (HR=1.61, 95% CI 0.81-3.17) but showed small or no associations with pediatric cancers: acute lymphoblastic leukemia (HR=0.97, 95% CI 0.64-1.45), acute myeloid leukemia (HR=1.01 (0.46-2.22), non-Hodgkin lymphoma (HR=1.05, 95% CI 0.66-1.66), central nervous system tumors (HR=1.18, 95% CI 0.68-2.05), neuroblastoma (HR=1.07, 95% CI 0.58-1.97), hepatoblastoma (HR=1.23, 95% CI 0.54-2.83), and germ cell tumors (HR=1.07, 95% CI 0.55-2.10).

Conclusions: We found little to no compelling evidence of associations between maternal depression or its treatment and pediatric cancers in offspring, which should be a reassuring finding for pregnant women.

Cardiovascular

Although diabetes remains a predictor of major limb amputation in chronic limb-threatening ischemia patients, smoking history may need to be more carefully considered

Sydney Browder* Sydney Browder Teresa Filipowicz Nicole Kelly Katharine McGinigle

Objective:

Smoking and diabetes are clear risk factors for peripheral artery disease and its worst form, chronic limb-threatening ischemia (CLTI). Although the co-occurrence of smoking and diabetes increases poor outcomes in general, the combined effect of these factors on the risk of major limb amputation has yet to be quantified in a CLTI population.

Methods:

This was a secondary data analysis of PREVENT III, a randomized controlled trial of CLTI patients undergoing bypass surgery from 2001-2003. Smoking status was defined as never, former, or current and history of diabetes was binary. Interaction between smoking and diabetes was assessed using a likelihood ratio test (LRT; $\alpha=0.05$). We used crude generalized linear models to estimate stratum specific risks of limb amputation at 1 year and calculate RRs.

Results:

The 1,421 participants were mean age 68±12 years, 27% non-White, 36% female, 74% former or current smokers, and 64% had diabetes. Within 1 year, 31% had a limb amputation. There was no significant interaction between smoking and diabetes (LRT=1.84; p=0.175). Current smokers without diabetes were the least likely to have an amputation (15%) and never smokers with diabetes were the most likely (44%) [Diff (95%CI) = 29% (21%, 36%), p<0.001]. Diabetics were more likely to have an amputation compared to non-diabetics, regardless of smoking status, while ever smokers were less likely to have an amputation compared to never smokers (Figure 1).

Conclusions:

Ever smokers had a lower risk of amputation compared to never smokers which was not originally hypothesized. We considered two explanations: 1) never smokers are less likely to develop CLTI than ever smokers; therefore, never smokers who develop CLTI may have more aggressive/extensive disease and 2) ever smokers are less likely to survive to experience a major amputation than never smokers (survivor bias). Covariate selection should be carefully considered when studying CLTI and other advanced, chronic diseases.

Forest Plot: Risk of Major Amputation
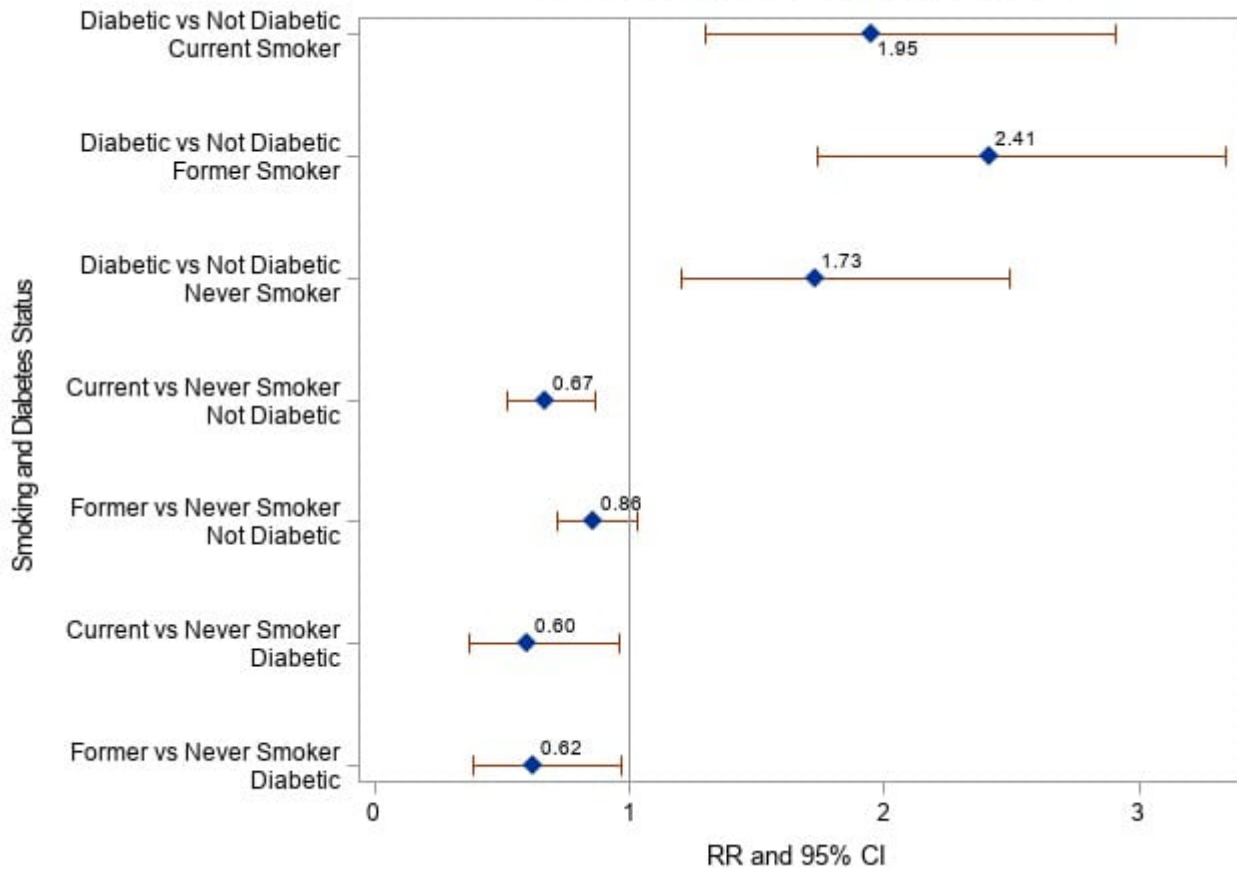
Sociodemographic predictors of cardiovascular health among low-income and racially and ethnically diverse children Subin Jang* Subin Jang Lenora Goodman Nancy E. Sherwood Simone A. French Alicia Kunin-Batson Junia N. de Brito

Background: The American Heart Association (AHA) identified health factors and behaviors as key measures for ideal cardiovascular health (CVH), known as Life's Essential 8 (LE8). Using LE8 (except sleep), we examined sociodemographic factors that were independently associated with CVH among children living in low income and racially/ethnically diverse households.

Methods: The analytic sample included 268 children who participated in the NET-Works randomized clinical trial and the NET-Works 2 prospective follow-up study. Sociodemographic factors were measured at baseline (aged 3.4±0.7yrs, 49% female; 63% Hispanic). At the 5-year follow-up visit (aged 9.4±0.7yrs), we calculated the total CVH scores (0-100) in addition to the score for each of 7 metrics: BMI percentile, plasma glucose, blood lipids (calculated as total – HDL cholesterol), blood pressure, smoke exposure, diet, and physical activity. Scores 80 to 100 indicated high CVH by AHA. Logistic regression models estimated odds ratios and 95% confidence intervals for the association between sociodemographic factors and CVH.

Results: The overall mean CVH score was 75.3±8.3. Thirty-two percent of the sample had high CVH (mean score 84.4±2.8) and 68% had low CVH (mean 71.0±6.4). Key factors driving high CVH scores were lower BMI percentile, lower non-HDL cholesterol, healthier diet, and higher physical activity. Sociodemographic factors associated with high CVH were higher household income (OR 3.37, 95% CI 1.67-6.78), parent's self-reported non-Hispanic White race (3.46, 1.62-7.39), advanced education (3.10, 1.52-6.35), and no participation in food assistance programs (WIC: 0.57, 0.33-0.97 and SNAP: 0.57, 0.34-0.97).

Conclusions: These findings highlight the importance of identifying groups at highest risk of poor CVH, such as socioeconomically disadvantaged populations, and developing strategies to address unique needs and barriers experienced by these children and families to enhance the CVH of all children.

Title: Titrating Antiplatelet Regimens in Peripheral Artery Disease Post-Revascularization Using Thromboelastography-Platelet Mapping (TEG-PM) Parameters: Adenosine Diphosphate Maximum Amplitude(ADP MA) and Arachnoid Acid Maximum Amplitude (AA MA) Fanah Hagos* Fanah Hagos Dua Anahita Patel Shiv Morrow Katherine Suarez Ferreira Sasha Patricia Lee Ivy

Background: Peripheral artery disease (PAD), resulting from atherosclerotic arterial occlusion, affects over 200 million individuals worldwide. Revascularization procedures, such as extremity artery bypass or endovascular stenting, are common to enhance limb blood perfusion. Thromboelastography with platelet mapping (TEG-PM) provides a comprehensive assessment of coagulation dynamics and holds potential for patient-centered thromboprophylaxis. **Aim:** (1) Evaluate the utility of ADP MA and AA MA, in conjunction with platelet aggregation/ inhibition. (2) Assess the impact of common comorbidities on TEG-PM values. **Methods**: Linear models used to examine time and comorbidity differences in ADP MA and AA MA, and Chi-squared tests to evaluate relationships between disease status and postoperative adverse events. Cox proportional hazards models assessed ADP MA and AA MA relationships with occlusion/stenosis in the intervention area, with cut point analysis for corresponding Kaplan-Meier curves. **Results**: A cohort of 194 patients, with a mean age of 72.0 years and a BMI of 26.6, the majority had hypertension (91%) and hyperlipidemia (91%), while 52.6% had diabetes. Diabetic patients exhibited significantly higher ADP and AA at both time points ($p \leq 0.0228$), contrasting with those with hyperlipidemia ($p \geq 0.144$). Cox proportional hazard analysis revealed a 2% increase in the risk of occlusion/stenosis with a 1 mm rise in AA MA (HR=1.02, 95%CI=1.00-1.04, p=0.031). Although ADP MA did not reach significance (HR=1.014, 95% CI=0.993-1.035, p=0.208), AA MA emerged as a significant predictor (HR=1.019, 95% CI=1.002-1.036, p=0.031). The optimal cut point for AA MA was identified as 49.4, yielding an AUC of 0.6186 in the univariable model. Furthermore, ADP MA had an optimal cut point of 49.3 with an AUC of 0.545 in the univariable model. **Conclusion:** findings underscore the potential of ADP MA/ AA MA as a meaningful indicator for predicting occlusion/stenosis events after revascularization.
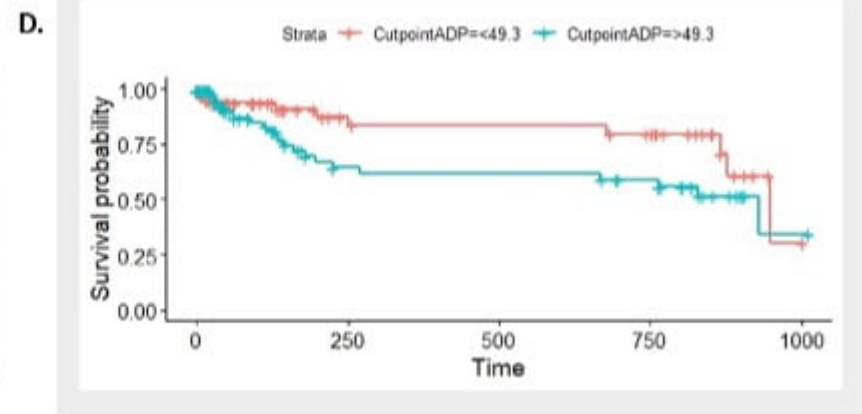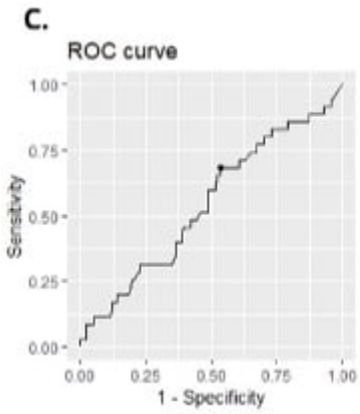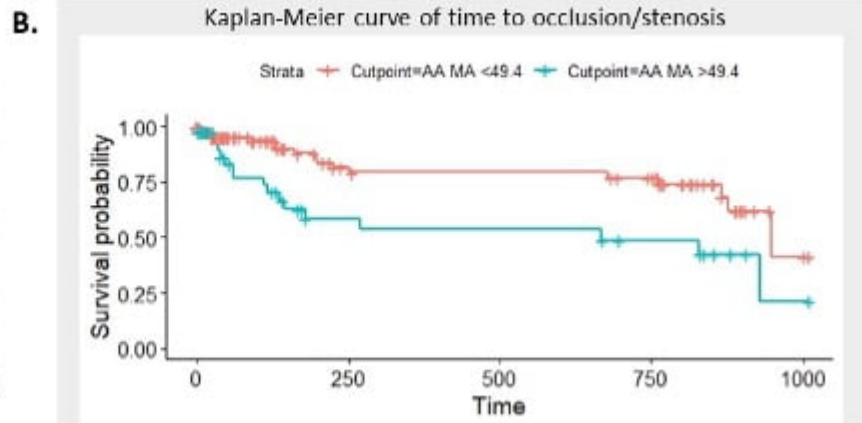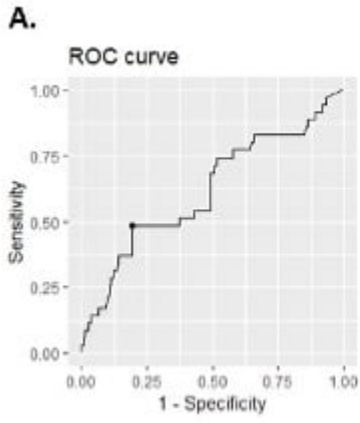
Association of smoking intensity with prevalence of radiographic abdominal aortic calcification: A cross-sectional study among community-dwelling older men Shabir Sarwary*

Shabir Sarwary John Schousboe Pawel Szulc Lynn Marshall

BACKGROUND

Abdominal aortic calcification (AAC) is a marker of cardiovascular risk. Smoking is associated with severe AAC; however, prior studies on this topic assessed smoking as a binary variable without accounting for the specific smoking habits.

METHODS

The association between smoking and AAC was assessed in 4,707 men from the Osteoporotic Fractures in Men Study. At baseline, smoking history (age initiated, frequency, age they quit) was assessed via self-reported questionnaires. Pack-years and age started smoking was categorized to 5 levels, quartiles for those who are current or former smokers. Time since quitting smoking was categorized to 6 levels, quartiles for those who were former smokers. AAC was assessed on the lateral lumbar spine radiographs using Kauppila's semiquantitative score. AAC severity was categorized as none (0, n=781), mild (1-4, n=1,865), and moderate/severe (5-24, n=2,061). Prevalence odds ratios (POR) and 95% CI were calculated using multinomial logistic regression adjusted for age, education, and social class status.

RESULTS

In the adjusted model, the odds of mild AAC were higher in the highest quartile of pack-years of smoking (42–111) compared to never-smokers (POR=2.46, 95% CI: 1.75, 3.44). Similarly, the odds of moderate/severe AAC were higher in the highest quartile of pack-years of smoking compared to never-smokers (POR = 8.33, 95% CI: 5.98, 11.59). POR increased across the quartiles of smoking for both mild and moderate/severe AAC. An overall pattern of decreasing POR was observed for both mild and moderate/severe AAC categories with increasing categories of time since quitting smoking, such as those with the most time since quitting smoking having the lowest prevalence of AAC.
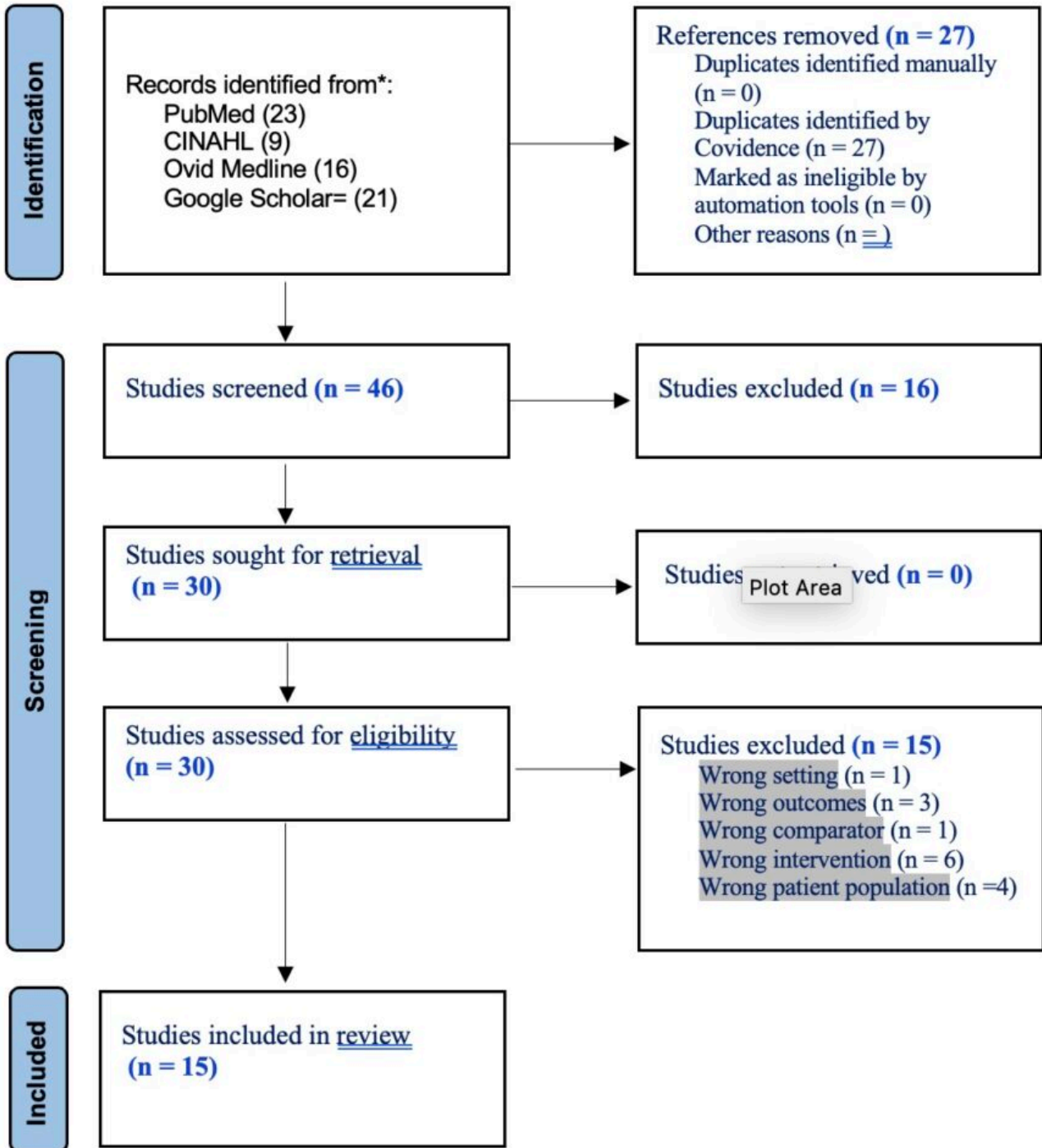
DISCUSSION

In this cohort of older men, heavy smoking was strongly associated with higher odds of AAC. Since smoking contributes to inflammation and oxidative stress, smoking cessation may result in slowing the progression of AAC among former smokers.

Evaluating the Efficacy of Thromboelastography with Platelet Mapping for Antiplatelet Titration in Peripheral Artery Disease After Lower Extremity Revascularization: A Comprehensive Literature Review Fanah Hagos* Fanah Hagos Dua Anahita Shiv Patel Morrow, Katherine Suarez Ferreira, Sasha Patricia Lee, Ivy

Background: Peripheral artery disease (PAD), affecting over 200 million people globally, has become endemic. Despite the increasing number of operative interventions, the prevalence of limb loss remains high. Objective: This literature review aims to assess the efficacy of Thromboelastography Platelet Mapping (TEG-PM) in titrating antiplatelet therapy post extremity revascularization surgery to prevent thrombosis. **Methods**: A comprehensive literature search was conducted across Ovid Medline, CINAHL, PubMed, and Google Scholar, using relevant Medical Subject Headings (MeSH) terms, from 2000 to December 2023. Inclusion criteria prioritized diagnostic accuracy, predictive value, and therapeutic implications of TEG parameters in PAD patients. Exclusion criteria ruled out studies unrelated to humans, vascular or endovascular surgery, or lacking sufficient TEG information. **Results**: The initial search yielded 68 references, with 22 duplicates identified. After screening titles and abstracts of 46 studies, 16 were excluded. Full-text assessment of 30 studies resulted in the inclusion of 15 relevant studies. Key themes emerged, emphasizing TEG-PM's efficacy in assessing antiplatelet therapy response, predicting thrombotic complications, and guiding personalized titration strategies post revascularization surgery in PAD patients. The studies demonstrated TEG-PM's ability to identify patients responsive or resistant to antiplatelet medications, facilitating tailored therapeutic interventions. Significant variability in response to mono- and dual antiplatelet therapy in PAD patients undergoing lower extremity revascularization was observed. **Conclusion:** This literature review highlights the growing role of TEG-PM in shaping antiplatelet titration strategies, studies suggest that TEG-PM can enhance precision in antiplatelet therapy, optimizing outcomes and reducing the risk of thrombotic and bleeding complications.

**Identification of studies via databases and registers**

Identification

Records identified from*:
  PubMed (23)
  CINAHL (9)
  Ovid Medline (16)
  Google Scholar= (21)

References removed (n = 27)
  Duplicates identified manually (n = 0)
  Duplicates identified by Covidence (n = 27)
  Marked as ineligible by automation tools (n = 0)
  Other reasons (n =)

Screening

Studies screened (n = 46)

Studies excluded (n = 16)

Studies sought for retrieval (n = 30)

Studies   ved (n = 0)
      Plot Area

Studies assessed for eligibility (n = 30)

Studies excluded (n = 15)
  Wrong setting (n = 1)
  Wrong outcomes (n = 3)
  Wrong comparator (n = 1)
  Wrong intervention (n = 6)
  Wrong patient population (n =4)

Included

Studies included in review (n = 15)

Cardiovascular

Sex differences in the multifactorial structural relationship between sugar-sweetened beverage intake and metabolic syndrome during adolescence WU, PEI-WEN* PEI WEN WU Yu-Ting Chin Sharon Tsai Wei-Ting Lin Chien-Hung Lee

Sugar-sweetened beverages (SSBs) are the primary source of dietary fructose intake. The metabolism of fructose involves an increase in uric acid (UA) and insulin resistance (IR), both of which are endogenous factors associated with metabolic disorders. Studies indicated that sex may modify the effect of endogenous factors on the aggregation of cardiometabolic abnormalities during adolescence. This study examined sex heterogeneity in the structural associations between SSB intake, UA, IR, and adolescent metabolic syndrome (MetS). A community-based cohort of 703 boys and 751 girls underwent assessments for dietary intake, physical activity, and clinical cardiometabolic outcomes. We applied structural equation modeling to evaluate sex differences in the multifactorial structural relationship across SSB intake, UA, homeostatic model assessment-based insulin resistance (HOMA-IR), and confirmatory factor analysis-derived MetS score (cMSs). The factor loadings for waist circumference and log-transformed triglyceride on the MetS construct were higher in boys (11.67 cm and 0.21 mg/dL) compared to girls (7.55 cm and 0.12 mg/dL). Adjusted for covariates, SSB intake had UA- and HOMA-IR-mediated effects on cMSs in both sexes. In boys, the two endogenous markers showed significant mediated effects on the association between consuming >500 mL/day of fructose-rich tea drinks (FTD) and cMSs. However, in girls, the indirect effect was only observed on the path of >500 mL/day FTD->HOMA-IR->cMSs. Our study helps to elucidate the effects of sex and endogenous markers on the structural relationship between SSB intake and the clustering of metabolic dysfunctions during adolescence.

Cardiovascular

A Multi-state Non-Markov Regression Model to Estimate Progression of Coronary Heart Disease (CHD) Ming Ding* Ming Ding Haiyi Chen Feng-Chang Lin

In chronic disease epidemiology, investigation of disease etiology has largely focused on one single endpoint, and progression of chronic disease as a multi-state process is understudied, representing a knowledge gap. Most of existing multi-state regression models require Markov assumption, which assumes that current state is independent of past states, and thus are unsuitable to estimate progression of chronic diseases that is largely non-memoryless. In this paper, we propose a new non-Markov regression model that allows past states to affect transition rates of current states. The key innovation is that by conditioning on past disease history, we divide disease states into substates to convert non-Markov to Markov process to estimate transition parameters. Specifically, we apply cause-specific Cox models (CSC) including past states as covariates to obtain transition rates (TR) of substates, as well as transition probability (TP) and state occupational probability (SOP) of substates. The transition parameters of disease states are calculated as weighted average of transition parameters of substates, where the weight is estimated based on distribution of past disease history. The significance of our model is that the division into substates allow to gain new mechanistic insight of chronic disease, and the transition parameters of disease states is highly suitable to describe progression of chronic diseases that exhibit non-Markov properties. We applied our model to describe progression of coronary heart disease (CHD) in the ARIC study, where CHD progression is modeled in five states: healthy, high risk (development of hypertension, hyperlipidemia, or type 2 diabetes), CHD, heart failure, and mortality. We obtained TR, TP, and SOP for each substate transition at each age (Figure). Our method has potential of wide application in chronic disease epidemiology.
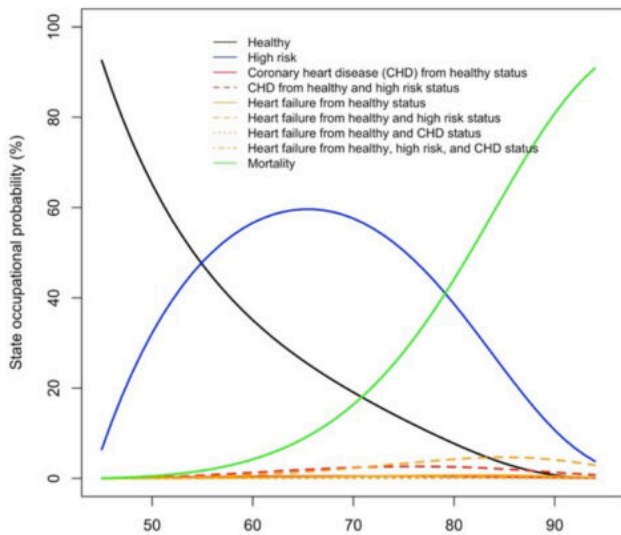
Transition rates
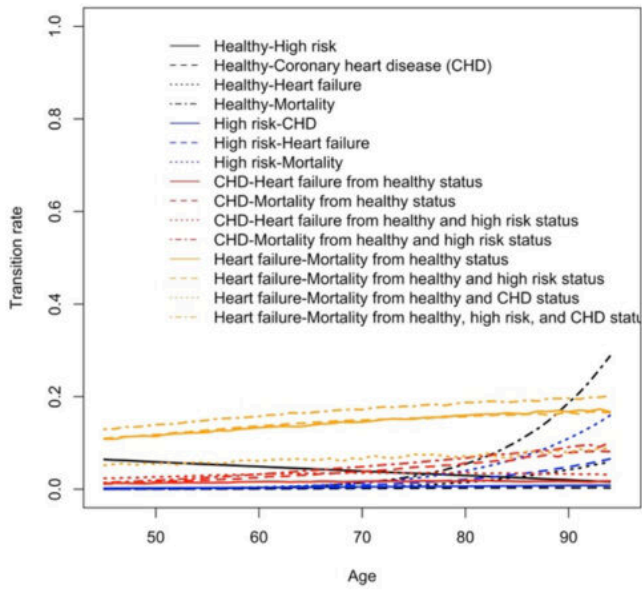
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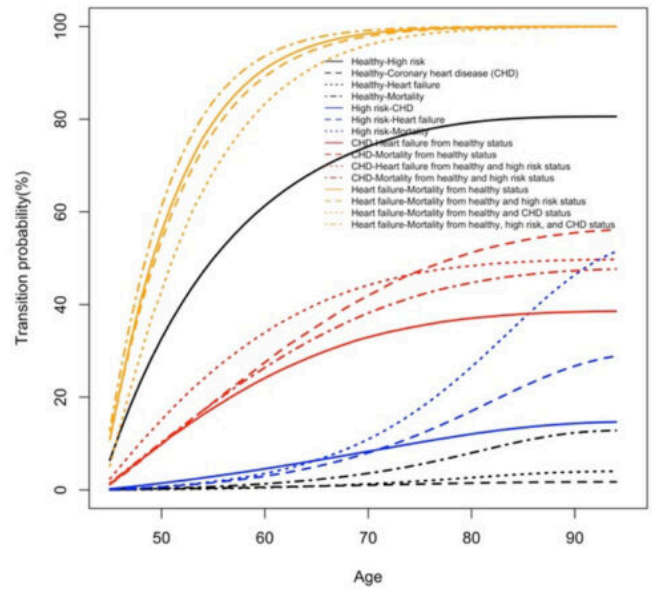
State occupational probabilities

Cardiovascular

Association of psoriasis with prevalence, incidence and progression of coronary artery calcification – the ELSA-Brasil cohort study William R. Tebar* William Tebar Vandrize Meneghini Giuliano Generoso Alexandre C. Pereira Marcio S. Bittencourt Raul D. Santos Itamar S. Santos Paulo A. Lotufo Isabela M. Bensenor

Introduction: Psoriasis is a chronic inflammatory disease which has been associated with a cardiovascular risk burden, including coronary artery calcium (CAC). However, investigation about psoriasis and CAC incidence and progression is still scarce.

Objective: To analyze the association of psoriasis with CAC prevalence, incidence and progression in the Brazilian Longitudinal Study of Adult Health (ELSA-Brasil).

Methods: Data from 3824 participants (51.0±8.9 years, 53.8% women) without cardiovascular disease and with CAC exams at baseline and after a 5-year follow-up were analyzed. CAC score (in Agatston units) was analyzed by computed tomography, while psoriasis was identified by reported medical diagnosis. CAC progression was dichotomously defined by Berry method (progression vs. no progression). The association of psoriasis with CAC prevalence, CAC incidence rate, and CAC progression was analyzed by Poisson regression with robust variance estimator and adjusted by sociodemographic factors, traditional risk factors, C-reactive protein and statin use. A sensibility analysis was performed excluding statin users.

Results: At baseline, participants with psoriasis (n=107; 2.8%) had higher prevalence of CAC≥100 than those without psoriasis (17.8% vs. 8.4%, p=0.001). CAC progression was observed in 61.9% (n=13 from 21) of participants with psoriasis and in 44.9% (n=326 from 726) of participants without psoriasis (p=0.123). Psoriasis was associated with prevalent CAC≥100 (Prevalence ratio [PR]: 1.61 [1.13; 2.29]) and incident CAC≥100 (Incidence rate ratio [IRR]: 2.40 [1.33; 4.34]) in fully adjusted analyses. Psoriasis was associated with CAC progression among non-statin users (PR: 1.63 [1.19; 2.23]) even after sociodemographic adjustment but not beyond traditional risk factors.

Conclusion: Psoriasis participants had higher prevalence and incidence of moderate-to-severe CAC burden beyond traditional risk factors.

Table 1. Association of psoriasis with prevalence, incidence and progression of coronary artery calcification in ELSA-Brasil cohort study.

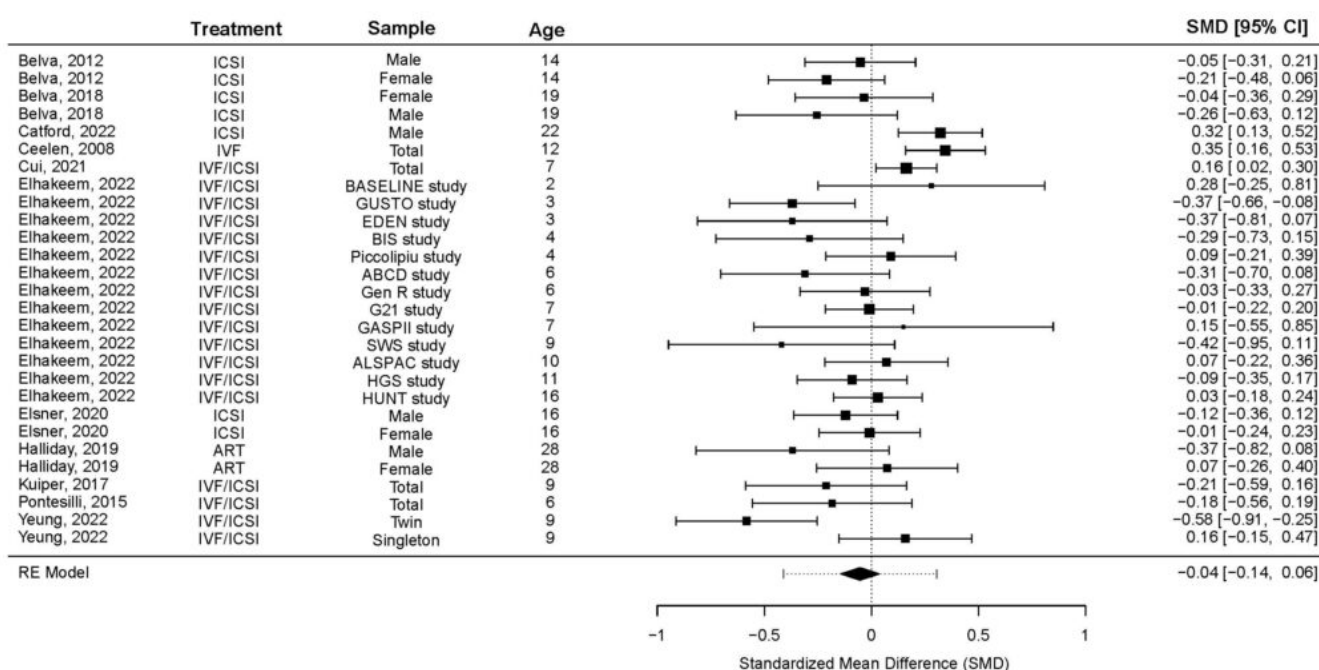| Statistical model adjustment	Unadjusted model	Sociodemographic factors	+ Traditional risk factors	+ C-reactive protein and statin use
	Baseline CAC>0 prevalence – PR (95% CI)			
Participants without psoriasis (n=3717)	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)
Participants with psoriasis (n=107)	1.20 (0.90; 1.59) p=0.208	1.06 (0.83; 1.34) p=0.663	0.97 (0.75; 1.24) p=0.795	1.01 (0.80; 1.29) p=0.914
	Baseline CAC≥100 prevalence – PR (95% CI)			
Participants without psoriasis (n=3717)	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)
Participants with psoriasis (n=107)	**2.12 (1.39; 3.22) p<0.001**	**1.62 (1.15; 2.28) p=0.005**	**1.56 (1.09; 2.22) p=0.015**	**1.61 (1.13; 2.29) p=0.008**
	5-year follow-up CAC>0 incidence – IRR (95% CI)			
Participants without psoriasis (n=2420)	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)
Participants with psoriasis (n=54)	0.90 (0.47; 1.73) p=0.758	1.02 (0.52; 2.01) p=0.959	1.04 (0.53; 2.04) p=0.916	1.08 (0.55; 2.14) p=0.828
	5-year follow-up CAC≥100 incidence – IRR (95% CI)			
Participants without psoriasis (n=3493)	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)
Participants with psoriasis (n=88)	1.92 (0.98; 3.76) p=0.056	**2.44 (1.27; 4.68) p=0.007**	**2.21 (1.21; 4.04) p=0.010**	**2.40 (1.33; 4.34) p=0.004**
Participants who met criteria (n=747)	CAC progression – PR (95% CI)			
Participants without psoriasis (n=726)	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)
Participants with psoriasis (n=21)	1.38 (0.98; 1.95) p=0.068	1.38 (0.99; 1.93) p=0.059	1.13 (0.75; 1.71) p=0.552	1.12 (0.74; 1.69) p=0.600
After statin users removed (n=609)				
Participants without psoriasis (n=592)	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)
Participants with psoriasis (n=17)	**1.60 (1.16; 2.21) p=0.004**	**1.63 (1.19; 2.23) p=0.002**	1.28 (0.86; 1.90) p=0.228	1.25 (0.85; 1.88) p=0.257

PR= Prevalence ratio; IRR= Incidence rate ratio; CI= Confidence interval; CAC= Coronary artery calcification. Sociodemographic factors were age, sex, race and education attainment; and traditional risk factors and biomarkers were smoking, alcohol consumption, physical inactivity, body mass index, hypertension, diabetes, total cholesterol and fasting glucose.

Cardiovascular

Infertility Treatment and Offspring Blood Pressure – A Systematic Review & Meta-analysis

Edwina Yeung* Edwina Yeung Priscilla Clayton Ian Alicia Livinski Diane Putnick

Studies have inconsistently observed that children conceived by in vitro fertilization (IVF), or intracytoplasmic sperm injection (ICSI) have higher blood pressure (BP) compared to children not conceived by assisted reproductive technologies (ART). We updated a 2017 meta-analysis and included data from contemporary cohorts and those with long follow-up. The protocol was registered on PROSPERO (CRD42022374232). Three databases and 4 grey literature sources were searched. Two authors screened 2493 records and extracted data from 35 included studies (from 51 publications). Data was analyzed using metafor and robumeta in R, allowing for robust estimation and clustering of effect sizes within cohorts. Unadjusted and covariate-adjusted statistics were analyzed separately as not all studies had adjusted measures. Covariates included maternal demographics (e.g., age, education, smoking), child characteristics (e.g., sex, age), and at times (25%) birth characteristics. Offspring were conceived between 1982 and 2016. Overall, 36 effect sizes from 24 unique cohorts compared BP between ART (N=4,851) and non-ART (N=8,151, reference) groups. No standardized mean difference (SMD) in systolic (β=0.04, 95%CI=-0.09–0.017), or diastolic (β=0.10, 95%CI=-0.05–0.24) BP by treatment was found, but heterogeneity was considerable (I2=77% for SBP; 88% for DBP). Adjusted analyses from 23 unique cohorts (N=2,220 treatment vs. N=39,778 non-treatment) similarly showed no difference for SBP (**Figure**) and DBP (β=-0.04, 95%CI=-0.17–0.10) but heterogeneity remained high (I2=63% for SBP; 85% for DBP). Removing 7 studies which adjusted for birth characteristics, as these may be mediators, made no material difference. Analyses were further stratified by type of treatment (i.e., IVF vs. ICSI vs. mixed), study quality, and birth year (<2000 vs. ≥ 2000) as potential moderators, but none reduced heterogeneity. In conclusion, conception by ART was not associated with offspring blood pressure in a meta-analysis, although considerable heterogeneity was observed.

Figure 1. Adjusted standardized mean differences (SMD) in systolic blood pressure comparing offspring conceived by ART vs. non-ART

Study	Treatment	Sample	Age	SMD [95% CI]
Belva, 2012	ICSI	Male	14	-0.05 [-0.31, 0.21]
Belva, 2012	ICSI	Female	14	-0.21 [-0.48, 0.06]
Belva, 2018	ICSI	Female	19	-0.04 [-0.36, 0.29]
Belva, 2018	ICSI	Male	19	-0.26 [-0.63, 0.12]
Catford, 2022	ICSI	Male	22	0.32 [0.13, 0.52]
Ceelen, 2008	IVF	Total	12	0.35 [0.16, 0.53]
Cui, 2021	IVF/ICSI	Total	7	0.16 [0.02, 0.30]
Elhakeem, 2022	IVF/ICSI	BASELINE study	2	0.28 [-0.25, 0.81]
Elhakeem, 2022	IVF/ICSI	GUSTO study	3	-0.37 [-0.66, -0.08]
Elhakeem, 2022	IVF/ICSI	EDEN study	3	-0.37 [-0.81, 0.07]
Elhakeem, 2022	IVF/ICSI	BIS study	4	-0.29 [-0.73, 0.15]
Elhakeem, 2022	IVF/ICSI	Piccolipiu study	4	0.09 [-0.21, 0.39]
Elhakeem, 2022	IVF/ICSI	ABCD study	6	-0.31 [-0.70, 0.08]
Elhakeem, 2022	IVF/ICSI	Gen R study	6	-0.03 [-0.33, 0.27]
Elhakeem, 2022	IVF/ICSI	G21 study	7	-0.01 [-0.22, 0.20]
Elhakeem, 2022	IVF/ICSI	GASPII study	7	0.15 [-0.55, 0.85]
Elhakeem, 2022	IVF/ICSI	SWS study	9	-0.42 [-0.95, 0.11]
Elhakeem, 2022	IVF/ICSI	ALSPAC study	10	0.07 [-0.22, 0.36]
Elhakeem, 2022	IVF/ICSI	HGS study	11	-0.09 [-0.35, 0.17]
Elhakeem, 2022	IVF/ICSI	HUNT study	16	0.03 [-0.18, 0.24]
Elsner, 2020	ICSI	Male	16	-0.12 [-0.36, 0.12]
Elsner, 2020	ICSI	Female	16	-0.01 [-0.24, 0.23]
Halliday, 2019	ART	Male	28	-0.37 [-0.82, 0.08]
Halliday, 2019	ART	Female	28	0.07 [-0.26, 0.40]
Kuiper, 2017	IVF/ICSI	Total	9	-0.21 [-0.59, 0.16]
Pontesilli, 2015	IVF/ICSI	Total	6	-0.18 [-0.56, 0.19]
Yeung, 2022	IVF/ICSI	Twin	9	-0.58 [-0.91, -0.25]
Yeung, 2022	IVF/ICSI	Singleton	9	0.16 [-0.15, 0.47]
RE Model				-0.04 [-0.14, 0.06]

Standardized Mean Difference (SMD)

Causal Inference

Causal Diagrams for Disease Latency Bias Ramin Rezaeianzadeh* Mahyar Etminan Ramin
Rezaeianzadeh Mohammad Mansournia

Objective: Disease latency is defined as the time from disease initiation to disease detection.
Disease latency bias (DLB) can affect epidemiological studies that examine the causal effects of
different exposures (eg, a drug) with a wide range of chronic diseases. Using casual diagrams we
demonstrate four scenarios where disease latency can introduce bias into causal epidemiologic
studies.

Methods: A number of epidemiologic studies have shown that benzodiazepines can increase the risk
of dementia. Some of these results could have been affected by DLB since the prodromal signs of
dementia could have preceded benzodiazepine use. We show 4 different causal directed acyclic
graphs (cDAGs). We define variables: E (benzodiazepine use), Y (diagnosed dementia), Y* (early
symptoms of dementia), U (unmeasured confounder) C are subjects censored from the study and M
is a mediator between Y* and E.

Figure 1. **Biasing path through an unmeasured confounder.** U represents the unmeasured
confounder 'insomnia'. DLB might be introduced when U is a common cause of Y* (early signs of
cognitive deficit secondary to dementia) and use of a benzodiazepine. A biasing path can be
introduced through the path.

$Y \leftarrow *Y \leftarrow U \rightarrow E$

Figure 2. **Biasing path through reverse causality bias.** Early signs of cognitive deficit years prior
to diagnosis of dementia can lead to use of benzodiazepines prior to dementia diagnosis. A biasing
path is created through Y* which acts as an unmeasured confounder $Y \leftarrow Y* \rightarrow E$

Figure 3. **Biasing path through Selection bias.** C is a collider on the path $E \rightarrow C \leftarrow Y* \rightarrow Y$. Subjects
who experience early cognitive adverse events of dementia (Y*) and an experience an adverse event
of benzodiazepines are censored from the study and analysis is done only among those who stay in
the study (represented with a boxed C=0).

Figure 4. **Biasing path through a mediator.** The effect of Y* is mediated on E through M (number
of physician visits). Early signs of dementia prompts patients to have more physician visits which will
make it more likely for them to be prescribed a benzodiazepine. Adjustment for M in these studies
can lead to

Conclusion: Disease latency bias is am important bias that might effect epidemiologic studies that
examine a latent outcome. Sensitivity analysis including probabilistic bias analysis can be
undertaken to control for this bias.

Causal Diagrams for Disease Latency Bias Mahyar Etminan* Mahyar Etminan Ramin Rezaeianzadeh Mohammad Ali Mansournia Mahyar Etminan

Objective: Disease latency bias (DLB) can affect epidemiologic studies that examine the causal effects of exposures (eg, a drug) with a wide range of chronic diseases. Using causal directed acyclic graphs (cDAGs), we demonstrate four scenarios where disease latency can introduce bias into causal epidemiologic studies.

Methods: Epidemiologic studies have shown that benzodiazepines can increase the risk of dementia. Some of these studies could have been affected by DLB as the prodromal signs of dementia could have preceded drug use. We show 4 different cDAGs related to this question with variables A (benzodiazepine use), Y (diagnosed dementia), Y* (early dementia symptoms), U (unmeasured confounder), C (censored subjects) and M (mediator between Y* and A).

Figure 1. **Biasing path through an unmeasured confounder.** U represents the unmeasured confounder 'insomnia'. DLB may be introduced when U is a common cause of Y* (early signs of dementia) and use of a benzodiazepine. A biasing path can be introduced through the path: Y←*Y←U→A.

Figure 2. **Biasing path through reverse causality.** Early signs of cognitive deficit can lead to benzodiazepine use years prior to diagnosis of dementia. A biasing path is created through Y*, acting as an unmeasured confounder: Y←Y*→A

Figure 3. **Biasing path through selection bias.** C is a collider on the path A→C←Y*→Y. Subjects experiencing early symptoms of dementia (Y*) and adverse events from benzodiazepine use are censored and analysis is done only in those who stay in the study (represented by a boxed C=0).

Figure 4. **Biasing path through a mediator.** The effect of Y* is mediated on A via M (number of physician visits). Early signs of dementia prompts patients to have more physician visits, and more likely to receive a benzodiazepine. Adjustment for M in these situations can close the biasing path.

Summary: DLB is an underrated bias that might methods such as probabilistic sensitivity analysis to better address it.
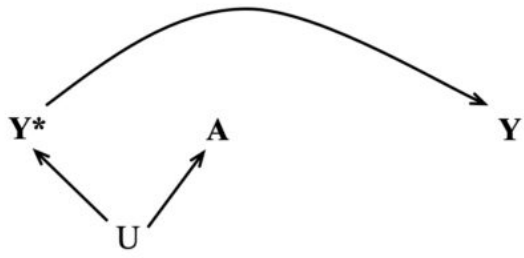
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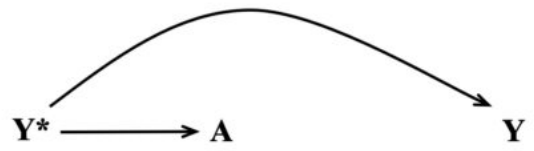
Figure 2

Figure 3

Figure 4

Causal Inference
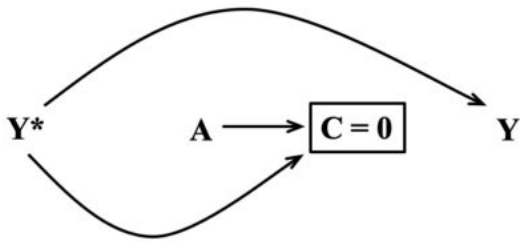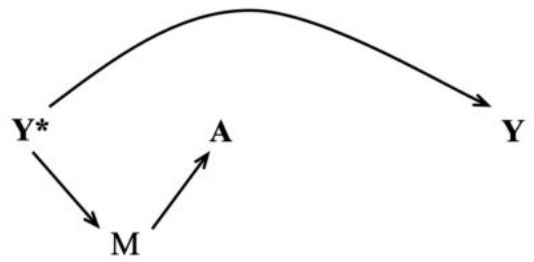
Everything and the kitchen sink? Improving our models for selective attrition among breast and lung cancer survivors and the impact on estimated aging trajectories Sophia Fuller* Sophia Fuller Sowmya Vasan Hailey Banack Alexandra Binder Elizabeth Cespedes Feliciano

In cancer research, evaluating long-term declines of physical function is complicated by differences in censoring between cancer survivors and cancer-free individuals as well as differences by cancer type, stage, and baseline functional status. Inverse probability of censoring weights (IPCW) can be used to account for selective attrition. The objective of this research is to compare two approaches to fitting IPCW: 1) IPCW generated using Super Learner (IPCW-SL) and 2) IPCW generated using a standard generalized linear model approach (IPCW-GLM). Super learner, an ensemble machine learning algorithm, is a prediction modelling technique useful as datasets become larger and computational efficiency increases. However, generalized linear models (GLMs) are still the default for estimating the probability of censoring. Using Women's Health Initiative data, we matched women with breast and lung cancer to women without cancer by age at diagnosis. We followed women up to 16 years after diagnosis (or index date) and predicted the probability of censoring at each follow up year using both a GLM and super learner with 10-fold cross validation. We used the predicted probabilities from these models to create stabilized IPCW-SL and IPCW-GLM and compared their relative performance across successive waves of follow-up. Women with late-stage cancer, especially lung cancer, had higher weights to account for the degree of censoring compared to earlier stage and cancer-free women. We next used these weights in generalized estimating equations to examine trajectories of physical function decline among breast and lung cancer survivors vs. age-matched women without cancer; we will examine how each weighting schema changes the estimated rate of physical function decline. As computational efficiency increases, ensemble prediction models are becoming more accessible and may outperform traditional methods.

Social Disconnectedness and Cognitive Functioning: An Application of a Novel Causal Inference Approach for Health Disparity Research Xi Wang* Xi Wang Toshiaki Komura Koichiro Shiba

Background: Social disconnectedness can be a threat to disparities in the cognitive functioning of older adults, yet prior research has examined its impacts on the population average outcome rather than its disparities.

Methods: We analyzed the longitudinal data of adults aged ^{3} 50 from the Health and Retirement Study (HRS; n = 11,322) and the English Longitudinal Survey of Aging (ELSA**;** n = 5,179). We assessed binary exposures of social isolation and loneliness at baseline. Cognitive functioning was measured four years after the baseline. We assessed disparities in cognitive functioning by income, wealth, education, and race. Controlling for 35 pre-baseline characteristics, we estimated the heterogeneous effects of disconnectedness on cognitive function using a causal forest algorithm. We simulated changes in the class-based and racial disparities in cognitive function under various interventional scenarios changing the exposure distributions.

Results: We observed existing disparities in both the exposure and the outcome. We found the population average association between social isolation and lower cognitive functioning in HRS (estimated ATE = -0.23; 95% CI: -0.35, -0.11) and ELSA (estimated ATE = -0.35; 95% CI: -0.54, -0.16). In HRS, we also found evidence of effect heterogeneity such that the association between social isolation and lower cognitive functioning was stronger among those with lower educational attainment and Black race but higher income and wealth. We found no effect of loneliness on cognitive functioning. Disparities in cognitive functioning were simulated to decrease under all hypothetical interventions reducing the prevalence of social isolation, particularly ones that addressed disproportionate distributions of the exposure itself.

Conclusion: Public health interventions reducing the population prevalence of social isolation and its disparities have the potential to narrow health disparities in cognitive functioning.
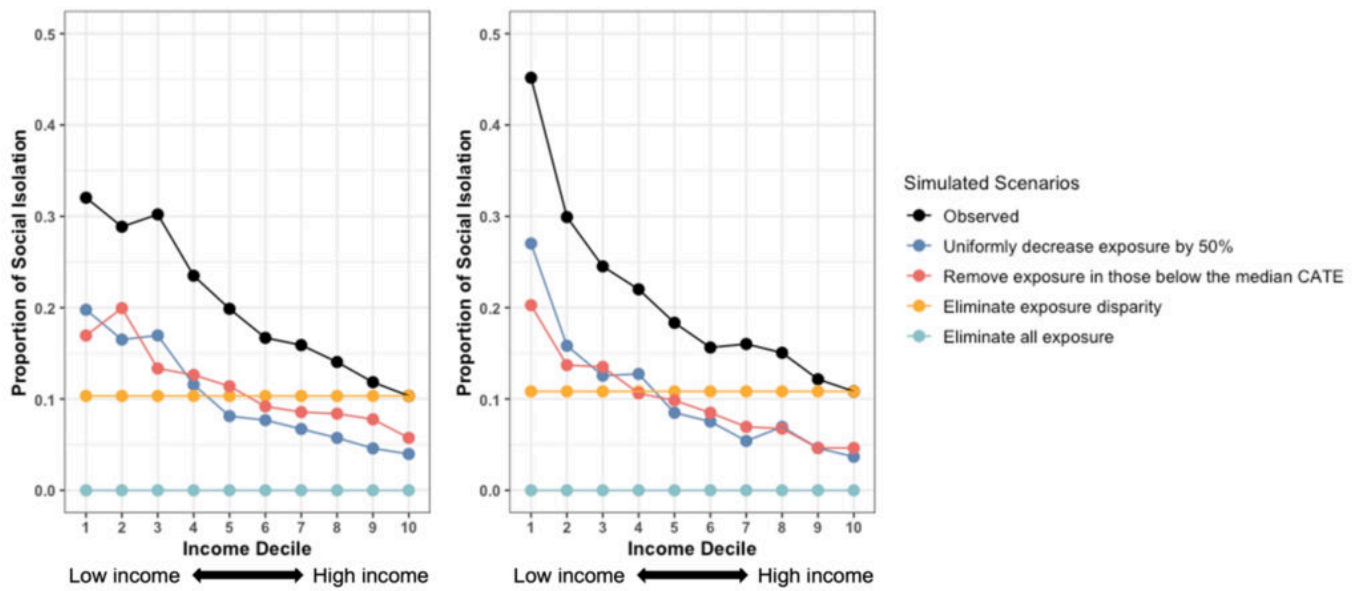
Figure 1: Comparison of income-based inequalities of social isolation in HRS and ELSA: existing vs. simulated scenarios.

Abbreviations: HRS, the Health Retirement Study; ELSA, the English Longitudinal Survey of Aging.

LATEBREAKER

Causal Inference

Decompression surgery with or without fusion in subgroups with degenerative lumbar spondylolisthesis Harrison Hansford* Harrison Hansford Margreth Grotle Tore Solberg Bjørnar Berg Christian Hellum Ivar Austevoll Tor Ingebrigtsen Issa Dahabreh Hopin Lee Matthew Jones James McAuley Aidan Cashin

BACKGROUND Lumbar spinal surgery is indicated for patients with degenerative spondylolisthesis (DS) who have minimal improvement with non-surgical care. Adding fusion to decompression has been shown in two RCTs to have no benefit beyond decompression alone and comes with increased costs and complications (Försth NEJM 2016; Austevoll NEJM 2021). However, it is suggested some subgroups benefit from additional fusion.

METHODS Using observational data from the NORSpine registry we emulated the NORDSTEN trial (Austevoll 2021) to compare decompression alone to with additional fusion. We included patients aged 18-80 with a diagnosis of DS and back or leg pain for ≥3mo. We excluded those with previous surgery at the level of the DS. We estimated the between-group mean difference on the Oswestry Disability Index and reoperation rate at 1-year post surgery, and risk of peri-operative complications. Subgroups investigated were: back pain intensity, BMI, sex, age, ASA score, smoking status, and difficulty walking. We adjusted for confounding using inverse probability of treatment weighting.

RESULTS From 2007-2021, 3817 patients underwent surgery for DS in NORSpine. We included 1409 patients who received decompression alone and 770 who received additional fusion surgery. Our primary outcome had estimate agreement with the index trial (trial=0.7/100 95%CI -2.8-4.3; emulation=1.8/100, 0.1-3.5), favoring fusion surgery. There was no additional risk of reoperation (RR=1.2, 0.89-1.84) and lower risk of complications (RR=0.62, 0.41-0.95) from decompression alone. The subgroup with back pain >6/10 had a 3.2/100 (0.6-6) greater treatment effect from fusion than those with lower pain. All other subgroups were not significantly different.

CONCLUSION There may be small benefits of adding fusion to decompression alone, with this effect larger in people with higher back pain. However, additional fusion comes with increased risk of adverse events and effect sizes are unlikely to be meaningful.

Assessing COVID-19 disease transmission timelines: a meta-analysis of global average and pooled distributions of SARS-CoV-2 incubation periods Liz Best* Liz Best Tony Cappello Alex Riordan Hannah Mazzotta Stephanie Tack Megan Henry Katrina Stadler Angie Shen

Background: Understanding the average and pooled distribution of COVID-19 incubation periods provides invaluable information when conducting public health and epidemiological assessments of potential or assumed SARS-CoV-2 exposures among individuals and populations. **Methods:** We conducted an updated systematic literature review, meta-analysis, and pooled distribution analysis of COVID-19 mean incubation period. We qualitatively reviewed 54 relevant publications and included 20 publications in our meta-analysis; 9 studies were used for pooled distribution estimation. Random effects models were used for calculation of the pooled estimates, including mean incubation period, by variant, by country, and mu and sigma distribution parameters. **Results:** The overall pooled mean incubation period was 4.37 days (95% CI: 4.16-4.59). Meta-RRs decreased with each subsequent variant, with the exception of the beta variant [novel: 5.65 days (95%, 5.02-6.28), alpha: 4.73 days (4.17-5.28), beta: 5.18 (95% CI: 4.93-5.43), delta: 4.23 days (95% CI: 3.91-4.54), and omicron: 3.54 days (95% CI: 3.24-3.84)]. Mean incubation period varied by country with the shortest mean incubation period in Spain [3.23 days (95% CI: 3.04-3.42 days)] and the longest mean incubation period in China [5.28 days (95% CI: 4.57-5.99 days)]. Pooled distribution analysis yielded a lognormal distribution of mu and sigma of 1.19 and 0.51. The highest probability timeline of exposure occurs between 2 and 4 days prior to symptom onset. **Conclusions:** Pooled risk estimates and distributions of COVID-19 incubation periods from this study can be used to help determine the most probable or likely timeline of exposures based on the date of symptom onset of individual suspected or assumed COVID-19 exposures, particularly in the absence or unavailability of individual case contact tracing, close contact testing, and genomic surveillance.

Does COVID-19 Increase the Risk of Subsequent Kidney Diseases More Than Influenza? A Retrospective Cohort Study Using Real-World Data Yue Zhang* Yue Zhang Nasrollah Ghahramani Vernon Chinchilli Djibril Ba

Background: Although case reports and observational studies suggest COVID-19 increases the risk of kidney diseases, definitive real-world evidence, especially in comparison with influenza, is lacking. Our study aims to assess the association between COVID-19 infections and subsequent kidney diseases, using influenza as a positive control and incorporating a negative control to establish clearer associations.

Methods: A large retrospective cohort study with strata matching was conducted using the MarketScan database with records from Jan. 2020 to Dec. 2021. We used the international classification of 10th revision (ICD-10) codes to identify individuals and build three cohorts, COVID-19, Influenza but no COVID-19 (positive control), and no COVID-19 / Influenza (negative control). The main outcomes were acute kidney injury (AKI), and chronic kidney disease (CKD). To evaluate the association between COVID-19 and the onset of kidney diseases relative to both control groups, we employed multivariable stratified Cox proportional hazards regression analysis.

Results: The study included 939,241 individuals with COVID-19, 1,878,482 individuals in the negative control group, and 199,071 individuals with influenza. After adjusting for demographics, comorbidities, and medication histories, COVID-19 was significantly associated with increased risks of AKI (HR: 2.75, 2.62-2.88) and CKD (HR: 1.38, 1.32-1.45), while influenza was associated with a modestly increased risk of AKI (HR: 1.23, 1.10-1.37) and had no impact on CKD (HR: 1.03, 0.92-1.14). Time-specific analyses indicated that while the HR for AKI declined from 0-180 days to 0-540 days, CKD's HR remained stable, with COVID-19's risk surpassing influenza's throughout follow-up (Figure).

Conclusion: COVID-19 infections were associated with a 2.4-fold risk of developing AKI and a 1.4-fold risk of CKD as compared to influenza. Greater attention needs to be paid to AKI and CKD in individuals after contracting COVID-19.
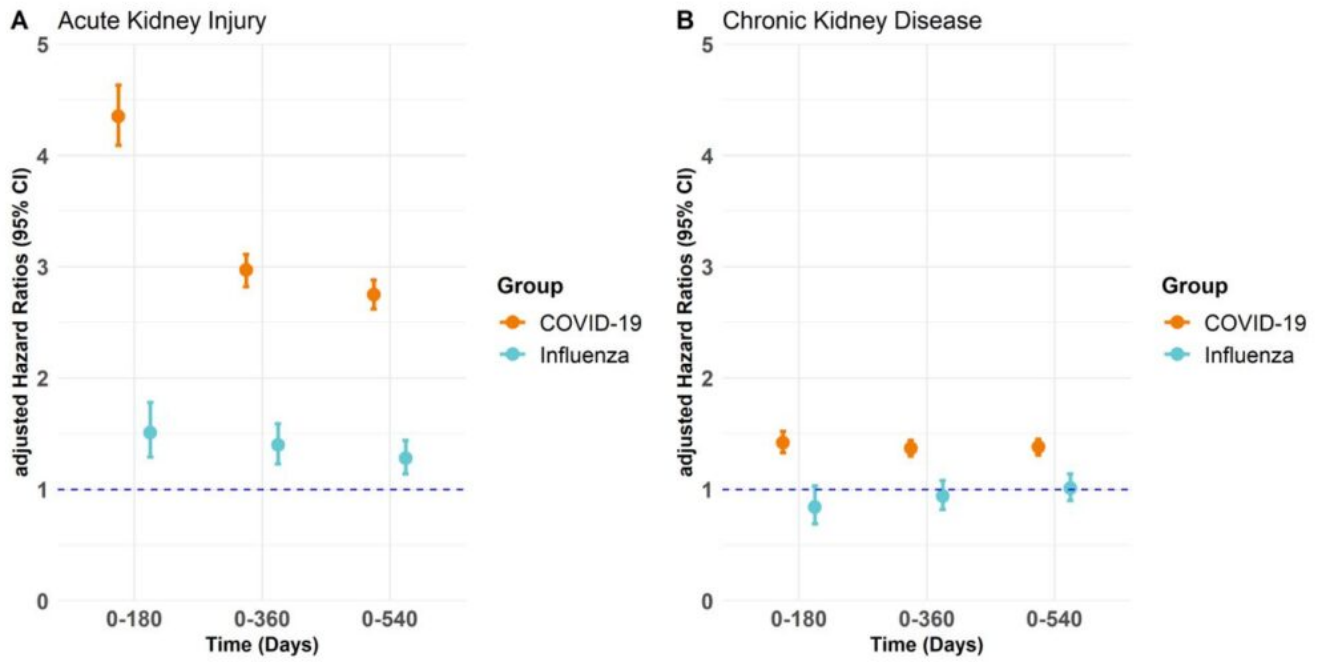
Figure: Exploratory Analysis of Chronic Kidney Disease and Acute Kidney Injury Risks Associated with COVID-19 and Influenza Comparing to Negative Control Across Three Time Intervals: 0–180, 0–360, and 0–540 Days (Hazard Ratios, 95% Confidence Interval).

LATEBREAKER

COVID-19 Pandemic

Flatland: 2-dimensional fixed effect models in meta-analyses of non-pharmaceutical interventions need to be upgraded to a dynamic, non-linear, high-dimensional world Brian Gurbaxani* Brian Gurbaxani

- Forest plots for the meta-analysis of interventions are flat, 2-dimensional, and tend to use linear fixed and random effects models as modes of analysis. By contrast, the effects of non-pharmaceutical interventions (NPI) on an epidemic live in a high-dimensional, non-linear world. These facts have been brought into dramatic relief by the recent COVID-19 pandemic, and in particular by the Cochrane Review's recent meta-analysis of NPI such as facemasks, handwashing, and social distancing for respiratory infections[1]. The Cochrane Review's conclusions for facemasks and COVID-19 in particular were inconclusive, and could not provide evidence for their efficacy, whereas a plethora of other studies have shown efficacy. A more nuanced review of Cochrane's results in the light of non-linear, dynamic modeling[2] and a lively exchange on these issues[3,4] has recently occurred in the pages of the American Journal of Public Health and the Journal of the American Medical Association[5], an important result of which is that linear fixed and random effects models are not the best way to approach the epidemiological data on NPI, as can be seen in even very basic dynamic models. In this talk we expand on this theme that dynamic models are needed to evaluate some interventions like facemasks and other NPI, because the interventions do not have a fixed effect over the variables of time, percentage of use, and attack rate of the pathogen. Importantly, the results show that if the design, duration, and statistical power of a randomized controlled trial of an NPI are chosen poorly, the study will likely show no effect, even when the NPI are performing exactly as predicted.

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LATEBREAKER

COVID-19 Pandemic

Association between COVID-19 re-infection and incidence of Post-Acute Sequelae of SARS-CoV-2 (PASC): a retrospective cohort study of essential workers Tesleem Babalola* Tesleem Babalola Sean Clouston Benjamin J. Luft Zennur Sekendiz

Background: Some people develop symptoms known as post-acute sequelae of SARS-CoV-2 (PASC) that may commence after the initial recovery from acute COVID-19 infection or continue from the initial illness. PASC is an emerging phenomenon yet to be fully understood, and identifying risk factors has been challenging. Thus, this study investigates the association between SARS-CoV-2 re-infection and the incidence of PASC among essential workers enrolled at Stony Brook University World Trade Center (WTC) Health Monitoring Program.

Method: This was conducted among 2513 cohort essential workers, mainly first responders residing on Long Island, NY, with confirmed polymerase chain reaction, antibody, or antigen positive test results for SARS-CoV-2 infection as of February 2024. Participants who reported experiencing at least one of the COVID-19-related symptoms lasting ≥4 weeks were categorized as PASC group, while those who did not were classified as non-PASC group. Adjusting for demographic variables (such as age & gender), lifestyle variables (such as smoking status), anthropometric variables (such as BMI), and other COVID-19-related variables (such as infection severity), we computed Incidence Rate Ratio (IRR) for the association between PASC and COVID-19 re-infection (frequency) using Poisson regression models.

Result: A total of 475 (18.9%) PASC patients were identified among the cohort. The cohort also had 403 (16%) participants with multiple COVID-19 infections. After adjusting for relevant demographic, lifestyle, anthropometric, and other COVID-19-related variables, we found a significant association between increased infection/re-infection (IRR = 0.248; p =0.012), severe COVID-19 infection (IRR = 3.103; p <0.001) and risk of experiencing PASC.

Conclusion: As we continue to understand more about the acute phase of SARS-CoV-2 infection, continuous effort should be directed toward reducing reinfection and severity.

COVID-19 Pandemic

The COVID-19 pandemic, COVID-19 disease, and perinatal health in California Shelley Jung*

Shelley Jung Emily Liu Dana Goin Kara Rudolph Mahasin Mujahid William Dow Jennifer Ahern

Adverse effects of COVID-19 on perinatal health have been documented, however there is a lack of research that separates individual disease from other changing risks during the pandemic period. We linked California statewide birth and hospital discharge data for 2019-2020, and compared health indicators among 3 groups of pregnancies: A) 2020 delivery with COVID-19, B) 2020 delivery with no documented COVID-19, and C) 2019 pre-pandemic delivery. We aimed to quantify the links between COVID-19 and perinatal health, distinguishing effects of individual COVID-19 disease (A vs B) from pandemic effects (B vs C). We examined the following health indicators: preterm birth, hypertensive disorders of pregnancy, gestational diabetes mellitus and severe maternal morbidity. We applied g-computation to estimate "average effect of treatment on the treated" risk differences (RD), and adjusted for individual and community-level confounders. Among pregnancies in 2020, those with COVID-19 disease had higher burdens of preterm birth (RD[95% confidence interval (CI)]=2.8%[2.1,3.5]), hypertension (RD[95% CI]=3.3%[2.4,4.1]), and severe maternal morbidity (RD[95% CI]=2.3%[1.9,2.7]) compared with pregnancies without COVID-19 (A vs B) adjusted for confounders. Pregnancies in 2020 without COVID-19 had a lower burden of preterm birth (RD[95% CI]=-0.4%[-0.6,-0.3]) and a higher burden of hypertension (RD[95% CI]=1.0%[0.9,1.2]) and diabetes RD[95%CI]=0.9%[0.8,1.1] compared with pregnancies in 2019 (B vs C) adjusted for confounders. Estimation with matching and targeted maximum likelihood estimation found essentially equivalent results. Protective associations of the pandemic period on preterm birth may be explained by socioenvironmental and behavioral modifications, while increased maternal conditions may be due to stress and other behavioral changes. To our knowledge, our study is the first to separate the effects of individual COVID-19 disease from the pandemic period on perinatal outcomes.

The association between county-level COVID-19 policy and self-reported depression among the Citizen Science Study participants

Hyelee Kim* Hyelee Kim Aaron Cozen Thomas Carton Madelaine Modrow Soo Park Sylvia Sudat Heather Kitzman Carmen Isasi Scott Zimmerman Jingxuan Wang Maria Glymour Jeffrey Olgin Gregory Marcus Mark Pletcher

Aim

We investigated the association between county-level COVID-19 policies and depression in a large digital cohort.

Method

We analyzed county-level policy data from the U.S. COVID-19 County Policy Database and individual depression scores from the COVID-19 Citizen Science Study between April 2020 and December 2021. County-level policies were combined and transformed into weekly indexes for 3 domains: containment and closure (n=13, ranges 0-13), public health (n=8, 0-8), and economic support (n=5, 0-5). Depression was measured by self-report using the Patient Health Questionnaire-8 (PHQ-8). We used a linear mixed model to estimate the association between each 4-week rolling averaged policy index and outcomes of PHQ-8 scores and major depressive disorder (MDD=1 [vs. 0] if PHQ-8≥10) with random intercepts for counties and individuals, adjusting for individual sociodemographic factors and county-level averaged COVID-19 cases and deaths.

Results

A total of 34,102 participants from 183 counties were included (mean age 51.2, 31.9% male, 7.4% Hispanic, 6.2% Asian, and 1.7% Black). A 1-unit increase in the containment and closure index over the previous 4 weeks was associated with a 0.07-unit higher PHQ-8 score (95% CI 0.06, 0.07) and 0.3% higher MDD RD (95% CI 0.2%, 0.3%). Increases in the public health index were associated with decreases in PHQ-8 (β -0.13; 95% CI -0.14, -0.12) and MDD risk (RD -0.4%; 95% CI -0.6%, -0.3%). The economic support index was not associated with PHQ-8 scores (β -0.01; 95% CI -0.04, 0.01) or MDD risk (RD 0.0%; 95% CI -0.2%, 0.2%). An increase in county-level COVID-19 deaths was associated with higher PHQ-8 scores (β 0.15; 95% CI 0.10, 0.20) and MDD risk (RD 0.7%; 95% CI 0.3%, 1.2%).

Conclusion

Containment and closure policies may have contributed to depressive symptoms in the short term, whereas active public health policies may have reduced depression risk. This study showed a promising opportunity for digital cohorts for better policy implementation.

The relationships between Greek membership, alcohol consumption, and SARS-CoV-2 incidence among college students Chen Chen* Chen Chen Christina Ludema Ming Li Molly Resenberg Jonathan T. Macy

This study tested the relationships between Greek membership, alcohol consumption, and SARS-CoV-2 incidence in a sample of college students during the Fall 2020 semester, while taking into account potential selection biases and measurement errors.

Data collection involved online baseline and bi-weekly follow-up surveys for 8 weeks, and baseline/endline antibody testing using BGI Colloidal Gold IgM/IgG rapid assay kits. Incidence was determined by seropositivity in the endline assessment for those who were seronegative at baseline. We specified logistic regression models to estimate odds ratios (OR) and 95% confidence intervals (CI), adjusting for age, gender, race, and RT-PCR history. Direct standardization generalized results to the IU undergraduate population, and a sensitivity analysis corrected for measurement error in negative predictive values (74.63%).

Key findings: Among the 808 college students with negative SARS-CoV-2 antibody tests at baseline, 5.2% tested positive 8 weeks later at endline. 22.4% of the sample were Greek members, and 7.7% tested positive for SARS-CoV-2 at endline, compared to 4.5% of non-Greek members. Higher alcohol frequency and hazardous alcohol behavior were observed among infected individuals. Greek members had a higher likelihood of getting infected compared to non-members (aOR = 2.01, 95% CI: 1.01, 4.00). Elevated alcohol consumption also increased infection odds, especially with hazardous behavior (aOR = 4.79, 95% CI: 1.34, 17.10). No significant Greek membership-alcohol consumption interaction was observed. Instead, Greek membership's effect on infection risk dropped from 2.01 (1.01, 4.00) to 1.59 (0.78, 3.26) after adjusting for alcohol use, suggesting that the impact may be through elevated alcohol consumption and risky behavior.

These findings offer valuable insights for public health interventions and university policies, particularly within the unique dynamics of Greek organizations in educational institutions.

Table 3. Statistics for Drinks by Greek membership

Greek Membership	N	Variables for alcohol consumption	N	Mean	SD	Median
Yes	303	Alcohol frequency	289	**10.06**	8.58	**8.00**
		Audit score	289	**7.83**	4.28	**7.00**
No	957	Alcohol frequency	909	**5.70**	8.11	**3.00**
		Audit score	923	**5.58**	4.86	**5.00**

Operational Implementation of Operation Expanded Testing in the Midwest Region Daniela Pusl* Daniela Pusl Lisa V. John Nancy McMillan Jeanne Ohrnberger Beverly Roberts

The Centers for Disease Control and Prevention (CDC) and US Health and Human Services (HHS) established Operation Expanded Testing (OpET), a nationwide surveillance and testing program to rapidly identify COVID-19 cases, reduce exposure, address outbreaks, and control spread of disease, in 2021. The Midwest Coordination Center (MCC), 1 of 3 OpET coordination centers, focused on making testing accommodating, effective, and accessible.

MCC organized staff and resources to support outreach and coordination in 16 states. MCC operations incorporated human and technological solutions to enable strong and continuous operational efficiency. MCC activated liaisons at state and local levels to conduct outreach, exchange information and coordinate with existing state and local programs and established physician and laboratory networks to order and perform tests. MCC's IT systems provided the digital platform to rapidly deploy processes, guidance, testing information, client support, and program data to maximize easy-to-implement testing procedures.

MCC enrolled 3357 sites, more than half the sites in the national program (n=6305) and conducted 2,671,972 tests in 19 months. MCC was able to serve areas with high demand and address gaps in testing accessibility for underserved populations, including communities with a Social Vulnerability Index >0.5 (n=429) and high-risk populations, such as long-term care and nursing home facilities (n=498). The average turnaround time was 21.8 hours, meeting CDC's 24-hour turnaround goal, with an average of 5329 tests per day.

MCC successfully established COVID-19 testing coordination across 16 states, addressing critical public health needs by identifying risks in asymptomatic, symptomatic, and confirmed positive cases to facilitate prompt action to reduce spread. The program enhanced COVID-19 testing availability in schools, underserved populations, and congregate settings, aiding in the reduction of spread and assisting with curbing outbreaks.

Wealth Accumulation, State Borders, and COVID-19: A Novel Exploration of COVID-19 Prevalence in Kansas City, Dec 2020 – Dec 2021 Victoria Fisher* Victoria Fisher Allison Boretsky Aveline Roderick Nadia Abuelezam

Background: Historical policies and structures within the United States have cultivated the political economy and socio-spatial demographics of today, largely informing health outcome disparities. It can be difficult to tease apart the impact of history from the influence of current policies. This novel exploration of Kansas City, Kansas (KS) and Missouri (MO) aims to understand how historical policy-resultant wealth concentration and accumulation and state-level COVID-19 responses are associated with COVID-19 prevalence.

Methods: COVID-19 data for December 2020 through December 2021 were sourced from the CDC. 2021 demographics were taken from the American Community 5-Year Survey. We conducted a linear mixed effect regression model to examine the state effect on prevalence outcomes. The main outcome was the log of COVID-19 prevalence per 10,000. The main predictor was state. Covariates included measures of affluence (percent of families with income greater than $125,000, percent employed professionally, and percent with a bachelor's degree or higher), age, and an interaction term between time and state.

Findings: For 2021, the average ZIP code COVID-19 prevalence per 100,000 person months was 4093 (95% CI: 3953, 4240). In the unadjusted model, MO had nearly 18% (95 CI: -1%, 40%) greater prevalence than KS. After controlling for affluence, the state effect was insignificant (8%, 95 CI: -10%, 27%). Affluence was significantly associated with 14% (95% CI: -21%, -5.8%) less COVID-19 prevalence; increasing age was associated with an 11% (95% CI: -22%, 1%) decrease in COVID-19 prevalence.

Discussion: Affluence and older age were strong predictors of lower COVID-19 prevalence across Kansas City ZIP codes, suggesting that historical policies that influenced wealth and resources have strong protective benefits. Affluence and age do not account for the total difference between KS and MO COVID-19 outcomes suggesting that COVID-19 policy differences were also impactful.

Autoimmune Disease and Long Covid Syndrome in Postmenopausal Women from the Women's Health Initiative Patrick Montine* Patrick Montine Danielle J Harvey Shawna Follis Monica Daniela Zuercher John Robbins Christian Sandrock Richard H White Lorena Garcia

Abstract: We analyzed the cross-sectional association between pre-existing autoimmune diseases (AID), specifically rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE), and the manifestation of Post-COVID Conditions (PCC) symptoms among postmenopausal women participating in the Women's Health Initiative. Postmenopausal women, having undergone an endocrinologic transition marked by decreasing estrogen levels, are susceptible to the development of AID. The paper aims to assess whether a history of AID is linked to PCC, employing the WHO PCC definition, among postmenopausal women with COVID-19. Participants who tested negative for COVID-19 and those who developed AID after December 31, 2019 were excluded. AID history was evaluated using unadjusted and adjusted logistic regression models, controlling for age, race and other confounders. Among 37,289 participants responding to COVID-19 Survey 2, 1237 reported positive COVID-19 results with 413 (33%) participants having PCC. The participants who reported positive COVID-19 predominantly comprising White (90%), Non-Hispanic (96%) individuals residing in urban areas (90%), with a median age of 83.79 ± 5.52. Preliminary results indicate a significant association between SLE (OR 3.13, 95% CI: 1.41-6.96, P < .01) and RA (OR 1.54, 95% CI: 1.03-2.29, P = .03) with PCC. Our findings suggest that postmenopausal women with pre-existing AID may be more predisposed to PCC, offering valuable insights for a deeper understanding of PCC mechanisms.

Diabetes

Racial and ethnic disparities of type 2 diabetes in the United States: the pathways through exercise in the Multi-Ethnic Study of Atherosclerosis Tong Xia* Tong Xia Roch A. Nianogo QingZhao Yu Tamara Horwich Preethi Srikanthan Kosuke Inoue Matthew Allison Karol E. Watson Liwei Chen

Introduction: In the United States, racial/ethnic minorities have persistently higher risks of type 2 diabetes (T2D) than White individuals. Engaging in less exercise may explain part of the differences. We aimed to examine whether and to what degree racial/ethnic differences in T2D were explained by variation in exercise.

Methods: We included adults (45–84 years) from the Multi-Ethnic Study of Atherosclerosis (MESA) cohort who were free of T2D in 2000–2002 (baseline) and followed until 2020 for incident T2D. We examined associations of race/ethnicity with T2D using Cox proportional hazard regressions. We assessed the proportion of racial/ethnic differences in T2D risk explained by habitual exercise (i.e., the average of exercise from baseline to develop T2D or until last contact if censored) using a causal mediation analysis approach.

Results: Among 5772 participants, 41.7%, 26.0%, 20.4%, 11.9% were Whites, Blacks, Hispanics, and Chinese Americans, respectively. Controlling for age, gender, and family history of diabetes, Hispanics [hazard ratio (HR) (95% confidence interval, CI): 2.02 (1.74–2.34)], Chinese Americans [1.50 (1.24–1.82)], and Blacks [1.66 (1.44–1.93)] had higher T2D risk than Whites. Compared to Whites, Hispanics [β (SE): -0.96 (0.15), P<0.001] and Chinese Americans [-1.07 (0.18), P<0.001] had lower exercise (metabolic equivalent of task-hour/day) levels, while Blacks [0.26 (0.16), P=0.11] had the same exercise level. Exercise explained 10.8% and 11.3% of racial/ethnic differences in T2D, comparing Hispanics and Chinese Americans to Whites, but did not explain racial/ethnic differences in T2D comparing Blacks to Whites.

Conclusions: Exercise may explain about one tenth of racial differences in T2D comparing Hispanics and Chinese Americans to Whites. Interventions on increasing exercise among Hispanics and Chinese Americans may help narrow racial/ethnic disparities in T2D and promote health equity.

Diabetes

Trends in racial/ethnic disparities in glycemic control among veterans with newly-diagnosed diabetes receiving primary care in the Veteran's Health Administration, 2008-2019 Simin Hua* Simin Hua Rania Kanchi Lorna E. Thorpe Rebecca Anthopolos Mark D. Schwartz Jay Pendse Andrea R. Titus

Background

Racial/ethnic disparities in glycemic control among Non-Hispanic Black (NHB) and Non-Hispanic White (NHW) veterans with type 2 diabetes (T2D) have been reported. This study examines trends in early glycemic control (EGC) by race/ethnicity to understand how disparities soon after T2D diagnosis have changed between 2008 and 2019 among cohorts of newly-diagnosed US veterans.

Methods

We estimated annual percent of EGC (average hemoglobin A1c<7%) in the first 5 years post-diagnosis among 840,789 veterans with newly-diagnosed T2D in primary care. We compared EGC by racial/ethnic group among cohorts defined by diagnosis year (2008-2010, 2011-2013, 2014-2016 and 2017-2019) using mixed effect models with random intercepts. We estimated odds ratios of ECG comparing racial/ethnic minority groups to NHW, adjusting for years of diagnosis, age group, sex and interaction of age and racial/ethnic group with years of diagnosis. We conducted secondary analyses using A1c≥9% in the first 5 years post-diagnosis.

Results

The average annual percent of veterans who achieved EGC during follow-up was 72.8%, 71.8%, 71.5%, and 76.2% in 2008-2010, 2011-2013, 2014-2016, and 2017-2019 cohorts respectively. All racial/ethnic minority groups were less likely to achieve EGC compared to NHW veterans in the 2008-2010 cohort. In cohorts after 2011-2013, NHB and Hispanic veterans were more likely to achieve EGC; however, Hispanic veterans were also more likely to have A1c≥9% within 5 years in all cohorts. EGC disparities for Non-Hispanic Asian, Native Hawaiian/Pacific Islander, and American Indian/Alaska Native veterans persisted during 2011-2016, but they were equally likely to achieve EGC as NHW veterans in the 2017-2019 cohort.

Conclusion

Overall EGC trends among newly-diagnosed veterans in VADR have been stable since 2008. Within that, EGC has improved in most racial/ethnic minority groups relative to NHW veterans. Efforts should continue to minimize disparities between racial/ethnic groups.

Neutrophil-to-lymphocyte ratio and immune cell proportion differences in at-risk children with and without type 1 diabetes Kirk Hohsfield* Kirk Hohsfield Patrick M. Carry Alex Romero Lauren A. Vanderlinden Marian Rewers Katerina Kechris Jill M. Norris Randi K. Johnson

Introduction:

Risk factors for type 1 diabetes (T1D) likely differ before and after the appearance of islet autoimmunity (IA), a critical stage of disease progression marked by the advent of autoantibodies. We investigated the neutrophil-to-lymphocyte ratio (NLR), a systemic inflammation biomarker, and immune cell proportions as risk factors for T1D in The Environmental Determinants of Diabetes in the Young (TEDDY) prospective cohort study.

Methods:

Using plasma DNA methylation (Illumina EPIC array) measured in a matched, nested case-control design, immune cell (B, CD4T, CD8T, monocyte, natural killer, and neutrophil) proportions were estimated via the Houseman method. We tested for differences in NLR and cell type proportions between T1D cases and controls using conditional logistic regression (NLR) and linear mixed effects models (cell types), adjusting for age, sex, and matching strata. Each cell type was modeled as a log ratio with neutrophils to account for the compositional data and exponentiated to be a mean difference cell proportion ratio (CPR). Analyses focused on two critical time points in the natural history of T1D: just before (pre-IA: 60 case-control pairs) and just after (post-IA: 76 case-control pairs) IA seropositivity.

Results:

No differences in NLR or cell proportions were identified pre-IA ($P>0.05$). However, both the NLR and cell-specific proportions differed post-IA. A one-unit increase in NLR led to an 86% decrease in T1D odds (OR: 0.14, 95% CI: 0.03, 0.77). Compared to controls, T1D cases had increased NK (CPR: 1.40, 95% CI: 1.02, 1.92), CD8T (CPR: 1.21, 95% CI: 1.02, 1.44), and CD4T (CPR: 1.16, 95% CI: 1.01, 1.33) cell proportion ratios post-IA.

Conclusions:

We identified expansion of key lymphocyte populations distinguishing T1D cases from controls post-IA, including NK, CD8T, and CD4T cells. Environmental factors or inflammatory triggers driving these immune cell changes may give clues to the etiology of T1D and should be investigated further.

Impact of the coal-to-clean energy policy on blood pressure in peri-urban adults in Beijing, China. Talia Sternbach* Talia Sternbach Xiaoying Li Xiang Zhang Ellison Carter Brian Robinson Chris Barrington-Leigh Guofeng Shen Wenlu Yuan Collin Brehmer Kaibing Xue Kennedy Hirst Shu Tao Yuanxun Zhang Sam Harper Jill Baumgartner

Household solid fuel use in China was responsible for an estimated 363,000 deaths in 2019, including 227,000 cardiovascular deaths. In 2013, the Chinese government launched a multi-city coal-to-clean energy policy designed to reduce household solid fuel emissions and improve air quality. The policy banned household coal burning and provided subsidies for electric or gas-powered heating. We took advantage of the staggered implementation of the ban across villages in peri-urban Beijing to investigate whether the policy impacted blood pressure (BP).

In winter 2018-19, we enrolled 1,003 participants in 50 Beijing villages that were eligible for but not enrolled into the policy and conducted follow-up campaigns in winter 2019-20 and 2021-22. Twenty of our 50 study villages were enrolled into the policy during the study (10, 7, and 3 villages in 2019, 2020, and 2021, respectively). Questionnaires and BP measurements were conducted by trained staff during household visits in each campaign. Brachial and central BPs were measured using an automated oscillometric device. We estimated the policy's impact on BP using a staggered difference-in-differences design with extended-two-way fixed effects estimators and village-level clustered standard errors. We also adjusted for age, sex, waist circumference, smoking, alcohol consumption, and high BP medication to improve precision.

Average treatment effects on the treated showed some evidence that the policy reduced systolic BP (-1.3 mmHg, 95% CI: -3.2 to 0.6), diastolic BP (-1.6 mmHg, 95% CI: -2.9 to -0.2), and central pulse pressure (-1.6 mmHg, 95% CI: -3.0 to -0.2). Diastolic BP reductions were more precise than those for systolic, and BP reductions were greater in villages treated in 2019 compared with those treated later. Clean energy policies that reduce harmful exposures may serve as a population-level intervention for BP in China to supplement higher-risk BP reduction strategies and behavioral modifications.

High Ambient Temperature in Pregnancy and Risk of Childhood Acute Lymphoblastic Leukemia Tormod Rogne* Tormod Rogne Rong Wang Pin Wang Nicole C. Deziel Catherine Metayer Joseph L. Wiemels Kai Chen Joshua L. Warren Xiaomei Ma

Background: High ambient temperature is increasingly common due to climate change and is associated with risk of adverse pregnancy outcomes. Acute lymphoblastic leukemia (ALL) is the most common malignancy in children, the incidence is increasing, and in the United States it disproportionately affects Latino children. We aimed to investigate the potential association between high ambient temperature in pregnancy and risk of childhood ALL.

Methods: We used data from California birth records (1982-2015) and California Cancer Registry (1988-2015) to identify ALL cases diagnosed <14 years and 50 times as many controls matched by sex, race/ethnicity, and date of last menstrual period. Ambient temperatures were estimated on a 1-km grid. Association between ambient temperature and ALL was evaluated per gestational week, restricted to May-September, adjusting for confounders. Bayesian meta-regression was applied to identify critical exposure windows. For sensitivity analyses, we evaluated a 90-day pre-pregnancy period (assuming no direct effect before pregnancy) and constructed an alternatively matched dataset for exposure contrast by seasonality.

Findings: Our study included 6,258 ALL cases and 307,579 controls. The peak association between ambient temperature and risk of ALL was observed in gestational week 8 (Figure), where a 5 °C increase was associated with an odds ratio of 1.09 (95% confidence interval 1.04-1.14) and 1.05 (95% confidence interval 1.00-1.11) among Latino and non-Latino White children, respectively. The sensitivity analyses supported this.

Interpretation: Our findings suggest an association between high ambient temperature in early pregnancy and risk of childhood ALL. Further replication and investigation of mechanistic pathways may inform mitigation strategies.
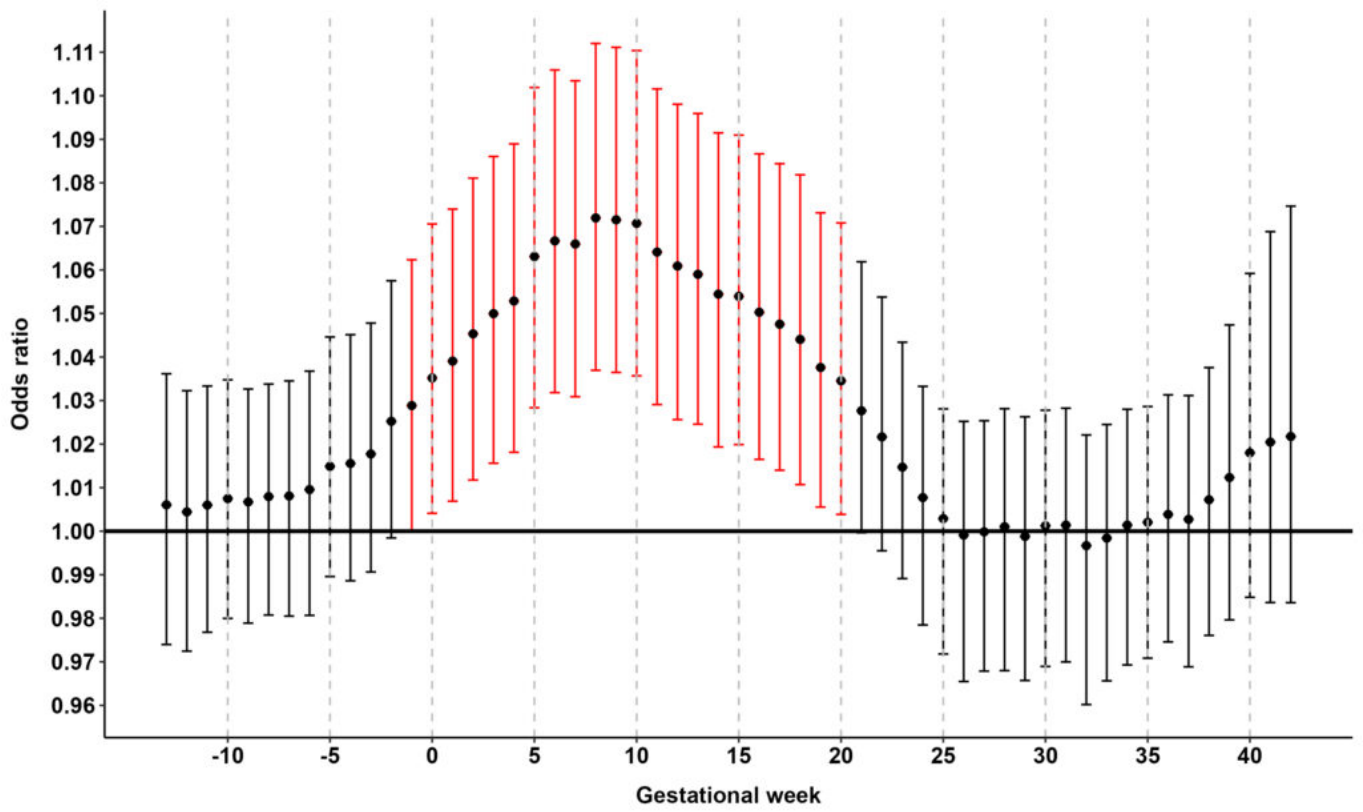
Associations of Land Cover, Greenness, Weather, and Community Type with Radiologic Sinus Inflammation Margaret Tomann* Margaret Tomann Brian S. Schwartz Annemarie G. Hirsch Jonathan Pollak Joseph Dewalle

Chronic rhinosinusitis (CRS) is a disease of the nasal and sinus mucosa with substantial direct and indirect costs for individuals and society and elevated risk of transition to lower airway diseases. Climate change-driven variation in weather and land use may contribute to increases in levels and allergenicity of aeroallergens. We aimed to evaluate associations of land cover, greenness, weather, and community type with radiologic sinus inflammation (RSI), an objective finding of CRS, using electronic health records from Geisinger in 37 counties of Pennsylvania.

In a nested case-control study we included individuals aged 18 – 80 years from 2008 – 2018. Cases (n = 2382) with RSI were identified using a validated text algorithm applied to sinus computed tomography scan reports. Controls (n = 11,910) were frequency matched on age, sex, and year. Land cover, greenness, and weather metrics were assigned in a 1250-meter residential buffer and incorporated 3-month latency and 3-month duration (L3D3). Sensitivity analyses evaluated 3-month latency, 6-month duration (L3D6). Logistic regression with robust standard errors was used to estimate associations (odds ratio [OR], 95% confidence interval [95% CI]) while adjusting for confounding variables.

Cases and controls (n = 14,289) had mean (SD) age of 49.5 (15.3) years, were predominantly non-Hispanic White (96%) and had mean (SD) contact time with Geisinger of 5.88 (3.29) years. Associations (OR, 95% CI) with L3D3 (primary analysis) were weaker than L3D6 (sensitivity). Increasing urbanization was associated with increased odds (vs. rural) of RSI: suburban – small town (1.25, 1.12–1.38), lower density urban (1.33, 1.17–1.53), higher density urban (1.47, 1.23–1.76). Increasing greenness was associated with increased odds (vs. quartile 1) of RSI: quartile 2 (1.00, 0.88–1.15), quartile 3 (1.15, 1.01–1.30), quartile 4 (1.20, 1.06–1.37). These associations suggest that air pollution and aeroallergens may each play a role in RSI.

Acute exposure to extreme summer heat increases risk of hospitalizations among adults with dementia Scott Delaney* Scott Delaney Angela Stegmuller Daniel Mork Danielle Braun Antonella Zanobetti

Background

As climate change accelerates, the frequency of hot summer temperatures will increase, which may impact neurological health. Socially marginalized adults and those with neurodegenerative diseases may be particularly vulnerable, but whether hot summer temperatures increase the risk of symptoms related to Alzheimer's Disease and related dementias (ADRD) remains understudied. We explored the impact of short-term exposure to extreme summer heat on hospitalization with ADRD diagnosis codes.

Methods

Health data is from adults aged 65+ enrolled in Medicare from 2000-2016. Using exposure data from GridMET, we calculated heat index distributions for May-August in each Koppen-Geiger climate subtype. We used these distributions to convert heat index values for each ZIP code to heat index percentiles for use as our exposure. In a time-stratified case-crossover design, we identified 209,269 cases, defined as first known hospitalization among adults with ADRD. We matched controls on week day, month, and year. We fit 14-day distributed lag nonlinear models using conditional logistic regression and cubic splines with degrees of freedom and knot placement based on AIC. We stratified analyses by climate type and demographic characteristics.

Results

Extreme summer heat indexes were associated with increased ADRD-involved hospitalization risk in some but not all climates. Lag-response relationships suggest effects extend 2-4 days after exposure depending on climate. Thus, the OR of hospitalization after 3 days of sustained exposure to heat indexes in the 99th vs 50th percentile was 1.03 (95% CI 1.02, 1.05) for Temperate zones; 1.03 (1.02, 1.04) for Continental zones; 1.03 (0.99, 1.06) for Arid zones; and 1.02 (0.96, 1.08) for Tropical zones. Importantly, the OR point estimate for Black versus White beneficiaries was approximately 3 times larger.

Conclusion

Extreme heat may increase risk of hospitalization among adults with ADRD and may exacerbate racialized health inequities.
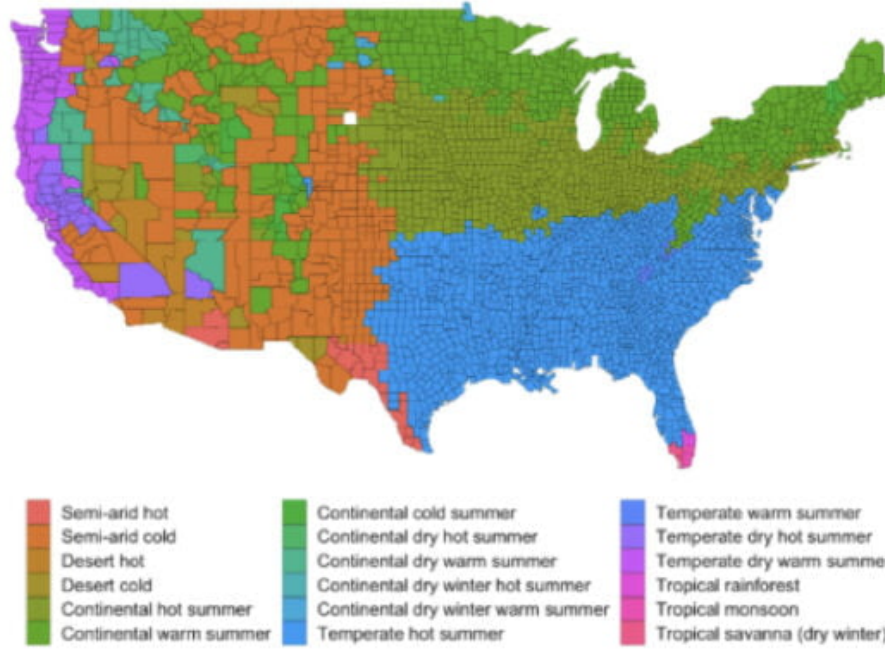
(a) Koppen-Geiger climate zones by county.
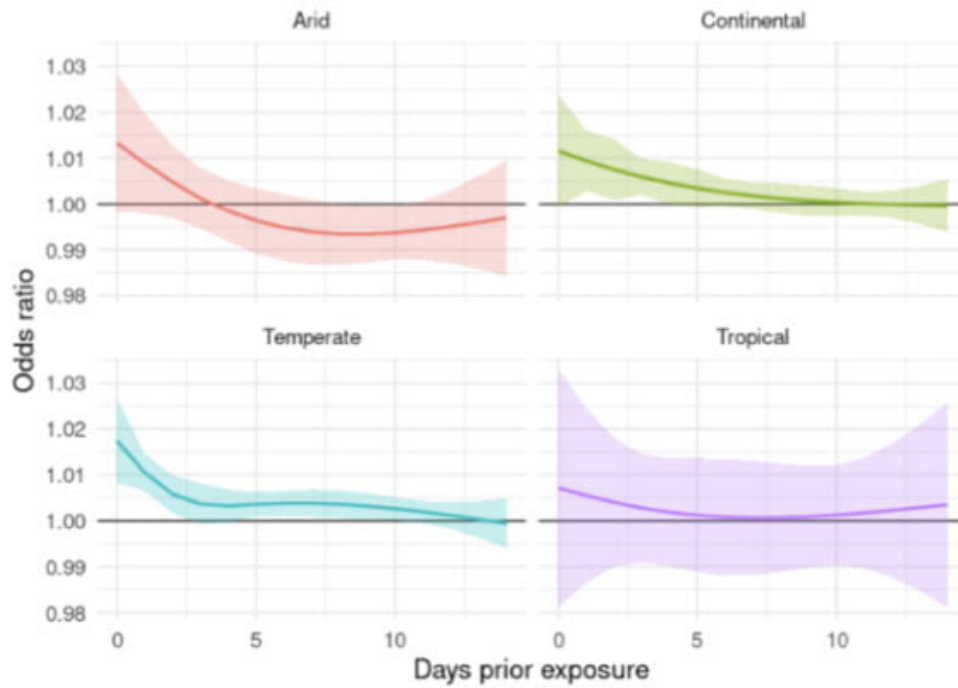
(b) Lag-response curves corresponding to exposure at the 99th (vs. 50th) percentile of each climate type's summer heat index distribution.

Environment/Climate Change

Excess moderate temperature days increase the risk of hospitalizations for cardiovascular conditions in multiple states Shannon Zenk* Melanie Sona Erin Liedtke Kelly Jones

Background: While it's known that extreme heat can affect cardiovascular health, the impact of moderately hot temperatures (below 37°C) is unknown.

Objective: Our study aims to quantify the relationship between exposure to moderately hot temperatures ranging from 27°C to 37°C and the risk of in-patient hospitalization for cardiovascular conditions. Additionally, we aimed to contextualize hospitalization risk variation within different climate regions.

Methods: Inpatient electronic medical record data for patients with cardiovascular conditions was obtained from the Healthcare Cost and Utilization Project (HCUP) database for Arizona (AZ), Mississippi (MS), and New York (NY) 2016-2019. Daily high temperature at the ZIP code level was used to explore the associations between temperature and rate of hospitalization. We performed Poisson regression, controlling for year and stratifying by state, to determine the change in risk associated with each additional day above moderately hot temperatures during the hottest season of the year (June-September).

Results: Our study comprised of a sample size of 2,079,043 cardiovascular-related inpatient hospitalization. An additional day at 27°C was linked to an increased risk in hospitalization for cardiovascular conditions in AZ (RR 1.30, 95% CI 1.28-1.32), MS (RR 1.24, 95% CI 1.23-1.25), and NY(RR 1.10, 95% CI 1.10-1.11). Furthermore, results demonstrate distinct temperature thresholds at which the risk of hospitalization markedly escalates compared to the risk observed at 27°C. Notably in NY (32°C, RR 1.23, 95% CI 1.22-1.23) and MS (36°C, RR 1.41, 95% CI 1.37-1.44). This observation underscores regional disparities in the impact of temperature on the rate of hospitalization.

Discussion: Recognizing that temperatures well below extremes do increase the risk of experiencing heat exacerbated or induced cardiovascular illness, resulting in inpatient hospitalizations, is critical to inform climate-appropriate heat warning policies.

Prenatal exposure to mixtures of endocrine-disrupting chemicals in association with obesity in childhood and adolescence Nuria Güil-Oumrait* Nuria Güil-Oumrait Vishal Midya Augusto Anguita-Ruiz Léa Maitre Mariona Bustamante Jose Urquiza Cathrine Thomsen Line Småstuen Haug Hector C. Keun Barbara Heude John Wright Rosemary McEachan Marina Vafeiadi Regina Grazuleviciene Rémy Slama Leda Chatzi Martine Vrijheid Damaskini Valvi

Objective: Prenatal exposure to endocrine-disrupting chemicals (EDCs) may contribute to childhood obesity, but only a few studies have tracked these associations into adolescence and analyzed EDCs as mixtures. We aimed to investigate the associations between prenatal exposure to EDC mixtures and obesity in childhood and adolescence.

Material and methods: We examined 1301 mother-child pairs from the Human Early Life Exposome (HELIX) project, involving birth cohort studies across 6 European countries. We analyzed 9 metals, 3 organochlorine pesticides, 5 polychlorinated biphenyls, 2 polybrominated diphenyl ethers, 5 perfluoroalkyl substances, 10 phthalate metabolites, 3 phenols, 4 parabens, and 4 organophosphate pesticide metabolites measured in urine and/or blood collected in pregnancy. BMI z-scores were calculated in childhood (6-12 years; N=1301) and adolescence (13-18 years; N=607), and overweight (including obesity) was defined using the WHO growth reference. We used penalized multi-group Bayesian Weighted Quantile Sum Regression (BWQSR) to assess the EDC mixture associations with overweight in childhood and adolescence, adjusting for confounders.

Results: The prevalence of overweight was 28.9% in childhood and 30.0% in adolescence. Adjusted multi-group BWQSR indicated that, in both childhood and adolescence periods, higher exposures to the metal mixture (OR [95%CrI] per quartile mixture increase = 1.47 [1.10, 1.98] and (1.10 [0.66, 1.79], respectively), and the organochlorine pesticide mixture (OR [95%CrI] = 1.48 [1.23, 1.79] and 1.46 [1.11, 1.97], respectively) were associated with higher odds for overweight. The PCB mixture was associated with lower odds of being overweight (OR [95%CrI] = 0.80 [0.66, 0.95] in childhood and 0.66 [0.50, 0.86] in adolescence).

Conclusion: Findings suggest that prenatal exposure to mixtures of metals and organochlorine pesticides is associated with higher odds of being overweight in childhood and through adolescence. Future analyses will explore chemical-by-chemical interactions within EDC mixtures in association with overweight, and potential underlying mechanisms by studying children's proteins and metabolomics profiles.

Association between annual health checkup attendance and functional disability among older survivors of the 2011 Japan Earthquake and Tsunami Hiroyuki Hikichi* Hiroyuki Hikichi Ichiro Kawachi

Objective: Research has demonstrated that participating in health checkups is associated with lower risks of physical and cognitive impairments in older adults. However, little is known about the association in older survivors of natural disasters. This study examined whether health checkup attendance could protect older survivors' functional capacity after the 2011 Japan Earthquake and Tsunami, considering time-dependent confounders.

Methods: With the dataset becoming available only recently due to advancements in data processing, we seized the opportunity to conduct a comprehensive analysis. We initiated a survey in Iwanuma City, 80 km west of the epicenter, seven months before the disaster, continuing with follow-up surveys every three years until 2022. The primary outcome was functional disability levels from the Japan long-term care database. The key explanatory variable was annual health checkup participation for metabolic syndrome and frailty, recorded by the local government. Time-dependent covariates included smoking, drinking, and daily walking, adjusted using marginal structural models. We also considered housing damage, loss of loved ones, and socio-demographics. The analysis included 1,481 individuals, excluding 18 with baseline functional disabilities.

Results: Among participants in the 5-wave panel surveys, 56.6% were women, and the baseline average age was 71.0 years. The result of marginal structural models showed that health checkup attendance was associated with lower levels of functional disability (Coefficient -0.08, 95% CI -0.10 to -0.05, p < .01).

Conclusions: Participating in annual health checkups was protectively associated with a lower risk of functional disability among older disaster survivors. We conclude that encouraging annual health checkup attendance could protect the health and well-being of older survivors, who are especially vulnerable following a major disaster.

LATEBREAKER

Environment/Climate Change

Environmental Justice Considerations on The Association between Socioeconomic Factors and Environmental Noise in Rhode Island Parks Ugoji Nwanaji-Enwerem* Ugoji Nwanaji-Enwerem Diana Grigsby-Toussaint Erica Walker

Introduction: In Rhode Island (RI) there are over 6.7 million annual visits to parks. Urbanization has resulted in an increase in noise pollution, including within parks. Studies show that noise exposure is associated with adverse health effects on physiological stress, cardiovascular disease risk, and mental health. Research also suggests disproportionate noise exposure in areas with lower socioeconomic status and high sociodemographic diversity. This research aims to explore associations between socioeconomic/demographic factors and sound levels in RI parks.

Methods: Thirteen parks in Providence, RI were studied during daytime hours in October-November 2023. Sound measurements were collected for five-minute periods at each park's center. Socioeconomic/demographic data were sourced from the US Census Bureau and American Community Survey. Pearson correlation and multilinear regression analyses assessed sound levels and median household income, percent population below the poverty level, and race/ethnicity.

Results: Positive correlations were found between A-weighted sound levels (LAeq) and percent Hispanic population (r=0.02, p=0.94). C-weighted sound levels (LCeq) correlated positively with percent Black population and percent below the poverty level (r=0.14, 0.13; p=0.7, 0.7). Negative correlations existed for LCeq with median household income (r=0.3, p=0.4) and LAeq with percent white population (r=-0.1, p=0.9). T-tests comparing Southside to West End parks showed differences greater than 3dBA and mean peak sound levels above 64dB (p=0.08). Multilinear regression revealed an inverse association between maximum A-weighted sound levels and median household income (β= -0.00165, p=0.886) and a positive association with percent Hispanic population (β= 0.05, p=0.7).

Conclusion: Although results were non-significant, trends suggest important environmental justice implications. Higher median household income was associated with lower sound levels, while higher percent Hispanic and Black populations correlate with higher LAeq and LCeq, respectively. This highlights environmental disparities, emphasizing the need for interventions to address disproportionate sound exposure, ensuring improved population-level health through both environmental and policy initiatives.

Environment/Climate Change

Long-term Exposure to Traffic-related Air Pollution and Cardiovascular Hospitalizations: Examining Health Disparities in 14 U.S. States Adjani A. Peralta* Adjani Peralta Yaguang Wei Joel Schwartz

Background

Cardiovascular diseases are a leading cause of morbidity and mortality in the U.S. Understanding the relationship between exposure to traffic-related air pollution and cardiovascular hospitalizations could help identify vulnerable populations and provide evidence for a revised EPA annual NO2 standard.

Methods

Using generalized linear models, we studied the impact of nitrogen dioxide (NO2) and elemental carbon (EC) exposure, specifically from traffic-related air pollution exposures, on the rate of all-cardiovascular (CVD) hospitalization in 14 U.S. states between 2000-2016. We aggregated hospitalization rates from the Health Cost and Utilization Project State Inpatient Databases and estimated annual PM2.5 exposures from a validated ensemble exposure model to the ZIP code level within each state. Covariates were attained from the decennial Census and the American Community Surveys. Multiplicative interaction terms were used to assess effect measure modification by race and poverty.

Results

For each 1-ppb increase in annual NO2 and 1-µg/m3 in EC, we found positive associations with all-cardiovascular hospitalization rates: NO2 1.0072% (95% CI: 1.0067,1.0077) and EC 1.27% (95% CI: 1.24, 1.29). Significant positive associations persisted at <58 ppb NO2 levels, the current annual US standard: NO2 1.0097% (95% CI: 1.0091, 1.010) and EC 1.22% (95% CI: 1.20, 1.25). We found evidence that both race and poverty modify the associations.

Conclusion

Prolonged exposure to traffic-related air pollution contributes to increased rates of all-cardiovascular hospitalization in 14 states, affecting populations even in areas with low NO2 levels. Vulnerability to CVD hospitalization persisted among Black individuals and in regions characterized by elevated poverty levels.

The Relationship between Long-Term Ambient Air Pollution Exposure, Neighborhood Environmental Vulnerability, and COVID-19 Pneumonia Morbidity in New York City Hospitalization Data Sneha Kannoth* Sneha Kannoth Cong Zhang Sandra S. Albrecht Alexander Azan Earle C. Chambers Min Qian Perry E. Sheffield Azure Thompson Jennifer A. Woo Baidal Stephanie Lovinsky-Desir Jeanette A. Stingone

Background

Research suggests geographic disparities in adverse COVID-19 outcomes are associated with air pollution. Social and structural factors at the neighborhood-level can lead to greater exposure to air pollution and increase vulnerability to the health effects of air pollution. We hypothesize that the link between air pollution and adverse COVID-19 is stronger in neighborhoods with social and structural factors that induce greater vulnerability to air pollution.

Methods

We used electronic health records from 5 New York City (NYC) health systems for COVID-19 hospitalizations (3/1-6/20/20), 11-year average air pollution ZIP Code estimates (particulate matter ($PM_{2.5}$), nitrogen dioxide (NO_2), black carbon (BC), ozone (O_3)) from the NYC Community Air Survey (2009-2019), and a neighborhood environmental vulnerability index (NEVI) using US Census and CDC data. We constructed Poisson regression models with robust standard errors to estimate the risk ratios of COVID-19 pneumonia for each pollutant, adjusting for age, sex, body mass index, smoking, history of asthma, diabetes, hypertension, and effect modification by tertiles of NEVI.

Results

The sample included 7501 patients, of which 490 had COVID-19 pneumonia. Greater chronic exposure to air pollutants NO_2 (RR:1.63; 95%CI:1.51,1.77), $PM_{2.5}$ (RR:1.37; 95%CI:1.27,1.48), and BC (RR:1.44; 95%CI:1.31,1.59) was associated with greater risk of COVID-19 pneumonia. Inverse results were observed for O_3 (RR:0.83; 95%CI:0.81,0.86). Relationships between chronic NO_2, $PM_{2.5}$, BC exposures and COVID-19 pneumonia were stronger among those living in areas of higher neighborhood-level vulnerability ($p<0.05$) (Fig1).

Conclusion

There is evidence to suggest that neighborhood-level vulnerability modifies the relationship between chronic air pollution exposure and COVID-19 pneumonia. Understanding the role that environmental exposures play in infectious disease severity requires understanding of community-level vulnerability to those exposures.

Fig1. Risk Ratios and 95% Confidence Intervals regarding the Relationship between Chronic Air Pollution Exposure and COVID-19 Pneumonia, within each Tertile Strata of Neighborhood Environmental Vulnerability Index (NEVI) in New York City (NYC)[1-2]
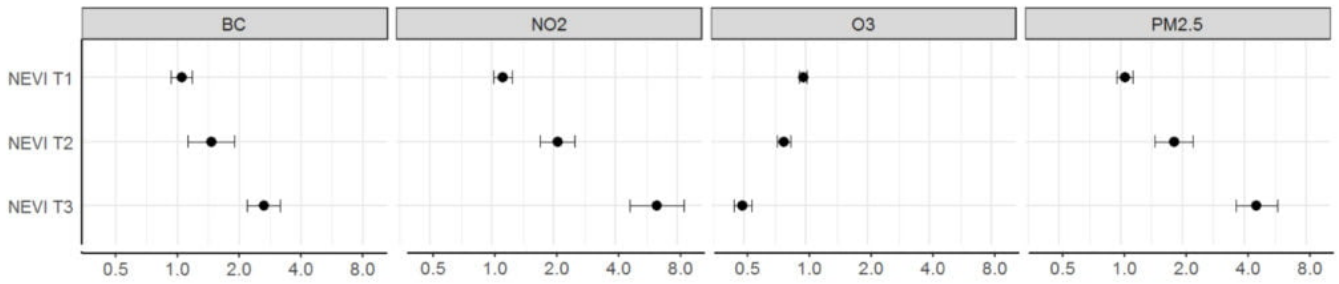
[1] Poisson regression model adjusted for age, sex, body mass index, smoking, history of asthma, diabetes, hypertension, and stratified by NEVI tertile, with NEVI T1 indicating the lowest neighborhood environmental vulnerability

[2] Data are from a harmonized repository of electronic health records from 5 NYC health systems, restricted to areas with >40% catchment

Environment/Climate Change

Association between Per- and Polyfluoroalkyl Substances and Liver Cancer Risk Xinyuan Zhang* Xinyuan Zhang Longgang Zhao Howard D. Sesso I-Min Lee Julie E. Buring Michelle Lai Philippe Grandjean Xuehong Zhang

Background

Liver cancer incidence in the US has tripled since the 1980s. The underlying causes likely include exposures from environmental toxins with carcinogenicity, e.g., per- and polyfluoroalkyl substances (PFASs) to which US populations are ubiquitously exposed. We aimed to study circulating levels of PFAS in nested case-control studies comparing liver cancer cases to both generally healthy controls and liver disease controls.

Methods

We identified 44 liver cancer cases from the Women's Health Study and the Physicians' Health Study, with 1:1 cancer-free controls matched by age, sex, and time of blood collection. We also identified 66 liver cancer cases from the Mass General Brigham Biobank, with 1:1 cancer-free, metabolic dysfunction-associated steatotic liver disease (MASLD) controls matched by the same criteria. The stored pre-diagnostic blood samples were assayed for major PFASs. We examined the associations of total and individual PFASs with liver cancer risk by comparing tertiles and comparing >90th versus <90th percentile using conditional logistic regression models, adjusting for smoking status, alcohol intake, obesity, and diabetes.

Results

Compared to healthy controls, the highest vs. lowest tertile of total PFAS was not significantly different for the risk of liver cancer (adjusted OR=1.09 (95%CI: 0.28-4.28). However, those at or above the 90th percentile of perfluorodecanoic acid (adjusted OR=7.96 (95%CI: 1.09-58.4)) and perfluoroundecanoic acid (adjusted OR=10.5 (95%CI: 1.06-103)), compared to those <90th percentile, had a statistically significant higher risk of liver cancer. Compared to MASLD controls, adjusted models did not find significant associations between total or individual PFASs and liver cancer risk (all P>0.05).

Conclusion

Certain PFAS at high levels might be associated with liver cancer risk, although evidence from larger scale studies is warranted, potentially informing policy making and regulation of various PFASs in the US and worldwide.

Table. Characteristics of liver cancer cases and controls from three cohorts in the study of pre-diagnostic blood PFASs.

	Women's Health Study and Physicians' Health Study		Mass General Brigham Biobank	
	Liver cancer case	Generally healthy control	Liver cancer case	MASLD control
Sample size, n	44	44	66	66
Time of blood collection, year, range	1982-1999	1982-1999	2010-2021	2010-2021
Age, year, mean (SD)	61.07 (10.24)	60.98 (10.21)	59.8 (11.9)	60.1 (11.9)
Sex, n (%)				
Female	28 (63.6%)	28 (63.6%)	21 (31.3%)	21 (31.3%)
Male	16 (36.4%)	16 (36.4%)	46 (68.7%)	46 (68.7%)
Current smoker, n (%)	20 (45.5%)	21 (47.7%)	10 (14.9%)	11 (16.4%)
≥1 alcoholic drink/week, n (%)	26 (59.1%)	21 (47.7%)	27 (40.3%)	37 (55.2%)
Body mass index, kg/m^2, mean (SD)	25.9 (4.4)	25.5 (3.3)	29.9 (5.8)	33.4 (7.3)
Diabetes, n (%)	5 (11.4%)	1 (2.27%)	30 (44.8%)	36 (53.7%)
PFAS, ng/mL, geometric mean (SD)				
Total PFAS	38.8 (18.6)	41.5 (21.9)	6.94 (0.66)	9.23 (0.93)
PFOA	4.03 (2.34)	4.76 (3.21)	1.30 (0.13)	1.57 (0.16)
PFOS	27.4 (13.2)	27.7 (13.4)	3.33 (0.35)	4.49 (0.60)
PFDA	0.18 (0.11)	0.16 (0.09)	0.14 (0.01)	0.19 (0.02)
PFUnDA	0.11 (0.09)	0.09 (0.07)	0.10 (0.01)	0.13 (0.02)

Abbreviations: PFAS, per- and polyfluoroalkyl substances; MASLD, metabolic dysfunction-associated steatotic liver disease; SD, standard deviation; PFOA, perfluorooctanoic acid; PFOS, perfluorooctanesulfonic acid; PFDA, perfluorodecanoic acid; PFUnDA, perfluoroundecanoic acid.

Atrazine use and markers of kidney function and nephrotoxicity among male farmers in the Biomarkers of Exposure and Effect in Agriculture Study Gabriella Andreotti* Gabriella Andreotti Joseph J Shearer Dale P Sandler Anna M Lukkari Richard Remigio Christine G Parks Vicky C Chang Venkata Sabbisetti Laura E Beane Freeman Amy Karger Jonathan N Hofmann

Background: Atrazine is a widely used herbicide that has been associated with malignant and non-malignant kidney disease and reduced kidney function in the Agricultural Health Study (AHS). However, little is known about the association between atrazine use and specific kidney disease biomarkers. **Objective:** We evaluated the associations between atrazine use and clinical biomarkers of kidney function and nephrotoxicity among male farmers in the Biomarkers of Exposure and Effect in Agriculture study, a sub-cohort of the AHS. **Methods:** We included 264 farmers with: 1) recent atrazine use (use within the last 3 months), nearly all of whom also had past use; 2) former atrazine use (top tertile of lifetime use but no recent use); and 3) no/low atrazine use (no recent use and no or low lifetime use). These groups (n=88 each) were frequency-matched on age and state of residence (Iowa, North Carolina). Markers were measured in serum (creatinine, cystatin C, urea nitrogen, uric acid) and urine (kidney injury molecule-1, albumin, creatinine). The 2021 CKD-EPI creatinine-cystatin C equation was used to calculate estimated glomerular filtration rate (eGFRcr-cys). The percent difference in these markers across groups of atrazine use was estimated using multivariable linear regression. **Results:** Recent atrazine users had lower eGFRcr-cys (-6.7%; 95%CI: -11.7%, -1.4%) and higher levels of serum creatinine (7.0%; 95%CI: 1.4%, 12.8%), cystatin C (7.4%; 95%CI: 1.2%, 13.9%), and uric acid (6.1%; 95%CI: -0.4%, 13%) compared to farmers with no/low atrazine use. Comparisons between farmers with former atrazine use and no/low use were null, except for an inverse association with blood urea nitrogen (-6.9%; 95%CI: -12.9%, -5.0%). **Conclusions:** Our findings add to the evidence that atrazine use, particularly among recent users, is associated with diminished kidney function. Additional studies are needed to clarify the mechanisms through which atrazine may contribute to kidney damage.

Association between prenatal and childhood exposure to particulate matter and asthmatic symptoms in the children of the Cyprus MEDEA Cohort Stefania Papatheodorou* Stefania Papatheodorou Nicole Alkhouri Veronica Wang Panayiotis Yiallouros Panayiotis Kouis Pinelopi Anagnostopoulou Petros Koutrakis

Background: Asthma is highly prevalent among children, especially in the eastern Mediterranean region, where desert dust storms heighten susceptibility to exacerbation of respiratory asthmatic symptoms.

Aims: To examine the association between prenatal and childhood exposure to PM2.5 and PM10 and the development of ever and 12-month asthma or asthmatic symptoms before clinical exam and interview within the Mitigating the Health Effects of Desert Dust Storms Using Exposure-Reduction Approaches (MEDEA) cohort in Cyprus.

Methods: The study included 3,773 MEDEA cohort children (7-13 years old) from Nicosia and Limassol. Prenatal and 12 months before the clinical exam and interview PM exposure was calculated for each participant. Logistic regression was used to evaluate the association between prenatal exposure and ever outcomes, as well as 12-month exposure and 12-month outcomes. The models were adjusted for demographics, clinical characteristics, family history, season and long-term trends, and climatic factors. We examined effect measure modification (EMM) by age, sex, and BMI.

Results: For each 1 μg/m3 increase in PM10 levels during the prenatal period, the odds of ever having wheezing increased by 3% (95% Confidence Intervals [CI]: 2% to 4%), and ever doctor-diagnosed asthma increased by 4% (95% CI: 2% to 6%). We did not find any association between 12-month PM exposure and asthma or asthmatic symptoms a year before the interview. There was an indication for EMM by sex, where male participants had higher odds (8%, 95% CI 5% to 10%) of ever asthma than females (-3%, 95% CI -5%-3%). There was no indication for EMM by age or BMI,

Conclusion: Our study shows that prenatal exposure to particulate matter increases the odds of having respiratory symptoms and asthma in children born in Nicosia and Limassol. Continued efforts are needed to identify the most vulnerable populations and develop strategies to reduce exposures and improve air quality.

Genetics

Using self-organizing maps to investigate the relationship between psychosocial factors and epigenetic aging in the Hispanic Community Health Study Sarina Abrishamcar* Sarina Abrishamcar Grace Christensen Jasmine K. Aqua Christian Dye Rebecca Jones-Antwi Anke Huels Jianwen Cai Carmen R. Isasi Robert C. Kaplan Karen N. Conneely Shakira F. Suglia

Background: Evidence suggests that psychosocial stressors are associated with epigenetic age acceleration (EAA), where one's predicted biological age based on DNA methylation (DNAm) exceeds their chronological age. While Hispanic/Latinos experience high rates of psychosocial stressors, most studies have been conducted in populations of European descent. **Objective**: We investigated whether exposure to multiple psychosocial factors is associated with longitudinal changes in EAA among 974 adults in the Hispanic Community Health Study/Study of Latinos. **Methods**: We utilized self-organizing maps (SOM), an unsupervised clustering method, to categorize participant exposure profiles and assess the joint effects of psychosocial factors (acculturation, discrimination, mental health, stressful life events, and low social support) on EAA. We measured DNAm from whole blood at two visits six years apart using the MethylationEPIC BeadChip and calculated EAA using the GrimAge clock and DunedinPACE (PACE) pace of aging biomarker. We used linear mixed-effect models to estimate the effect of exposure cluster on change in EAA across the two timepoints adjusting for age and gender. **Results**: The SOM algorithm identified four clusters of participants, with Cluster 1 containing the highest levels of all psychosocial factor exposure and Cluster 4 containing the lowest levels, relative to the other clusters. We found evidence of EAA across all exposure clusters. Compared to Cluster 4 participants, Cluster 1 participants had the highest GrimAge EAA and fastest PACE (β [95%CI]=1.22[0.51,1.93] years & 0.03[0.01,0.05], respectively), followed by Cluster 2 (0.65[0.03,1.27] years & 0.02[-0.004,0.03], respectively), and finally Cluster 3 (0.57[-0.06,1.20] years & 0.02[0.004,0.04], respectively). **Conclusion:** Exposure to multiple psychosocial stressors was associated with EAA over time, providing insight into how biological aging may contribute to health disparities among Hispanic/Latino populations.

[3] **[4]**

[1] **[2]**

■ Hispanic Stress Inventory	■ Depression	■ Perceived Stress
■ Racism	■ Anxiety	■ ACEs
■ Social Support	■ Chronic Stress	■ Traumatic Stress
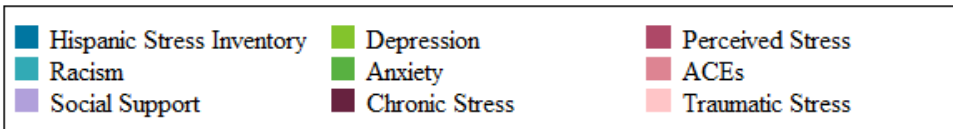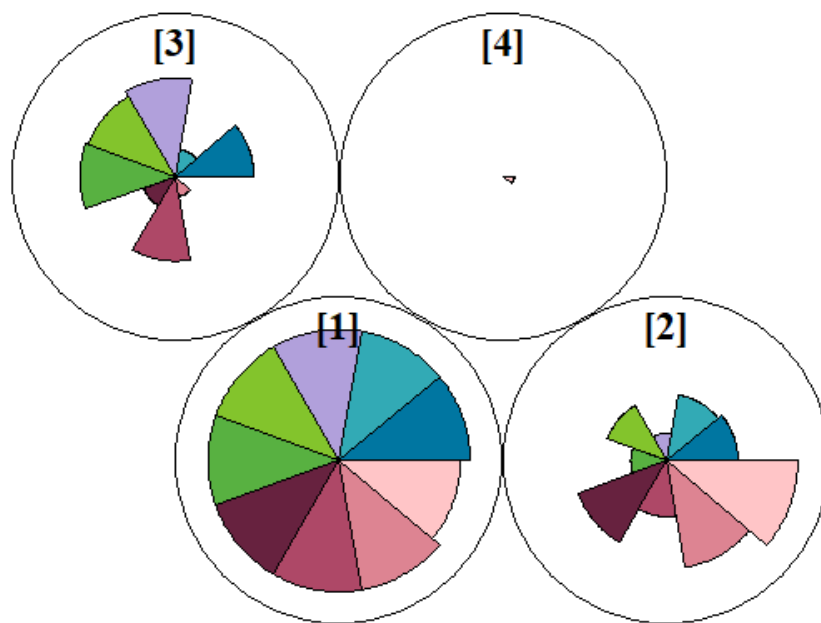
Genetics

Racial Identity as a Modifier of Genetic Risk Scores for Alzheimer's Disease and All Cause Dementia Peter Buto* Peter Buto Anna M. Pederson Dorothy Chen Kendra D. Sims Catherine Schaefer Sarah F. Ackley Minhyuk Choi M. Maria Glymour Thomas J. Hoffmann

withdraw

Is There a "PRS Paradox" In Prostate Cancer Survival Studies? – Investigating Potential Bias in Genetic Studies of Prostate Cancer Survival Anqi Wang* Anqi Wang Konrad H. Stopsack Lorelei A. Mucci Anna Plym

Background: Polygenic Risk Score (PRS) has been shown to robustly stratify the overall prostate cancer risk, with a stronger association with aggressive versus non-aggressive diseases. In contrast, case-only studies indicate that higher PRS is associated with a lower to neutral risk of prostate cancer death, implying potential biases. Two underlying biases should be considered: 1) collider-stratification, which occurs when conditioning on case status and may skew the distribution of unmeasured confounders; and 2) lead time, resulting from potential earlier detection of cancer in men with higher PRS due to effects on prostate specific antigen (PSA) levels.

Methods: Simulations with a hypothetical cohort of 100,000 cancer-free men were used to evaluate the aforementioned biases. Absolute risks of cancer incidence and mortality by PRS were incorporated in the simulations, derived from prior prostate cancer GWAS studies.

Results: In the presence of collider bias, the Relative Risk (RR) for the PRS on the risk of prostate cancer death tends to be underestimated in case-only studies. We show that in instances of a null observed association (RR=1.0), the true RR could be at least 1.3, assuming no other sources of bias. The magnitude of collider bias is positively correlated with the RRs of unmeasured confounders on prostate cancer incidence and mortality (Figure). In the context of lead time bias, our simulation demonstrates that earlier diagnosis in men with higher PRS artificially extends perceived survival time. For example, detection 2.5 years earlier than average could reduce a true RR of 1.1 to an observed RR of 1.0.

Conclusion: Our simulations show that the observed inverse association of PRS with prostate cancer survival may be attributable to bias. Given its potential role in determining prostate cancer prognosis, it is crucial to distinguish the true PRS impact on prostate cancer prognosis in case-only studies.

Figure. The Impact of Unmeasured Confounder U on Collider Bias in PRS and Prostate Cancer Death Associations
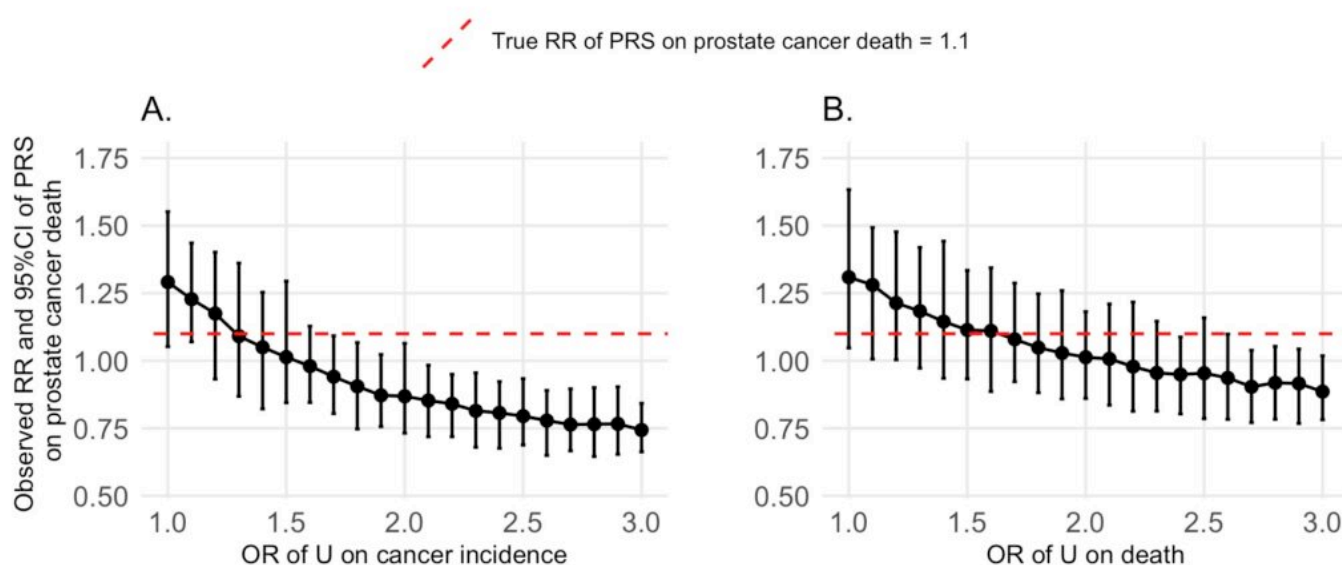
LATEBREAKER

Genetics

Association of Diet Quality with Nonalcoholic Fatty Liver Disease Varies by Genetic Susceptibility

Song-Yi Park* Homa Sadeghi Unhee Lim David Bogumil Lynne Wilkens Veronica W Setiawan Iona Cheng Loïc Le Marchand

A healthy diet is the first-line therapy for nonalcoholic fatty liver disease (NAFLD). However, it remains unknown if the protective effect of a healthy diet on NAFLD varies by genetic susceptibility. In the Multiethnic Cohort (MEC), we previously reported an inverse association between high diet quality as determined by Healthy Eating Index (HEI-2015) score (via self-administrated food frequency questionnaires) and NAFLD risk and developed a polygenic risk score (PRS) with 21 genetic variants for NAFLD in MEC. In this study, we evaluated the cross-sectional HEI-NAFLD association across the PRS levels and carrier status of 21 variants in 542 NAFLD cases (>5% liver fat on magnetic resonance imaging without excessive alcohol intake) and 965 non-cases in the MEC Adiposity Phenotype Study.. We applied logistic regression models adjusted for age, energy intake, total body fat, and population stratification using 5 principal components. We observed significant interaction of HEI with the PRS and carrier status of the PNPLA3 and COBLL1 risk variant (Pinteraction≤0.001). Higher tertiles of HEI, compared with the lowest tertile, were inversely associated with NAFLD in the lower 80% of the PRS [OR for 2nd tertile=0.67 (95% Cl: 0.49-0.91); OR for 3rd tertile=0.51 (0.36-0.72)], while no significant HEI-NAFLD association was detected in the top 20% PRS [ORs and 95% CIs for the 2nd and 3rd tertiles: 1.25 (0.63-2.51) and 0.64 (0.33-1.24) respectively]. Similarly, the inverse HEI-NAFLD associations were more prominent in non-carriers and carriers of one risk allele for PNPLA3 and COBLL1, but not among the carriers of two risk alleles in these loci. In conclusion, our results suggest that the association of a healthy diet with NAFLD differs by genetic susceptibility. If replicated in independent data and prospective studies, this gene-diet interaction can provide important insights to precision intervention strategies to lower the risk of NAFLD.

Global Health

Joint Associations of Individual- and Community-level Women's Empowerment with Complete use of Maternal Healthcare Utilization in 34 Sub-Saharan African Countries Yun-Jung Eom* Yun-Jung Eom Rockli Kim

Background: Gender norms and practices in a community may importantly shape individual's access to healthcare. However, evidence on the associations between women's empowerment (WE) and pregnancy-related healthcare are restricted to individual-level analysis. We examined how individual- and community-level WE are jointly associated with complete use of maternal healthcare services in sub-Saharan Africa (SSA).

Methods: We pooled data from Demographic and Health Surveys (post-2010) across 34 SSA countries (N=194,905). Complete care was defined as having four or more antenatal care visits, facility delivery, and postnatal care. Based on a globally validated survey-based WE index (SWPER), a composite variable was constructed for individual- and community-level WE in terms of attitude to violence, social independence, and decision-making: low-low (reference), low-high, high-low, and high-high. Sociodemographic factors were adjusted in multilevel linear probability models.

Results: One-third of women (35.4%) completed all pregnancy-related healthcare. Highly empowered women living in high empowered communities (high-high) had the highest probability of complete care (b=0.059; 95% CI=0.051,0.066 for attitude to violence, b=0.117; 95% CI=0.109,0.125 for social independence, and b=0.074; 95% CI=0.066,0.081 for decision-making). Less empowered women living in highly empowered communities (low-high) had a greater likelihood of receiving complete care than highly empowered women living in less empowered communities (high-low), which was particularly evident in social independence domain.

Conclusion: We found a strong contextual effect of WE on maternal healthcare utilization. Together with strengthening individual women's agency, policies to change community-level gender norms are needed to encourage less empowered women to engage in maternal healthcare practices in SSA.

Figure 1. Associations between joint categories of individual- and community-level women's empowerment and complete care[a] (N=194,905)
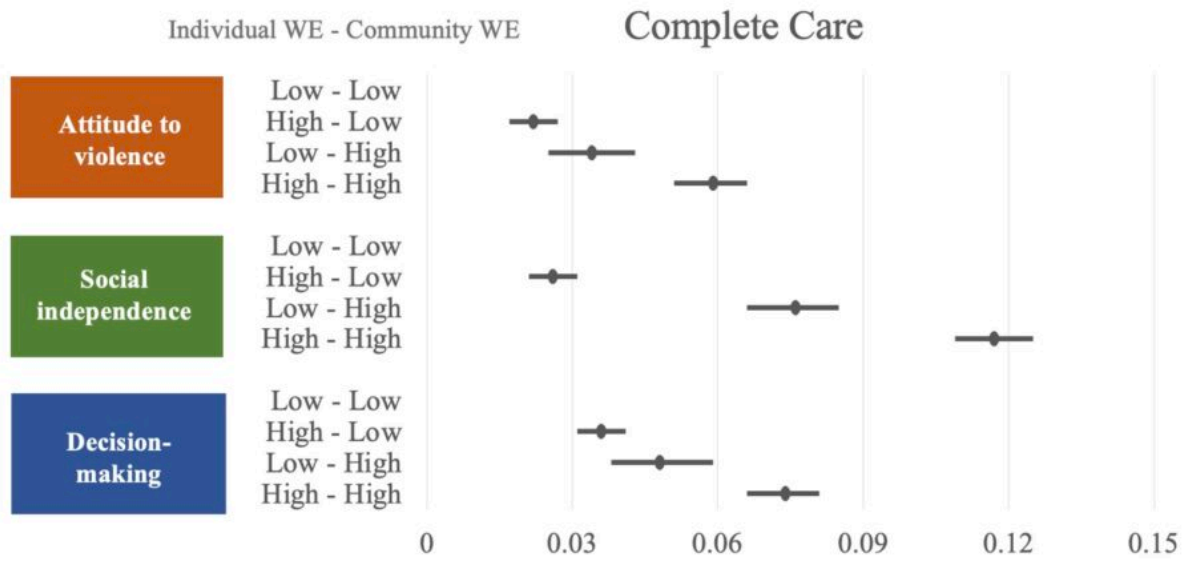
a. Complete care indicates women who visited antenatal care >=4 times, had facility delivery with skilled birth attendants, and received any postnatal care.
b. Black dots and lines indicate the coefficients and 95% confidence intervals, respectively.
c. Individual-level covariates are as following: women's age at birth, number of children aged under 5, birth order, place of residence, household wealth index, and survey year.

Global Health

Community health workers, communities, and child development trajectories: A value-added approach Caitlin Hemlock* Caitlin Hemlock Ann M. Weber Emanuela Galasso Maria Dieci Lisy Ratsifandrihamanana Lia C.H. Fernald

Interventions to improve child development in low-resource settings are often delivered through home visits by community health workers (CHWs), but many have not exhibited substantial gains for young children. This analysis aimed to determine the relative effectiveness, or value-added, of CHWs on cognitive development outcomes in a home-visiting trial and to examine if any characteristics of the CHW or community were associated with effectiveness. We analyzed data from the 4 treatment arms of a cluster RCT conducted in 100 communities in rural Madagascar (2014-2016). CHWs (1 per community) and enrolled children were surveyed at baseline and two years later. Child cognitive development scores were assessed using the Ages and Stages Questionnaire-Inventory (ASQ-I) and were internally age-standardized. We estimated value-added by estimating CHW/community-level fixed effects on ASQ score change from baseline to endline, conditional on baseline score and child and household characteristics. We also assessed associations between CHW and community-level characteristics and gains in ASQ. We analyzed data from 1456 children present at baseline and endline. CHW/community value-added ranged from -1.68 SD to 1.31 SD and explained 26% ASQ change score variance. CHWs with another income-generating position were associated with a 0.54 SD (95% CI: 0.22, 0.87) increase in ASQ score from baseline to endline. Higher gains in ASQ were also associated with communities that had healthcare, education, and transportation infrastructure and were less geographically dispersed. We found positive value-added of CHWs with another income-generating activity, potentially from better intervention delivery or improved economic resources, and in communities with improved infrastructure and accessibility. Careful consideration of the contexts in which child development interventions are implemented and potential correlates of improved CHW performance are crucial for improved outcomes.

Health Disparities

Race/ethnicity-specific associations of the combined effects of extreme temperature exposures and neighborhood socioeconomic disadvantage on birth outcomes in Harris County, Texas Wei-Jen Chen* Wei-Jen Chen Elaine Symanski Allan C. Just Kristina W. Whitworth

Evidence suggests that exposure to high temperatures during pregnancy and living in disadvantaged neighborhoods increases risks of preterm birth (PTB) and low birth weight (LBW) among newborn infants. However, the impact of these combined exposures has not been examined.

A retrospective cohort study was conducted using 123,138 singleton live birth records in Harris County, Texas (11/2018–12/2020). Census tract-level daily maximum air temperatures, assessed using the "XGBoost-IDW Synthesis" model, were linked to mothers' residence at delivery and averaged across their gestational period. Average temperatures were dichotomized at the 90th percentile (i.e., 29.35 ℃). Neighborhood disadvantage was assigned based on the census tract-level Area Deprivation Index and categorized as high/low based on the median. Modified Poisson regression was applied in the entire sample to evaluate associations of combined exposures to temperature and neighborhood disadvantage with either PTB or LBW, adjusted for covariates. We also conducted stratified analyses to explore the differential impact of these combined exposures for non-Hispanic White (NHW), non-Hispanic Black (NHB), and Hispanic mothers.

Relative to those experiencing lower temperatures during pregnancy and living in less deprived neighborhoods, PTB risk was elevated for women who experienced high temperatures and lived in the more deprived neighborhoods (Risk Ratio (RR), 95% Confidence Interval (CI): All Women: 3.93, 3.69–4.17; NHW: 5.25, 4.43–6.23; Hispanic 3.93, 3.63–4.24; NHB: 3.57, 3.22–3.95). For LBW, RRs were also elevated for women with these combined exposures (All Women: 3.74, 3.49–4.02; NHW: 4.19, 3.28–5.35, Hispanic: 4.12, 3.74–4.53; NHB: 3.25, 2.91–3.62).

Our study provides evidence of the racial/ethnic differences in the combined effects of high temperatures and neighborhood disadvantage on birth outcomes, highlighting the importance of considering neighborhood-level stressors in environmental and perinatal health disparities.

Health Disparities

Predictors of Pediatric Respiratory Disease in New York State Erin Ryan Kulick* Erin Kulick Marina Oktapodas Feiler Jack McClamrock

Pediatric respiratory-related hospitalizations are disproportionally distributed across racial and ethnic populations in the US. Current research has mainly focused on smaller homogenous populations making the true burden of disease across diverse populations largely unknown. Statewide existing data was leveraged to examine the distribution and predictors of pediatric acute respiratory disease using data from the New York State (NYS) Department of Health Statewide Planning and Research Cooperative System (SPARCS). This administrative claim database contains 98% of all hospitalizations in NYS, allowing us to examine a diverse population regarding race, ethnicity, insurance status, and geography. The study sample included pediatric discharges in NYS from 2009-2017. Patient characteristics, diagnoses, treatments, and billing were collected for hospitalizations or ED visits. Diagnoses are established using ICD-9/10 codes at the first two diagnostic positions. The primary outcome was all-cause respiratory discharges. Distributions of sociodemographic characteristics were calculated as proportions for categorical variables. Differences in sociodemographic characteristics between overall and acute respiratory hospitalizations were tested using chi-squared tests. Log-binomial regression was modeled to identify sociodemographic predictors of respiratory hospitalizations.

Over 2.9 million acute respiratory hospitalizations among pediatric patients were identified (18% of all pediatric hospitalizations), with 91% being emergency department visits. The risk of a respiratory hospitalization was highest among those who were >1-5 years, Black race, and Hispanic or Multi-ethnic (Table 1). This descriptive study identified pediatric populations at high risk for acute respiratory hospitalizations using a highly representative sample and reducing selection bias. Next steps include consideration of environmental and structural determinants of health and individual respiratory outcomes.

Table 1. Sociodemographic Predictors of Acute Respiratory Pediatric Hospitalizations in New York State, 2009-2017

Characteristics	Risk Ratio	95% Confidence Interval
Age (years), n (%)		
<=1	1.43	1.42, 1.43
>1-5	2.18	2.17, 2.19
6-12	1.72	1.72, 1.73
13- <18	(ref)	(ref)
Sex, n (%)		
Male	(ref)	(ref)
Female	0.94	0.94, 0.95
Race, n (%)		
White	(ref)	(ref)
Black	1.63	1.63,1.64
Asian	1.04	1.03,1.05
Multi-Racial	1.18	1.16, 1.20
Other	1.24	1.24, 1.25
Ethnicity, n (%)		
Hispanic	1.28	1.28, 1.29
Non-Hispanic	(ref)	(ref)
Multi-Ethnic	1.28	1.26, 1.30
Insurance Type, n (%)		
Private	1.04	1.04, 1.05
Public	1.14	1.14, 1.14
Uninsured	(ref)	(ref)

Health Disparities

The Racial Opportunity Gap and Fine Particulate Air Pollution in California Stacey Alexeeff*
Stacey Alexeeff Joel Schwartz Rachel Morello Frosch Madeline Somers Jamal Rana Stephen Van Den
Eeden

Background: Disadvantaged populations often live in neighborhoods with higher levels of
pollution. The Racial Opportunity Gap (ROG) is a recently developed place-based measure of
structural racism that reflects differences in intergenerational economic mobility by race. Its
relationship to fine particulate air pollution (PM2.5) has not yet been studied.

Methods: Annual PM2.5 data on a 1km grid was from a published ensemble model of Dr. Schwartz.
We computed the 10-year average PM2.5 concentrations during 2007-2016 for each census tract
and categorized as low ($<=9.0$), moderate (9.1-12.0), high (12.1-15.0) and very high (15.1-20.0)
based on Environmental Protection Agency regulation levels. We obtained publicly available
intergenerational income distribution data for white and black individuals in the same census tract
born to parents at the 25th percentile of the national income distribution. We computed ROG,
defined as the difference in these measures. We visualized the crude means by PM2.5 categories
using bar plots. We fit a linear mixed effects model accounting for spatial correlation to estimate
associations between economic mobility measures and PM2.5 concentrations.

Results: White children in families at the 25th income percentile moved up to much higher income
percentiles in adulthood (43.8-46.3; Figure), but Black children only moved up to the 33.2-35.2
income percentile in adulthood, resulting in substantial gaps by race (p-values<0.0001). Census
tracts with lower PM2.5 had greater economic mobility for white adults (Figure), and this difference
was statistically significant in regression models (p-value=0.0046). Census tracts with lower PM2.5
also had slightly greater economic mobility for black adults, although this difference was not
statistically significant (p-value=0.2352).

Conclusions: We found advantaged census tracts with lower air pollution and higher white
economic mobility. The Racial Opportunity Gap was high in all PM2.5 categories.

Economic Mobility and Air Pollution
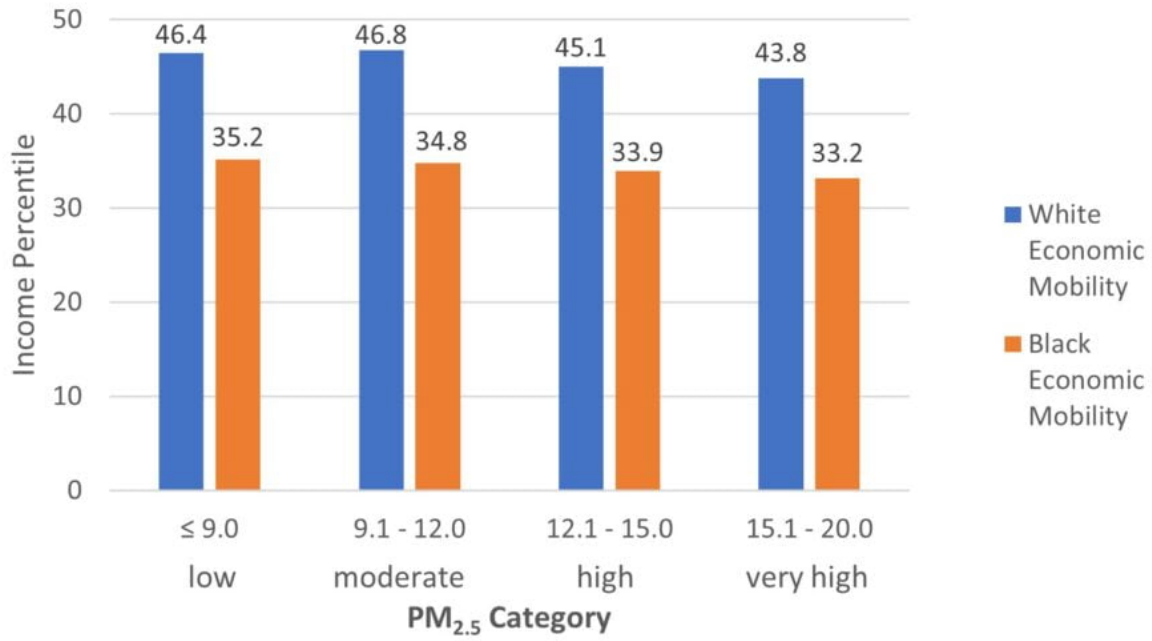
Disparities in HPV Vaccination in the MIdwest region of the US Kristyne Mansilla Dubon*
Kristyne Mansilla Dubon Edward Peters Abraham Mengist

Human papillomavirus (HPV) incidence rates in the Midwest region range between 10 to 13 per 100,000. HPV infection is strongly associated with cancers that are preventable through vaccination. Current guidelines require two or three doses for complete HPV vaccination, depending upon age. Despite recent improvements, the HPV vaccination proportion remains below the Healthy People-2030 80% goal, with lower completion rates among racial and gender minorities. Our objective was to examine the differences in vaccination status among teens and young adults living in the Midwest region of the US. In 2023, we conducted a cross-sectional knowledge attitude and practice survey administered through Qualtrics using their survey panels. The population consisted of participants aged 13 to 26 years old residing in the Midwest region of the US who had agreed to participate in the survey. We estimated summaries of sociodemographic characteristics and conducted a bivariate analysis to identify potential predictors of vaccination status. Lastly, we fitted a generalized ordered logit model to examine disparities in vaccination status. We observed that 30% of participants (n=1306 had completed the vaccination series, almost 10% had initiated HPV vaccination, 35% were unvaccinated, and 25% were unsure of their vaccination status. The adjusted model included age, gender, ethnicity, and educational level. We found that as age increases, the odds of not being vaccinated decrease (aOR 0.9 95% CI 0.85-0.96) . Self-identified female participants had lower odds of being unvaccinated than male participants (aOR 0.68, 95% CI:0.52-0.92). Black or African Americans and American Indian or Alaska Native had almost 3 and 2.5 times, respectively, higher odds of not knowing whether they were vaccinated or not compared to White participants (aOR 0.68, 95% CI:0.52-0.92). Participants with less than a high school education had higher odds of not knowing if they were vaccinated than participants with a graduate education (aOR 2.56, 95% CI:1.01-4.18). These findings suggest that age, race, gender, and educational level are associated with vaccination status and knowledge of vaccination status among the participants in the study. The study's findings highlight sociodemographic barriers affecting HPV initiation and completeness and provide a guide to prioritize public health interventions that target minority groups to enhance vaccination rates.

Development and Validation of a Breast Cancer Risk Prediction model for Puerto Rican women Mary V Diaz Santana* Mary Diaz Santana Molly Rogers Clarice Weinberg Dale Sandler

Background

Breast cancer (BC) is the leading cause of cancer death among Hispanic women. Country of birth has been reported to modify BC risk in this population of women. Compared to Hispanic women in the US, BC mortality rates are higher in Puerto Rico (PR). BC risk prediction models are needed to identify women at high risk who would benefit from early detection. Previously developed risk prediction tools for Hispanic women have been reported to underestimate or overestimate risk in Hispanic women. We seek to develop a BC risk prediction model, specific to Puerto Rican women, that includes socioeconomic determinants of health.

Methods

We used data on Puerto Rican women (315 cases; 348 controls) from the ATABEY case-control study to estimate BC relative risk and attributable risk for each woman. Puerto Rican-specific absolute risks were estimated by accounting for SEER age-specific and country-specific BC incidence and competing mortality from the PR Cancer Registry. We validated our model in prospective data from 1,108 Puerto Rican participants from the Sister Study. We assessed model performance by calibration (expected/observed (E/O) cases) and discrimination accuracy (AUC). The model was built using the Individualized Coherent Absolute Risk Estimator R package.

Results

The Puerto Rican-specific risk model included age at menarche, age at first full-term pregnancy, family history of breast cancer, biopsy for benign breast disease, and socioeconomic factors. In independent data from the Sister Study, the Puerto Rican-specific model was well calibrated (E/O) ratio 1.02 (95%CI, 0.71-1.47). The AUC was 0.71 (95%CI, 0.60-0.81).

Conclusions

This is the first absolute risk model that is specific to Puerto Rican women. Discriminatory accuracy for this model was higher than what has been reported using the Hispanic Risk Model. This suggests that the use of the Puerto Rican-specific risk prediction model can improve breast cancer risk stratification for Puerto Rican women.

Figure 1: Performance in terms of the sensitivity and specificity for the Puerto Rican-specific breast cancer risk model

AUC=0.709

Health Disparities
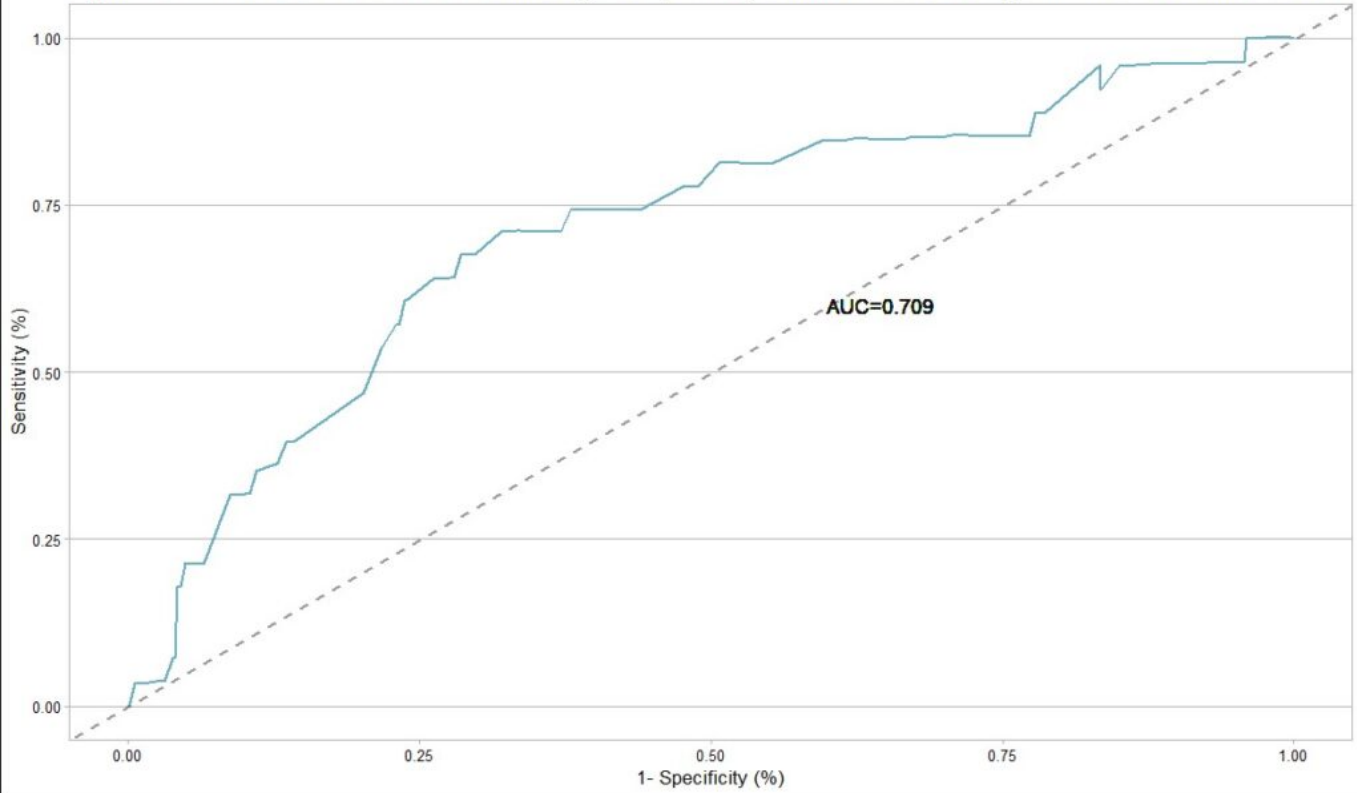
Beyond Credentials: Understanding Educational Gradients in Cognitive Function at Midlife
Eric Grodsky* John Warren Eric Grodsky Chandra Muller

INTRODUCTION: A substantial body of research points to the persistence of educational credential gradients in cognitive function across the life course, from early adulthood through old age. Fewer studies have considered the roles of educational opportunities and achievements early in the life course in shaping (1) educational credential gradients or (2) variation in cognitive function among those with the same credentials. As a result, researchers underestimate the contribution of education writ large to variation in cognitive performance later in life. METHODS: We analyze data from the nationally representative High School and Beyond (HSB)cohort, which has followed ~25,500 people from high school in 1980 through age ~60 in 2021-22. The 2021-22 round of HSB gathered high quality measures of cognition across multiple domains; the 1980-1992 rounds gathered extensive information about educational opportunities, achievements, and attainments. RESULTS: We demonstrate that high school educational opportunities, and especially academic achievements, account for most of the credential gradient in cognition on selected cognition measures among adults who attended high school in the U.S. in 1980 as they approach 60 years of age. High school educational opportunities and academic achievements also help account for some of the variation in cognition among those with the same educational credential. CONCLUSION: Educational credentials commonly employed to understand the contribution of education to cognitive aging therefore risk both mischaracterizing and understanding the contributions of education to cognitive function and change over the life course.

Health Disparities

Sex Differences in Psychological Distress and its Risk Factors Among U.S. Adult Immigrants, 2005-2018 Maryam Elhabashy* Maryam Elhabashy David Adzrago Faustine Williams

Introduction. Psychological distress, an array of non-specific symptoms of stress, anxiety, and depression, is a mental health condition associated with increased likelihoods of adverse physical and mental health outcomes. Limited research explores sex differences in psychological distress and its risk factors across minority communities, especially immigrant population. This study aims to estimate the prevalence of psychological distress and its sociodemographic and behavioral health risk factors among male and female immigrants. **Methods.** Drawing from the 2005-2018 National Health Interview Surveys (NHISs) data, this study analyzed a sample of male (n=21,082) and female (n=24,984) adult immigrants using weighted multivariable logistic regression analyses. **Results.** Psychological distress was more prevalent among females (22.68%) compared to males (15.58%). Among the demographic factors, older age (i.e., ≥65 vs. 18-25 years) was a significant protective factor for males than for females. Males aged 55-64 also had significantly low odds of experiencing psychological distress; no significant difference was observed among females. Being overweight was a significant protective factor for males, while being overweight or obese was a significant risk for females. For the behavioral factors, alcohol drinking and smoking were significant risk factors among males and females, with males with current or former alcohol drinking status having greater risks while females with current or former smoking status had greater risks. Regarding chronic disease, males exhibited more significant risks with 1-2 chronic diseases, while females had more significant risks with ≥3 chronic diseases. **Conclusions.** This study shows that prevalence and risk factors of psychological distress differ across male and female immigrants. Therefore, more sex-specific considerations should be addressed in mental health research and interventions to address the needs of male and female immigrants.

Association of cumulative adverse social determinants of health score with insufficient sleep duration among U.S. adults. Kelley M. Pascoe* Kelley Pascoe Yilda Macias Pandora L. Wander Alyson J. Littman

Introduction: Insufficient sleep duration is associated with individual adverse Social Determinants of Health (SDoH) and with poor health outcomes. However, the association with cumulative adverse SDoH is unclear.

Methods: Using 2022 Behavioral Risk Factor Surveillance System data from 35 U.S. states and two territories (n=236,406) we examined the association of self-reported insufficient sleep duration (<7 hours) with cumulative adverse SDoH scores among adults. We fit binomial logistic regression models using grouped-linear adjustment for SDoH scores and indicator variables for sex, age, and race/ethnicity to estimate unadjusted and adjusted weighted PR (PR and aPR) and 95% CI. We assessed interactions by sex and race/ethnicity.

Results: Participants were mostly non-Hispanic white (77%), employed (51%), coupled (57%), and had a college degree or higher (44%). Approximately 32% of participants reported insufficient sleep. For every unit increase in SDoH score the prevalence of insufficient sleep was 24% higher after adjusting for sex, age and race/ethnicity (aPR=1.24, 95%CI: 1.23-1.26). Race/ethnicity modified the association between SDoH score and insufficient sleep. The association between SDoH score and insufficient sleep was stronger among non-Hispanic Asians (aPR: 1.96, 95% CI: 1.70, 2.26), intermediate among Hispanic (aPR: 1.34, 95% CI: 1.01, 1.80), non-Hispanic whites (aPR: 1.32, 95% CI: 1.30, 1.33), and non-Hispanic other race groups (aPR: 1.30, 95% CI: 1.14, 1.49), and weaker among non-Hispanic Black (aPR: 1.16, 95% CI: 1.13, 1.20) and non-Hispanic American Indian/American Native (aPR: 1.02, 95% CI: 0.80, 1.28) groups, adjusting for age and sex. Associations did not differ by sex.

Conclusion: Higher adverse SDoH scores are positively associated with insufficient sleep duration. Future research should examine underlying mechanisms linking cumulative SDoH experiences and sleep health.

Figure 1. Forest plot of the Association between Social Determinants of Health (SDoH) and Insufficient Sleep Duration (<7hours) by Race/Ethnicity.
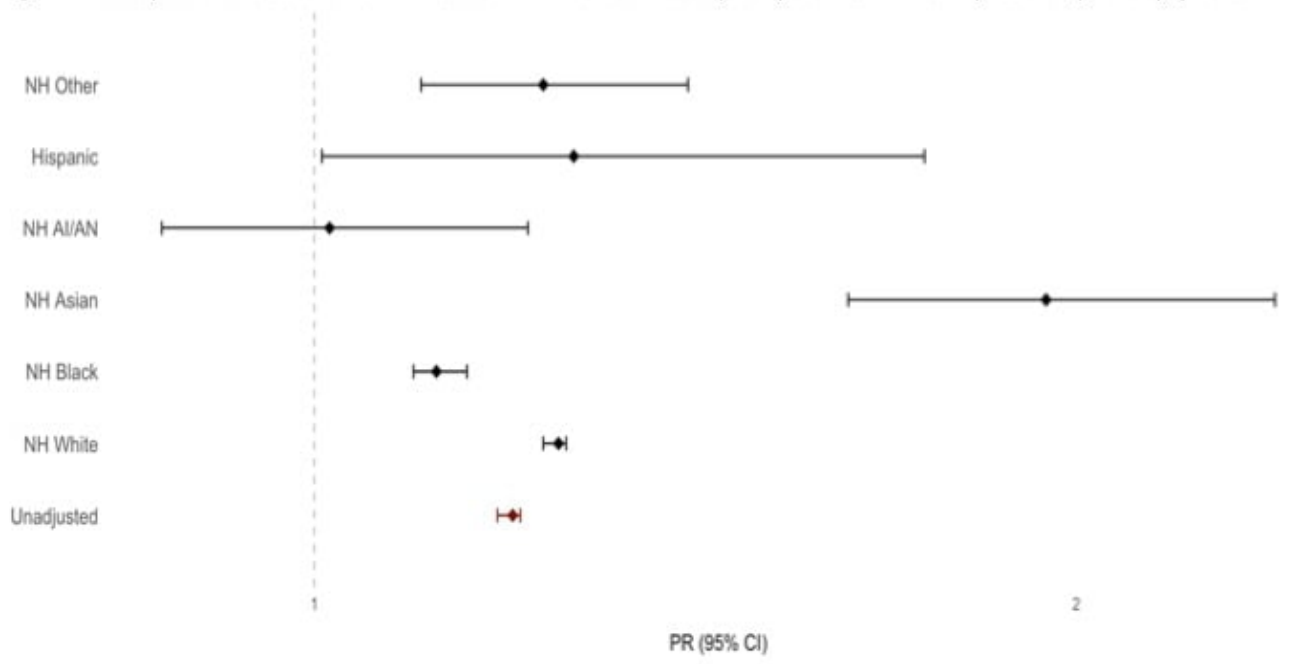
Using a target trial to estimate the causal effect of health technology on racial disparities

Chloe Bennett* Chloe Bennett Rob Cavanaugh Louisa Smith

The burden of type 2 diabetes (T2D) disproportionately affects Black people, perpetuating health inequities. Continuous glucose monitors (CGM), which improve glycemic control and reduce complications, have the potential to mitigate racial disparities in T2D outcomes.

This ongoing study uses the target trials framework to estimate the causal effect of CGM initiation on racial inequities in hemoglobin A1c levels, a key indicator of diabetes control. We specified a target trial with the following design: non-Hispanic Black and White individuals with T2D and no prior CGM use are assigned to one of two treatment strategies: either initiate CGM use or continue with standard monitoring. Differences in A1c between the Black and White participants within each treatment arm after 1 year will quantify disparity in diabetes control.

This target trial is currently being emulated using data from the NIH All of Us Research Program, which includes electronic health records and surveys. Eligible participants are 18+ with self-reported T2D. Initial analyses found 17,507 participants with self-reported T2D; 9312 (53%) met eligibility criteria at least once. Eligible participants contributed a median of 5.66 years of data. The average A1c when participants first met eligibility criteria was 7.7% (Black participants) and 7.2% (White).

The emulation uses a repeated design: time zero begins every time A1c lab results are recorded, as long as eligible participants have no recorded use of a CGM within the year prior. Baseline confounding, including by baseline A1c level, is adjusted for via inverse-probability weighting to estimate an intention-to-treat effect. Pooling over all trials, we can estimate the difference in differences in A1c after 1 year between Black and White individuals across treatment and control groups. Results will be discussed in the context of the use of (1) health technology to address disparities and (2) the target trials framework to study them.

Overall and firearm-related homicide disparities across county, race and ethnicity, age, and sex in the United States, 2000-19 Paula Strassle* Paula Strassle Laura Dwyer-Lindgren Erik J Rodriquez Parkes Kendrick George A. Mensah Eliseo J. Pérez-Stable

Homicide is one of the leading causes of death in the US, especially among adolescents and adults ages <45. While research has consistently found racial/ethnic homicide disparities, the intersection between geography, race/ethnicity, sex, and age have not been comprehensively assessed. We applied validated small-area estimation methods to death registration data from the US National Vital Statistics System and population data from the US National Center for Health Statistics to estimate homicide (overall and firearm-related) rates by county, race/ethnicity, age, and sex from 2000–19. Estimates were corrected for misreporting of race/ethnicity and age-standardized to the 2010 Census. In 2019, the national homicide rate was 6.1 (95% uncertainty interval: 6.0–6.2) deaths per 100,000; 76.1% of homicides (75.5–76.6) were firearm-related. The highest rates were among Black males ages 15–24 (74.6 [72.3–77.0]) and 25–44 (70.0 [68.4–71.4]), followed by AIAN males ages 25–44 (33.5 [28.6–38.8]) and 15–24 (24.5 [19.2–31.0]). Among females, rates were highest among AIAN females ages 25–44 (10.2 [8.1–13.0]) and Black females ages 15–24 (9.6 [8.9–10.3]) and 25–44 (9.1 [8.7–9.6]). Rates among AIAN and Black males (Fig) and females ages <65 increased in most counties from 2000–2019. Oklahoma counties had some of the largest increases among AIAN males. In 2019 homicide rates were >100 in 119 and 90 counties (out of 1488) for Black males ages 15–24 and 25–44, respectively. Among AIAN males ages 25–44, 3 out of 474 counties had rates >100. For AIAN females ages 25–44, homicide rates were >20 in 19 counties (13 in Alaska). Similar trends were seen for firearm-related homicide. Homicide remains a significant public health concern in the US, especially among AIAN and Black males and females. These results provide important nuance in homicide disparities and motivate research to identify drivers and develop and implement effective interventions in places and populations of greatest need.

Change in age–standardised mortality (%), 2000 to 2019
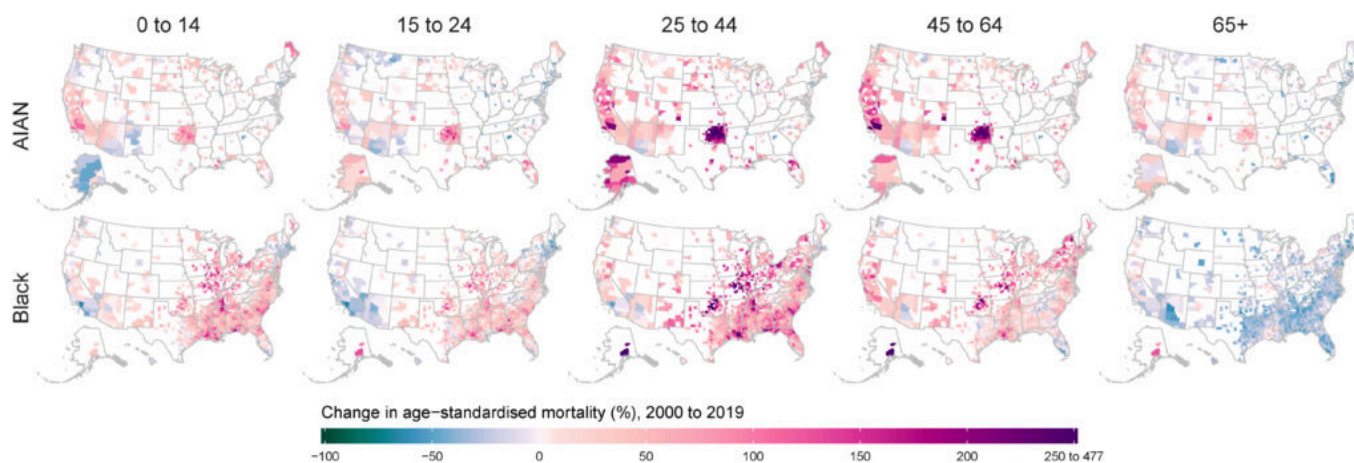
Census-Tract Level Social Vulnerability and Preterm Birth in California Jocelyn Burridge*

Jocelyn Burridge Rebecca Baer Christina Chambers

Background: Preterm birth (PTB) is a leading cause of neonatal morbidity and mortality. Existing literature has shown that community factors influence risk of PTB. This has led to increasing use of the Social Vulnerability Index (SVI) as a proxy for individual risk factors.

Objectives: This study investigated the association between SVI and PTB and explored the moderating effect of SVI on risk of pregnancy-induced hypertension in relation to PTB.

Methods: This retrospective study utilized linked hospital discharge and vital statistics data from all pregnancies in California 2018-2021 from the UC San Diego Study of Outcomes in Mothers and Infants (SOMI). The study sample consisted of 1,022,097 singleton livebirths linked to the CDC's 2020 SVI metrics by census tract. SVI was categorized in quintiles (Very Low, Low, Moderate, High, Very High), determined by socioeconomic status, household composition, racial/ethnic status, and housing/transportation metrics. Pregnancy-induced hypertension was identified by ICD code. PTB (<37 weeks) was obtained from vital statistics. Logistic regression models were adjusted for maternal age, insurance status, education, body mass index, nulliparity, pre-existing hypertension, smoking, and rural-urban classification. An interaction term for pregnancy-induced hypertension and SVI was tested in the model.

Results: Significant associations were found between PTB and successively higher SVI quintiles compared to Very Low SVI quintile, adjusting for confounders (see table). Highest risk was in the Very High SVI quintile (adjusted odds ratio [aOR] 1.34, 95% Confidence Interval [CI] 1.30, 1.39). Increased risks were also seen for very preterm birth (<32 weeks) (Very High vs Very Low SVI: aOR 1.81, 95% CI [1.66, 1.97]). A significant interaction between hypertension and SVI was found, suggesting SVI amplifies the impact of hypertension on risk of PTB.

Conclusion: There was a significant correlation between higher SVI and PTB at the census tract level. This highlights the potential for SVI as a predictive tool for assessing risk of PTB and underlines the need for targeted interventions in high SVI regions.

Model of Association Between Overall SVI and Preterm Birth

	All Preterm <37 weeks		Moderate Preterm (32-36 weeks)		Very Preterm (<32 weeks)	
	Unadjusted OR	Adjusted OR	Unadjusted OR	Adjusted OR	Unadjusted OR	Adjusted OR
Composite SVI						
Very low SVI	Ref	Ref	Ref	Ref	Ref	Ref
Low SVI	1.06 (1.03, 1.09)*	1.04 (1.00, 1.07)*	1.05 (1.02, 1.09)*	1.03 (0.99, 1.06)	1.13 (1.03, 1.23)*	1.12 (1.01, 1.29)*
Moderate SVI	1.14 (1.11, 1.17)*	1.11 (1.07, 1.14)*	1.11 (1.08, 1.15)*	1.08 (1.04, 1.12)*	1.40 (1.29, 1.52)*	1.34 (1.22, 1.46)*
High SVI	1.25 (1.21, 1.28)*	1.25 (1.21, 1.29)*	1.21 (1.18, 1.25)*	1.21 (1.17, 1.25)*	1.56 (1.44, 1.69)*	1.59 (1.45, 1.74)*
Very high SVI	1.35 (1.31, 1.38)*	1.34 (1.30, 1.39)*	1.3 (1.27,1.38)*	1.29 (1.25, 1.33)*	1.75 (1.62, 1.89)*	1.81 (1.66, 1.97)*

*Significant at p<0.05

Adjusted for individual-level maternal age, payer, BMI, nulliparous, education level, urban/rural status, ever smoking, any hypertension

Excess death and population attributable risk fraction of major cause of death due to area-level socioeconomic inequalities in Japan from 2015 to 2020 Yuri Ito* Yuri Ito Aoi Kataoka Tomoki Nakaya Manami Inoue Tomotaka Sobue Naoki Kondo

Background

Socioeconomic inequalities in health have long been a global issue. Health Japan 21, Japan's health promotion plan, has focused on reducing health inequalities by bottoming up the health of subpopulations with low socioeconomic status (SES). To prioritize subpopulations for the plan's target, we estimated excess deaths and population attributable risk fractions due to socioeconomic inequalities (EDSI and PAFSI) for major causes of death by sex and age group.

Method

The areal deprivation index (ADI) was used to establish area-based SES. We categorized municipalities into the ADI quintile weighted by population size; Q1 is the least deprived, and Q5 is the most deprived group. EDSI was calculated as the difference between the observed number of deaths and expected deaths of the Q2–Q5 groups, with Q1 as the standard population, and PAFSI was the proportion of EDSI in the observed death. We calculated the mortality of the six major causes of death (Cancer, Heart disease, Cerebrovascular disease, Pneumonia, Accidents, and Suicides) obtained from vital statistics from 2015 to 2020.

Results

For all ages, the largest EDSI was Cancer in men (12,118) and Heart disease in women (9,066). The largest PAFSI was Accidents in men (23.1%) and women (20.6%) of all ages. For the less than 75 years old group, the largest EDSI was Cancer in both men and women, and the largest PAFSI was Accidents. By age group, the largest EDSI showed in the 0-39 years was Suicides in men and Cancer in women, the 40-64 years were Cancer for both sexes, the 65-74 years were Cancer in men and Heart Disease in women, and 75 years and older were Cerebrovascular disease in men and Heart disease in women. Cancer, Heart disease, Cerebrovascular disease, and Accidents had the largest PAFSI in those aged 0-39 years, Pneumonia in those aged 40-64 years and Suicide in those aged ≥ 75 years.

Conclusion

EDSI and PAFSI differed by sex and age. We need to consider the priority of intervention to reduce the deprivation gap based on the figures for both EDSI and PAFSI.

The influence of primary tumor site on colon cancer death among adult patients ≥ 45 years old diagnosed with colon cancer between 2010 and 2017. Akpevwe Amanda Ojaruega*

Akpevwe Amanda Ojaruega

Introduction: Colon cancer poses a significant health challenge, impacting a considerable portion of the population aged 45 years and older in the United States. Over the past decade, research has increasingly recognized the heterogeneity of colon cancer, highlighting the pivotal role that the primary tumor site may play in influencing disease progression and patient outcomes. This study delves into the intricate relationship between primary tumor location and death from colon cancer among individuals aged 45 years and older diagnosed with colon cancer in the USA during the years 2007 to 2017.

Methods: Our study included 111,789 adults ≥ 45 diagnosed with colon cancer from January 2010 to December 2017, identified from the Surveillance, Epidemiology, and End Results (SEER) research plus 18 registries' released in November 2020. We used univariable and multivariable logistic regression models to examine the association of race/ethnicity and death from colon cancer. We adjusted for clinical and socio-demographic factors associated with primary tumor site at diagnosis and colon cancer death to control for potential confounding.

Results: Primary tumor tumor site at diagnosis was significantly associated with colon cancer death at ($p < 0.001$). Hepatic flexure tumors had the highest odds of colon cancer-related death (aOR=1.8 [95% CI: 1.23-1.30]). Non-Hispanic blacks had higher odds of colon cancer-related death than non-Hispanic whites (aOR=1.61 [95% CI: 1.51-1.71]). Patients diagnosed at more advanced ages(80+ group) experienced poorer outcomes (aOR=7.64 [95% CI: 7.02-8.31]), correlating with existing literature linking age and survival rates.

Conclusion: Colon cancer death is significantly associated with the site of the primary tumor. This finding plays a pivotal role in guiding treatment plans, comprehending metastatic patterns, and grasping the molecular characteristics associated with different colon cancer tumor sites.

Centering Health Equity in Epidemiologic Research: An Introduction to the Health Equity Research Production Model Dustin Duncan* Dustin Duncan

Privilege is one of the primary causes of structural inequality and health inequality. As structural inequality increases globally, there will undoubtedly be an increase in health inequity; this has driven a commensurate increase in health equity research. The increased focus on health equity may lead to important evidence-based policy changes, potentially leading to changes in health and reductions in inequities in health. However, it is not enough to rectify health inequities. This paper introduces the Health Equity Research Production Model to the field of population health and health equity research because there is no current model in the literature focused on research production, including redressing issues of equity, fairness and justice in the production of research. The Health Equity Research Production Model focuses on research production using a framework of accountability and aims to remediate the compounded effects of privilege through systems and systems change. It prioritizes equity in the: (1) engagement with and centering of communities studied in research in all phases, (2) identities represented within research teams, (3) consideration of identities and groups awarded research grants, and (4) consideration of identities and groups considered for research products (e.g., peer-reviewed publications). This inclusive scientific approach–which directly addresses privilege inherent within the existing research production model—aims to deconstructs existing systems. The goal of the Health Equity Research Production Model is to facilitate accountability for prioritizing equity in academic research in an existing system structured on inequality, including by centering minoritized and marginalized academicians and researchers including to expand pipeline to reflect communities in need of research, creating fairness in research production while also improving the quality of the health equity research produced.

Equity in Community Engagement in Research

Prioritizes the importance and voice of community in research

Equity in Research Teams

Expand career opportunities for researchers from non-traditional backgrounds

Health Equity Research Production

Expand career opportunities for researchers from non-traditional backgrounds

Equity in Research Grants

Expand funding for researchers from non-traditional backgrounds

Equity in Research Papers

Expand opportunities for papers for researchers from non-traditional backgrounds

Assessing Maternal and Infant Health in Latino Populations Through Secondary Data Analysis Sueny Paloma Lima do Santos* Sueny Paloma Lima Ilana Chertok

Maternal-infant health is a critical global concern, particularly among the Latino populations. Our study seeks to explore complex health concerns by synthesizing data from multiple population-data sources. We used data from the Guatemalan Demographic and Health Surveys (DHS) to investigate the relationship between the quality of antenatal care and pre-pregnancy folic acid intake. Using the Pregnancy Risk Assessment and Monitoring System (PRAMS), we assessed the role of pre-pregnancy BMI on the relationship between pre-pregnancy folic acid intake and breastfeeding duration among Hispanic mothers in the US. National Health and Nutrition Examination Survey (NHANES), we assessed the mediating role of diet quality in the relationship between food insecurity and obesity among Hispanic children and adolescents. In Guatemala (N=9,523), 84.6% took pre-pregnancy folic acid, and 11.9% had adequate antenatal care. Mothers with no antenatal care (AOR=0.04, 95% CI 0.02-0.06) and those with intermediate quality antenatal care (AOR=0.58, 95% CI 0.44-0.77) had lower odds of folic acid intake compared to those who received adequate antenatal care. Among Hispanic mothers in the US (N=27,671), stratifying by pre-pregnancy BMI, among mothers with normal weight and obesity, compared to folic acid intake 4-6 times per week, there was a lower likelihood of breastfeeding when mothers did not take folic acid (AOR=0.702, 95% CI 0.503-0.978 and AOR=0.641, 95% CI 0.425-0.967, respectively). In NHANES (N=7,190), the indirect effect was found to be 0.0098, indicating partial mediation by diet quality. Food insecurity's direct effect on obesity was 0.0543. The total effect, which accounts for direct and indirect effects, was 0.0641, suggesting a combined influence of food insecurity and diet quality on obesity among this population. Understanding the complex interplay between prenatal and postpartum behaviors among Latino mothers is crucial for promoting health equity.

Health Disparities

Counseling Women of Reproductive Age about Emergency Preparedness, Changes in Provider Attitudes – Fall DocStyles Survey, United States, 2021-2023 Jerome Leonard* Jerome Leonard Romeo R. Galang Rebecca Hall Carrie Shapiro-Mendoza Jessica R. Meeker

Natural disasters and severe weather emergencies are increasing in frequency and severity. Women of reproductive age – including pregnant, postpartum, and lactating populations – face unique challenges during disasters that may be mitigated by emergency preparedness. A survey of healthcare provider attitudes and practices related to counseling women of reproductive age on emergency preparedness was administered in 2021 and 2023. Our analysis assesses changes in reported provider attitudes and practices comparing 2021 to 2023. Data were collected through Porter Novelli DocStyles, a web-based opt-in panel survey of healthcare providers in the United States. We calculated frequencies and confidence intervals (CI) of provider responses using R 4.3.0, and differences were assessed based on CI review. There were 1,503 respondents in the 2023 sample, including family practitioners (35%), internists (31%), obstetrician/gynecologists (Ob/Gyns) (17%), physician assistants (8%), and nurse practitioners (8%). Compared to the 2021 sample (n=1,503), a higher percentage of providers in the 2023 sample report emergency preparedness plans as very important from 51% (95% CI: 48%, 53%) to 56% (95% CI: 53%, 58%), counseling patients on emergency preparedness as very important from 31% (95% CI: 29%, 33%) to 42% (95% CI: 40%, 45%) and having counseled patients on emergency preparedness plans from 30% (95% CI: 27%, 32%) to 37% (95% CI: (34%, 39%). Compared to the 2021 sample, 2023 providers overall reported feeling similar levels of confidence in counseling patients on emergency preparedness plans from 53% (95% CI: 51%, 56%) to 51% (95% CI: 49%, 54%). However, Ob/Gyns reported a decrease in confidence from 70% in 2021 (95% CI: 64%, 75%) to 52% in 2023 (95% CI: 46%, 59%). These findings underscore the need for healthcare provider resources to support emergency preparedness counseling for this population.

Changes in COVID-19 mortality disparities among people with HIV in Florida after introduction of COVID-19 vaccine. Tendai Gwanzura* Tendai Gwanzura Mary Jo Trepka Diana Sheehan Tan Li Levente Juhasz Giselle Barreto Shelbie Burchfield

Previous studies have identified sociodemographic variations in COVID-19 mortality rates, including factors such as age, race/ethnicity, and geographic location, both before and after the availability of the COVID-19 vaccine. However, there is limited research on this relationship among people with HIV (PWH). This study therefore aimed to compare sociodemographic disparities in COVID-19 mortality among PWH before (January 1, 2020 – April 30, 2021) and after (May 1, 2021 – December 31, 2021) the introduction of COVID-19 vaccines. Using 2020-2021 Florida HIV surveillance data and ZIP Code-level Social Vulnerability Index (SVI), a multilevel competing risks model estimated risk of COVID-19 death among PWH, before and after vaccine availability. The adjusted hazard ratio (aHR) decreased post-vaccine for individuals aged 50 to 65 (after vaccine: aHR 4.23, 95% confidence interval [CI] 2.23–7.98; before vaccine: aHR 5.39, 95% CI 2.66–10.93) and those over 65 (after vaccine: aHR 9.19, 95% CI 4.83–17.47; before vaccine: aHR 17.15, 95% CI 8.45–37.49) compared to those aged 18 to 34. Post vaccine, disparities in the hazard of death from COVID-19 were eliminated for Hispanics (after vaccine: aHR 0.99, 95% CI 0.66–1.49; before vaccine: aHR 2.23, 95% CI, 1.57–3.16), but not for Non-Hispanic Blacks (after vaccine: aHR 1.43, 95% CI, 1.02–2.0; before vaccine: aHR 1.81, 95% CI, 1.30–2.52) compared to Non-Hispanic Whites (NHW). PWH who resided in areas of high social vulnerability had a higher risk of death post-vaccine (aHR 1.70, 95% CI 1.03–2.80), but not pre-vaccine availability (aHR 1.36, 95% CI 0.89–2.07). Potential reductions in age and race/ethnic disparities in COVID-19 mortality were observed following the availability of the COVID-19 vaccine. However, PWH in the most socially vulnerable areas did not show improvements, suggesting a need for targeted interventions to boost vaccine uptake and eliminate disparities in these communities.

Prevalence estimates of disability, overall and by functional disability domains, among adults and children in national population-based surveys in US Qi Cheng* Qi Cheng Yan Wang Allison Boda Seman Joseph Holbrook Catherine E. Rice

Background: The six standardized disability questions developed by the Census Bureau and used in the American Community Survey are population-level measures of functional disability in 6 domains (ACS-6: hearing, vision, mobility, cognition, self-care, and independent living). This analysis examined the range of disability prevalence estimates in adults and children from national population-based surveys using ACS-6.

Methods: Using 2017 or/and2018 data from ACS, BRFSS, CPS, NHANES, NHIS, and SIPP, we calculated disability prevalence for adults aged ≥ 18 years and children aged 5-17 years by survey accounting for their complex survey design. Z-tests assessed statistically significant differences (p<.05) between survey estimates.

Results: Among adults, disability prevalence ranged from 27.2% (CI: 26.9-27.5) in BRFSS to 12.1% (11.7-12.5) in CPS (p<.05). Variation in prevalence existed across functional domains of disability, with mobility disability consistently having the highest prevalence (Figure 1a). Disability prevalence for children also varied across surveys, from 15.1% (13.1-17.6) in NHANES to 5.4% (5.4, 5.5) in ACS (p<.05). Variation in prevalence across domains of disability also existed, with cognition disability consistently having the highest prevalence across all surveys (Figure 1b).

Conclusion: Given the variation in disability prevalence across surveys using the ACS-6 question set, cautious interpretation of estimates from a single survey may be needed. Understanding how survey purpose, sampling design, response rate, and statistical weighting influence disability prevalence across national surveys may help stakeholders interpret and use estimates.

Reduced transitions to a nursing home among residents of assisted living facilities: a target trial Derek R. Manis* Derek Manis David Kirkwood Stacey Fisher Wenshan Li Peter Tanuseputro Zain Pasat Colleen Webber Andrew P. Costa

Background: The rapid expansion of assisted living suggests an increasing share of clinically frail older adults use it as a substitute for a nursing home. We examined transitions to a nursing home among residents of assisted living facilities relative to community-dwelling home care recipients.

Methods: We conducted a retrospective cohort study using the target trial framework in Ontario, Canada. We obtained linked, individual-level health system administrative data from residents of assisted living and home care recipients who applied for a bed in a nursing home from 04/01/14 to 03/31/19; these individuals were followed until 03/31/22. We examined any transition, long-stay transitions, and short-stay transitions to a nursing home among those in assisted living who resided there for at least one year before their application to a nursing home. We used inverse probability weighted marginal structural Cox models to control for time-varying and time-invariant confounding.

Results: There were 10,012 residents of assisted living (Mean [SD] age 87.9 [6.56] years, 72% female) and 131,679 home care recipients (Mean [SD] age 84.5 [7.47] years, 61% female) who applied for a bed in a nursing home (N = 141,691; 95,744.6 person-years). Residents of assisted living facilities had 11.6 fewer (76.4 v. 88.0) transitions to a nursing home per 100 person-years; 13.2% of the transitions among those in assisted living were prevented. Residents of assisted living had a decreased hazard of any transition (HR 0.46, 95% CI 0.45-0.47), a long-stay transition (HR 0.47, 95% CI 0.46-0.48), and a short-stay transition (HR 0.16, 95% CI 0.13-0.21) to a nursing home at any point during the follow-up period.

Conclusions: Residents of assisted living facilities mostly age in place, despite their clinical complexity and needs for ongoing health care. The integration of assisted living into the continuum from home to institutionalized nursing home care informs health system capacity and planning.
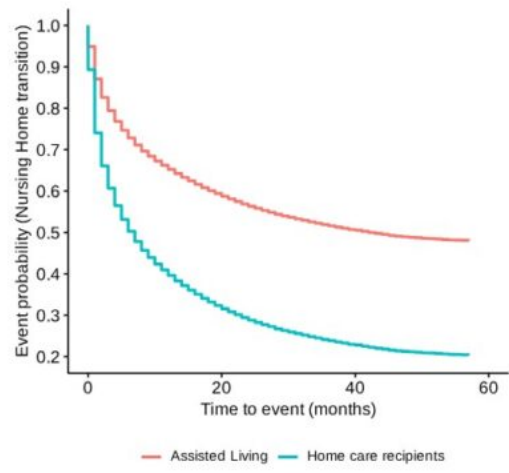
Who Uses Telehealth, Where, and When? Exploring Use of Psychiatric and Primary Care in Electronic Health Records of Patients with Depression

Catherine Ettman* Catherine Ettman Jason Straub Grace Ringlein Carly Lupton Brantner Elizabeth Chin Elena Badillo Goicoechea Priya Dohlman Fernando S. Goes Elizabeth A. Stuart Peter P Zandi

While telehealth has the possibility to improve access to healthcare for some, it may create disparities for others who may not have access to it. We sought to understand: 1) are there differences in who uses telehealth; 2) do telehealth usage patterns differ across primary versus psychiatric care? Using electronic health record data for two cohorts of patients with depression in a large U.S. academic medical system, we assessed telehealth use for primary care and psychiatric care from July 1, 2020, through December 31, 2023. Our sample includes patients ages >10 years in the Johns Hopkins Medicine System with a depression diagnosis with appointments in the Department of Psychiatry (n=15,218) or Johns Hopkins Community Physicians (n=44,243). We estimated the odds ratio of an appointment happening over telehealth versus in-person using multivariable logistic regression with random effects at the patient level (to account for repeated visits) for each patient characteristic: sex, age, race and ethnicity, employment, area deprivation index (ADI), insurance, and psychiatric co-morbidities (i.e., history of substance use disorder (SUD), anxiety disorder, and suicidal ideation or attempt). First, the following characteristics were associated with greater use of telehealth in both psychiatric and primary care from July 1, 2020, through October 21, 2023: female sex, White race, full-time employment, private health insurance, lower ADI, ages 18-64, and co-morbid anxiety. Second, we found that the following patient groups were more likely to use telehealth when controlling for all other patient characteristics and appointment characteristics (time of day, day of week, month, lead time) across both psychiatric and primary care: age (18-64 years), employment, lower ADI, and anxiety. In fully adjusted models, age, employment, and living in higher socio-economic areas were associated with lower odds of using telehealth, suggesting that access to resources may be a central driver of differences in telehealth use. Telehealth use may be concentrated among patients with higher socioeconomic status. Efforts to improve access to telehealth can help to reduce inequities in access to mental health treatment between patients with more and fewer economic resources.

LATEBREAKER

Health Services/Policy

Impact of a sugar-sweetened beverage tax on non-communicable diseases mortality in Brazil, according to income levels Luciana B Nucci* Luciana Nucci Carla C Enes Flavia M Sarti Wolney L Conde

Consumption of sugar-sweetened beverages (SSBs) is associated with an increased risk of chronic non-communicable diseases (NCD). Taxes on SSBs have been successful in reducing consumption and NCD prevalence in several countries. In Brazil, discussions are underway regarding the implementation of such taxes. This study aims to estimate the number of averted deaths in Brazil after a 20% tax on SSBs, considering patterns of consumption of different income levels.

Cross- and own-price elasticities for SSBs after a 20% tax were estimated considering consumption patterns of the population, and of the 25% poorest and richest. Data from Brazil's nationally representative Household Budget Survey (2017-18) was used to estimate the mean total energy intake (in kcal/day) before and after the tax. Mortality data for 2019 for CVD, diabetes, cancer, COPD, kidney, and liver diseases was extracted from the Brazilian Mortality Information System. BMI was included as a mediator variable, which was calculated using self-reported data from the 2019 National Health Survey. The Preventable Risk Integrated ModEl (PRIME) was used to estimate the number of deaths averted by a 20% tax on SSBs. Uncertainty intervals (UI) were calculated using Monte Carlo analysis, with all parameters included in the model by sex and 5-year age groups (from 15 to 85+).

The estimated number of deaths that would have been averted in 2019 was 7,170 (95%UI: 6,185-8,233) for the entire population, 10,118 (95%UI: 9,183-11,020), and 20,247 (95%UI: 18,024-22,372) for the poorest and richest income patterns of consumption, respectively. The proportion of averted deaths for those under 75 years of age would be 41% for the whole population and ~58% for both incomes. Most averted deaths would be from CVD (~65%) and diabetes (~25%).

A SSB tax might be an effective fiscal policy to decrease the consumption of SSB and NCD mortality in Brazil, especially when we consider different income patterns of consumption.

Housing instability is associated with higher prevalence of recent methamphetamine, cocaine, and opioid use among people with HIV in the US Joseph A Delaney* Bridget Whitney Heidi M Crane Dominique Heinke Stephanie A Ruderman L Sarah Mixson Robin M Nance Amanda L Willig Sonia Napravnik Kenneth H Mayer Laura Bamford Edward Cachay Jeffrey Jacobson Rob J Fredericksen Lydia N Drumright Joseph A Delaney

Background

There is growing evidence that lack of stable housing may make people with HIV (PWH) more vulnerable to substance use. In particular, MCO (Methamphetamine, Cocaine, and/or Opioid) use is associated with increased health concerns and social stigma.

Methods

We included PWH in clinical care in the Centers for AIDS Research Network of Integrated Clinical Systems (CNICS) cohort from 2019 or later who completed a patient reported outcome assessment in a cross-sectional analysis. We estimated associations between the most recent self-reported housing stability response and the closest preceding or concurrent MCO use assessment using relative risk regression adjusted for age, sex, race/ethnicity, and CNICS clinical site. Housing stability was assessed using a single item: "In the past month, how would you describe your living situation?"; response options: 'Homeless,' 'Unstable,' 'Stable,' 'Don't know'. Substance use was assessed via the ASSIST as any use in the past 3 months of any of the MCO substances.

Results

Our study included 5,580 PWH (average age: 52; 81% male; 41% White, 42% Black, 11% Hispanic; average time in care: 9.5 years), of which 5,075 (91.0%) reported stable housing. Overall, 10.9% of participants reported recent use of ≥1 MCO (7.2% Methamphetamine, 4.3% Cocaine, 2% Opioids). PWH who reported a housing status other than stable were 2.94 (95%CI: 2.51-3.43) times more likely to report MCO use compared to those stably housed (Figure). PWH who were unhoused were the most likely to report MCO use (RR=3.91, 95%CI: 3.20-4.77).

Conclusion

Lack of stable housing, particularly being unhoused, was associated with an increased burden of substance use among PWH. This finding highlights that housing instability is associated with increased negative health consequences and should be prioritized an important social determinant of health among this vulnerable population. Increased access to substance treatment programs remains vital to improving outcomes of PWH.

Associations Between Housing Instability and MCO Use
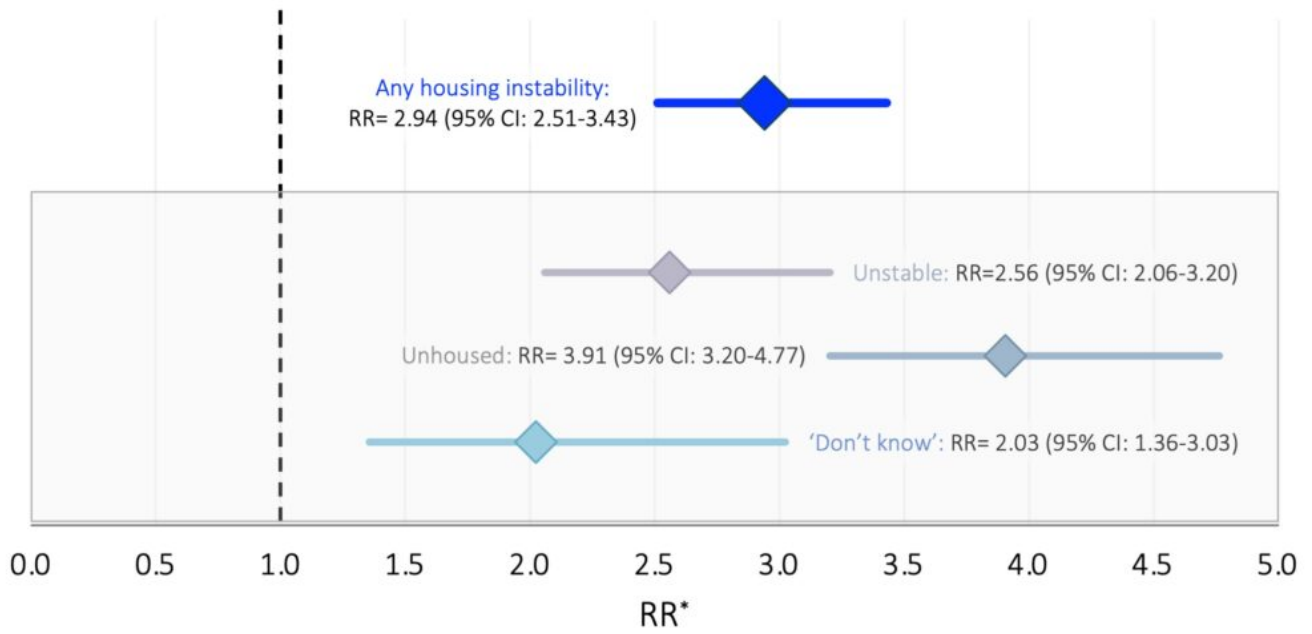
Any housing instability:
RR= 2.94 (95% CI: 2.51-3.43)

Unstable: RR=2.56 (95% CI: 2.06-3.20)

Unhoused: RR= 3.91 (95% CI: 3.20-4.77)

'Don't know': RR= 2.03 (95% CI: 1.36-3.03)

RR*

*Relative risk regression estimates adjusted for age, race/ethnicity, birth sex, and site; reference group: stable housing.

A geospatial analysis of public transit access to HIV pre-exposure prophylaxis (PrEP) providing clinics in metro-Atlanta Noah Mancuso* Noah Mancuso Patrick Sullivan

Background: Young Black and Hispanic men experience high HIV incidence in the US and rely on public transit more than White men. HIV pre-exposure prophylaxis (PrEP) is a highly effective HIV prevention method, but challenges with access remain. We describe public transit access to PrEP providing clinics in the metro-Atlanta region.

Methods: Census block groups (CBGs) from four Atlanta counties were joined with CBG-level sociodemographic data from the 2016-2020 American Community Survey. PrEP clinics in Georgia were identified in a national directory. Population-weighted centroids of each CBG were used to calculate the 10 closest PrEP clinics; the Google Maps Distance Matrix API was used to calculate travel time by public transit. CBGs were considered public transit deserts if no public transit option was available or if transit time was >45 minutes. Multivariable log-binomial regression was used to describe associations between public transit deserts and CBG-level race, ethnicity, age, and income.

Results: Of the 2,466 Atlanta CBGs, 23% had no access to a PrEP clinic by public transit. The average transit time to the nearest PrEP clinic was 37 minutes; 489 CBGs housing 729,941 residents had transit times >45 minutes. A 5% increase in the proportion of males aged 25-34; of people living under the poverty line; or of Hispanic people living in a CBG were each associated with a decreased prevalence of being defined as a public transit desert [aPR=0.61 (0.56, 0.66); aPR=0.75 (0.71, 0.78); aPR=0.96 (0.94, 0.98)]. There was no association with Black race.

Conclusion: Many Atlantans do not have access to a PrEP clinic by public transit. Public transit access to PrEP is better for CBGs with more HIV prevention priority populations. To increase PrEP access in public transit deserts, the geographic spread of PrEP clinics should be expanded, travel subsidiaries should be provided for ride-sharing services, and telemedicine and pharmacy PrEP programs should be widely available.

Transit time to nearest PrEP clinic

Time to clinic (min)
- 1.4 to 18.6
- 18.6 to 27.1
- 27.1 to 36.0
- 36.0 to 49.8
- 49.8 to 392.0
- No Public Transit Available

Highways

PrEP Clinics

The factors Associated with Sexually Transmitted Infections (STI) Screening among Women in the United States. Shilpa Patil* SHILPA PATIL Dr. Malinee Neelamegam

Background – Although many STIs are preventable, STI rates in the U.S. have continued to rise. According to the CDC's Sexually Transmitted Disease (STD) Surveillance 2021 annual report, more than 2.5 million cases of chlamydia, gonorrhea, and syphilis were reported. During 2020-2021, the chlamydia and gonorrhea rate among women increased by 2.4%, whereas the primary and secondary syphilis rate among women increased by 55.3%.

STI screening among women is crucial to protecting individual health and preventing the spread of infections. This study aims to determine the factors associated with STI screening among women of childbearing age in the U.S.

Methods – This study is a secondary data analysis of the 2017-2019 National Survey of Family Growth (NSFG). The screening process involves interviewing individuals aged 15 to 49 from selected households about sexual health and collecting optional urine samples for STI testing, with financial incentives offered for participation. Bivariate analysis is done using chi-square tests, and multivariate analysis is done using logistic regression methods.

Results – Respondents comprised 26.45% (n= 1624) Hispanic and 73.55% (n= 4517) non-Hispanic women (4.54% (n = 279) other races, 21.59% (n= 1326) African American, 47.42% (n=2912) White). Ages range from 32.34% at 15-25 years, 37.01% at 25-35, to 30.65% at 35-49 years. Only 32% of women underwent STI screening in the past year.

STI screening was significantly associated with having a usual place of care(aOR: 1.44, 95% CI 1.14-1.83), possessing public health insurance (aOR 1.48, 95%CI 1.11-1.99), achieving higher education levels (aOR 2.88, 95% CI 2.03, 4.07), being unmarried (aOR 1.57, 95% CI 1.17 – 2.10), and identifying as Hispanic (aOR 1.55, 95% CI 1.20-1.99) or non-Hispanic Black (aOR 2.22, 95% CI 1.60-3.07). Conversely, older age categories exhibited a lower likelihood of receiving STI screening.

Conclusion – The study emphasizes the critical need for a multi-pronged approach to boost STI screening in U.S. women, focusing on increased healthcare access, enhanced health literacy, and tailored public health messaging that addresses women's diverse backgrounds and relationship statuses. It also calls for age-specific interventions to heighten STI risk awareness and underscore the importance of regular screening, advocating for a comprehensive strategy to foster proactive and informed sexual health management across all age groups.

Regional and socioeconomic disparities in HIV prevalence among reproductive-aged women in The Gambia: an analysis of national survey Amadou Barrow* Amadou Barrow Dr Yan Wang

Background: Human Immunodeficiency Virus (HIV) infection is a major public health issue in The Gambia with a higher prevalence among women. Regional and socioeconomic disparities in HIV epidemiology have not been well studied in developing countries. Understanding the variations and determinants of HIV infection is important for tailoring responses, particularly in rural areas. This study analyzed the regional and socioeconomic disparities in HIV prevalence among women of reproductive age.

Methods: We analyzed data from 4487 reproductive-aged women in the 2013 Gambia Demographic and Health Survey (GDHS) using bivariate analyses and multilevel regression to estimate adjusted prevalence ratios (aPR) for associations between HIV infection and regional, sociodemographic, sexual history, and healthcare factors. The Lorenz curve, concentration index, slope, and relative indices of inequality for HIV prevalence were used to analyze socioeconomic disparities. Statistical significance was set at 5.

Results: The HIV-weighted prevalence was 2.1% (urban: 2.4%; rural: 1.8%). After controlling for confounders, rural residence (aPR=0.50, 95% CI: 0.26, 0.97), ages 35-39 years (aPR=5.03, 95% CI: 1.45, 17.51), richest household wealth (aPR=0.33, 95% CI: 0.12, 0.94), and ≥2 lifetime partners (aPR=3.31, 95% CI: 2.01, 5.44) were identified. Significant pro-rich disparities existed for maternal age, 6.7 times higher (95% CI: 3.8, 9.9) relative HIV prevalence for lowest versus highest position; pro-poor disparities for maternal education, 53% lower (95% CI: 0.23, 0.71) relative prevalence for lowest versus highest position. Significant inequalities in pro-poor HIV prevalence for ≥2 lifetime partners by household wealth (Conc. index=-0.069, SE=0.024), and education (Conc. index =-0.054, SE=0.020); no recent STIs (Conc. index =-0.013, SE=0.004) and no insurance (Conc. index =-0.012, SE=0.043) and recent sexual activity (Conc. index =-0.010, SE=005) by education.

Conclusions: Marked regional and sociodemographic HIV disparities exist among Gambian women. Targeting higher-risk women in urban settings, middle age groups, lowest wealth quintiles, and those with multiple partners could help address population-level socioeconomic HIV inequalities.

HIV / STI

Predictors of guideline-adherent screening for cervical cancer among women living with HIV in the Bronx, New York Danya Birnbaum* Danya Birnbaum Jenny Shen Chloe Teasdale Breanne Lott Jessica Atrio Howard Strickler Heidi E. Jones

Background: Cervical cancer screening is essential care. Using the Einstein-Rockefeller-CUNY Center for AIDS Research (ERC CFAR) Clinical Cohort database, we examined factors associated with screening among women living with HIV (WLH) receiving care in the Montefiore Health System (MHS), the largest provider of HIV care in the Bronx, New York.

Methods: WLH aged 21-65 years receiving HIV care (2+ lab tests) within 18 months at MHS between 2014-2019 were included. Those who received cervical cancer screening ≤18 months from their date of entry were coded as screening-adherent, based on annual screening guidelines for WLH. Potential predictors of screening explored included: age, race/ethnicity, socio-economic status, CDC-defined HIV acquisition group, hepatitis C virus status, insurance type, pregnancy and hormonal contraceptive use during observation period, and HIV viral load (VL; using test closest to entry date). We ran multivariable logistic regression of screening using stepwise modeling, keeping variables with p≤0.15 in the final model.

Results: Of 2,553 WLH, 1,794 (70.3%) were screened for cervical cancer within the first 18 months of observed person time. WLH who had acquired HIV through injection drug use (IDU) [aOR: 0.67; 95% CI: 0.49, 0.92] vs. non-IDU and those with detectable HIV (VL >10,000 [aOR: 0.67; 95% CI: 0.53, 0.85], VL 100-10,000 [aOR: 0.56; 95% CI: 0.43, 0.73] vs. <100 copies/ml) were less likely to receive cervical cancer screening. WLH who used any hormonal contraception had 3.22 times [95% CI: 2.34, 4.41] the odds of screening as those not using hormonal contraception.

Conclusions: Nearly one-third of WLH receiving HIV care in the Bronx did not receive cervical cancer screening within 18 months of care. WLH with uncontrolled viral load and those who acquired HIV via IDU were more likely to not have been screened, indicating the importance of targeted outreach and alternative screening modalities, such as self-sampling and mobile clinics.

The association between county-level social vulnerability and childhood vaccination rates at time of primary school entry James Buckley* James Buckley Patrick Maloney Alison Keyser-Metobo Derek Julian

Background: We examined the association between county-level social vulnerability and vaccination completion rates among Nebraska children entering primary school during the 2021-2022 academic year.

Methods: Data on county-level vaccination rates were drawn from the Nebraska State Immunization Information System. Rates were assessed for the Measles, Mumps, and Rubella (MMR), Polio, Varicella, Diphtheria, Tetanus, and Pertussis (DTaP), and the Hepatitis B (HepB) vaccines. A combined rate for all vaccines was also assessed. Social Vulnerability Index (SVI) scores were drawn from the CDC/ATSDR Geospatial Research, Analysis & Services Program. We assessed the relationship between vaccine uptake and social vulnerability using multivariate Poisson regression modeling.

Results: The mean childhood county-level vaccine rate was 69.14% for MMR, 68.84% for Polio, 68.81% for Varicella, 61.14% for DTaP, 82.84% for HepB and 57.89% overall. Socioeconomic Status (Theme 1) was associated with decreased rates of combined vaccination completion [0.85(0.74,0.97)]. Household Characteristics (Theme 2) was associated with increased rates of combined vaccination completion [1.41(1.30,1.53)] and each individual vaccine. Racial/Ethnic Minority Status was associated with decreased rates for combined vaccine completion [0.77 (0.71,0.85)] and for each individual vaccine. Housing Type/Transportation (Theme 4) was not associated with the rate of combined vaccine completion [1.06(0.94,1.20)] but was associated with increased rates of vaccination for Polio [1.24(1.11,1.39)], HepB [1.11 (1.00,1.23)], and DTaP [1.14(1.01,1.28)].

Conclusion: SVI is a critical tool for evaluating the relationship between specific aspects of social vulnerability and childhood vaccination uptake and can be used to inform and evaluate future interventions. Additional research should be conducted to evaluate the underlying causes of decreased vaccination uptake among racial and ethnic minorities.
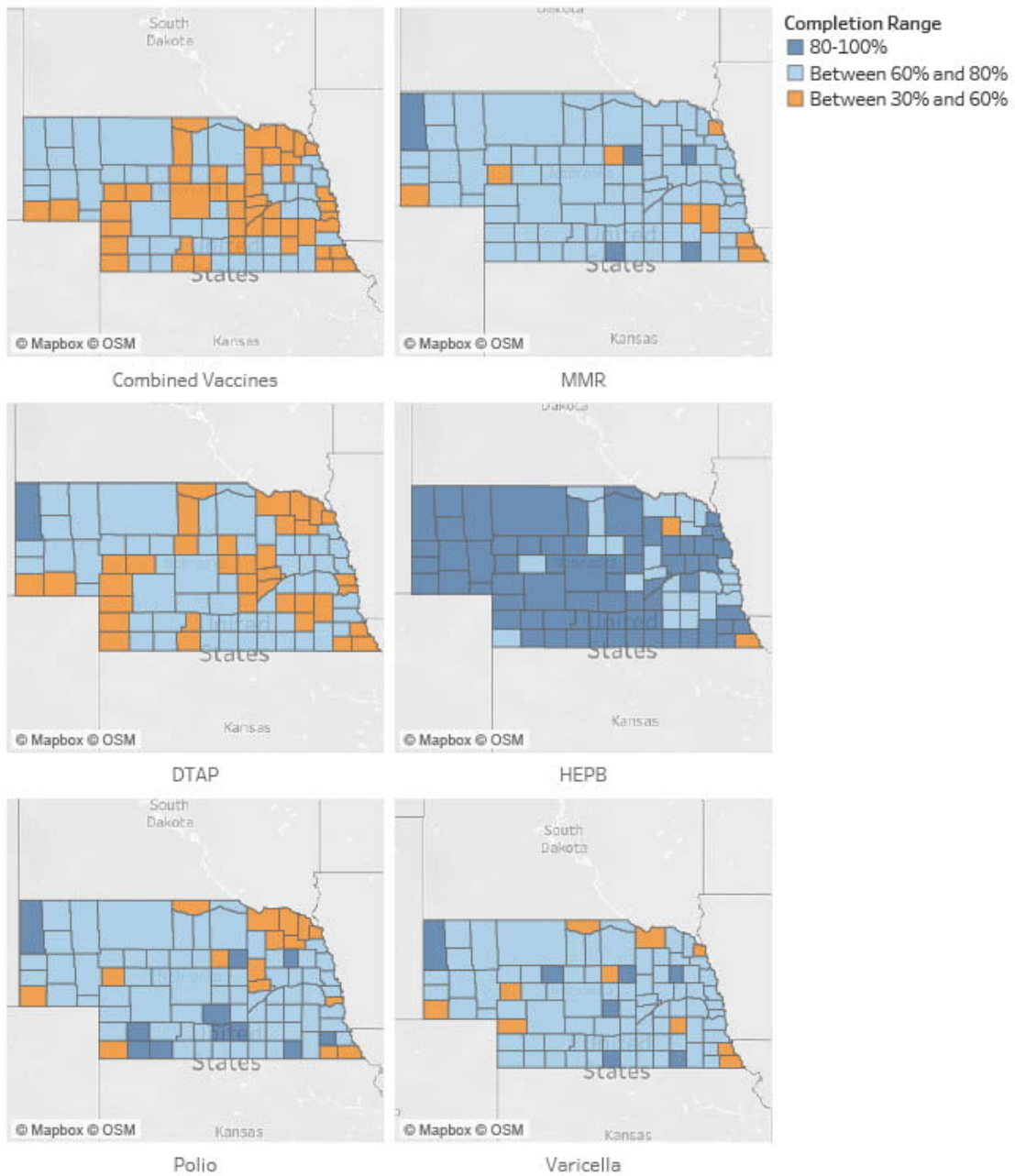
Figure 1: Vaccination Rates by Series and County at Time of Primary School Entry, 2021-2022

The Effect of Time Since First Dose of Measles-Mumps-Rubella (MMR1) Vaccine on Measles Immunity

Archchun Ariyarajah* Archchun Ariyarajah Natasha S. Crowcroft Kevin A. Brown John Wang Jeff Kwong Shelly Bolotin

Background

Canada eliminated measles in 1998. However, immunity from the MMR vaccine can wane in elimination settings. Our study examines the impact of time since first dose (MMR1) on measles immunity.

Methods

We conducted a retrospective cohort study on 37,412 individuals in Ontario, Canada who underwent measles IgG antibody testing in 2014-16. Health administrative databases provided sociodemographic and health data. Vaccination was ascertained using physician billing claims data at 12-15 months of age. We measured measles antibody geometric mean concentration (GMC) and immunity defined as ≥275mIU/mL, with sensitivity analyses at ≥200mIU/mL and >120mIU/mL. We used multivariable negative binomial and logistic regression models with restricted cubic splines to estimate GMC and susceptibility, respectively, adjusting for confounders, across eliminated and endemic settings.

Results

Measles antibody GMC decreased substantially in the first 10 years post-MMR1 and decline slowed thereafter. In the cohort born in a measles elimination setting (data available 1-17 years), antibody GMC declined significantly from 2194.4mIU/mL (95%CI, 2038.9-2349.9) in year 1 to 992.4mIU/mL (95% CI, 951.7-1033.2) by year 10, and to 782.6mIU/mL (95% CI, 751.7-813.5) by year 17. At a [3]275mIU/mL protection threshold, 25% (95% CI, 23-27%) were susceptible to measles by the seventeenth year, but at >120mIU/mL, susceptibility was 4% (95% CI, 3-5%). In the cohort born in a measles endemic setting (data available 15-25 years), antibody GMC declined from 821.7mIU/mL (95%CI, 802.6-840.9) in year 15 to 725.5mIU/mL (95%CI, 706.0-745.0) by year 25. At a [3]275mIU/mL protection threshold, 28% (95% CI, 26-30%) were susceptible to measles by year 25, but at >120mIU/mL, susceptibility was 4% (95% CI, 3-5%).

Discussion

These results align with previous studies; however, susceptibility interpretation depends on the protection threshold. More research examining waning measles immunity in elimination settings is needed.

Infectious Disease

Shigella is the leading cause of bystander pathogen exposure to antibiotics due to diarrhea treatment
Stephanie A. Brennhofer* Stephanie A. Brennhofer Timothy L. McMurry James A. Platts-Mills Joseph A. Lewnard Elizabeth T. Rogawski McQuade

Pathogens carried asymptomatically at the time of antibiotic treatment experience selection pressure despite not being the intended target of treatment (i.e., bystander pathogens), which can contribute to antimicrobial resistance. We aimed to quantify the amount of bystander exposures that could be attributed to the treatment of individual diarrheal pathogens to inform the value of pathogen-specific diarrhea interventions. We analyzed 15,697 antibiotic courses from 1,715 children aged 0-2 years across 8 sites in the MAL-ED birth cohort study. Pathogens present in a diarrheal stool sample at a high quantity previously determined to be etiologic were considered the cause of antibiotic courses for diarrhea. Pathogens detected in the most recent stool up to 30 days prior to an antibiotic course were considered bystanders. We calculated incidence rates and proportions of bystander pathogen (enteroaggregative E. coli (EAEC), Campylobacter, enterotoxigenic E. coli (ETEC), atypical enteropathogenic E. coli (aEPEC), typical enteropathogenic E. coli (tEPEC), and Shigella) exposures due to 10 leading causes of diarrhea. The incidence rate of bystander pathogen exposures to antibiotics was the highest due to treatment of Shigella (32.5 bystander exposures to any antibiotic per 100 child-years), of which, 10.0 and 7.1 were exposures to macrolides and fluoroquinolones, respectively (Figure). However, only 4.4% of all antibiotic exposures to bystander pathogens were due to Shigella, given the many causes of antibiotic use in this population. The next leading causes of bystander pathogen exposures were rotavirus (18.4 bystander exposures to any antibiotic per 100 child-years), sapovirus (16.3), adenovirus 40/41 (16.1), and ETEC (14.7). Pathogen-specific interventions for diarrhea such as vaccines could prevent some of this burden of bystander exposures to antibiotics.

Figure: Incidence rates per 100 child-years of bystander pathogen exposures to antibiotics and the proportion of exposures due to treatment of etiology-specific diarrhea
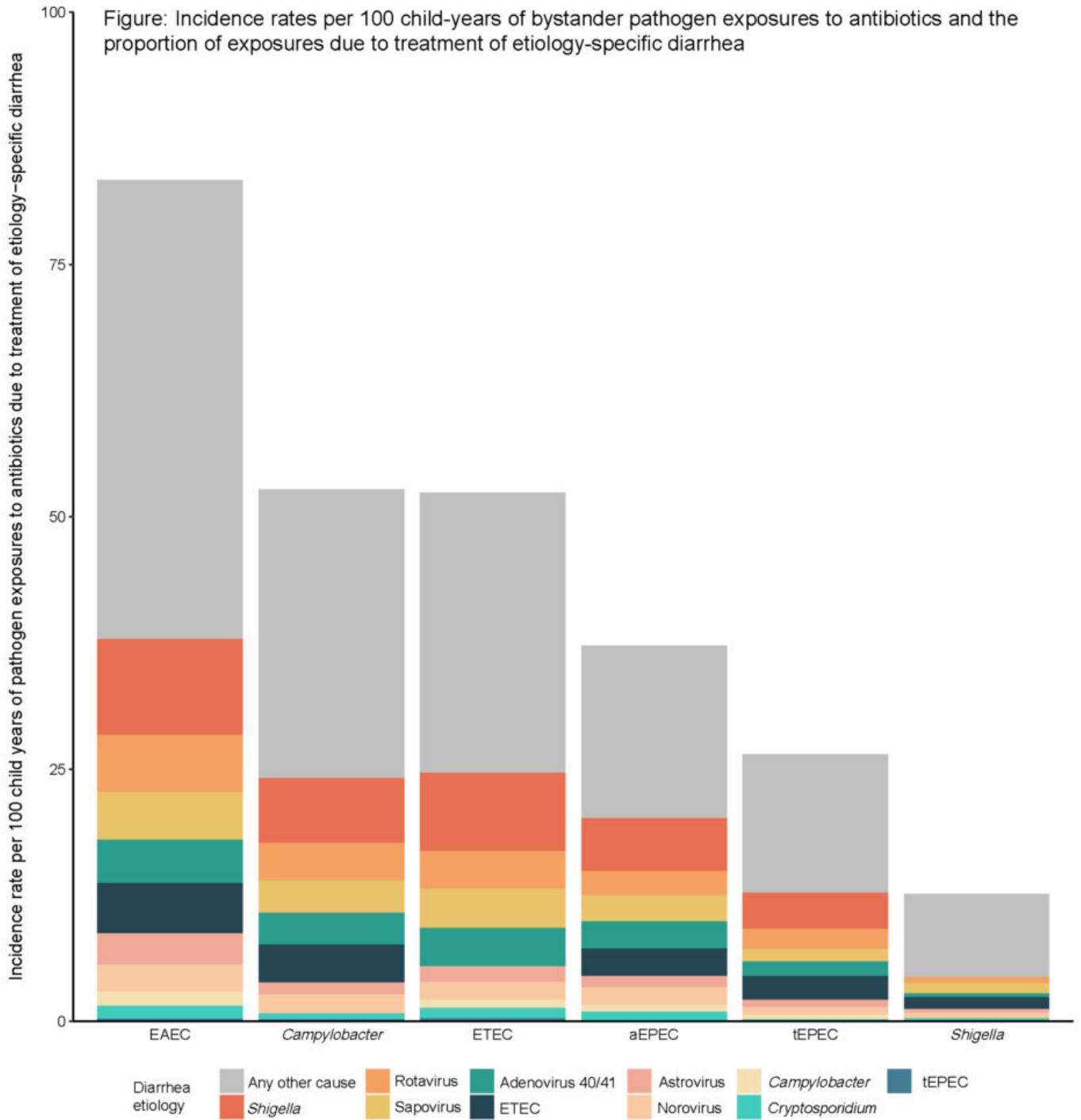
Caption: EAEC = enteroaggregative *E. coli*; ETEC= enterotoxigenic *E. coli*; aEPEC = atypical enteropathogenic *E. coli*; tEPEC = typical enteropathogenic *E. coli*

Infectious Disease

Bias in rotavirus vaccine effectiveness estimates due to missing vaccination cards in a Uganda case-control evaluation Jordan Cates* Jordan Cates Hellen Aanyu-Tukamuhebwa Julia Baker Cissy Nalunkuma Eleanor Burnett Kaudha Elizabeth Annet Kisakye Goitom Gebremedhin Weldegebriel Jacqueline Tate Jason M. Mwenda Paul Gastañaduy

Background: Card-confirmed vaccination status is essential to estimate vaccine effectiveness (VE) accurately, yet card ascertainment is often incomplete, especially in low-resource settings. We aimed to quantify the potential bias in rotavirus VE estimates due to exclusion of children without card-confirmed vaccination status.

Methods: Children aged 4-11 months were enrolled in a hospital-based test-negative case-control evaluation of rotavirus VE in Uganda from July 2018- December 2022. Logistic regression was used to estimate the odds ratio (OR) of at least one dose of rotavirus vaccine between cases (children with laboratory-confirmed rotavirus diarrhea) and non-rotavirus "test-negative" diarrhea controls, adjusted for age, season, and site. VE was calculated as 100*(1-adjusted OR). VE restricted to children with card-confirmed vaccination status was compared to VE when imputing the vaccination status for children without a vaccine card. Multiple imputation was performed assuming a multivariate normal distribution with 40 imputations, including variables for rotavirus test result, receipt of rotavirus vaccine, and demographics associated with missing vaccine cards.

Results: Among 186 cases and 632 controls, 48% and 44% were missing vaccine cards, respectively. Among 96 cases and 352 controls with card-ascertained vaccination status, 92% and 94% received at least one dose of rotavirus vaccine, respectively. Among 90 cases and 280 controls with imputed vaccination status, an estimated 88% and 93% were vaccinated. Among children with card-confirmed vaccination, the adjusted VE was 56% (95% confidence interval [CI]: -10%, 82%). In the multiple imputation analysis, the adjusted VE was 50% (95% CI: -25%, 80%).

Conclusions: Rotavirus VE restricted to card-confirmed children was slightly higher compared to multiple imputation. This illustrates the use of multiple imputation to assess the magnitude and direction of potential selection bias due to low card ascertainment.

Infectious Disease

Estimating Diphtheria Reproduction Numbers – Update from the analysis of the 2022 -2023 Diphtheria Outbreak in Kano State (Nigeria) Raoul M KAMADJEU* Raoul M KAMADJEU Oyeladun Okunromade Bola Lawal Muzammil Mohammed

Nigeria has been affected by a large diphtheria outbreak since late 2022, with the epicenter in Kano State from which with 13899 cases (9895 confirmed) were reported. This study focuses on evaluating the basic reproduction number of diphtheria within the ongoing outbreak in Kano State.

We obtained diphtheria outbreak line-list from Aug 2022 to Dec 2023 from Nigeria CDC (NCDC). The effective reproductive number (Rt) a variation of the basic reproduction number reflecting population changing immunity levels and outbreak control measures. Four methods were employed: Exponential Growth (EG), Maximum Likelihood Estimation (ML), Time-Dependent (TD) and Sequential Bayesian (SB). The generation time, needed for estimating Rt, was approximated using the serial interval distribution between onset dates of symptoms for each of the Local Government Area, a State sub-administrative unit. Analyses assumed a chain of transmission in a population initially susceptible, mixing freely, with no imported cases. We used the R0 package in R Studio.

Results revealed two distinct patterns of the outbreak in Kano: a period of low but constant transmission for the first 300 days, with a daily incidence below 25 cases, followed by an explosive burst reaching a peak of 125 cases. The generation time distribution, based on 2,349 values, fits a lognormal distribution with mean = 1.91 and standard deviation = 1.33. Rt estimates were 1.19 (95% CI: 1.17, 1.20) using EG, 1.09 (95% CI: 1.02, 1.73) with ML, and ranged from 0.2 to 3.3 with TD, and 1.0 to 3.19 with SB, reflecting changing transmission dynamics. The observed trend in cases was best modelled by EG, ML, and TD.

This analysis aimed to update the reproduction rate of the diphtheria outbreak in Kano, offering insights into transmission dynamics to inform and adapt control measures. While Rt estimates align with existing findings, caution is necessary in interpretation due to inherent assumptions in their estimation.

Figure 1: Estimating Diphtheria Reproduction Numbers - Update from the analysis of the 2022 -2023 Diphtheria Outbreak in Kano State (Nigeria)
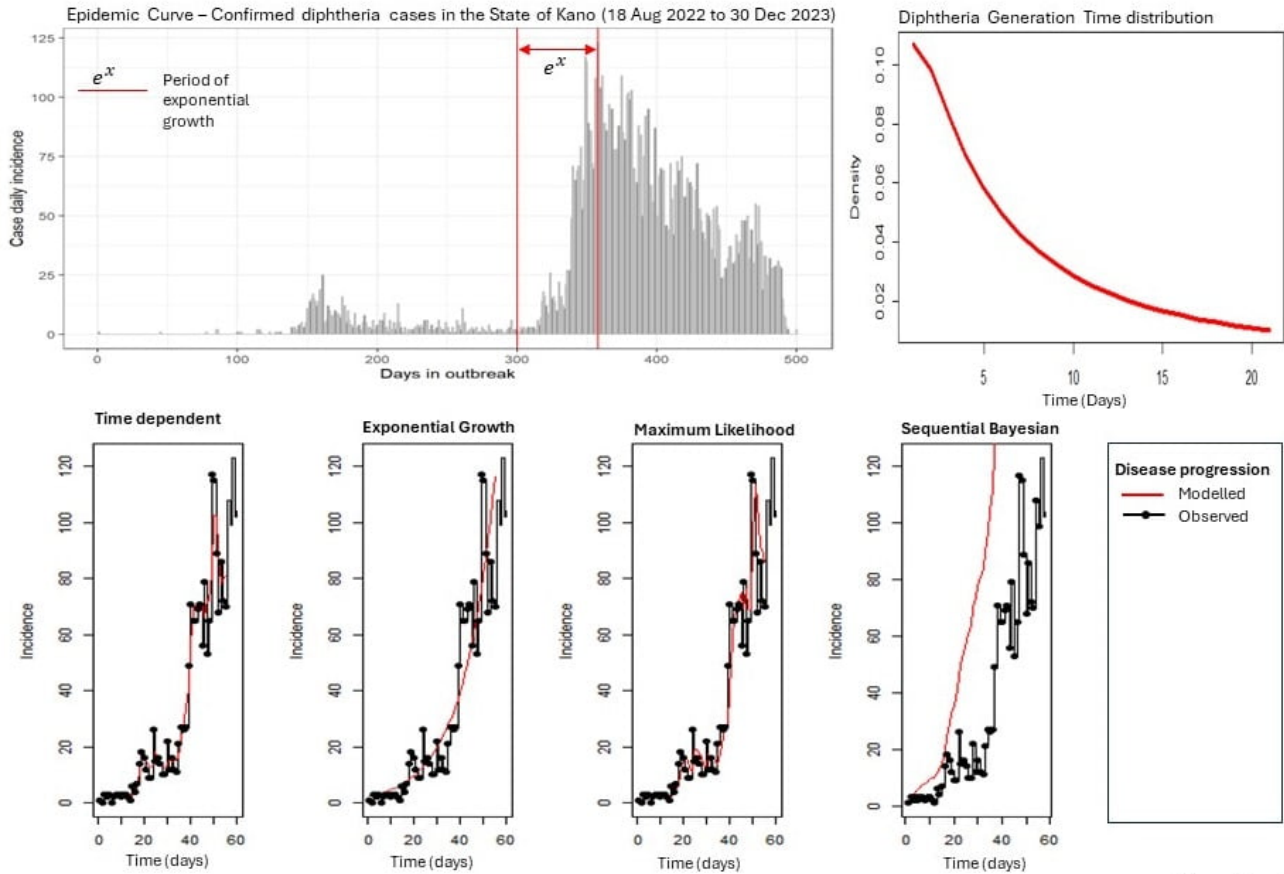
Assessing coverage of recommended vaccinations for older adults: An analysis of the Canadian Longitudinal Study on Aging Angelina Sassi* Angelina Sassi Nicole E. Basta Christina Wolfson

Preventing infectious diseases among older adults is crucial to healthy aging. The risk associated with influenza, pneumococcal pneumonia, herpes zoster (HZ), and COVID-19 can be significantly reduced via vaccination. Assessing vaccine uptake of these recommended vaccines is an important first step in identifying opportunities to improve prevention efforts among older adults. The Canadian Longitudinal Study on Aging (CLSA) provides a unique opportunity to estimate vaccination coverage for multiple vaccines among a large cohort of older adults where extensive data has been collected. Using CLSA data from 2018-2021, we aimed to go beyond national estimates reporting the uptake of each vaccine to determine the proportion of Canadian adults aged 65 years and older who are "fully vaccinated" (received influenza vaccine within the past 12 months and received pneumococcal and HZ vaccine in their lifetime, as recommended), "under vaccinated" (vaccinated with at least one of these vaccines but not all), and "non-vaccinated" (not vaccinated with any of these vaccines). We then aimed to evaluate the association between multiple socio-demographic and health care utilization factors and being under-vaccinated and non-vaccinated, compared to being fully vaccinated, using multivariable, multinomial logistic regression models. Of the 10,432 adults aged 65 and older eligible for our analysis, 51.4% were under-vaccinated due to missed influenza, pneumococcal, or HZ vaccination (95% CI: 50.5 – 52.4%). Specifically, 18.5% missed HZ vaccine only (95% CI: 17.8 – 19.3%), 13.2% missed both HZ and pneumococcal vaccines (95% CI: 12.6 – 13.9%), 9.7% missed pneumococcal vaccine only (95% CI: 9.2 – 10.3%), and 10% missed influenza vaccine (only or with one other vaccine) (95% CI: 9.4 – 10.5%). Additionally, 17.3% were non-vaccinated (95% CI: 16.6 – 18.1%). These results provide new insights into gaps in vaccine uptake among Canadian older adults and indicate key areas for future interventions.

Effect of Seasonal Malaria Chemoprevention (SMC) on malaria transmission: Analysis of 2021 malaria rates in Nouna, Burkina Faso Elisabeth Gebreegziabher* Elisabeth Gebreegziabher Mamadou Ouattara Ali Sié Mamadou Bountogo Boubacar Coulibaly Valentin Boudo Thierry Ouedraogo Elodie Lebas Huiyu Hu Benjamin F. Arnold Thomas M. Lietman Catherine E. Oldenburg

Objective

Seasonal malaria chemoprevention (SMC) is the administration of sulfadoxine–pyrimethamine (combination of a broad-spectrum antibiotic, sulfadoxine and antiparasitic pyrimethamine) and amodiaquine to children aged 3-59 months at monthly intervals four times during the high malaria transmission season. Using data from the Community Health with Azithromycin Trial (CHAT), a randomized controlled trial of 278 villages in Nouna Burkina Faso, passive surveillance data of clinic visits and national malaria control program (NMCP) data on SMC administration, this study aimed to describe malaria incidence rates in the presence of SMC and compare malaria rates in the weeks after administration of SMC.

Methods

For each health post in the study area, we calculated the malaria diagnoses counts by epidemiological (epi) week. We used CHAT census data to obtain denominators, number of children by health post, to estimate the malaria rates for each epi week in 2021. Negative binomial regression was used with person weeks used as offset and standard errors clustered by health post to obtain incidence rate ratio (IRR) comparing malaria rates over the four rounds of SMC administration weeks to the first, second-, and third-weeks post administration.

Results

In 2021, SMC was administered in four rounds four weeks apart between July and September, on epi weeks 27, 31, 35 and 39. SMC was administered during malaria peak weeks (Incidence rate (IR)= 8.4, 95% CI (6.8 to 10.1) per 1000 person weeks). Malaria rates were still high through December, after fourth/last round of SMC (IR range 10-15 cases per 1000 person weeks). There was substantial reduction in malaria rates in the 3 weeks post SMC, but not in linear fashion. Compared to administration weeks, malaria rates were lower by 36%, 37% and 23% in the first, second and third week after administration (IRR= 0.64, 95%CI (0.55 to 0.76), 0.63, 95%CI (0.55 to 0.73) and 0.77, 95%CI (0.67 to 0.88) respectively).

Conclusion

Our findings suggest that four rounds of administration may not adequately cover the malaria transmission season. A fifth round of SMC could be helpful. The greatest decline in malaria rates post SMC was in the first two weeks after administration and rates started to increase by week 3. SMC appears effective but short-lived.

Incidence rate of non-severe malaria per person-week with 95% CIs
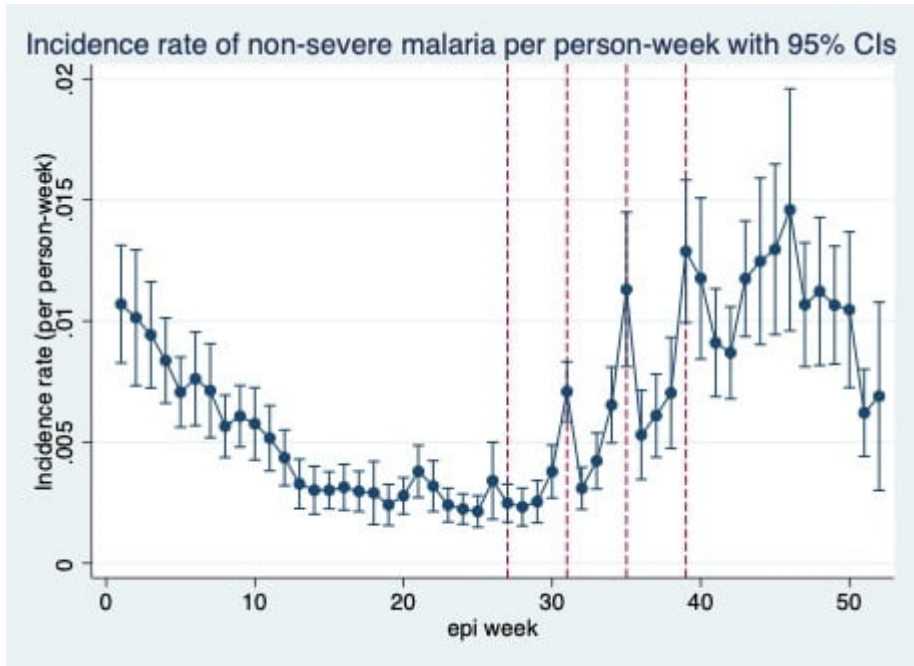
LATEBREAKER

Infectious Disease

Norovirus GII.17 and Sporadic Medically-Attended Acute Gastroenteritis in Oregon and Washington, 2023-2024 Mark Schmidt* Mark Schmidt Laura Tsaknaridis Holly Groom Judy Donald Sarah Vertrees Ayo Ojebode Lisa Morrow Carly Crocker Katherine Carlson Emma Viscidi

Background: When norovirus genotype GII.17 emerged in Asia in 2014, there were concerns that it would replace GII.4 as the globally predominant strain associated with acute gastroenteritis. Outside of several isolated outbreaks, this worry has largely not yet been realized. Here we describe developing results from a prospective, community-based surveillance study of medically-attended acute gastroenteritis (MAAGE) in the northwestern U.S.

Methods: Beginning November 15, 2023, we have been conducting daily recruitment of Kaiser Permanente Northwest (KPNW) patients of all ages with MAAGE diagnoses. We enrolled participants who completed a baseline survey and self-collected a stool specimen for testing at the Oregon State Public Health Laboratory (OSPHL). Norovirus detection was assayed through real-time polymerase chain reaction; Sanger sequencing was subsequently performed on specimens testing positive. We include here results received through February 23, 2024.

Results: To date, we have tested 255 stool specimens, of which 34 (13%) were positive for norovirus. Genotyping has been completed for 19 (56%): 9 (47%) were GII.17, 5 (26%) were GII.4, and one each was GI.3, GI.5, GII.3, GII.8, and GII.12; 8 are untypable and 7 are pending. Only one person with GII.17 reported contact with someone with AGE symptoms prior to their illness.

Conclusion: In this first analysis of an ongoing community-based study, the high proportion of GII.17 genotypes – and low proportion of GII.4 – detected among sporadic MAAGE cases is unexpected and notable. Our 2014-2016 similar study found 54% and 2% of 228 typable norovirus strains were GII.4 and GII.17, respectively. CDC outbreak data showing a recent doubling in outbreaks due to GII.17 further suggest the emergence of GII.17 as a cause of gastroenteritis within the U.S. Our findings underscore the importance of ongoing surveillance to characterize the genetic epidemiology of norovirus, especially to inform norovirus vaccine development.

Correlations between high-risk businesses for respiratory pathogen transmission and neighborhood social factors in Wisconsin Andrew Hoover* Andrew Hoover Kate Duchowny Chihua Li Lauren MacConnachie Rohini Perera Lindsay Gypin Robert Melendez Philippa Clarke John Kubale Grace Noppert

Introduction

Business types play a key role in neighborhood respiratory pathogen spread, including COVID-19, yet few studies have investigated what business types are high-risk and why. This study presents a novel measure that characterizes business types according to their hypothesized risk for respiratory pathogen transmission and examines the relationship between the proportion of high-risk businesses in a neighborhood and neighborhood social factors.

Methodology

Using business density data from the National Neighborhood Data Archive (NANDA), we created a score to identify business types that may be high risk for respiratory pathogen transmission. Scores for each business type were derived from the average number of visits and time spent there sourced from Advan Research mobile phone data, and our conceptualization of the most prevalent interactions occurring there. Business types with a score of 8 or higher were labeled "high risk" and businesses with a score lower than 8 were labeled "low risk". We calculated the proportion of businesses in each Wisconsin census tract that were classified as "high risk" and examined Pearson correlations with neighborhood disadvantage, affluence, and population density from NANDA, across Wisconsin census tracts.

Results

Scores for 67 business types ranged from 2 to 11 with a mean of 7.30 (Figure 1). The proportion of high-risk businesses (mean: 0.26; SD: 0.10) was statistically significantly correlated with neighborhood disadvantage ($r = 0.32$; $p < 0.01$), affluence ($r = -0.16$; $p < 0.01$), and population density ($r = 0.17$; $p < 0.01$), across Wisconsin census tracts.

Conclusions

Our novel tool can be used to identify neighborhoods that may be most vulnerable to respiratory pathogen outbreaks due to the businesses operating within them. Using this tool, we found that neighborhoods with higher proportions of high-risk businesses tend to have fewer social resources, suggesting an even greater potential for respiratory pathogen burden.
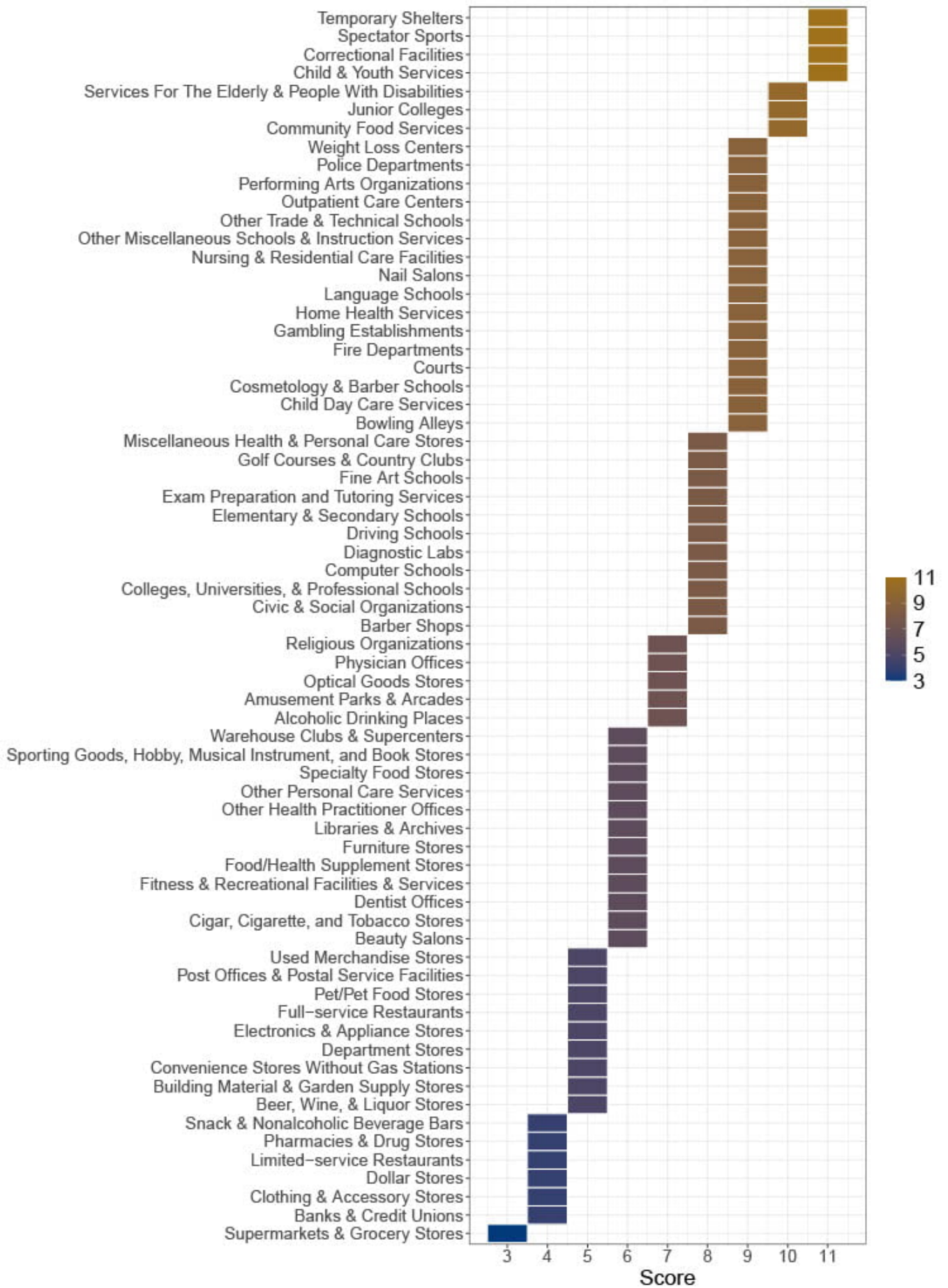
Neonatal outcomes among people vaccinated against COVID-19 during pregnancy in the United States, December 2020-September 2022 Stacey L Rowe* Stacey L Rowe Annette K Regan Sheena G Sullivan Flor Munoz Jennifer Griffith Matthew Coates Onyebuchi A. Arah

Background: Vaccination against COVID-19 is recommended during pregnancy to protect pregnant people and infants against severe disease. Whilst the safety of COVID-19 vaccination during pregnancy is well-established, there is limited evidence on the incidence of congenital abnormalities among infants born to vaccinees.

Methods: We assembled a national cohort of pregnancies ending 11 December 2020–30 September 2022 using Merative™ Marketscan® Commercial & Medicaid Databases. COVID-19 vaccines were identified from outpatient and inpatient drug records. Neonatal outcomes were identified from hospital inpatient encounters, and included: major structural birth defects; microcephaly and other congenital abnormalities including ankyloglossia (tongue-tie). Incidence of neonatal outcomes was calculated by insurance type (public versus private). Associations between maternal COVID-19 vaccination and outcomes were estimated using Poisson regression.

Results: We identified 550,590 pregnancies ending in livebirth, of which 14.3% were vaccinated during pregnancy. 5,448 (1%) infants born to vaccinated individuals had a major structural birth defect and 1,203 (<1%) had microcephaly. There were no variations in the incidence of these conditions by insurance type; however, incidence of ankyloglossia was higher among privately-insured people (5.4% versus 2.8%). COVID-19 vaccination during pregnancy was associated with ankyloglossia in the privately-insured cohort (aIRR 1.20; 95% CI 1.16, 1.25) but not in the publicly-insured cohort (aIRR 0.72; 95% CI 0.65, 0.79). Insurance type was identified as an effect modifier.

Discussion: Monitoring neonatal outcomes is an important element of maternal vaccine program evaluation. Previous studies have suggested that maternal vaccination is associated with ankyloglossia. Our findings demonstrate that this effect is modified by insurance type, indicating that previously reported associations may be influenced by residual/uncontrolled confounding.

Incidence and seroprevalence of Lyme disease in high-risk occupational groups in North America and Europe

Emma Viscidi* Emma Viscidi Elizabeth Devore Rhonda Bohn

Background and Objectives: Lyme disease, a tick bite–transmitted infection caused by Borrelia burgdorferi complex spirochetes, is the most common tick-borne illness in North America and Europe. A 2021 systematic literature review and meta-analysis found that 14% of the world's population is B. burgdorferi seropositive. Previous studies have reported higher risk of Lyme disease in certain occupational groups; however, contemporary data synthesizing findings on the burden in high-risk occupational groups is needed. The purpose of this research is to describe the incidence and seroprevalence of Lyme disease in high-risk occupational groups in contemporary studies from North America and Europe.

Methods: A targeted literature search was conducted to identify relevant subject headings and text words (incidence, seroprevalence, Lyme disease, and high-risk populations). Results were limited to English-language human studies of adult populations in North America and Europe published between 2013 and 2023.

Results: Thirteen studies were identified that met the inclusion criteria and employed robust, population-based study designs. All studies explicitly defined the underlying study population and described sampling strategies aimed at ascertaining a representative sample of that study population. In 3 United States studies that reported on Lyme disease among soldiers, higher prevalence or incidence rates were observed in soldiers compared with the general United States population. In studies conducted in European countries, foresters, farmers, and other outdoor workers had higher seroprevalence than the general populations in those countries (**Figure**).

Conclusion: There is evidence that specific occupational groups, such as farmers, foresters, and soldiers, are at higher risk for Lyme disease. These occupational groups may be a desirable target population for Lyme disease clinical trials and preventive vaccines.

Figure. Seroprevalence of *Borrelia burgdorferi* in High-Risk Occupational Groups Versus General Populations, by Country (2012-2023)
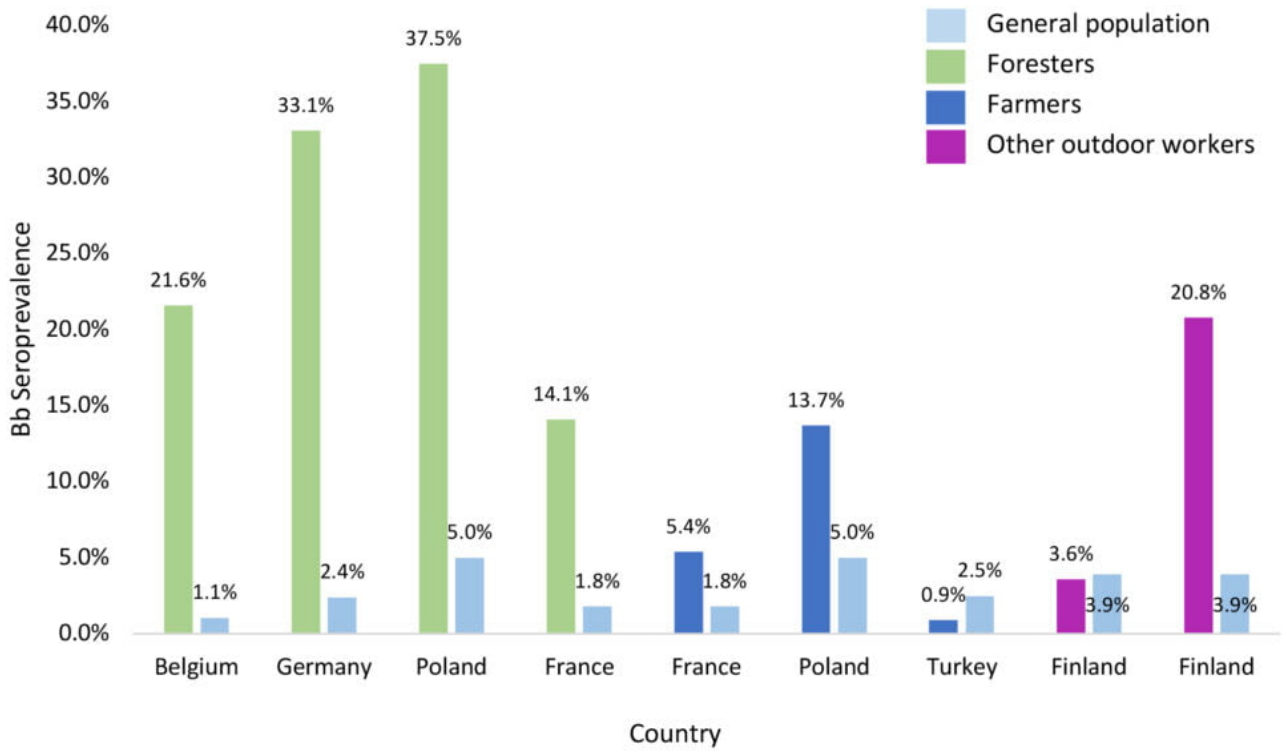
Bb, *Borrelia burgdorferi*.

Assess the factors contributing to Tuberculosis missed opportunities in Arkansas, 2009-2021 Danielle Boothe* Danielle Boothe Namvar Zohoori Clare Brown Ruofei Du Joseph Bates Leonard Mukasa Sean Young

Background: The Arkansas Department of Health (ADH) conducts routine high-risk-based Tuberculosis (TB) screening on various subpopulations known to be at risk for TB and Latent Tuberculosis Infection (LTBI). There needs to be more knowledge on patient-level factors associated with TB cases that were missed based on the screening strategies. This study aims to determine characteristics associated with missed TB opportunities.

Methods: The study design is a retrospective cohort using surveillance and genotyping data. A TB missed opportunity is a case of active TB reported in Arkansas that should never have occurred, given the prevailing intervention strategies in the state. There are ten missed opportunities criteria; the top three include persons born before 1951, previously reported cases of LTBI, and homeless individuals. The predictor variables are sputum smear, chest cavitary evidence, sex, race/ethnicity, genotypic clustering, public health region, and diagnosis year. Generalized estimating equations analysis assessed factors associated with TB missed opportunities.

Results: A total of 1015 persons with TB disease were reported to the ADH TB Program between 2009 and 2021. Of those, 547 (53.9%) were categorized as TB missed opportunities, with the majority, 260 (47.5%) being persons born before TB treatment in 1951. After adjusting for all predictor variables, being white non-Hispanic substantially increased the odds of being classified in the missed opportunity group (adjusted OR = 5.18; CI: 3.18, 8.45). Black non-Hispanic had an increased odds of 2.71 (CI:1.60, 4.59). Having evidence of chest cavitary and being in a genotypic cluster decreased the odds of being classified in the missed opportunity group by 35% and 32%, respectively.

Conclusion: Given Arkansas's current strategy, fifty-four percent of cases could have been prevented. Knowing the factors associated with TB missed opportunities can assist the program in prioritizing sub-populations known at risk for TB and LTBI. Furthermore, efforts are underway to construct an LTBI registry.

Infectious Disease

The association between health care access and shingles vaccination among older adults in Virginia, United States Chidozie Declan Iwu* Chidozie Declan Iwu Pramita Shrestha Miguel Martinez Alyson J Littman Julia Hood

Introduction: Shingles is a debilitating vaccine preventable disease that poses a health threat to older adults. Two vaccines against shingles have been approved and recommended for adults 50+ years old in the United Sates. This study aimed to assess the association between healthcare access and shingles vaccination among older adults, as well as the impact of COVID-19 pandemic on vaccine uptake.

Methods: This was a cross-sectional study among 50+ years adults in Virginia (n=16,576) using data from the Behavioral Risk Factor Surveillance System (2018, 2019, and 2020). We calculated unweighted prevalence of shingles vaccination by health insurance and access to primary health care provider (used as proxies for health care access) and in relation to the COVID-19 pandemic (pre vs. during). Log binomial regression models were used to estimate weighted prevalence ratios (PR), adjusting for potential confounders.

Results: Shingles vaccination was substantially higher among those with healthcare access compared to those without. Specifically, shingles vaccination was 40% among those with health insurance vs. 12% among those without, and 41% among those with a primary healthcare provider vs 18% among those without. Shingles vaccination was 47% during the COVID-19 pandemic vs. 36% before. People with health insurance [adjusted PR (aPR): 2.03 (95% CI: 1.44 – 2.86)], and access to primary health care provider [aPR: 1.99 (95% CI: 1.65 – 2.41)] were approximately twice as likely to receive shingles vaccine compared to those without health insurance and access to primary health care provider. There was 26% higher likelihood of receiving the shingles vaccine during the pandemic compared to pre-pandemic [aPR:1.26 (95% CI: 1.20 – 1.33)].

Conclusion: This study highlights the pivotal role of health care access on shingles vaccine uptake among older adults. The observed rise in vaccine prevalence during the pandemic reinforces the role of public health initiatives and awareness in vaccine uptake.

Injuries/Violence

Association of mild traumatic brain injury and risk of musculoskeletal injury among United States service members Alexander Ivan B. Posis* Alexander Ivan Posis James M. Zouris John J. Fraser Amy Silder Daniel J. Crouch Pinata H. Sessoms Andrew J. MacGregor

Background: Mild traumatic brain injury (mTBI) is associated with higher subsequent musculoskeletal injury (MSKI) risk. However, there is limited research on the association of mTBI on MSKI risk and if it is modified by sex among a large cohort of United States (US) service members (SMs) with extended follow-up while in service.

Methods: This retrospective cohort study included 777,811 SMs (mean age = 20.5 ± 3.4 years; 18.9% female; 53.7% White; mTBI = 2.6%) who enlisted between 2016-2020 and had medical record data until 2023. mTBIs were identified using International Classification of Disease, 10th revision codes defined by the Armed Forces Health Surveillance Division. Incident MSKI events were identified by anatomical complex, primary tissue type affected and International Classification of Functioning, Disability and Health codes. We used multivariable accelerated failure time models to estimate time ratios (TR) and 95% CIs, adjusted for demographic and military-relevant characteristics, for the association between mTBI and subsequent MSKI risk. We assessed effect measure modification (EMM) by sex testing an mTBI-by-sex interaction and conducted sex-stratified models.

Results: During 1,590,992 person-years of follow-up, there were 543,463 MSKI events (crude rate = 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 MSKI, relative to no mTBI. There was evidence to suggest EMM by sex (p-interaction <0.01). In sex-stratified models, mTBI was associated with a 41% (TR = 0.59, 95% CI 0.54-0.65) reduction in time to injury among females only and 54% (TR = 0.46, 95% CI 0.43-0.48) among males only.

Conclusions: In this large cohort of US SMs, mTBI was associated with shorter time to MSKI. The association was modified by sex, such that males had faster mTBI-associated time to MSKI compared to females. Findings suggest the importance of considering mTBI history and sex when assessing MSKI risk.

Injuries/Violence

Estimating the effect of Florida's red flag gun law on firearm mortality rates Catherine Gimbrone* Catherine Gimbrone Kara Rudolph

In response to the deadly Parkland high school shooting in 2018, Florida's legislature enacted a red flag law permitting the temporary removal of firearms from individuals who pose a danger to themselves or others. Unlike liberal states that have passed similar laws, Florida was one of the first conservative and largely pro-firearm states to pass a law restricting gun ownership. Notably, firearm homicides have increased over time in the US and are a leading cause of death among younger populations, yet there has been little research into the effects of red flag laws on firearm homicide deaths. To address this gap, we employed augmented synthetic control methods to estimate the effect of Florida's law on subsequent firearm homicide, non-firearm homicide, firearm suicide, and non-firearm suicide mortality rates using yearly data from CDC Wonder from 2009 to 2021, and excluding 2018 to account for lagged effects. A weighted synthetic unit with similar pre-period trajectories of covariates and outcomes to Florida was constructed from 23 conservative states lacking similar gun laws. Models estimated causal mortality rate differences between synthetic and treated units with jackknife+ confidence intervals and were adjusted for socio-demographic and economic factors. We found that firearm homicide rates decreased significantly below the expected value following the passage of Florida's red flag law (RD: -0.93, 95% CI: -1.68,-0.54), whereas non-firearm homicide rates did not (RD: 0.13, 95% CI: -0.12, 0.41). Trends among firearm (RD: -0.67, 95% CI: -1.57, 0.06) and non-firearm suicide rates (RD: -0.68, 95% CI: -2.28, 0.35) both declined, yet neither were significant. In conclusion, the enactment of red flag laws may serve to reduce the growing burden of firearm homicides in the US.

Figure 1. Homicide mortality rate differences between synthetic control and treated units stratified by firearm method following the enactment of Florida's red flag law
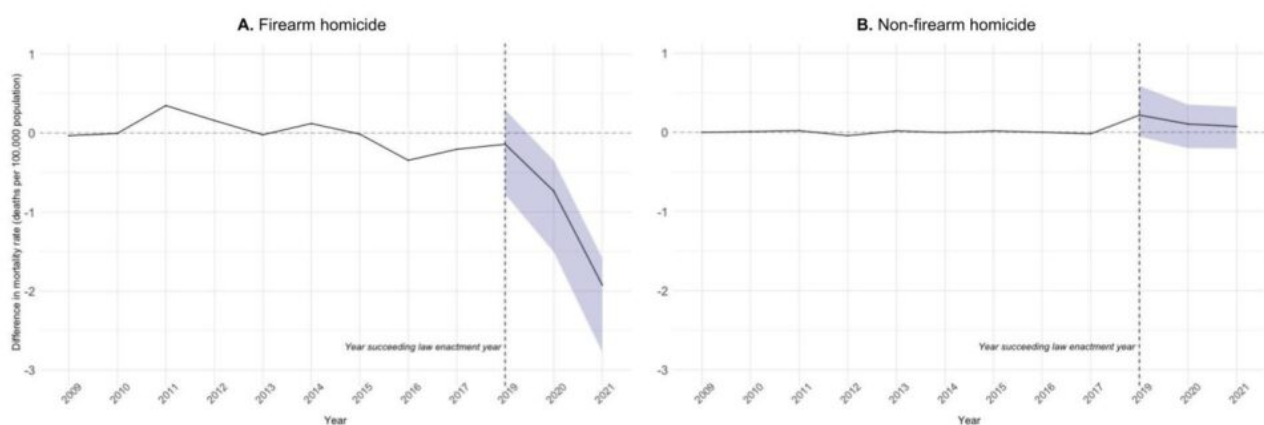
Housing stability and firearm violence: A natural experiment utilizing COVID-19 eviction moratoria in the United States Christina A. Mehranbod* Christina A. Mehranbod Carolyn S. Fish Ariana N. Gobaud Brady R. Bushover Daniel C. Semenza Christopher N. Morrison

Background

Firearm violence is a significant cause of morbidity and mortality in the US, particularly in communities with high housing instability. Evictions contribute immensely to housing instability, disproportionately affecting racialized and minoritized groups. Eviction moratoria implemented during COVID-19's peak offers insights into housing stability's impact on firearm violence. This study uses eviction moratoria as a natural experiment to examine associations with shootings in US cities.

Methods

We obtained shooting data from the Gun Violence Archive (2018-2021), eviction moratoria information from Princeton University, and eviction filing counts from the Eviction Lab (2020-2021). Major US cities with eviction moratoria, shooting data, and filing counts were included. Autoregressive integrated moving average (ARIMA) models were applied to weekly time series data. First, we estimated the impact of moratoria on city-wide shootings from 01/2018 – 04/2021. We also employed ARIMA models to examine variations in eviction filings and shootings from 1/2020 – 04/2021. Next, we applied these ARIMA models specifically to a subset of census tracts theoretically most impacted by evictions — census tracts in the top quartile for renter instability and with a higher-than-city-average percentage of residents racialized as Black.

Results

The analysis included 23 cities. Protective effects of eviction moratoria were estimated in 9 (39%) cities, though some 95% CIs included the possibility of negative associations. For example, in Albuquerque, NM, an eviction moratorium was associated with a significant decrease of 0.01 shootings per 10,000 population per week (95% CI: -0.037, -0.006). Negative effects of eviction filings on shootings were estimated in 11 (48%) cities, though some 95% confidence intervals included possible positive associations. In the subset of census tracts, results were similarly mixed, and no significant effects were found in the relationship between filings and shootings.

Conclusions

Eviction rates may be an important contributor to firearm violence. However, the study of eviction moratoria and filings on shooting rates showed inconsistent results, highlighting the need for further research into the complex drivers of housing instability and community firearm violence.

Injuries/Violence

Associations Between a High School Program Related to Inclusivity and Self-Reported Interpersonal Violence Victimization among United States High School Students Ann Richey* Ann Richey Avanti Adhia Ali Rowhani-Rahbar

Introduction: Adolescent interpersonal violence is a critical public health issue that can lead to adverse health outcomes. Inclusive school climates can potentially decrease interpersonal violence victimization, and schools can promote inclusive school climates through school programs.

Methods: We used 2018 School Health Profiles data to obtain school program information and 2019 Youth Risk Behavior Surveillance System data to obtain adolescent interpersonal violence victimization reports. Principals answered yes/no to the question, "Does your school have any clubs that give students opportunities to learn about people different from them, such as students with disabilities, homeless youth, or people from different cultures?" Associations between state-level proportions of high schools with that program and self-reported interpersonal violence victimization among high school students were tested using weighted logistic regression.

Results: State-level proportions of the high school program ranged from 56% to 100%. For every 10-unit difference in state-level proportions, higher proportions were associated with lower odds of a student self-reporting forced sexual intercourse (OR=0.88, 95% CI=0.84-0.93), sexual violence (OR=0.96, 95% CI=0.92-1.01), sexual teen dating violence (TDV) (OR=0.99, 95% CI=0.94-1.05), bullying victimization at school (OR=0.88, 95% CI=0.85-0.91), and electronic bullying victimization (OR=0.89, 95% CI=0.85-0.93). For every 10-unit difference in state-level proportions, higher proportions were associated with higher odds of a student self-reporting physical TDV (OR=1.03, 95% CI=0.97-1.08).

Conclusion: Results suggest preliminary evidence of associations between school programs related to inclusivity and adolescent interpersonal violence victimization. Further research is needed to understand the mechanisms behind this relationship and how schools can promote inclusive programs to effectively reduce interpersonal violence victimization.

Mental Health & Alcohol Abuse: Descriptive Epidemiology Using the All of Us Research Program Aeisha Thomas* Drenen Magee Aeisha Thomas

Alcohol Use Disorder (AUD) has been shown to be highly associated with Depression and Anxiety. Medical research has historically lacked diversity; thus, we hypothesize the existence of possible undiscovered connections between these conditions, especially within underrepresented populations.

To help address this, our descriptive epidemiology study uses the diversity, size, and biologically and behaviorally rich nature of the All of Us Research Program database (AoU) to describe, in parallel, Depression or Anxiety and AUD within AoU; hoping to complement past studies, or, potentially, find novel distributions.

This cross-sectional study describes the demographic data pertaining to race and sex assigned at birth in cohorts built from the AoU Personal and Family Health History Survey (Controlled Access, v7) (PFHHS). These were *AUD and Depression, AUD alone, Depression alone,* and *Neither* (AUD/D Cohorts). Corresponding cohorts for AUD and Anxiety were also built in parallel (AUD/A Cohorts). Thus, eight cohorts were designed to describe Depression or Anxiety alongside AUD within AoU.

PFHHS participants (n = 185,232) are: 64.0% Female, 33.8% Male, 1.2% Other; 71.4% White, 9.4% Black or African American, and 19.2% Other Minorities.

For the AUD/D Cohorts the distributions were: (a) Overall, 2.4% AUD and Depression, 1.3% AUD, 27.1% Depression, and 69.3% Neither, (b) White population (n = 132,239), 2.7% AUD and Depression, 1.4% AUD, 28.9% Depression, and 67.0% Neither, and (c) Black population (n = 17,335), 2.0% AUD and Depression, 1.4% AUD, 22.6% Depression, and 74% Neither.

For the AUD/A Cohorts the distributions were: (a) Overall, 1.7% both AUD and Anxiety, 1.9% AUD, 19.8% Anxiety, and 76.6% Neither, (b) White population, 1.3% AUD and Anxiety, 2.1% AUD, 21.5% Anxiety, and 74.7% neither, and (c) Black population, 1.3% both, 2.0% AUD, 21.2% Anxiety, and 81.6% Neither.

These descriptions add to previous research, demonstrating the value of the AoU's unique landscape.

Global Trends in Adolescent Loneliness, 2000-2022 Sophia L. Freije* Sophia Freije Isaac C. Rhew Yolanda N. Evans KC Gary Chan Daniel A. Enquobahrie

Background: Some studies suggest adolescent loneliness has increased globally in recent years, but none of these reports have examined data collected after the onset of the COVID-19 pandemic. We characterized global trends in loneliness among adolescents from 2000 to 2022.

Methods: We used methodologically comparable, nationally-representative, cross-sectional surveys administered by the Programme for International Student Assessment in 2000, 2003, 2012, 2015, 2018, and 2022 to 15- to 16-year-olds from Organization for Economic Co-operation and Development member countries (n=37 countries, 1,409,084 students). Responses to six questions regarding loneliness in the school context (e.g. "other students like me") were dichotomized as strongly agree/agree vs. strongly disagree/disagree. Time trends for each loneliness item (outcome) were tested using two-piece Poisson regression models with survey year as the predictor, sex and parental education as covariates, and a knot at the year 2015. Confidence intervals were corrected for clustering within countries.

Results: The prevalence of each loneliness measure increased from 2000 to 2022, with the largest increases observed in 2015. Responses to loneliness items were moderately correlated (correlation coefficients range: 0.29 to 0.52). Prior to the 2015 inflection point, the prevalence of each loneliness measure was positively associated with a later survey year, with prevalence ratios (PRs) ranging from 1.02 for disagreement with "I feel like I belong" (95% CI: 1.01, 1.04) to 1.07 for "I feel like an outsider" (95% CI: 1.06, 1.08). Following the 2015 inflection point, PRs were null or negative ("I feel like an outsider" PR: 0.98, 95% CI: 0.97, 0.999; "I feel like I belong" [disagree] PR: 0.98, 95% CI: 0.97, 0.999).

Conclusion: To our knowledge, this is the most recent global estimation of adolescent loneliness. Our findings indicate an increasing trend in loneliness from 2000 to 2015, followed by null or decreasing levels. Factors that contribute to these observations need investigation.

Figure: Prevalence of Loneliness Measures in 15-16-year-old adolescents from 37 countries, 2000 to 2022

Mental Health
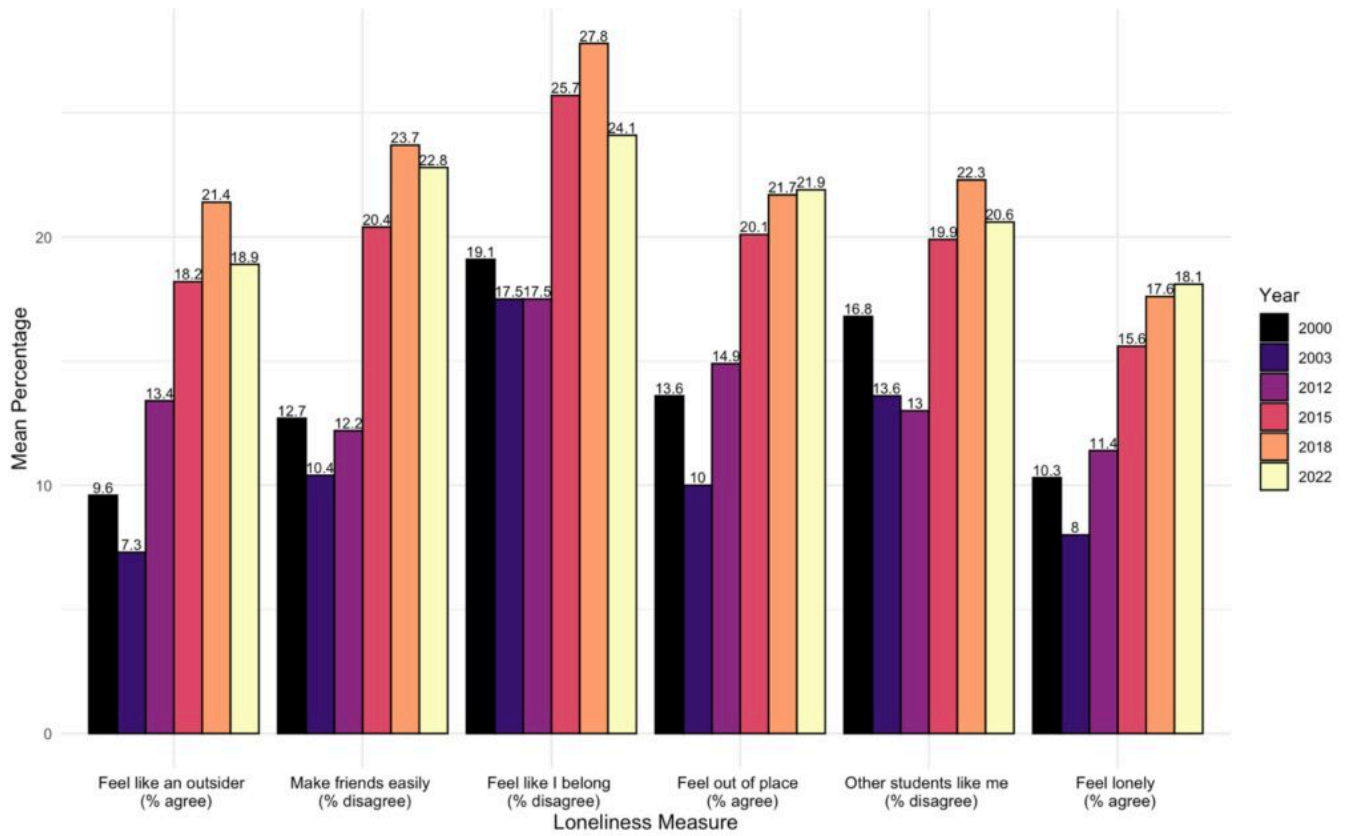
Suicidality and Major Depressive Episode among Young Adults Aged 18 to 25 Iva Magas* Iva Magas Samantha Brown Jennifer Hoenig

Background: Suicide is the second leading cause of death among young adults aged 18 to 25 and a major public health concern. This study's main objective was to examine the relationship between suicidal behavior, major depressive episode (MDE) and gender among young adults 18 to 25 in the U.S.

Methods: Data from the 2021 and 2022 National Surveys on Drug Use and Health (NSDUH) were analyzed. The population included 33,600 young adults aged 18 to 25. Data were stratified by gender and associations with suicidal ideations were analyzed using the χ2 test, overall and among young adults with MDE. Respondents were asked whether they had seriously thought, planned, or attempted to kill themselves in the past 12 months. The MDE was defined using DSM-5 criteria.

Results: The prevalence of suicidal thoughts (15.9% vs. 11.2%), plans (6.1% vs. 4.1%), and attempts (3.1% vs. 1.8%) was significantly higher among young adult females aged 18 to 25 than males in this age group (p<0.001). Young adult females were also more likely to have higher prevalence of MDE compared to males aged 18 to 25 (25.4% vs. 14.0%; p<0.001). In line with previous studies, our analyses show suicidal behaviors are far more common among those with MDE. Moreover, 43.6% of young adults aged 18 to 25 with an MDE had suicidal thoughts, 17.7% suicide plans, and 8.3% have attempted suicide during the 2021-2022 survey years. No gender differences in suicidal behaviors among young adults who experienced an MDE in the past year was found.

Conclusions: While gender differences were found for MDE and suicidality respectively, no gender differences were found for suicidality among young adults with MDE. This finding further highlights the nuanced and complex nature of suicidality. Further research is needed to better understand if the severity of MDE mediates the association between gender and suicidal thoughts, plans, and attempts.

Pharmacotherapy guideline concordance for major depressive disorder and its link to functioning via symptom change Mason T. Breitzig* Mason Breitzig Fan He Lan Kong Guodong Liu Daniel A. Waschbusch Jeff D. Yanosky Erika F. H. Saunders Duanping Liao

Background: Alleviation of symptom severity for major depressive disorder (MDD) is known to precede a lagged improvement of functioning. However, the degree to which adherence to pharmacotherapy guideline recommendations is associated with this recovery process remains unclear. This study investigated whether greater pharmacotherapy guideline concordance (quantified by the GCA-8) is associated with better functioning via reducing MDD symptom severity.

Methods: Data from 1,403 adults (67% female, 85% non-Hispanic/Latino White, mean age of 43 years) with non-psychotic MDD from the Penn State Psychiatry Clinical Assessment and Rating Evaluation System (PCARES) registry (visits from February 1, 2015, to April 13, 2021) were eligible for analyses. Cross-sectional mediation analysis was used to explore the total, direct, and mediated effects of the association between the GCA-8 and World Health Organization Disability Assessment Schedule 2.0 (WHODAS; score standard deviation [SD]: 10.32), with Patient Health Questionnaire depression module (PHQ-9) scores as the mediator. Analyses were adjusted for sociodemographic and clinical characteristics.

Results: The total effect from mediation analysis indicated that a 1 SD increase in patients' GCA-8 score (representing better concordance) was associated with a 0.53 improvement in patients' 1-year mean WHODAS score (n=851; β=-0.53; P value=.01). Additionally, 96.6% (95% CI: [31.1%, 100.0%]; β=-0.51; P value=<.001) of the total effect was mediated by the change in MDD symptom severity. The direct effect of the GCA-8 on the mean WHODAS score, independent of PHQ-9 change, was nonsignificant (β=-0.02, P value=.92).

Conclusions: We cross-sectionally observed that higher pharmacotherapy guideline concordance is associated with better self-reported functioning in patients with MDD, possibly via improvement of MDD symptom severity; future research should employ longitudinal designs with repeated measurements to elucidate the directionality.

Leveraging mental health communication inequities among Latinx populations to further our understanding of mechanisms of mental health stigma Melissa DuPont-Reyes* Melissa DuPont-Reyes Alice Villatoro Lu Tang

Background: Public communication about the diathesis-stress model—the interactive neurobiological-psychosocial component causes of mental illness—has promoted reception to treatment yet violent/dangerous stereotypes have increased too. These efforts have diffused in English-language media only. We leveraged high vs low diffusion of mental health communication across diverse language/cultural media exposure among Latinx populations to examine the effects of neurobiological-psychosocial causal beliefs on help-seeking via stigma and treatment beliefs.

Method: A quota US-based Latinx sample ages 13-86 (N=2058) self-completed assessments (α=.72-.94) in 2021 ascertaining: frequency of Spanish/Latinx and English media use and mental health content scanning/seeking; beliefs about mental illness neurobiological-psychosocial causes—genetics, brain chemistry, environment, stress; treatment—improves with treatment or on its own; stigma—violent/dangerous, bad character, unwilling to socialize; and help-seeking to healthcare providers or family/friends. Structural equation models estimated direct effects of neurobiological-psychosocial beliefs from Spanish/Latinx and English media exposures on help-seeking behaviors via treatment and stigma beliefs, net individual/family factors.

Results: Spanish/Latinx media was negatively associated with neurobiological-psychosocial causal beliefs while English media was positively associated, indicating greater diathesis-stress information in English vs Spanish/Latinx media (p<.01). Neurobiological-psychosocial causal beliefs were then positively associated with treatment and rejection beliefs (p<.01) simultaneously. Rejection beliefs in turn reduced help-seeking to healthcare professionals and family/friends (p<.05); no significant association was observed for treatments beliefs on either help-seeking outcome.

Conclusion: Public communication about the diathesis-stress model appears to have increased treatment beliefs at the expense of increasing stigma beliefs that impede help-seeking. Innovation in public mental health communication is urgently needed to counter stigma and health inequity.

Mental Health

Examining the cross-sectional and prospective associations between naturally occurring changes to school public health unit engagement regarding mental health and adolescent anxiety and depressive symptoms: Findings from Wave 6 (2017-18) and Wave 7 (2018-19) of the COMPASS Study Stephen Hunter* Stephen Hunter Carla Hilario Scott T Leatherdale Karen Patte Brendan T Smith Roman Pabayo

Background: Adolescence is a critical period for targeting mental health and schools provide unequivocal access to adolescents for initiatives to occur. The research objective was to examine the association between schools' engagement with their local public health unit (PHU) regarding mental health and adolescent anxiety and depressive symptomology.

Methods: Linked longitudinal data from wave 6 (2017-18) and wave 7 (2018-19) of the Cannabis, Obesity, Mental health, Physical activity, Alcohol, Smoking, and Sedentary behaviour (COMPASS) study in Canada was used. Adolescents (n = 27 473) reported their anxiety and depressive symptomology via questions from the 7-Item Generalized Anxiety Disorder (GAD-7) and Center for Epidemiological Studies Depression Revised (CESD-R-10), respectively. Schools' (n = 112) engagement with their local PHUs regarding mental health each year was reported via administrative surveys. Multilevel logistic regression analyses were used to determine if PHU engagement was a significant predictor of anxiety or depression at baseline and at follow-up, while controlling for individual-, school, and area-level covariates.

Results: Adolescents attending schools that engaged with their local PHU had greater odds of anxiety at baseline (OR = 1.30, 95%CI: 1.10, 1.53) and the probability was significantly higher over time compared to those who attended schools with no PHU engagement at baseline. Adolescents attending schools that engaged with their local PHU had a greater odds of reporting depression at baseline (OR = 1.18, 95%CI: 1.02, 1.36); however, the probability over time remained the same, compared to those who attended schools with no PHU engagement at baseline.

Conclusion: Schools' engagement with their local PHU regarding mental health did not mitigate increases in students' anxiety or depression symptoms over one year. A more nuanced inquiry into the frequency, type, duration, and target populations of mental health initiatives is required.

Using a causal decomposition approach to estimate the contribution of employment to differences in mental health profiles between men and women Christa Orchard* Christa Orchard Elizabeth Lin Laura Rosella Peter Smith

Background: Mental health disorders are known to manifest differently in men and women, however our understanding of how gender interacts with mental health and well-being as a broader construct remains limited. Employment is a key determinant of mental health and there are historical differences in occupational roles among men and women that continue to influence working lives. The goal of this study is to explore differences in multidimensional mental health between men and women, and to quantify how these differences may change if women had the same employment characteristics as men.

Methods: Working-age adults (25-64) were identified through a household survey in Ontario, Canada during 2012. We created multifaceted measures of employment to capture both employment and job quality, as well as multidimensional mental health profiles that capture mental health disorders and well-being using survey data. A causal decomposition approach with Montecarlo simulation methods estimated the change in differences in mental health profiles between men and women, if women had the same employment characteristics as men.

Results: Women were more likely to exhibit clinical mood disorders compared to men, with men more likely to exhibit absence of flourishing without a diagnosable disorder. Among those who were flourishing, women more often expressed at least some life stress compared to men. When women were assigned men's employment characteristics, which amounted to an increase in employment and higher quality employment, some of the gender differences in risk of clinical mood disorder decreased. However, differences between men and women in the remaining mental health profiles increased.

Conclusions: This study provided an estimate of the contribution of employment to the observed differences in multidimensional mental health between men and women. This adds to the literature by including a broader range of mental health indicators than disorders alone, and by formalizing the causal framework used to study these relationships.

Association Between Medicaid Insurance and Poor Mental Health among Insured Adults (18-64 years old) in Washington State: Analysis of BRFSS Data (2018-2019) Hiwot Weldemariam* Ekua-Yaaba Monkah Hiwot Weldemariam Betelhem Muno

Introduction

The prevalence of poor mental health in the United States is substantial, but there are barriers to accessing mental health care. Medicaid insurance, while expanding eligibility to many people, may pose obstacles that limit inaccessibility to services, more so than most forms of private insurance. The primary aim of this study was to investigate the association between Medicaid insurance coverage and recent self-reported poor mental health, both in aggregate and for specific types.

Methods

We used data from the 2018 to 2019 Washington State Behavioral Risk Factor Surveillance System survey. We included a total of 12,739 adults aged 18 to 64 years, and compared the prevalence of poor mental health for 14 or more days within the month preceding the survey between persons enrolled in Medicaid and those who had other forms of health insurance, adjusting for confounders by means of the Mantel-Haenszel method.

Results

The prevalence of poor mental health for more than 14 days during the prior month was 27.9% (N=466) among 1,780 individuals enrolled in Medicaid, which was 2.45 times higher than the corresponding prevalence in persons with other forms of health insurance. The magnitude of the association was similar after adjusting for confounders such age, race and ethnicity, income, and sex.

Conclusion

These data suggest that having Medicaid insurance is associated with poor self-reported mental health. However, the interpretation of the association is uncertain, given the possibility that poor mental health could potentially influence the type of insurance a person has. Conducting longitudinal studies that track individuals over time would offer a more comprehensive understanding of the temporal dynamics between insurance status and mental health outcomes.

Mental Health

Does perceived caregiver HIV stigma and depression increase adolescent neuro-behavioral difficulties? A mediation analysis in the asenze cohort Amaleah Mirti* Amaleah Mirti Leslie Davidson Jeremy Kane Gabriella Norwitz Rachel Gruver Kathryn Watt Chris Desmond Adele Munsami Nonhlanhla Myeza

Introduction:

People living with HIV (PLWH) often experience HIV related stigma that is, in turn, associated with several negative health outcomes including depression, harmful drinking, and intimate partner violence. Despite knowledge of these proximal impacts of HIV stigma on PLWH, less is known about the impact that HIV stigma has on the health and behavior of adolescents in the care of PLWH.

Methods:

Utilizing data from adolescents and their primary caregivers from the population-based Asenze cohort study in KwaZulu-Natal (KZN), South Africa, we conducted a path analysis to determine if caregiver depression [operationalized as mental health functioning] is a mediator of the hypothesized association between caregiver HIV stigma and adolescent neurodevelopmental behavior including internalizing and externalizing behaviors.

Results:

Results suggest good model fit and a statistically significant relationship between caregiver HIV stigma and caregiver mental health functioning. However, neither the direct nor indirect (including potential mediator caregiver mental health functioning) effect of HIV stigma on adolescent behavioral difficulties was statistically significant.

Conclusion:

This paper bolsters findings from other studies in KZN, as well as South Africa at large, on the relationship between HIV stigma and mental health for PLWH. Moreover, it highlights the importance of understanding HIV from a psychosocial perspective and reaffirms the need for mental health resources in populations with large numbers of people living with HIV.

Sex Differences in Anti-hypertensive Medications and PTSD Incidence in a Trauma Cohort

Sophie Selbe* Sophie Selbe Travis Evans Timothy L. Lash Henrik Toft Sørensen Jaimie Gradus Jennifer Sumner

Studies have documented protective associations between some antihypertensive (AHT) medications and the development or maintenance of posttraumatic stress disorder (PTSD), but few include samples large enough to examine multiple AHT classes or sex differences in one sample. Our study fills this gap in the literature.

Data came from a trauma cohort established from the Danish national health care and social registries from 1994 to 2016. All members of the cohort experienced one or more of the following traumatic experiences: fire/explosion, transportation accident, exposure to a toxic substance/medical complications, traumatic brain injury, assault with or without a weapon, pregnancy-related trauma, suicide death of a family member. The outcome was incident PTSD. The exposed group redeemed prescriptions for AHT medications including beta blockers, angiotensin II receptor blockers (ARBs), angiotensin-converting enzyme inhibitors (ACEIs), and calcium channel blockers within 60 days before their traumatic event. For the unexposed group, five persons who never redeemed an AHT medication were matched to the exposed group on age, sex, trauma type, and year. We ran descriptive analyses followed by Cox proportional hazards regression adjusted for marital status, income, and Charlson Comorbidity Index score to estimate hazard ratios (HR) and 95% CIs for the associations between AHT medication class and incident PTSD.

We observed a protective effect for calcium channel blockers and the development of PTSD for both women (HR=0.79; 95% CI=0.29,2.17) and men (HR=0.49; 95% CI=0.22,1.09). A slight protective effect was observed for beta-blockers in men and women; while ACEIs showed near-null effects. ARBs however displayed a protective effect in women (HR=0.47; 95% CI=0.11,2.11), but not protective in men (HR=1.35; 95% CI=0.50,3.61).

Overall, results suggest that there are sex differences among the previously documented protective effects of AHT medications on the development of PTSD.

Table 1. Rate of developing PTSD among persons on antihypertensive medications at the time of trauma compared to those not on antihypertensive medications at the time of trauma. Unadjusted models and models adjusted for marital status, income, and Charlson Comorbidity Index score at the time of trauma.

Sex	Model	Calcium Channel Blockers		ACE Inhibitors		Beta Blockers		Angiotensin II Receptor Blockers	
		HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI
Women	Unadjusted	0.70	(0.28-1.73)	0.84	(0.36-1.95)	0.89	(0.56-1.42)	0.41	(0.12-1.38)
	Adjusted	0.79	(0.29-2.17)	1.08	(0.39-3.01)	0.92	(0.56-1.51)	0.47	(0.11-2.11)
Men	Unadjusted	0.66	(0.35-1.25)	1.11	(0.65-1.90)	0.96	(0.59-1.56)	1.03	(0.43-2.49)
	Adjusted	0.49	(0.22-1.09)	0.94	(0.49-1.86)	0.85	(0.47-1.54)	1.35	(0.50-3.61)

Notes. HR = Hazard Ratio derived from Cox Proportional Hazard Regression Model.

A Four Step Iterative Approach in Estimating Prevalence in the Presence of Misclassification Bias in a Population Sample and Selection Bias in a Convenience Sample

Christoffer Dharma* Christoffer Dharma Peter Smith Dionne Gesink Travis Salway Victoria Landsman Michael Escobar

Self-reported measures of membership in stigmatized groups or behaviours (e.g., sexual orientation or drug use) are prone to misclassification within population surveys (PS). Community-based convenience samples (CS) typically increase participation and identification from marginalized groups, but they are subject to participation and sampling biases due to non-probabilistic sampling. Using either one of these surveys to calculate prevalence of an outcome in a marginalized population can lead to a biased estimate. We propose a four-step iterative approach that uses information from both surveys that builds on existing methods to obtain a more informed prevalence estimate.

First, Adjusted Logistic Propensity (ALP) is used to generate pseudoweights in the CS data to make the covariate distribution more aligned with the PS data. Second, using Bayes formula, we calculate the probability of being misclassified among those who did not report to be in the group of interest in the PS based on the ALP-weighted CS data. Third, their group memberships are imputed using the probability of misclassification calculated in step 2. Finally, we can calculate the prevalence using either the PS or CS. With the PS, multiple imputation is run m times and prevalence estimates are pooled. With the CS, during each iteration, we use the new combined sets of individuals with characteristics of interest to apply ALP back into the CS, which are then pooled into a single estimate.

We provide an example of calculating the prevalence of any existing mental health diagnosis among sexual minority men in Canada. The prevalence estimates from the two surveys were closer together after the four-step process was applied; the unadjusted prevalence from the PS was 19.97%, while prevalence from CS was 25.72%. After adjustment, the PS prevalence was 18.69% (95% CI: 14.73, 25.02), while for the CS, it was 21.59% (95% CI: 19.22, 23.92). Advantages and disadvantages of the proposed method will be discussed.

Methods/Statistics Emma Kileel* Emma Kileel Alana Brennan Matthew Fox Jennifer Weuve Jacob Bor

Background: The regression discontinuity design, a quasi-experimental technique used to estimate the causal effect of an intervention when random assignment is not possible, is gaining traction in epidemiologic research. This method leverages measurement error, typically regarded as a source of misclassification and bias in epidemiology, to emulate a random treatment assignment. It is unclear how the degree of measurement error impacts the ability of the regression discontinuity method to obtain valid and precise estimates of effect.

Methods: We simulated a dataset of 50,000 observations each with a value representing an HbA1c test result, the assignment variable, measured without error. At the diabetes diagnosis value of 6.5%, we simulated a discontinuity in the probability of outcome, Y, of 20%, representing the "true" estimate of effect. We simulated nondifferential measurement error by generating error terms randomly sampled from a normal distribution with specified means and standard deviations. Error terms were added to simulated HbA1c values to represent measured HbA1c values. True versus measured HbA1c values were compared to calculate sensitivity (Se) and specificity (Sp) of the assignment variable. Local linear regression was used to estimate the intent-to-treat (ITT) effect (risk difference).

Results: The ITT estimate did not vary substantially across degrees of measurement error (Table). When HbA1c was measured with very little error (Error SD=0.05, Se=99.5%, Sp=99.6%), the ITT estimate of effect was 20.7% (95% CI: 17.9, 23.5%). Even in scenarios of extreme measurement error (Sp<50%) the ITT estimate was 20.9% (95% CI: 18.1, 23.8%). When the Se was less than 50% the ITT estimate was 22.6% (95% CI: 19.5, 25.7%).

Conclusion: Using simulation methods, we demonstrated that even in the presence of large degrees of measurement error and corresponding misclassification, there was no bias in the ITT effect estimate when using a regression discontinuity design.

Table. Sensitivity and specificity of measured versus true HbA1c values by degree of measurement error and resulting intent-to-treat effect estimates (risk differences).

Mean of error term	Standard deviation of error term	Sensitivity [Pr(Measured HbA1c $\geq$ 6.5 | True HbA1c $\geq$ 6.5)]	Specificity [Pr(Measured HbA1c $\leq$ 6.5 | True HbA1c $\leq$ 6.5)]	Risk Difference (95% CI)
0.0	0.00	100%	100%	22.4% (19.3, 25.5%)
0.0	0.05	99.5%	99.6%	20.7% (17.9, 23.5%)
0.0	0.10	99.0%	99.1%	21.7% (18.6, 24.8%)
0.0	0.50	95.5%	95.6%	19.4% (16.5, 22.4%)
0.0	1.0	91.4%	91.5%	19.9% (16.8, 22.9%)
0.0	1.5	87.4%	87.3%	20.6% (18.1, 23.2%)
0.0	2.0	84.3%	83.3%	19.4% (17.0, 21.8%)
4.0	9.0	77.5%	43.8%	20.9% (18.1, 23.8%)
-4.0	9.0	43.3%	74.9%	22.6% (19.5, 25.7%)

Paired censoring in matched cohort studies Alexander Breskin* Alexander Breskin Michael Webster-Clark

Informative censoring remains a threat to internal validity in matched cohort studies even in the absence of uncontrolled confounding. Several methods exist to address informative censoring bias (e.g., inverse probability of censoring weighting (IPCW)). 'Paired censoring' analysis, in which both members of a matched pair are censored when the first member is censored, has recently been proposed and implemented, particularly in vaccine safety studies. Conditions under which this approach yields unbiased estimates of risks and incidence rates have yet to be elucidated.

We identified 3 necessary conditions for paired censoring to be valid. First, the outcome and competing events must not be terminal, meaning people remain under follow-up after their first event and can experience multiple events. Second, the treatment effect must be constant across levels of covariates driving informative censoring. Finally, only time-fixed covariates may drive informative censoring.

For demonstration, we conducted a simulation estimating the effect of a two-dose vaccine series on injection site reaction under four scenarios (Figure 1): a) non-terminal outcome, null effect, censoring depending on baseline covariates; b) non-terminal outcome, effect measure modification, censoring depending on baseline covariates; c) non-terminal outcome, null effect, censoring depending on a time-varying covariate; and d) terminal outcome. In each scenario, we estimated effects with a naïve estimate unadjusted for informative censoring and paired censoring. In scenario (a), the unadjusted estimate was biased while the paired censoring approach was not. In scenarios (b), (c), and (d), both estimates were biased, but the paired censoring approach slightly attenuated the bias.

Researchers should consider these conditions when accounting for informative censoring in matched cohort studies. If they are not met, alternatives to paired censoring such as IPCW should be used (given their own conditions are met).
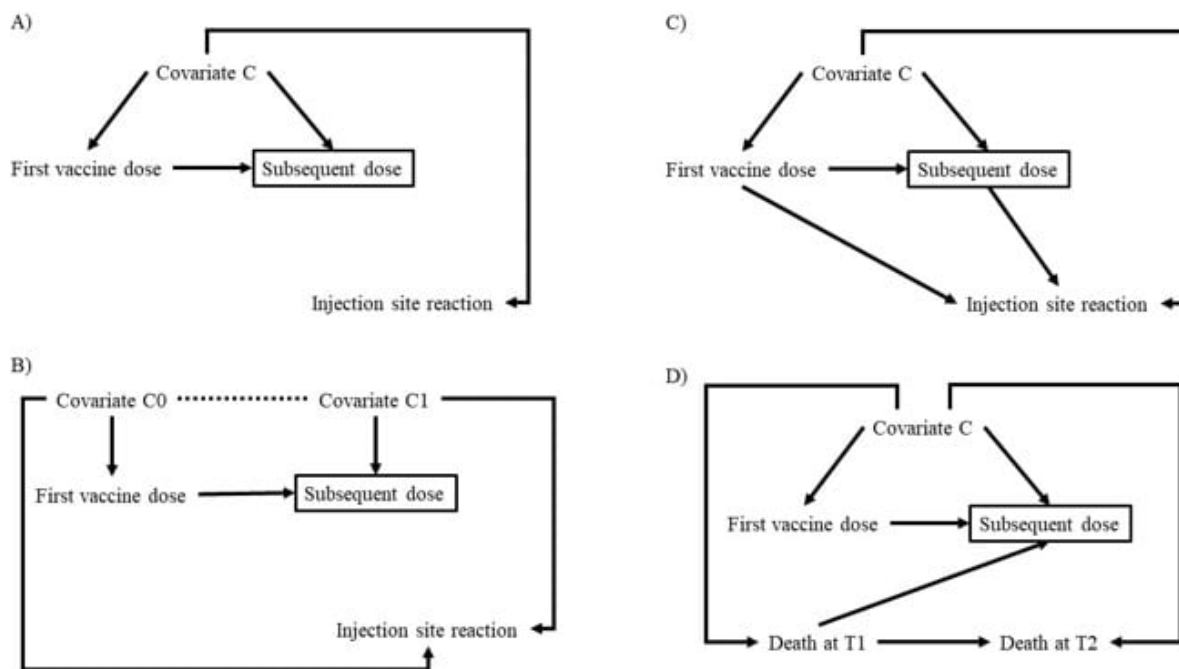
Figure 1: Directed acyclic graphs for the effect of a two dose vaccine on injection site reaction (Panels A-C) or death (Panel D) representing: the base case scenario of no effect measure modification and selection bias due to baseline confounders (Panel A), a scenario with effect measure modification (Panel B), a scenario with selection bias due to a time-varying covariate that is also a confounder (Panel C), and finally a scenario with a terminal outcome that makes it impossible to observe the second dose (Panel D).

Using an Online Panel to Crosswalk Alternative Exposure Measures in Two Studies: Deriving Comparable Estimates of the Effect of Physical Activity on Self-Rated Health Anna M. Pederson* Anna M. Pederson Scott C Zimmerman Peter Buto Yingyan Wu Eleanor Hayes-Larson Paola Gilsanz Elizabeth Rose Mayeda Rachel Whitmer M. Maria Glymour

Different assessments of physical activity (PA) across studies pose a major challenge when estimating effects of PA on health. We fielded an online survey (Qualtrics and Centiment) to develop a crosswalk between PA questions as asked in 2 cohorts: the Health and Retirement Study (HRS) and the Kaiser Healthy Aging and Diverse Life Experiences (KHANDLE) study. We compared associations of each question version of heavy PA and self-rated health, and whether associations differed by cohort.

Panel participants (n=2,335) were asked about heavy PA frequency as phrased in both HRS (4-level Likert scale) and KHANDLE (5-level Likert scale). HRS (n=11,094) and KHANDLE (n=1,823) participants aged 65+ self-rated their health (5-level Likert scale). We distance matched each HRS participant to 5 panel participants based on the HRS PA question and then imputed their responses to the KHANDLE PA question from the matched panel participants' responses (and vice versa). We pooled the imputed data and regressed self-rated health on heavy PA.

The measurement survey included panel participants aged 50+; 63% Female; 22% Hispanic, 25% Black, 26% White, and 27% Other racial/ethnic identity. In this sample, responses to HRS and KHANDLE versions of the heavy PA questions were moderately correlated ($R2 = 0.47$). In the pooled data, when using the HRS PA question with a 4-level PA scale, a 1 unit higher heavy PA was associated with better self-rated health (b=0.21 [0.20,0.22]), although the associations differed by cohort (interaction b=-0.089 [-0.107,-0.071]). When using the KHANDLE question version with a 5-level PA scale, heavy PA was associated with better self-rated health (b=0.13 [0.12,0.14]), and the association was similar across cohorts (interaction b=0.006 [-0.011,0.023]).

Fielding a survey with multiple question versions allows us to directly compare findings across multiple studies and pool or meta-analyze studies.
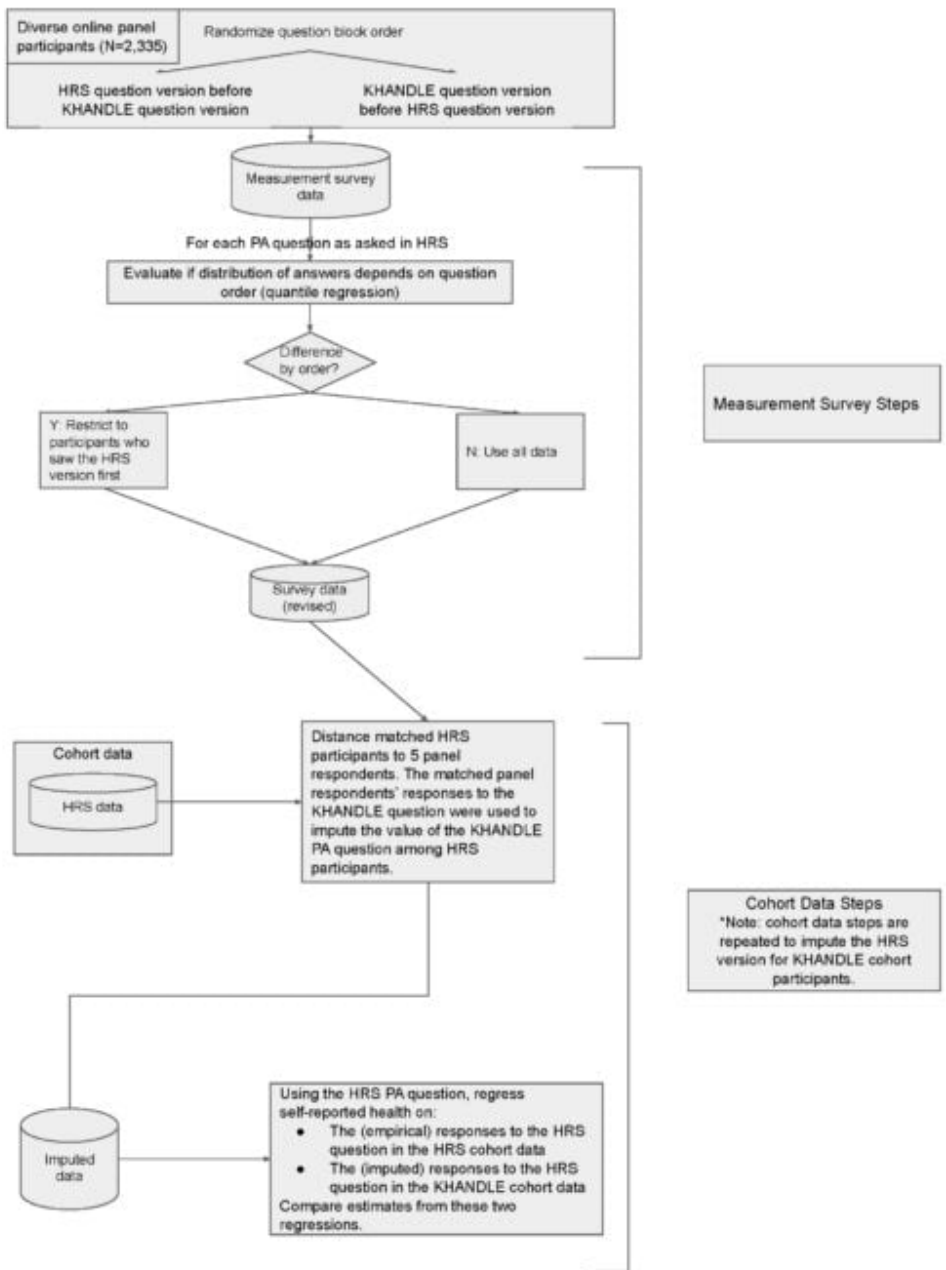
Enhancements to the Modified Kalman Filter for Small Domain Estimation Lauren Rossen*

Lauren Rossen Makram Talih

Measuring and tracking health disparities for small subpopulations can be challenging because direct estimates for small subgroups may be unstable or unreliable due to small sample sizes or small numbers of events. As a result, estimates for small subgroups may not meet data presentation standards, and analysts may need to aggregate data over larger areas, time periods, or groups to obtain reliable estimates, jeopardizing their timeliness and public health relevance. The Modified Kalman Filter (MKF) is a statistical modeling tool developed in 2011 for the purposes of small domain estimation, borrowing strength over time and across groups to produce more reliable model-based estimates for small subgroups. Recent enhancements to the MKF macro have been made to allow for additional flexibility in modeling non-linear trends, along with improving the transparency and usability of the tool.

Simulated data based on the National Health and Nutrition Examination Survey and the National Health Interview Survey were used to assess the performance of the enhanced MKF approach relative to direct survey estimates based on the root mean squared error (RMSE).

Model-based estimates using the enhanced MKF tool resulted in marked improvements in RMSE relative to direct estimates, with larger improvements seen for smaller sample sizes. Improvements were seen across a wide array of analytic scenarios, including outcomes with higher or lower prevalence, trends that varied from linear to cubic, trends that were shared or varied by group, as well as trends that involved unequally spaced time points. In all cases, relative RMSEs were smaller for model-based estimates than direct estimates. Gains in equivalent sample size of up to 420% were observed.

The enhanced MKF macro can be used to produce model-based estimates of health outcomes for small subpopulations, which will improve the availability of data for the assessment and monitoring of disparities in small groups.

Figure. Model-based (purple) and direct (gray) estimates of obesity prevalence and 95% confidence intervals among persons 65 years and older by race/ethnicity: Simulated cubic trends from 1999-March 2020.
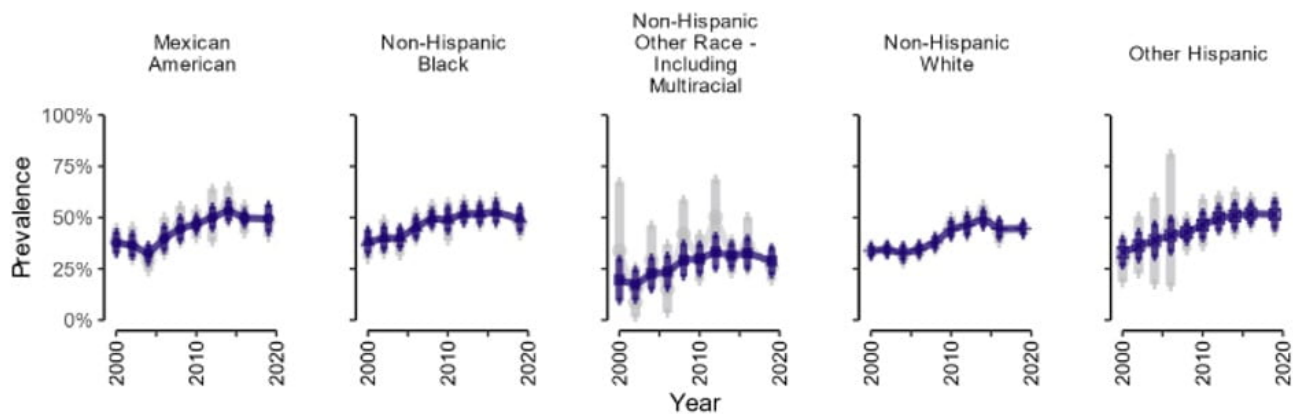
The Complex Estimand of Clone-Censor-Weighting When Studying Treatment Initiation Windows Quoa Her* Michael Webster-Clark Yi Li Sophie Dell'Aniello Robert Platt

Clone-censor-weighting (CCW) helps researchers compare treatment regimens that are indistinguishable from one another at baseline without relying on landmark dates or creating immortal person time. One application of the design in observational data is comparing outcomes of starting treatment in specific time windows (e.g., starting inhaled corticosteroids 30 days or from 30 to 180 days following hospitalization for chronic obstructive pulmonary disease exacerbation). Unfortunately, the hypothetical intervention that underlies the quantity that CCW estimates in such cases is more complex than it may seem.

We show that using CCW to study a regimen such as "start treatment prior to day 30" estimates the potential outcome of a hypothetical intervention where A) prior to day 30, everyone follows the treatment start distribution of the study population and B) everyone who has not initiated by day 30 initiates on day 30. Figure 1 illustrates how the resulting cumulative initiation probability would vary for four populations following different patterns of treatment initiation. We further show that allowing all initiators prior to day 30 to contribute to inverse probability of censoring weights (IPCW) estimates the effect of an impossible intervention where those who are forced to start on day 30 have the exposure history of those who started prior, creating bias. This bias is removed if only those who initiate on day 30 contribute to IPCW.

Finally, we demonstrate these findings via a simple simulation and show that, in some special cases, this treatment effect collapses to something more interpretable and those who initiate prior to day 30 can contribute to IPCW. While CCW is an excellent way to estimate outcomes of interventions such as "start by 30 days," providing information on the timing of treatment initiation and the plausibility of cumulative treatment effects generally provides key context on the underlying intervention.

Figure 1: Cumulative proportion of the population initiating over 30 days under the hypothetical intervention corresponding to a CCW analysis of a "start day 30 days" regimen in four populations with varying treatment initiation patterns.
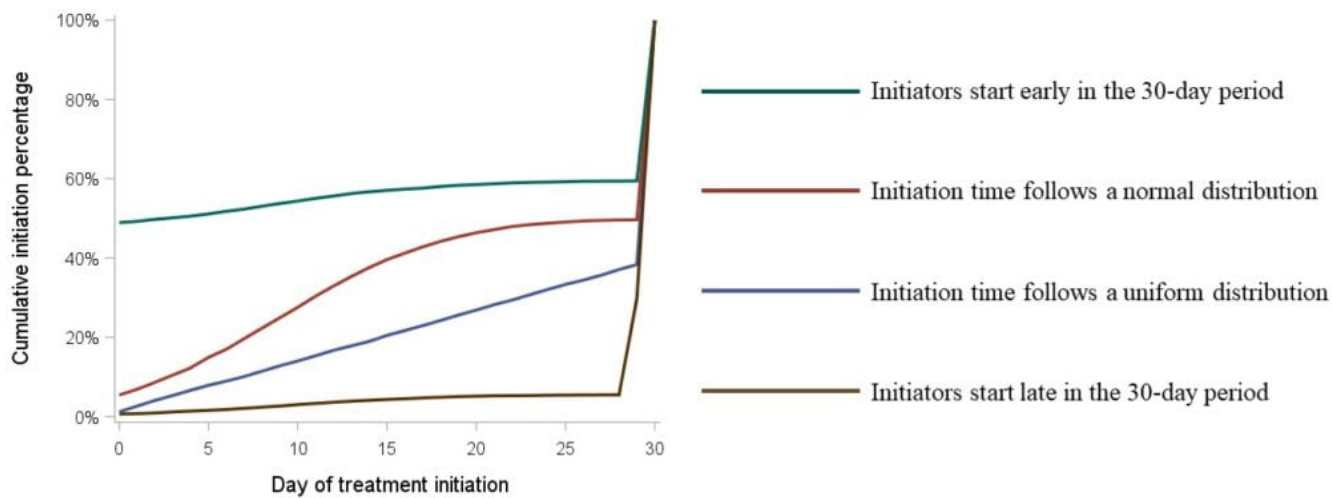
Using Transportability Methods for Subgroup Analyses Quoa Her* Michael Webster-Clark
Anthony Matthews Robert Platt

Subgroup analyses are a key part of epidemiologic research. Unfortunately, they often yield imprecise treatment effect estimates (or false positives for heterogeneity) because the analytic populations are restricted to members of the subgroup; those not in the subgroup do not contribute information.

While this works when A) there is no difference in the true treatment effect between members and non-members or B) the true treatment effect differs between non-members and members conditional on measured covariates, these two cases are not exhaustive. The true treatment effect may differ marginally between members and non-members but be equal if we account for measured covariates that modify the treatment effect of interest. In such cases, methods developed to transport estimates to external target populations can reduce variance in subgroup estimates.

We explored this using data from the PRIME trial of panitumumab on one-year progression free survival (PFS) in patients with metastatic colon cancer for the subgroup of Hispanic individuals (a small group with a differing prevalence of a key tumor gene). We 1) weighted non-Hispanic White participants to resemble Hispanic participants in terms of key effect measure modifiers, 2) combined unweighted Hispanic participants and weighted non-Hispanic White participants in one data set, and 3) analyzed the weighted cohort, obtaining 95% confidence limits from percentiles of 1,000 bootstrap iterations. While a Hispanic-only analysis estimated a decrease in PFS at one-year of 17% (95% C.I. -8.8%, 45%), an analysis including reweighted non-Hispanic Whites was much more precise (8.7%, 95% CI -5.3%, 22%) while still differing from the full population estimate (-1.0%, 95% CI: – 7.5%, 5.9%).

While this method is not suitable for every subgroup (e.g., it would create bias if used to study the tumor gene that directly modified the treatment effect), it can improve precision without ignoring other measured effect measure modifiers.

Robustness of effect estimates to varying model specifications: an application to statin use and risk of dementia using data from a large healthcare plan Erin Ferguson* Erin Ferguson Scott C Zimmerman Chen Jiang Minhyuk Choi Travis J Meyers Thomas J Hoffmann Paola Gilsanz Jingxuan Wang Akinyemi Oni-Orisan Rachel A Whitmer Neil Risch Ronald M Krauss Chirag Patel Catherine A Schaefer M Maria Glymour

Background: Model specification includes decisions such as sample eligibility; confounder selection; and operationalization of exposure and outcome measures. Effect estimates that are robust to a wide range of reasonable model specifications are most convincing. We assessed variation in the estimated association between statin initiation and risk of Alzheimer's disease and related dementias (ADRD) across many model specifications.

Methods: For 1.5 million Kaiser Permanente Northern California members who initiated statins between 2000-2015, linked electronic health records from 2000-2020 were used to identify ICD diagnoses of ADRD. We compared estimated effect of statin initiation on ADRD incidence from Cox models across 8,200 distinct covariate combinations, considering demographics and clinical factors. We next compared estimates across 1,253 datasets holding the covariate set constant but varying the restriction of multiple enrollments, burn-in and re-enrollment periods, excluding participants with mild cognitive impairment, and changing trial follow-up duration.

Results: Across alternative covariate adjustment sets, the estimated HR for statin initiation ranged from 0.91 to 1.23. Adjusting for diabetes history increased the variance of point estimates (Fig 1A) while age adjustment increased point estimates (1B). Adjustment for other covariates (e.g. healthcare utilization (1C) and low-density lipoprotein cholesterol (1D)) had smaller impacts. Across all datasets using the most adjusted covariate set, the point estimate for statin initiation ranged from 0.94-1.39 (average HR 1.07; SD=0.05), and 61% of these estimates were statistically significant. The variance of estimates across all specifications (variance of ln(HR)=.004) was nearly 6 times larger than the variance of any specific estimate within a single specification (average variance of the ln(HR)=.0007).

Conclusions: The association between statin initiation and ADRD varied based on model specification.

Figure 1. Scatterplots of point estimates versus their standard error for 8,200 models when adjusted (blue) or not adjusted (grey) for: (A) history of diabetes, (B) age at baseline, (C) healthcare utilization, and (D) low-density lipoprotein cholesterol. Estimates for the most adjusted model are represented by the red dot.
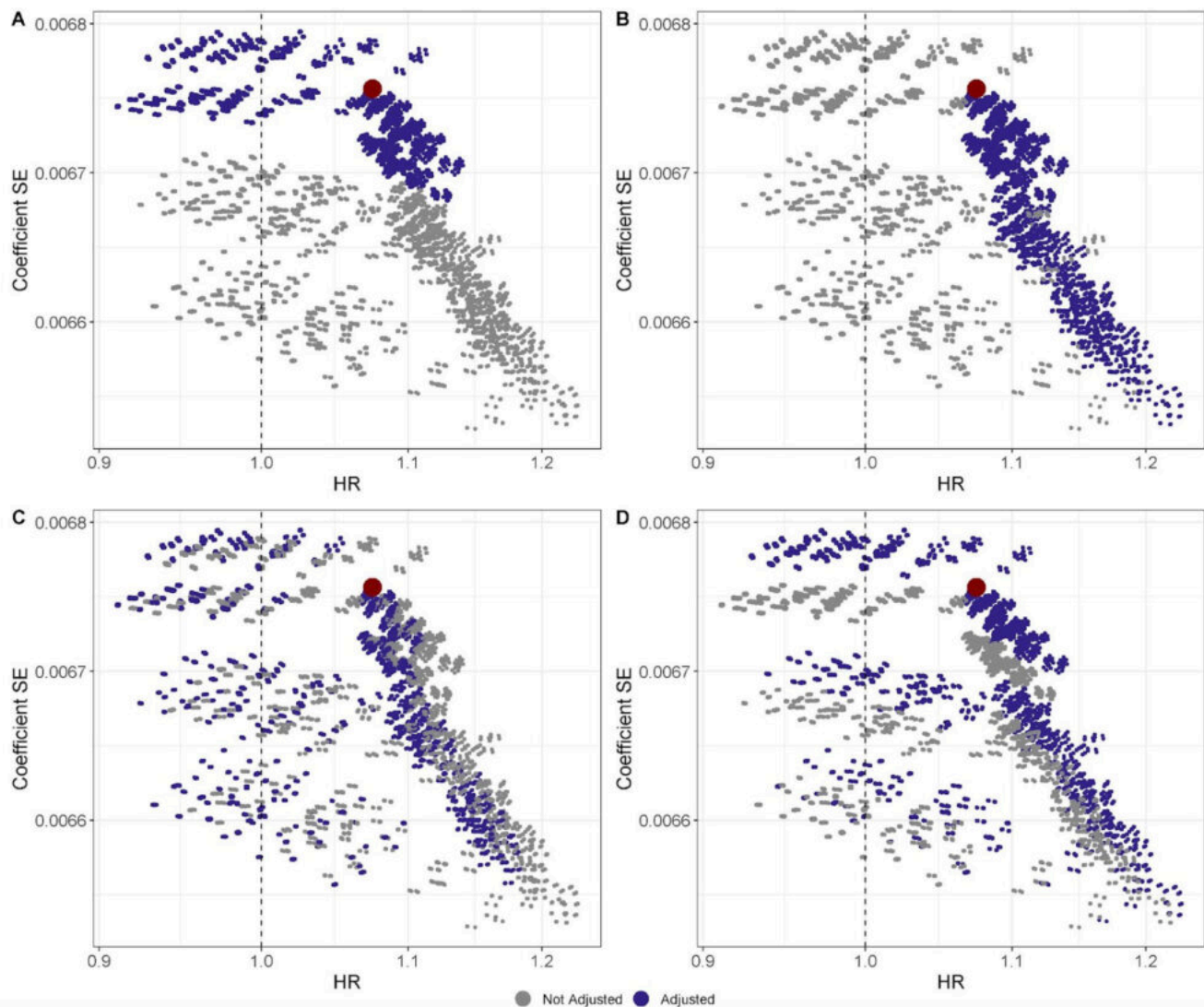
Utilization of locally estimated scatterplot smoothing (LOESS) regression to estimate missing weights in a longitudinal cohort of breast cancer patients Kristina Johnson* Alexa Zimbalist Kelly Radimer Janise Roh Isaac Ergas Charles Quesenberry Marilyn Kwan Lawrence Kushi

Background: Weight data is vital to longitudinal studies that aim to understand how body size may impact breast cancer prognosis. Incomplete data is common in such studies and can lead to biased study results if ignored. Traditional methods to handle missing data rely on making assumptions about missing data patterns. In this study, locally estimated scatterplot smoothing (LOESS) regression models are explored as a data-driven option to minimize missing weight data in a longitudinal cohort of women with breast cancer.

Methods: We identified 10,782 women diagnosed with invasive breast cancer from 2005-2013 at Kaiser Permanente Northern California. Outpatient weights from 2 years pre-diagnosis to 10 years post-diagnosis were included. LOESS regression models were fit to each individual's weight measurements and subsequently used to estimate weights at baseline (breast cancer diagnosis) and 6 follow-up time points (6, 12, 24, 48, 72, and 96 months post-baseline). The LOESS-estimated weights were compared to a traditional method of selecting the weight measurement closest to each timepoint within a time window of 90 days.

Results: LOESS models identified fewer weights compared to the traditional method at baseline (85% vs 92%). However, LOESS models identified considerably more weights at later follow-up periods, particularly at follow-ups 48, 72, and 96 months post-baseline (48 mths: 85% vs 75%; 72 mths: 78% vs 62%; 96 mths: 69% vs 51%). At baseline and the 6 follow-up timepoints, the weight measurements identified by both methods were highly correlated and more than 80% of the weights differed by 2.50 kilograms or less.

Conclusions: LOESS regression identified more weights at follow-up times further away from breast cancer diagnosis in comparison to the traditional method of weight identification. LOESS regression makes effective use of available longitudinal data and may be a beneficial tool to minimize missing longitudinal data in future studies.

Improving Global Burden of Disease Study Male Chlamydial and Gonococcal Infection Estimates via Female Data: a Sex-Ratio Exploratory Model Betyna Berice* Betyna Berice Hannah Han Maegan Ashworth Dirac

Background:
Chlamydia and gonorrhea are common sexually transmitted infections (STIs) and major public health issues worldwide. The overall prevalence of chlamydia and gonorrhea in many countries remains uncertain, with many studies conducted in males at high risk, and notable scarcity of data amongst average-risk males. In contrast, female data are typically collected during antenatal visits. Consequently, accurately quantifying the prevalence in males poses a challenge compared to females. We compared two approaches to estimating the prevalence of these diseases in males, one that borrows information for countries without male data from male data from countries in the same region, and one that borrows information from female data in the same country.

Methods:
Point-prevalence data were extracted from studies of chlamydia and gonorrhea reporting for male, female, or both-sex samples. Sex-specific data-points from the same study were paired to calculate log-sex ratios, which were modeled using the Meta-Regression, Bayesian, Regularized, Trimmed (MR-BRT)tool. These ratios were used to split both-sex datapoints into sex-specific datapoints. Sex-specific data-points were then modeled using a Bayesian meta-regression modeling tool, DisMod-MR 2.1 to estimate age, sex, and location specific prevalence of chlamydia and gonorrhea between 1990 and 2021. In approach one, the outputs of DisMod were considered final estimates of prevalence for both males and females. In approach two, the outputs of DisMod for females were combined with modeled sex-ratios to produce estimates for males in the same location, year, and age-group.

Findings:
Twenty-five studies provided male and female-specific data points for chlamydia, and 12 studies provided male and female-specific data points for gonorrhea. To assess performance of our two approaches, we compared the root mean square error (RMSE) of our male DisMod estimates to the male estimates produced by combining female estimates with modeled sex-ratios. RMSE for approaches one and two were similar; 0.035 and 0.040, respectively, for chlamydia, and 0.008 vs. 0.014, respectively, for gonorrhea, meaning that our two approaches performed similarly in fitting to male data.

Interpretation:
Overall, our two approaches to estimating prevalence of chlamydia and gonorrhea in males perform similarly in-sample. Our next step is to assess out-of-sample performance to determine if male estimates for locations with no local data are more reliably produced via DisMod (borrowing strength from males in other countries in the region) or via sex-ratio methods (borrowing strength from females in the same country). In order to enhance chlamydia and gonorrhea estimates and to provide up-to-date policy-relevant information on their respective trends, we need more population-based data for both males and females.

Methods/Statistics

All Covariates Are NOT Created Equal in Regression Calibration: Severe Bias in Causal Effect May Be Induced by Using Biomarkers to Calibrate True Nutrient Intake Wenze Tang*

Wenze Tang Zihan Qian Molin Wang

Regression calibration is a popular tool used to correct the bias induced by measurement error in continuous exposures. When estimating the causal effect of nutrient intakes on health outcomes, recent studies frequently used nutrient-derived biomarkers, also known as proxies, to calibrate true nutrient intakes, which are typically measured within small feeding studies. For example, a recent study used serum carbohydrate to calibrate true carbohydrate intake and found that higher carbohydrate density (i.e. percentage of energy intake from carbohydrate) was protective of a range of chronic disease outcomes, largely contradicting other sources of evidence. One explanation for such finding may be that using biomarkers to calibrate true nutrient intake can be subject to severe bias, as the biomarkers themselves may be mediating the causal effect of interest, resulting in a violation of the surrogacy assumption, a critical condition required for the validity of the regression calibration method. In this study, we demonstrate, both theoretically and through simulation studies, that the regression calibration estimators cannot be used to identify the total or the controlled direct effect when a proxy of the true exposure such as biomarker is a mediator between the true exposure and outcome. This is proved by quantifying the bias induced when the regression calibration method is inappropriately applied to such mediation settings under simple linear models. Assuming no exposure-proxy interaction, the bias becomes greater when the effect of the proxy on the outcome is greater, or when the correlation between the true exposure and the proxy is close to zero or one. We additionally quantified the bias when an exposure-proxy interaction is present. Finally, we conducted Monte Carlo simulations under a variety of scenarios to investigate the magnitude of finite sample bias for both continuous and binary outcomes.

Methods/Statistics

Optimizing Environmental Surveillance Rebecca Smith* Rebecca Smith Anwesha Chakravarti Bo Li

Environmental surveillance requires collection of samples meant to represent a generalized risk in a specific area. For example, mosquito traps are used to test for the presence of West Nile virus (WNV) in mosquito populations, playing a crucial role in monitoring risk and informing response. But how do you decide where take a sample for environmental surveillance? What makes a good sampling site?

We present a multi-step statistical approach for using longitudinal environmental sampling data to determine the value, or score, of a location in predicting an outcome of interest. This score is then used to understand what landscape, infrastructure, demographic and socioeconomic factors are associated with predictive ability. As a practical example, we apply this method to mosquito trapping in the Chicago metropolitan area and its suburbs and its ability to predict human cases of WNV. We find a minimum threshold for human population in the vicinity of the trap is necessary for overall prediction, with a weighting towards prioritizing sensitivity due to the low number of cases and severity of disease. However, different landscape factors become important for maximizing either sensitivity or specificity of the prediction, indicating that the optimal sampling location may vary based on the relative importance of each of these values.

This approach enables resource-limited environmental surveillance programs to identify better locations for their sample collection, which may help in reducing the number of samples needed while increasing their individual efficiency.

Comparative analysis of methods for identifying multimorbidity patterns among people with opioid use disorder in Ontario, Canada Myanca Rodrigues* Myanca Rodrigues Glenda Babe Tea Rosic Brittany B. Dennis Richard Perez Claire de Oliveira Sameer Parpia Lehana Thabane Zainab Samaan

Background:

Multimorbidity is defined as the co-occurrence of two or more (2+) chronic conditions. As the prevalence of chronic conditions increases, identification of patterns of co-occurring illnesses is crucial to health system planning. Cluster analysis is a commonly used method to identify multimorbidity patterns. However, to-date, studies have focussed on hierarchical cluster analysis (HCA), with a paucity of research examining non-hierarchical cluster analytic methods, such as K-means analysis.

Objective:

Our primary aim was to compare multimorbidity patterns using two methods – HCA and K-means clustering – in our cohort of people with OUD in Ontario, Canada.

Methods:

We linked observational cohort data collected from 3,430 people receiving treatment for OUD between 2011 and 2021 in Ontario, Canada to provincial health administrative databases. We identified 18 chronic conditions, commonly used in multimorbidity studies in Ontario, using ICD-10-CA diagnostic codes and the diagnostic codes of physician billing claims, and followed the cohort over an eight-year period in the data holdings. We used HCA and K-means clustering to identify multimorbidity patterns. Analyses were stratified by sex, with results compared for each method.

Results:

HCA identified 4 clusters for males, and 2 for females. K-means identified 3 multimorbidity patterns for each sex. Although there were some differences by sex and method of analysis, two combinations of disease were observed consistently across sexes and both methods: (i) diabetes, hypertension and stroke, and (ii) asthma and chronic obstructive pulmonary disease.

Conclusions:

Our study findings illustrate that multimorbidity patterns vary depending on the method of analysis used (HCA vs. K-means). We found that HCA was useful for large research datasets for an in-depth examination of multimorbidity, whereas K-means may be better used to identify disease clusters found in clinical practice.

Neurology

Use of U.S. Administrative Data in Muscular Dystrophy Research: A Scoping Review Anne Lyon Havlik* Anne Havlik Natalie Street Seth Perlman Jamie Zimmerman Catharine Riley

Muscular dystrophies (MD) are a group of hereditary muscle disorders that result in progressive muscle weakness, decreasing mobility, and declining quality of life over time. Administrative healthcare data are a valuable resource that can augment public health surveillance and research, especially when small sample sizes are a challenge. A systematic literature search of Medline, Embase, CINAHL, and Scopus was performed to learn how U.S. administrative data have been used to study MD and identify opportunities and gaps in the research. Key search terms used were related to MD, administrative health data, and healthcare utilization, which retrieved 1,270 bibliographic records; 854 unique abstracts and 53 full-text articles were reviewed. A standardized abstraction form was completed by 2 independent reviewers. Fifty studies met eligibility criteria and were included in the review. Studies used different approaches to MD case ascertainment, resulting in methodological and data quality heterogeneity. Seventeen publications included only claims administrative data, 9 included only inpatient administrative data, no publications included only outpatient administrative data, and 24 publications included at least 2 of these administrative data sources and other sources. Fifteen publications focused on pediatric populations, defined as including individuals less than 21 years of age. Thirty-five publications included populations outside of pediatric ages. Gaps identified include addressing differences in ICD code usage for MD subtypes, characterizing MD in young adult and older populations, and utilizing standardized diagnostic criteria as well as multiple sources of ascertainment. This is the first scoping review of MD research using administrative data. Public health implications may include enhanced evidence-based decision-making for individuals living with MD and their healthcare providers.

LATEBREAKER

Neurology

Socioeconomic status and Parkinson's disease in the Cardiovascular Health Study Mireya Long* Mireya Long John D. Beard Evan L. Thacker W. T. Longstreth Shu-Ching Hu Lana M. Chahine

Previous studies about the relationship between socioeconomic status (SES) and Parkinson's disease (PD), a neurodegenerative disease, are few and produced conflicting results. In addition, most of these studies were limited by information bias, lacked prospective data, and lacked multiple measures of SES. The purpose of our study was to utilize the advantages of the Cardiovascular Health Study (CHS) to estimate associations between SES and PD in the US older adult population. CHS is a prospective cohort study of 5,888 adults, including 165 incident PD cases through 2006, from four US communities who were at least 63 years old at enrollment during 1989/90 and 1992/93. SES factors included education, occupation (lifetime and current), and income measured by survey at enrollment. Information on PD was ascertained using a variety of sources and final PD status was adjudicated by two movement disorders specialists. We used log-binomial regression models to estimate risk ratios (RR) and 95% confidence intervals (CI) to estimate associations between SES and PD adjusted for confounders. Compared to participants who worked in professional/technical/managerial/administrative occupations, participants who worked in sales/clerical service occupations had a RR of 1.69 (95% CI: 1.04, 2.77), and those who worked in craftsman/machine operator/laborer/farming/forestry occupations, a RR of 1.67 (95% CI: 1.02, 2.74) after adjusting for confounders. Participants who reported a total combined family income, before taxes, for the past 12 months of $5,000 – $7,999, compared to those who reported $16,000 – $24,999, had a RR of 2.08 (95% CI: 1.16, 3.76) after adjusting for confounders. No other SES factor was significantly associated with PD. We found that income and lifetime occupation may be related to incident PD in CHS. Our results should be confirmed by future studies that use larger samples and dates of PD diagnosis.

Food Insecurity Increases Cardiovascular Mortality Risk Among Latino Americans with Arthritis Sri Banerjee* Sri Banerjee Jagdish Khubchandani May Beydoun Kayla Landry Kayla Landry Michael Goins Jacqueline Gavino Heather Esnaola Ashley Hamm

Food insecurity continues to be increasing, especially after the COVID-19 pandemic. However, complex chronic diseases are connected to food insecurity that result in increasing the risk of other diseases. Hunger, the most extreme form of food insecurity and interrupted eating patterns can have harmful consequences on physical health. In this study we wanted to determine if arthritis is connected to food insecurity among Latino Americans.

The National Health and Nutrition Examination Survey (NHANES) is a nationally representative survey with Latino American respondents from the survey, who were 20 years or older between the years 1999-2010 being included in the analysis with mortality follow-up through December 31, 2019. Food insecurity was determined by the USDA Household Food Security Survey Module questionnaire. Arthritis was determined by physician-diagnosed self-reported data. CVD mortality rate was determined from major cardiovascular disease as the underlying cause of death (*ICD-10: I00-I78*) among United States adults. Complex samples Cox regression was used to assess if food insecurity influenced the relationship between arthritis and cardiovascular (CVD) mortality.

Percent mortality among individuals with arthritis was 6.5% among males and 11.8% among females with mean follow-up of 10.4 years. For CVD mortality, the overall unadjusted hazard ratio (HR) for arthritis to no arthritis was 5.10 (95% confidence interval [CI], 3.43-7.59, p < 0.001). The adjusted HR was elevated, 2.62 (CI 1.32-5.20, p < 0.01), among individuals who had arthritis and food insecure but close to 1.0 (1.09 CI 0.32-3.75, p = 0.53) among individuals who had arthritis and food insecure, after adjusting for medical and demographic risk factors. Similar patterns were not observed within the general population.

This study was the first time that anyone has determined in unadjusted and adjusted models that food insecurity and arthritis combined has worse outcomes than arthritis alone from a nationally representative sample. This was tested to prevent joint diseases and lead to improved outcomes. Food insecurity screening needs to be improved as well to prevent disease. Also, the ethnic disparities on the effect of food insecurity are important to determine. This way disparate dietary patterns and eating habits can be influenced by a person's ethnicity.

Nutrition/Obesity
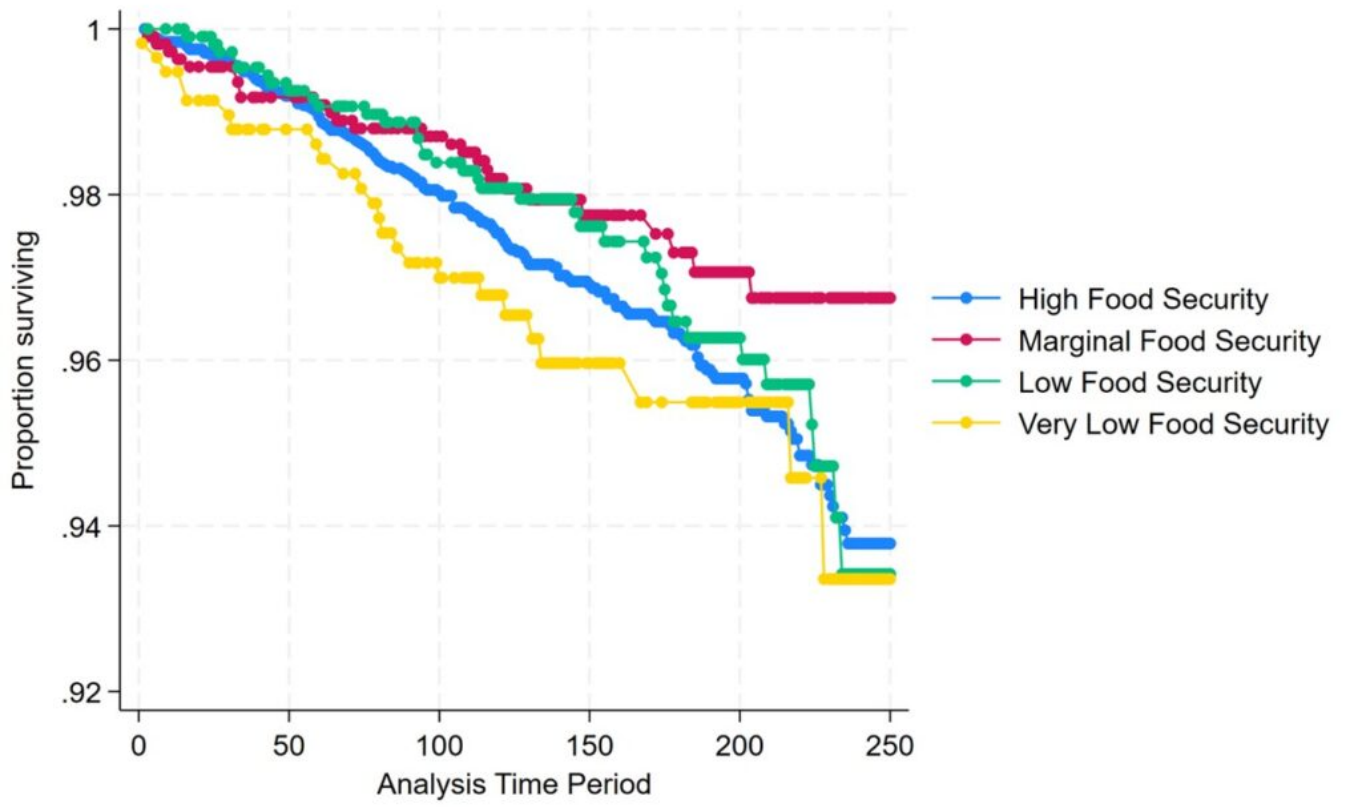
Adolescent dietary patterns in relation to blood leukocyte DNA methylation of circadian genes Jennifer T. Lee* Jennifer Lee Jaclyn M. Goodrich Dana C. Colinoy Karen E. Peterson Martha Maria Tellez-Rojo Alejandra Cantoral Libni Olascoaga-Torres Edward A. Ruiz-Narvaez Erica C. Jansen

Background:

The circadian rhythm, regulated by circadian genes, is involved in multiple metabolic processes and is responsive to diet. The epigenetic modification of DNA methylation (DNAm) is a potential mechanism through which dietary patterns impact health by altering the circadian gene regulation.

Methods:

We conducted secondary cross-sectional analysis of adolescents from the Early Life Exposure in Mexico to ENvironmental Toxicants (ELEMENT) cohort. Dietary intake assessed from a semi-quantitative food frequency questionnaire, three dietary patterns were derived using principal component analysis. Blood leukocytes DNAm was measured with Infinium MethylationEPIC BeadChip to obtain data from 707 CpG sites from 18 circadian genes. Linear regression models was used to examine associations between dietary patterns and circadian genes DNAm, adjusted for age, sex, socioeconomic status, batch effects, and estimated blood cell proportions. A 20% false discovery rate using the Benjamini-Hochberg method was applied to correct for multiple testing. Sex-stratified associations were examined. The Cauchy test (ACAT) was used to assess gene-specific associations.

Results:

Sample included 246 males and 277 females (14.50 ± 2.12 years). A Meat & starchy foods pattern was positively associated with a CpG site, cg19170589, within a CpG island of RORA (β=5.31e-3, 95% CI 2.46e-3 to 8.15e-3, q=0.194). An Eggs, milk & refined grain ("breakfast") pattern was negatively associated with cg13146553 in the gene body of RORA (β=-5.20e-3, 95% CI -7.76e-3 to -2.64e-3, q=0.061) in males. No associations were found with the Plant-based & lean proteins pattern. The ACAT showed significance between Meat & starchy foods pattern with CLOCK (p=0.034), and "breakfast" pattern with NPAS4 (p=0.015).

Conclusion:

Findings suggest dietary patterns among adolescents could result in epigenetic modification of circadian genes, particularly in RORA. Future research may explore the association in a longitudinal design.

Nutrition/Obesity

Temporal Dietary Patterns and Dietary Quality in Older Adults in the US Tuo Lan* Tuo Lan

Background: Although when we eat is as important as what we eat to maintain good health, not much is known about what types of "temporal" dietary patterns exist in a population.

Objective: To identify the temporal dietary patterns (TDPs) that incorporate timing and frequency of eating occasions and examine their associations with diet quality in older adults.

Methods: Adults (mean age = 63 y, n=883) in the Interactive Diet and Activity Tracking in AARP (IDATA) Study completed six 24-hr recalls using ASA24 over 12 months. TDPs based on energy intake were identified by a two-stage hierarchical clustering method that integrates optimal transport and the dynamic time warping distances. Diet quality was assessed by the Healthy Eating Index (HEI)-2015 based on adherence to dietary guidelines for Americans. The analysis of covariance was used to examine mean HEI score by temporal dietary patterns, adjusting for sex, age, race/ethnicity, and BMI.

Results: Four TDPs were identified: morning-to-evening (44.7%), evening-to-night (30.0%), uniform (21.4%) and early morning eating patterns (3.9%, Figure). Individuals with the evening-to-night eating pattern tended to be younger, male, overweight or obese, and have a higher daily energy intake (2151 vs mean=2067 kcal/day), while those with early morning eating tended to be older, non-White. People with a uniform eating pattern tended to have a shorter eating duration (12.4 hours vs mean=13.2 hours) and lower eating frequency (4.2 vs mean=5.2 times/day). Diet quality differed by TDPs (P<0.001). Evening-to-night eating pattern had the lowest HEI-2015 score (mean=58 out of 100), whereas a uniform eating pattern had the highest HEI-2015 score (mean = 62.7). HEI-2015 scores for morning-to-evening and early-morning patterns were 60.6 and 61.9, respectively.

Conclusions: Diet quality is affected by what people eat but also by when they eat.
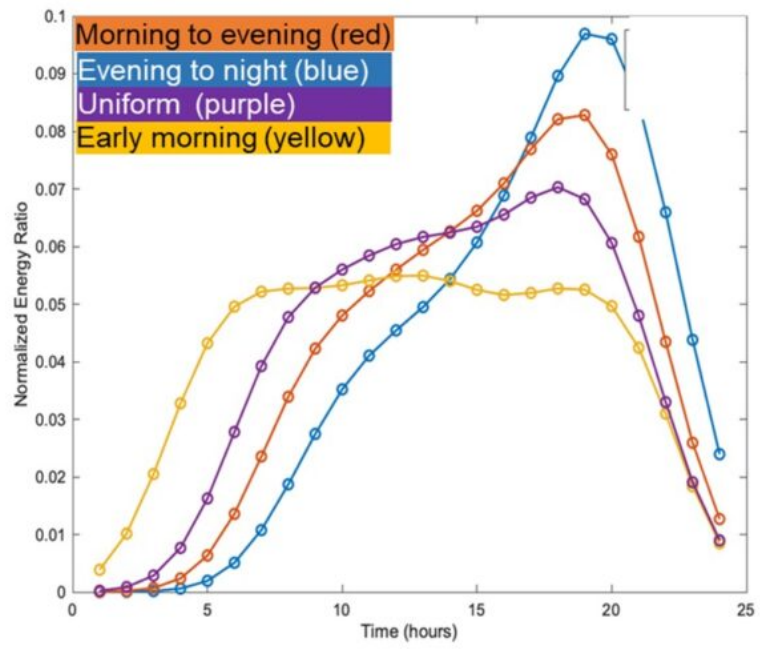
The Impact of Short-Term Exposure to Volatile Hydrocarbons on Fertility: Perspectives from the GuLF Study Rebecca N Noga* Rebecca Noga Jake E. Thistle Elizabeth M. Kamai Patricia A. Stewart Mark R. Stenzel Caroline P. Groth Tran B Huynh Gurumurthy Ramachandran Sudipto Banerjee W. Braxton Jackson II Kate Christenbury Richard K. Kwok Kaitlyn G. Lawrence Dale P. Sandler Lawrence S. Engel Stephanie M. Engel

Background: Petrochemicals benzene, toluene, ethylbenzene, xylene, n-hexane (BTEX-H) and other hydrocarbons have been linked to adverse reproductive health outcomes. Few studies have examined exposures in relation to fertility. **Methods**: We used data from the Gulf Long-Term Follow-Up (GuLF) Study, a longitudinal study of oil spill response and clean-up (OSRC) workers and nonworkers following the 2010 Deepwater Horizon disaster. Of 32,608 participants who enrolled (2011-2013), 10,068 workers (31%) completed a follow-up interview that collected information on fertility (2018-2021). We included participants aged 18-37 at time of exposure with no prior history of infertility and (women) with no history of hysterectomy who were still menstruating at follow-up, resulting in 3,434 participants (2,804 men, 630 women). We defined infertility as no pregnancy conception after 12 months of attempt. Cumulative average exposure to BTEX-H and total hydrocarbons (THC) chemicals were estimated via a job exposure matrix linking air monitoring data to detailed work histories collected at enrollment. We used logistic regression to assess odds ratio (OR) of infertility in relation to BTEX-H and THC exposures, adjusted for age, marital status, education, income, and smoking status. **Results**: Among those eligible, 10% of men and 12% of women reported no pregnancy after 12 months. In men, log-unit increases in BTEX-H and THC levels were all associated with increased odds of infertility (e.g., toluene OR: 1.24, 95%CI: 1.03, 1.49; xylene OR: 1.33, 95%CI: 1.02, 1.75). In women, associations between exposures and infertility were less evident. The odds of infertility were higher with exposures above the median (e.g., toluene OR: 1.44, 95%CI: 0.87, 2.41; ethylbenzene OR: 1.21, 95%CI: 0.73, 2.02). **Discussion**: Short-term exposures to BTEX-H and THC may be associated with increased odds of infertility. Given the exposures' pervasiveness, these associations have large implications for the public.

Occupational

Assessing the impact of unionization on the relationship between workload and health among California janitors Kevin Ru* Kevin Ru Melissa Afterman Max Blumberg Dominic Pina Javier Freire Carisa Harris Ellen Eisen

Background: The COVID-19 pandemic placed substantial strain upon janitorial workers seeking to meet increased cleaning demands. Prior studies among California (CA) janitors found high workload groups had greater odds of adverse physical and mental health outcomes. Yet, there is limited insight on the impact of unionization on these relationships which our study sought to quantify.

Methods: We conducted a cross-sectional survey in 2022 of CA janitors from the Service Employees International Union (SEIU) and a non-union organization, the Maintenance Cooperation Trust Fund (MCTF). Workload exposure was assessed across 16 common tasks, accounting for intensity, frequency, and duration of each to calculate an overall workload index score. These were then categorized into low, medium, and high workload groups. Severe pain was measured using a 10-point numeric scale across 4 body regions while prevalence of anxiety and depression was determined using the PHQ-9 and GAD-7 surveys respectively. Logistic regression was used to assess for associations, adjusting for age and sex.

Results: For severe pain, union workers (N=240) saw 4.19-fold increased odds [95% CI: 1.51-11.64] compared to the reference group in contrast to the 13.35-fold odds in non-union workers (N=120) [95% CI: 4.37-40.77]. For anxiety and depression, high workload groups for both union (N=221) and non-union (N=123) had 2.25-fold [95% CI: 0.9-5.62] and 2.23-fold [95% CI: 0.59-8.45] increased odds respectively compared to the low workload group.

Conclusion: Non-union janitors had increased odds of severe pain prevalence compared to union. In contrast, for depression/anxiety, there was a high prevalence across all janitors, reflecting the mental burden they often face. This study has shown that these associations are worth further exploration and understanding in addressing and reducing occupational health disparities among janitors in California.

Occupational

Childhood and adolescent residential and farm pesticide exposures and inflammatory bowel disease incidence in a U.S. cohort of women
Dazhe Chen* Dazhe Chen Jennifer M.P. Woo Christine G. Parks Kaitlyn G. Lawrence Katie M. O'Brien Robert S. Sandler Dale P. Sandler

Evidence suggests that the human gut microbiome is an important contributor to the pathogenesis of autoimmunity and is affected by early life environmental exposures. Pesticide exposures have been associated with altered gut microbiome in animals and some autoimmune diseases in humans, but no study has examined early-life pesticide exposures in relation to inflammatory bowel disease (IBD). We used data from the Sister Study (2003-2021) to examine self-reported residential and farm pesticide exposures during childhood or adolescence in relation to incident IBD diagnosis after study enrollment. We estimated Hazard Ratios (HR) and 95%CIs using Cox models, with age as the time scale, adjusting for race and ethnicity, attained education, smoking, and birth year. We identified 1,151 self-reported incident IBD cases among 49,263 participants without IBD at enrollment. IBD hazards were elevated among those whose childhood residence was regularly treated with pesticides (HR: 1.26, CI: 1.09, 1.45), including those who ever personally applied the pesticides (HR: 1.47, CI: 1.04, 2.08), compared to those who were never exposed during childhood. We also observed a positive association between IBD and exposure to broadcast pesticide sprays before 1975 (i.e., time of DDT ban) (≥6 times vs. never HR: 1.42, CI: 1.17, 1.74). Among participants who lived on a farm during childhood for ≥1 year (N=9,370), IBD hazards were higher among those who were in crop fields during pesticide application (HR: 1.58, CI: 1.04, 2.40) and who ever personally applied pesticides on crops (HR: 1.79, CI: 1.19, 2.68) or livestock (HR: 1.63, CI: 1.05, 2.54) during childhood or adolescence compared to those without the specified exposure. Results were similar for ulcerative colitis alone (N=945) and when using a stricter definition for IBD that incorporated IBD surgery and medication. Findings provide preliminary evidence on early-life pesticide exposure as a novel risk factor for IBD.

LATEBREAKER

Occupational

Identifying Emerging Issues in Work-related Chronic Disease through Research Partnerships: The NIOSH Chronic Disease Prevention Program Taylor Shockey* Taylor Shockey Raquel Velazquez-Kronen Lauralynn McKernan-Taylor Todd Stueckle Kim Anderson

Background: The National Occupational Research Agenda (NORA) is an innovative partnership program designed to enhance occupational health research and workplace practices. The NIOSH Cancer, Reproductive, Cardiovascular, and Other Chronic Disease Prevention cross-sector (CRC) within NORA works with industry, labor, trade, and academic partners to reduce and prevent occupational chronic disease. The CRC reviewed its 2017 – 2023 program to assess research activity in order to identify strengths and areas for improvement.

Methods: Project plans with CRC goals were gathered from NIOSH databases, while published papers from these projects were identified through searches of scientific reference databases. Projects and papers were coded to each industry sector to evaluate research activity and outputs.

Results: From 2017-2023, 305 projects were funded across 35 CRC-related research activity goals involving 7 industry sectors. Projects examined a diverse range of topics including work stress and cardiovascular disease (CVD), per- and polyfluoroalkyl substances analysis of worker serum samples, and exposure to waste anesthetic gases within the healthcare sector. CRC research yielded important findings including identifying associations between maternal nail technician work during pregnancy and congenital heart defects, and shiftwork in police officers leading to biological changes that increase CVD risk. Areas for improved research effort included work organization interventions to reduce CVD in healthcare and transportation workers, and interventions to reduce adverse reproductive outcomes in service workers.

Conclusion: CRC projects continue to quantify workplace exposures, associated effects, and evaluate interventions to reduce chronic diseases. The CRC actively collaborates with labor, trade, industry professionals and researchers interested in occupational chronic diseases, and is currently seeking partnerships to establish a neurological and renal disease working group.

Occupational

A prospective cohort study on workplace discrimination and risk of alcohol abuse in U.S. workers Jian Li* Jian Li Liwei Chen

Objective: Although growing evidence has suggested that discrimination is a risk factor for alcohol misuse, most previous studies focused on general unspecific discrimination and research on workplace discrimination is sparse. To our best knowledge, there are only 3 cross-sectional studies, all from the U.S., indicating strong associations of workplace discrimination with negative alcohol drinking behaviors. This study aimed to provide the first instance of research evidence examining the prospective association of workplace discrimination with the risk of alcohol abuse.

Methods: Using data from the Midlife in the United States (MIDUS), 1102 workers who had no alcohol abuse at baseline and were followed up to 9 years were included. Workplace discrimination at baseline was measured using a validated 6-item instrument and categorized into three levels by tertile, while alcohol abuse at both baseline and follow-up was assessed using a modified 4-item Michigan Alcoholism Screening Test (MAST). Multivariable Poisson regression was performed to estimate the associations.

Results: The incident alcohol abuse at follow-up was 4.08%. Workers who experienced high exposure to workplace discrimination had a higher risk of alcohol abuse (adjusted RR and 95% CI = 3.15 [1.16, 8.52]) compared to those with low exposure, adjusting for age, sex, race, marital status, education, household income, smoking, leisure-time physical activity, alcohol drinking frequency, and major depressive episode at baseline. A trend analysis showed an exposure-response manner. Further adjustment for other psychosocial work factor (i.e., job strain) did not change the strength of association.

Conclusion: We found workplace discrimination was prospectively associated with a higher risk of alcohol abuse among U.S. workers. Given the impact of alcoholism on disease burden, policy attention regarding interventions addressing discrimination at work is warranted.

County-Level Environmental Quality and Risk of Hypospadias in Arkansas Lydia Famuyide*

Lydia Famuyide Jenil Patel Wendy N. Nembhard

Hypospadias, one of the most common genital defects in boys, affects about 1 in 125 liveborn boys. Although the etiology of hypospadias is most likely due to an interplay of genetic and environmental factors, the exact etiology remains unknown. Several studies have examined the association between a single environmental exposure and the risk of hypospadias, but few have assessed the possible effects of multiple environmental exposures simultaneously. Thus, we aimed to address this gap by assessing the association between cumulative maternal prenatal environmental exposures and hypospadias occurrence in offspring.

We conducted a retrospective cohort study using data from the 2006-2010 Arkansas environmental quality index (EQI), its domains (air, water, land, sociodemographic, and built), and related county-level estimates, matched to data on infants diagnosed with hypospadias and identified from the Arkansas Reproductive Health Monitoring System born 1993 – 2014. We classified the EQI and its domains into quartiles. Crude and adjusted prevalence ratios (PR) and 95% confidence intervals (CI) were estimated from Poisson regression analyses to estimate the association between EQI and the prevalence of hypospadias.

For overall EQI, we observed a higher prevalence of hypospadias among boys born to women living in areas with fair environmental quality, compared to those living in areas with excellent environmental quality (PR=1.43; 95% CI=1.10, 1.87). We found no statistically significant association between the water domain and the prevalence of hypospadias. We also found that boys born in areas with fair air quality had a higher prevalence of hypospadias, compared to those born in areas with excellent air quality.

Our results suggest that while there is a potential positive association between overall poor environmental quality and the prevalence of hypospadias, the specific domains of sociodemographic, air, land, and built environments may play distinct roles.

Cerebral Palsy and the Hispanic-Immigrant paradox in California Births From 2000-2015

Giselle Bellia* Giselle Bellia Zeyan Liew Haoran Zhuo Tormod Rogne

Abstract

Introduction: Previous studies have shown significant racial disparities in Cerebral Palsy (CP) outcomes. Although, the Hispanic population is understudied despite it being the fastest growing minority group in the U.S. Data shows poorer general health outcomes among U.S.-born Hispanic women compared to their foreign-born counterparts. This analysis aims to investigate whether incidence of CP in Hispanic women's offspring differed by the mother's birthplace.

Methods: This statewide cohort study investigated live births that were registered in the California birth records during 2000 to 2015 and were linked to California Department of Developmental Services (DDS) records. Non-Hispanic mothers were excluded from the primary model, resulting in a cohort of 4,233,966 births containing 5,476 CP cases. A sensitivity analysis of only Mexican mothers included 3,514,470 births and 4,515 CP cases. Multivariable logistic regression models were used to estimate odds ratios for CP diagnosis by maternal nativity, adjusting for sex, birth year, mother's age and education, father's age, trimester of prenatal care onset, parity, and multiple births.

Results: CP was 12% more likely to occur in the offspring of U.S.-born Hispanic mothers compared with the offspring of foreign-born Hispanic mothers (OR = 1.12; 95% CI: 1.05-1.19). Similar results were found for Mexican mothers (OR = 1.13; 95% CI: 1.05-1.21) where odds of CP diagnosis were greater among U.S.-born mothers.

Conclusions: In line with previous research into other health outcomes, CP was more likely to be diagnosed in the offspring of Hispanic women born in the U.S. compared to offspring of foreign-born Hispanic women. Future policymakers and investigators working with Hispanic populations should carefully consider how mothers' nativity might be affected by policy and influence developmental disorder outcomes, including for neurological disorders such as CP.

Cerebral Palsy and the Hispanic-Immigrant paradox in California Births From 2000-2015

Giselle Bellia[a*], Maya Wilcox[b*], Tormod Rogne [ab], Haoran Zhuo [ac], Zeyan Liew [ac]

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[b] Department of Chronic Disease Epidemiology, Yale School of Public Health, New Haven, Connecticut
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*These two authors contributed equally to this work

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Trends in on-time vaccination by rural-urban commuting area, National Immunization Survey-Child, 2015-2021 Sophia R. Newcomer* Sophia Newcomer Sarah Y. Michels Alexandria N. Albers Rain E. Freeman Christina L. Clarke Jason M. Glanz Matthew F. Daley

Background: The US Advisory Committee on Immunization Practices (ACIP) recommends multiple vaccine series, most involving several doses, from ages 0-19 months. Most surveillance efforts track completion of series by the 2nd birthday. However, vaccination timeliness is a more sensitive measure of disease protection and quality of immunization services received. Our objective was to quantify trends in on-time vaccination among US children by rural-urban commuting area (RUCA), a measure of urbanicity and rurality.

Methods: We analyzed data from CDC's 2015-2021 National Immunization Survey-Child for children born 2014-2018. Zip code of residence, which is a restricted variable, was merged with RUCA categories from the USDA's Economic Research Service. Our outcome was on-time receipt of the combined 7-vaccine series, determined by comparing the ages when children received vaccine doses to ACIP-recommended ages. We tested an interaction between birth year and RUCA in a log-linked binomial regression model adjusted for socioeconomic, demographic, and household factors. Analyses accounted for the complex survey design.

Results: Among n=59,361 children, 87.7%, 7.1%, and 5.3% lived in metropolitan, micropolitan, or small town/rural RUCAs. Overall, on-time vaccination increased from 28.4% (95% CI: 26.9-29.9%) among children born in 2014 to 36.4% (95% CI: 34.9-38.0%) in 2018. There were differences in this unadjusted trend by RUCA (Figure 1). In the multivariable model, there was a 6.2% average annual increase (95% CI: 4.5-8.0%) in on-time vaccination for children in metropolitan areas. While the trend did not differ for micropolitan versus metropolitan areas (interaction adjusted prevalence ratio [aPR]: 1.02, 95% CI: 0.96-1.08), the rate of improvement was less in small town/rural versus metropolitan areas (interaction aPR: 0.93, 95% CI: 0.87-0.99).

Conclusions: On-time vaccination in early childhood has improved nationally, though rural-urban disparities have widened.

Trends in on-time vaccination by age 24 months among US children born 2014-2018, National Immunization Survey-Child
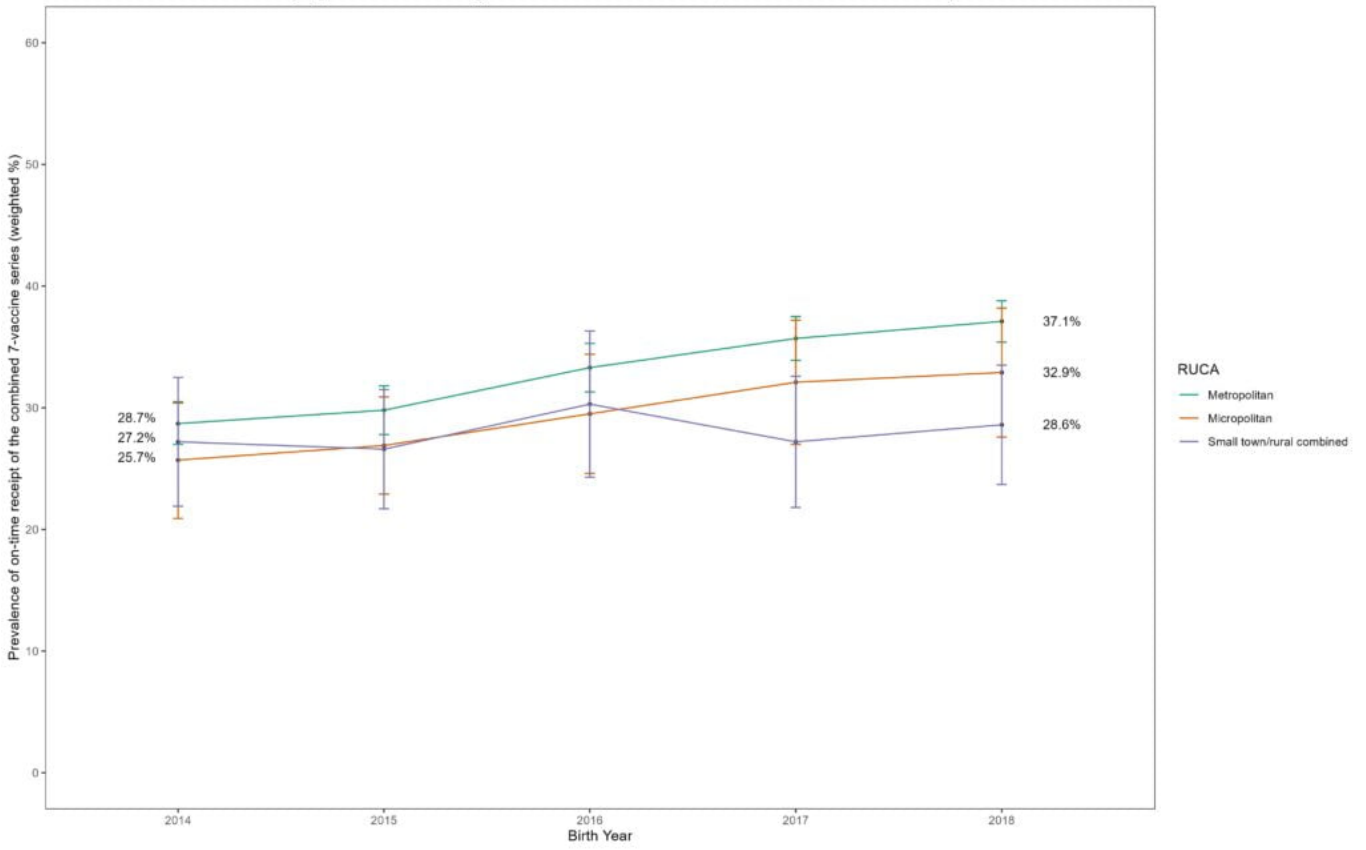
Associations between diphenhydramine and specific birth defects stratified by imputed indication, National Birth Defects Prevention Study and Birth Defects Study to Evaluate Pregnancy exposureS Eva Williford* Meredith Howley Eva M Williford Sarah C Fisher Martha M Werler Julie M Petersen Suzanne M Gilboa Craig Hansen Elizabeth C Ailes Mollie Wood Marilyn L. Browne

Diphenhydramine is used for various indications, including nausea and vomiting in pregnancy, allergy relief, and as a sleep aid. While diphenhydramine has been associated with increased risk for a small number of specific birth defects, findings from National Birth Defects Prevention Study (NBDPS; 1997–2011) were largely null. Yet, confounding by indication may persist as NBDPS did not collect indication. Data from Birth Defects Study to Evaluate Pregnancy exposureS (BD-STEPS; 2014–2019), a study conducted subsequent to NBDPS in a subset of sites, included questions on indication. Thus, we sought to use BD-STEPS data to impute missing indication in NBDPS data and generate estimates of the association between diphenhydramine and 12 birth defects in the combined data stratified by indication.

Cases included infants, stillbirths, or terminations with a birth defect. Controls included live born infants without a birth defect. Mothers of cases and controls reported early pregnancy medication use and BD-STEPS participants reported indication. We used a sequential regression multivariate imputation approach and created 50 datasets imputing missing values, including indication. We used Firth's logistic regression with propensity scores to calculate adjusted odds ratios (ORs) and 95% confidence intervals (CIs) for the association between diphenhydramine and each birth defect stratified by indication. We pooled ORs across the 50 imputed datasets using Rubin's rules.

In NBDPS and BD-STEPS, 461 cases (2–3% of each birth defect) and 341 controls (2%) reported early pregnancy diphenhydramine use; 66% were missing indication, which were all NBDPS participants. The pooled ORs for the 12 defects across the three indications ranged from 0.6 to 2.0; all CIs included the null. Our findings confirm previous NBDPS null findings and suggest that confounding by indication is likely not a large source of bias in studies of early pregnancy diphenhydramine use and the 12 birth defects analyzed.

Association between diphenhydramine and birth defects, stratified by indication.
Odds Ratio and 95% Confidence Intervals

Legend: Nausea and Vomiting in Pregnancy — Sleep Aid — Allergy
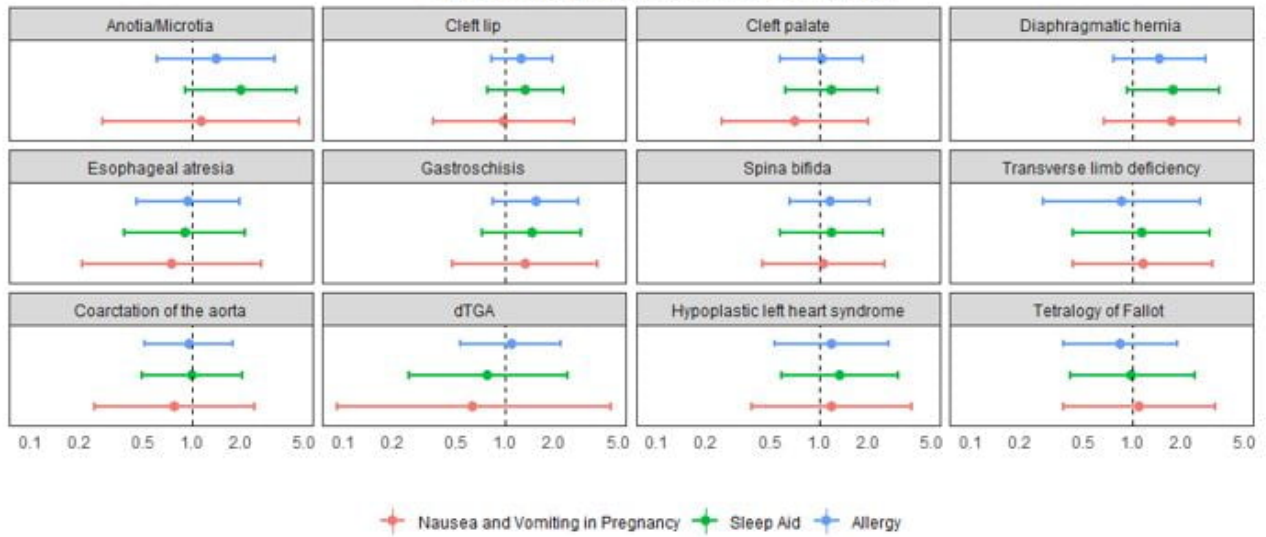
Abbreviations: d-TGA=d-transposition of the great arteries

Perinatal & Pediatric

A Target Trial of Pre-conception Switch from a Legacy Medication to a New Medication – An Application to Antiretroviral Therapy and Birth Outcomes
Ellen Caniglia* Ellen Caniglia Rebecca Zash Modiegi Diseko Judith Mabuta Mompati Mmalane Shahin Lockman Gloria Mayondi Gaerolwe Masheto Joseph Makhema Roger Shapiro

Background: In-utero exposure to certain medications have differential effects on adverse birth outcomes. The introduction of new medications with more favorable safety profiles offers an opportunity to reduce risk by switching from high- to lower-risk medications prior to pregnancy. We emulated a target trial of pre-conception switch from a legacy high-risk medication (nevirapine, NVP) to a new lower-risk medication (dolutegravir, DTG) among individuals with HIV on adverse birth outcomes.

Methods: The Tsepamo Study has performed birth outcomes surveillance at delivery sites in Botswana since 2014. Among individuals on legacy HIV medication (NVP) in 2016, when the programmatic switch to DTG as standard of care began, we compared those who switched to DTG and then became pregnant with those who did not switch prior to pregnancy. We estimated adjusted risk ratios (RRs) for stillbirth, neonatal death, preterm delivery, very preterm delivery, small-for-gestational-age (SGA), very SGA, and combined endpoints of any adverse or severe adverse outcome. We also evaluated low (<50kg) and high (80kg) early pregnancy weight and hypertension in pregnancy.

Results: Of 4,265 eligible individuals, 26% switched from NVP to DTG prior to pregnancy. Comparing switchers with non-switchers, RRs (95% CIs) were 0.82 (0.75, 0.89) for any adverse and 0.84 (0.71, 1.00) for any severe adverse outcome. These differences were driven by SGA and very SGA (**Figure, Left Panel**). Switchers were less likely to have low and more likely to have high early pregnancy weight (**Figure, Right Panel**). Sensitivity analyses indicated little evidence for time-trends in birth outcomes over the study period.

Conclusions: Switching from legacy to newer medications with more favorable safety profiles prior to conception can improve birth outcomes. Among individuals with HIV, switching from NVP to DTG prior to pregnancy may reduce the risk of low maternal weight in early pregnancy and fetal growth restriction.

Figure: Adjusted risk ratios and 95% confidence intervals for adverse birth outcomes (Left Panel) and maternal pregnancy weight and hypertension (Right Panel), comparing pre-conception switchers (NVP to DTG) to non-switchers (NVP), in the Tsepamo Study.
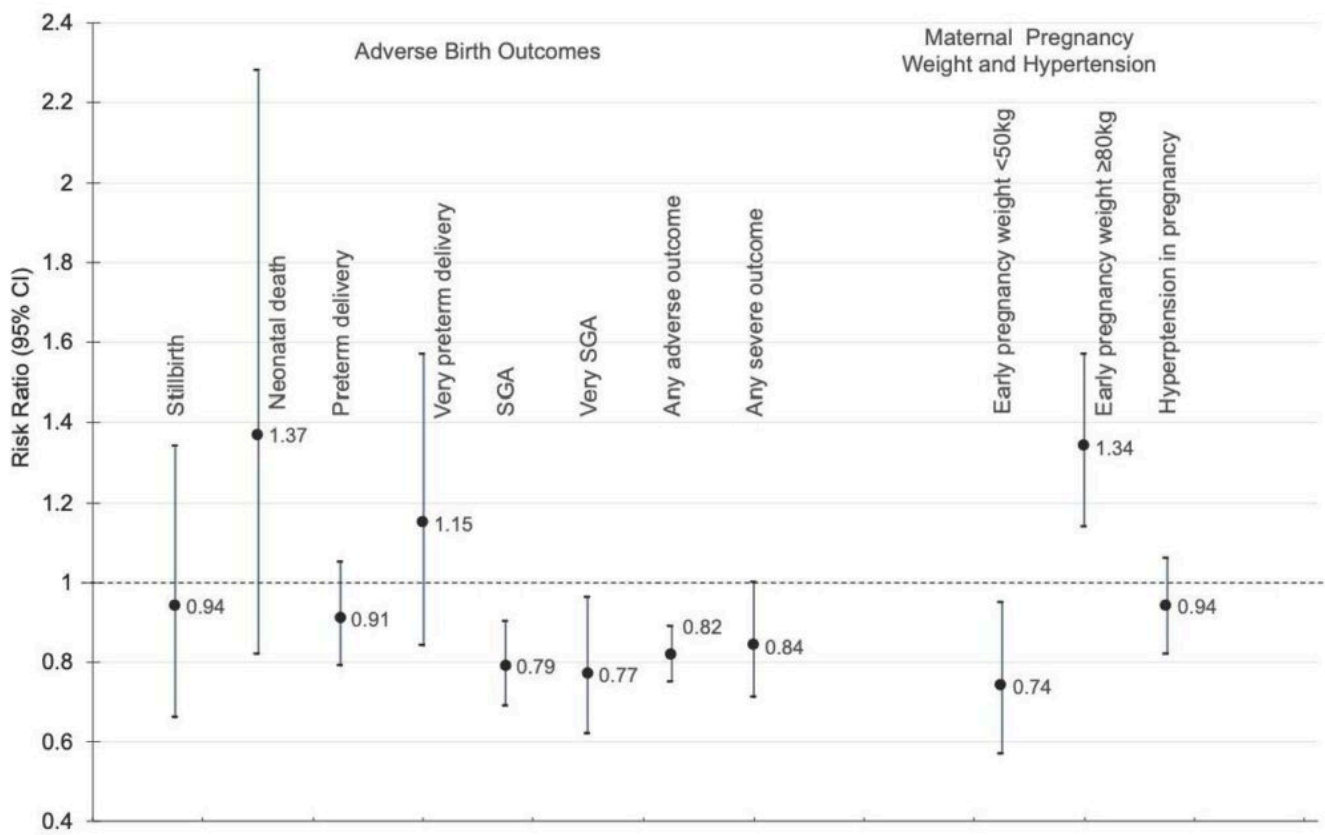
Risk in non-switchers (unadjusted)											
3.9%	1.5%	19.7%	4.2%	25.3%	11.4%	42.8%	17.2%		9.9%	17.6%	25.4%

The association between high residential mobility and maternal perinatal mental health

Katherine Bowers* Katherine Bowers Alonzo Folger Lili Ding

The housing crisis across the U.S. accelerated during the covid-19 pandemic and unstable housing remains a critical obstacle for low-income families. High residential mobility has been associated with poor developmental outcomes in children, potentially due to disruptions in school, medical care, and social support networks. In addition, mobility issues may have an intergenerational effect through stress and the associated emotional health of caregivers who experienced instability. The Pregnancy and Infant Development (PRIDE) Study is a longitudinal birth cohort, nested within a home visiting program that aims to understand how maternal adversity affects child development. We estimated the association between maternal residential mobility and perinatal mental health, a risk factor for poor developmental outcomes in children. **Methods.** Among n=258 moms, we summarized the mobility experience and employed correlations and linear regression, adjusting for socioeconomic factors, to estimate the association between lifetime residential moves and maternal early adversity (ACEs), discrimination, and the maternal perinatal health constructs of depression and anxiety. **Results.** Mothers (mean age 24.8 +/-5.6 years) experienced between 0 and 25 moves in their lifetime, averaging .26 +/-.20 moves/year (median = 0.21, or moving residence every 5 years). The Pearson correlation coefficient between moves/year and perinatal depression was r=0.10 (p value=0.08), and anxiety was r=0.13 (p value=0.03). Adjusting for maternal income and education, moves/year was positively associated with perinatal depression (range 0-24; β=4.03, 95% CI: 0.61, 7.44), and anxiety (range: 0-24; β=3.75, 95% CI: 0.62, 0.68). There were also statistically significant associations between lifetime moves and maternal ACEs (range 0-10; β=6.77, 95% CI:5.26, 8.28) and experiencing discrimination (range: 9-50; β=9.30, 95% CI: 3.39, 15.21). **Conclusions.** The effects of residential mobility are complex. In the PRIDE cohort, an increase in maternal lifetime moves was positively associated with mental health impairment at the time of pregnancy, early adversity, and current experiences of discrimination. Additional analyses are planned to better understand how a mother's mobility experience affects her perinatal mental health.

Association Between Neonatal Abstinence Syndrome Incidence and Male Twin Birth Patterning in the US Parvati Singh* Parvati Singh Alaxandria Crawford

The patterning of male twin live births in a population may respond to adverse socioecological conditions, characterized by research as "collective optimism". In concordance with expectations from the theory of selection in utero which posits that populations respond to adverse circumstances by altering the sex ratio of offspring, studies show a decline in male twins following increased suicides at the population level. The quantification of "collective optimism" through suicides, however, does not offer a direct link to birth outcomes. We use the monthly incidence of births diagnosed with Neonatal Abstinence Syndrome (NAS, withdrawal condition in newborns resulting from prenatal exposure to addictive substances) as a direct indicator of population-level exposure to harmful substances in-utero, and examine consequent changes in the patterning of male twin live births in the US. We utilize national monthly counts of male twin live births, male singleton live births from CDC WONDER, and national monthly counts of NAS births from the National Inpatient Sample database (2003-2019, 204 months). Our analytic data comprise a total of 1,129,713 male twin live births, 333,291 NAS births and 33,850,336 male singleton births, with a monthly mean of 5538, 1634 and 165,933 respectively. We apply ARIMA time-series methods to examine whether male twin live births decline within 0-4 months following higher-than-expected increase in monthly counts of NAS births, controlling for male singleton births and autocorrelation. Results from time-series analyses indicate a decline in male twin births 4 months following increased NAS births in the US, with 100 additional NAS births preceding a decline in 12 male twin live births 4 months later. Our findings contribute to our understanding of the complex interplay between societal challenges and reproductive outcomes, and underscore the potential impact of substance use crises on the biological responses within populations.
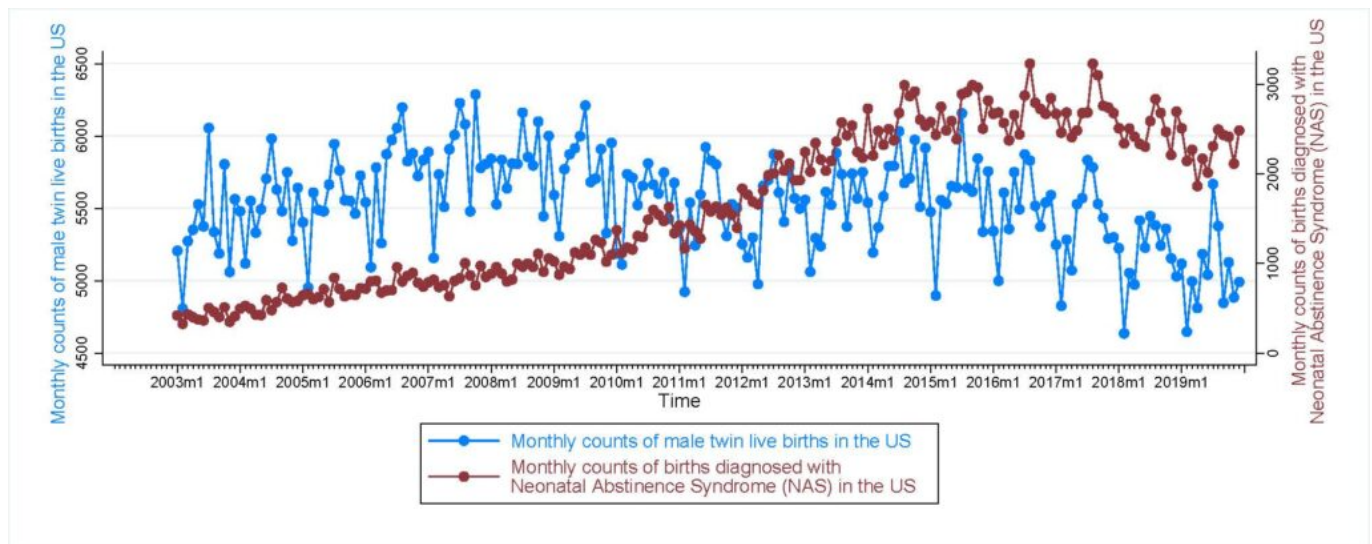
Male twin live births following a universal basic income program in Alaska: A population-level test of selection in utero Parvati Singh* Parvati Singh Nicholas Mark Sarah Cowan

Economic certainty and optimism about the future may underlie birth patterns in a population. In the US, the Alaska Permanent Fund Dividend (PFD), disbursed to all persons residing in the state of Alaska, exhibits a sizeable fertility response. PFD disbursements began in 1982 following operationalization of the Trans-Alaska Oil Pipeline System, with annual payments ranging from $600-$2500, currently ongoing. Increased economic certainty from the PFD may increase optimism about the future, with implications for birth cohort composition and fitness.

The theory of selection in utero posits that unfavorable external circumstances increase sex-specific spontaneous abortions (or miscarriages) during pregnancy, with higher likelihood of male fetal loss relative to female. As a corollary, periods of social prosperity may precede an increase in male live births owing to better survival and reproductive success during favorable external circumstances. Male twin gestations appear particularly sensitive to selection in utero and occupy the left tail of the gestational frailty distribution. Multiple studies report changes in the patterning and volume of male twin live births as a strong marker of external circumstances, including ambient stress and collective optimism.

We examine whether the odds of male twin live births increased within 3-6 months (consistent with prior research) following month and magnitude of amounts disbursed through the Alaska PFD using Alaska vital statistics birth data from 1980 to 2019. We use Autoregressive Integrated Moving Average (ARIMA) time-series methods to account for autocorrelations in births. Results from ARIMA analyses indicate an increase in the odds of male twin live births 3 months following $1000 increments in PFD receipt (coefficient = 0.0016, $p < 0.05$). These results remain consistent upon outlier adjustment. Our finding supports reduced selection in utero following increase in income receipt from the Alaska PFD.

Pre-Pregnancy and First-Trimester Hair Cortisol Predicts Preterm Birth in Pregnant Women in Perú: A Causal Inference Model Richard Künzel* Richard G. Künzel Yinxian Chen Sixto E. Sanchez Marta B. Rondon Nelida I. Pinto Elena Sanchez Clemens Kirschbaum Linda Valeri Karestan C. Koenen Bizu Gelaye

Approximately 87% of pregnant women in Perú have experienced at least one traumatic life event. Traumatic life events and other forms of psychological stress have frequently been associated with preterm birth (PTB), but the underlying biological mechanisms remain unclear. A promising biological mechanism is the hypothalamic-pituitary-adrenal (HPA) axis, a system involved in both, stress, and pregnancy regulation.

Investigating N = 1,808 pregnant Peruvian women, we examined the effect of pre-pregnancy and first-trimester hair cortisol (HCC) and hair cortisone concentrations (HCNC), which are novel chronic biomarkers of the HPA axis, on the risk of PTB. Using propensity scores to create stabilized inverse probability weights, we construct marginal structural models for causal association estimation.

While both independent one-log-unit increases from the population-mean pre-pregnancy HCC (Risk Ratio (RR) = 0.87; 95%CI: 0.64, 1.19) and HCNC (RR = 0.82; 95%CI: 0.59, 1.14) were associated with decreased risk of PTB, first-trimester HCC (RR = 1.50; 95%CI: 1.13, 2.01) and HCNC (RR = 1.41; 95%CI: 1.06, 1.87) were linked to increased PTB risk. Interestingly, if HCNC had been elevated in both, pre-pregnancy and first trimester, the increased PTB risk due to the elevated first-trimester HCNC would have been attenuated (RR = 1.07; 95%CI: 0.75, 1.52) compared to a HCNC increase only in the first trimester (RRpre-pregnancy*first trimester = 0.76, 95%CI: 0.63, 0.91). Furthermore, the HCNC/HCC ratio, which is thought to represent 11β-HSD-2 activity, was negatively associated to PTB in all occurrences.

Our findings show that corticosteroid levels before and in early pregnancy are linked to PTB risk. Moreover, our results implicate that the temporal trajectory of chronic corticosteroid concentrations, which may be influenced by previous experiences of traumatic life events or psychological distress, is crucial for PTB prediction.

Adverse childhood experiences and timing of pubertal onset in a racially and ethnically diverse cohort of adolescents in Northern California Ai Kubo* Sara Aghaee Julia Acker Julianna Deardorff Ai Kubo

Earlier puberty is associated with mental and physical health conditions throughout the life course. Girls who experience psychosocial stress appear to develop earlier than their peers. Adverse childhood experiences (ACEs) increase the risks of numerous chronic conditions. Previous studies on childhood adversity and puberty were limited by small samples, limited puberty data (i.e., age at menarche only), exclusion of boys, and racially/ethnically homogeneous samples.

We used a diverse cohort of 21,728 boys and 19,319 girls born at a Kaiser Permanente Northern California facility from 2003-11. Pubertal outcomes were determined using pediatrician-assessed Tanner stages during routine well-child visits. Girls are assessed for breast development (thelarche) and their first menses (menarche); boys are assessed for testicular enlargement (gonadarche); and both are assessed for pubic hair development (pubarche). Exposure is the highest reported ACEs score, measured using the standard 10-item questionnaire which has been administered during pediatric visits since 2021. We used adjusted Weibull and logistic regression models.

There were clear dose-effect relationships between ACEs and earlier pubertal timing in girls (p<0.01). Associations were greatest among girls with ≥7 ACEs (thelarche: adjusted HR=1.28, 95% CI=1.01-1.61; pubarche: HR=1.25, 95% CI=1.00-1.57; menarche (ref= ≥12 years): adjusted OR= 1.73, 95% CI=1.17-1.54), compared to those with no ACEs. There were significant interactions between ACEs and race/ethnicity in the thelarche models, with the strongest associations found in White and Black girls. There were no associations among boys.

These results suggest that girls' pubertal timing is more vulnerable than boys to exposure to early life adversities. Because early puberty is linked to numerous adverse outcomes over the life course, screening for ACEs and intervening with high-risk children early will help improve adolescent mental health and reduce disparities.

Why has gastroschisis been increasing over time and why is it more common in infants of young mothers? Rashida S. Smith-Webb* Rashida Smith-Webb Gary M. Shaw Peter H. Langlois Cynthia A. Moore Martha M. Werler National Birth Defects Prevention Study

Background: Gastroschisis, a severe abdominal wall defect, is more prevalent in infants of young mothers and has been increasing over the past decades. Various factors have been associated with an increased risk for gastroschisis independent of maternal age. However, studies have not systematically explored whether these factors can explain the time trend or age association. We examined whether factors previously associated with gastroschisis in the National Birth Defects Prevention Study (NBDPS) can explain the increasing prevalence over time and the inverse association with maternal age.

Methods: We used data from the NBDPS for gastroschisis cases and controls with delivery dates from 1997-2011. We calculated crude ORs for the time trend (birth years 2005-2011 vs. 1997-2004) and maternal age (<25 vs. 25+ years). We then evaluated the potential confounding effects of 18 factors separately (exposures: alcohol, cigarettes, illicit drugs, oral contraceptives, cold/flu+ fever, genitourinary infection, polycyclic aromatic hydrocarbons (PAHs), diet quality, BMI; reproductive: parity, interpregnancy interval; social: race, acculturation, income). We considered an exposure a confounder if the crude OR (cOR) for the time trend or maternal age changed by at least 10% in logistic regression models.

Results: The cOR for the time trend was 1.28; 95% CI: 1.14, 1.44, and was attenuated by at least 10% after adjustment for exposure to PAHs (any occupational OR = 1.12; 0.96, 1.30; cumulative across all jobs OR = 1.11; 0.96, 1.30). The cOR for young maternal age was 7.76 (6.71, 8.97). The maternal age OR was attenuated after adjusting for paternal age by 30% (OR = 5.43; 4.55, 6.48) and parity by 15% (OR = 6.62; 5.71, 7.68). Adjustment for other factors did not materially change the cORs for either the time trend or maternal age.

Conclusion: None of the parental exposures examined substantially accounted for the increasing time trend or the higher prevalence among younger mothers.

Association between density of food retailers and fitness centers and gestational diabetes mellitus in Eastern Massachusetts Matthew Shupler* Stefania Papatheodorou Matthew Shupler Jochem Klompmaker Michael Leung Joshua Petimar Jean-Philippe Drouin-Chartier Peter James Anna Modest Michele Hacker

Background: Few studies have investigated the association between the food and physical activity environment with the risk of gestational diabetes mellitus (GDM) with conflicting results.

Methods: Medical records from 68,779 pregnant individuals living in Eastern Massachusetts from 2000-2016 were linked by residential address to the density of supermarkets, fast-food restaurants, full-service restaurants, convenience stores, and fitness centers at 500-, 1000- and 1500-meter (m) buffers. Two indices ('healthy food index'; 'restaurant ratio') assessed the relative availability of healthy versus unhealthy food retailers. Multivariable logistic regression quantified the association between exposure variables and GDM odds, adjusting for individual and area-level characteristics. Effect modification by socioeconomic status (SES) was assessed using the Area Development Index (ADI).

Findings: In the fully adjusted model, pregnant individuals living in areas with the highest density of fast-food restaurants had higher odds of GDM compared to individuals living in areas with the lowest density (500 m (odds ratio (OR):1.17 95%CI:[1.04,1.34]), 1000 m (1.36 95%CI:[1.16,1.59]), and 1500 m (1.15 95%CI:[0.97,1.36]). While other exposure variables were not associated with GDM odds, there was significant effect modification by ADI. Among participants living in the lowest SES (highest ADI) neighborhoods, those living in the highest supermarket density tertile had significantly lower odds of GDM at all buffers (500 m; 1000 m; 1500 m. The association between fast-food restaurant density with GDM odds was greater in lower SES areas.

Interpretation: A greater number of fast-food establishments, particularly in low SES neighborhoods, and a lower density of supermarkets in high SES areas were associated with higher GDM risk in Eastern Massachusetts.

500 m buffer

Fast food restaurant density

Healthy food index

Restaurant ratio

Supermarket density

Odds of gestational diabetes (95%CI)

1500 m buffer

Fast food restaurant density

Healthy food index

Restaurant ratio

Supermarket density

Odds of gestational diabetes (95%CI)

Food environment exposure (ref='Low')
- High
- Medium
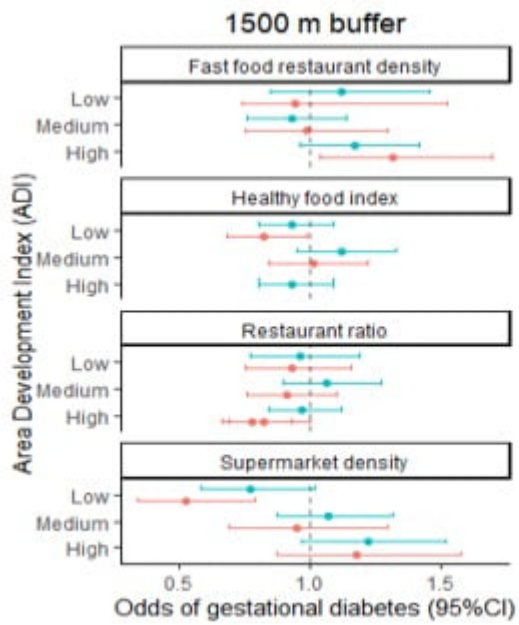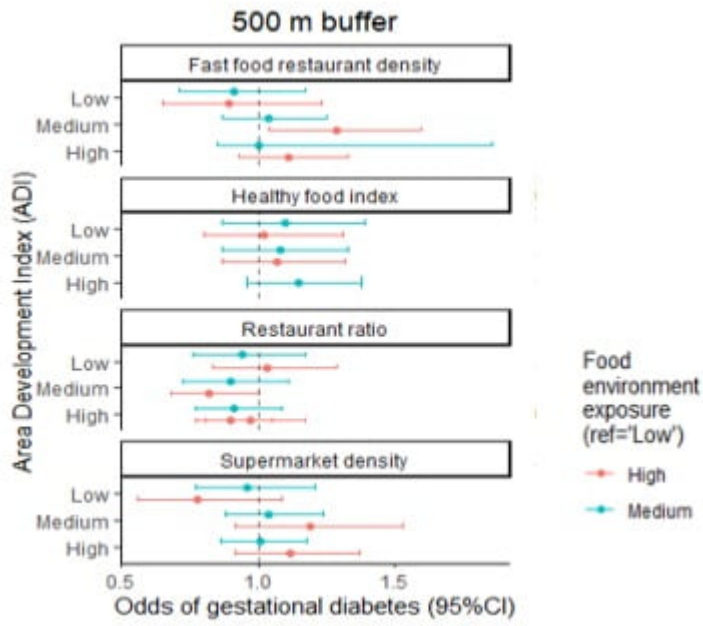
A Statewide Sibling Study of Cerebral Palsy in California Haoran Zhuo* Haoran Zhuo Tormod Rogne Zeyan Liew

Background and Aim Sibling design has gained popularity in epidemiologic research, but no study has been performed for cerebral palsy (CP). We developed the first sibling study on CP to evaluate the robustness of several identified and suspected risk factors of CP against uncontrolled confounding.

Methods Within a cohort of singleton births of 2007-2015 in California and CP diagnosis ascertained from a statewide registry, we identified discordant siblings (1213 CP and 1544 non-CP siblings) born to the same biological mothers. We performed logistic regression on the full cohort and conditional logistic regression on the sibling data to evaluate the associations between CP and a priori selected maternal factors (e.g. pre-pregnancy BMI, cigarette smoking, gestational weight gain), pregnancy/obstetric complications (e.g. preeclampsia, gestational diabetes, infections), and neonatal adverse birth outcomes (e.g. preterm birth, low birth weight, low Apgar score). Sensitivity tests were performed to evaluate the impacts of the carryover effect and generalizability when using sibling design.

Results The association between a strong risk factor, preterm birth, and CP was robust in the full cohort (OR=4.6, 95% CI 4.3-4.9) and the sibling analysis (OR=3.3, 95% CI 2.6-4.2). Similar findings were also on other investigated neonatal factors and maternal obstetric complications. On the contrary, the observed associations between maternal pre-pregnancy BMI, gestational preeclampsia, and gestational diabetes in the cohort (ORs range 1.2-1.4) were attenuated towards the null among siblings. Although maternal insufficient gestational weight gain and cigarette smoking were consistently associated with CP in the sibling data, our sensitivity analysis indicated that these lifestyle factors may be susceptible to the carryover effect. Other assumptions, such as the generalizability of the sibling analysis to the full cohort, did not impact our findings.

Conclusions Several investigated maternal and neonatal factors of CP remain robust in the sibling design, while uncontrolled confounding needs to be considered for pre-pregnancy BMI and some pregnancy complications. We demonstrated that if appropriately applied, a sibling design is useful to enhance causal inference of the etiological research findings of CP.

Akkermansia muciniphila modifies the association between prenatal metal exposure and childhood depressive symptoms Kiran P. Nagdeo* Kiran P. Nagdeo Vishal Midya Jamil Lane Libni A. Torres-Olascoaga Gabriela Gil Martínez Megan K. Horton Chris Gennings Martha Maria Téllez-Rojo Robert O. Wright Manish Arora Shoshannah Eggers

Background: Emerging research suggests that prenatal metal exposure and gut microbiome (GM) disruptions are associated with depressive disorders. Akkermansia muciniphila, a GM bacteria, has been studied for its potential antidepressant effects. However, its role in influencing the association between prenatal metal exposures and depressive symptoms in later childhood is not known. We investigated whether the presence of A. mucinipnila in the GM of 9-11-year-olds modifies the associations between specific groups of prenatal metal exposures (metal-clique) and concurrent depressive symptoms.

Methods: We leveraged existing data from a subset of 112 participants in the Programming Research in Obesity, Growth, Environment, and Social Stressors (PROGRESS) cohort. Metal concentrations (Pb, As, Cd, Cr, Zn, Se, Sb, Cu, Cs, Co, Mn) were measured in 2nd and 3rd trimester maternal whole blood. Stool samples were collected at 9–11 years of age and underwent GM assessment by metagenomic sequencing. A. muciniphila presence was detected using GM data. Children's Depression Inventory (CDI) was administered to 9-11-year-olds. We used a combination of interpretable machine learning and regression framework to identify specific groups of prenatal metals that are predictive and associative with depressive symptoms.

Results: We identified a three-component metal-clique consisting of high Zn and low Cr in the second trimester and low Co in the third trimester, characterizing a sub-group of 40.9% children. This metal-clique was significantly associated with increased log-transformed, t-scored CDI score (log-tCDI)(b[95%CI]=0.08[0.02,0.13]). The presence of A. muciniphila was associated with significantly decreased log-tCDI(b[95%CI]= -0.13[-0.21,-0.04]). Among children with no A. muciniphila, this metal-clique was significantly associated with increased log-tCDI (b[95%CI]=0.11[0.05,0.18]); whereas, for children with A. muciniphila, this same metal-clique, was associated with decreased depression score (b[95%CI]=-0.05[-0.16,0.06]).

Conclusion: We found suggestive evidence that A. muciniphila may modify the association between prenatal exposure to a particular group of metals (or metal-clique) and depressive symptoms in late childhood.

(A) Association with log(t-CDI), prenatal metal cliques and Akkermansia muciniphila

Metal clique:high Zn at 2T & low Cr at 2T & low Co at 3T (40.9%)

Indicator for No Akkermansia Muciniphila (77.3%)

Indicator for children with Metal clique but No Akkermansia Muciniphila (31.8%)

Indicator for children with Metal clique and Akkermansia Muciniphila (9.1%)

Beta (95% CI)
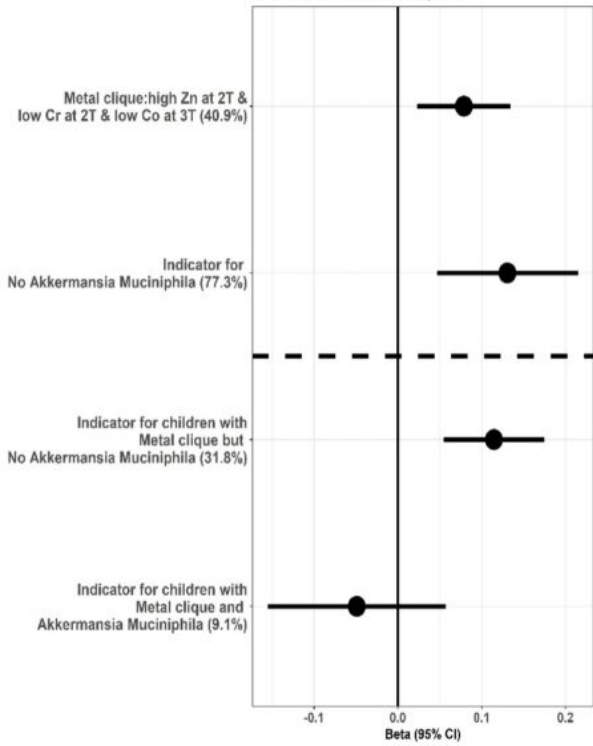
(B) Spearmen correlation between metal clique, its components and absence of Akkermansia Muciniphila

	Co at 3rd trimester	Zn at 2nd trimester	Cr at 2nd trimester	Metal clique	Indicator for absence of Akkermansia Muciniphila
Indicator for absence of Akkermansia Muciniphila	-0.02	0.08	0	0.01	1
Metal clique	-0.39	0.28	-0.63	1	0.01
Cr at 2nd trimester	0.12	-0.12	1	-0.63	0
Zn at 2nd trimester	-0.2	1	-0.12	0.28	0.08
Co at 3rd trimester	1	-0.2	0.12	-0.39	-0.02

Corr
-1.0 -0.5 0.0 0.5 1.0

Perinatal & Pediatric
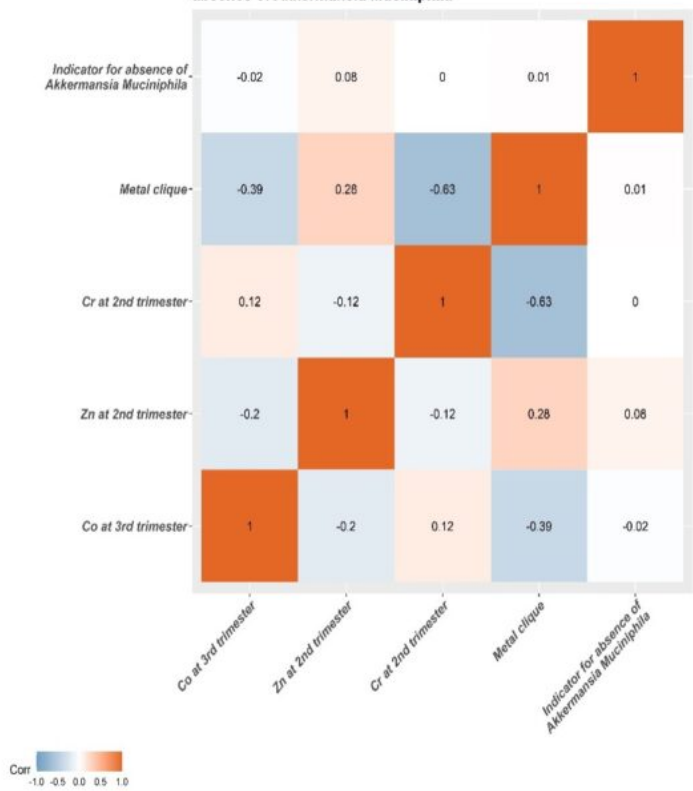
Childhood maternal depression and offspring's brain cortical and subcortical volumetric change Yuna Koyama* Yuna Koyama Henning Tiemeier

Maternal depression is a known risk factor for children's abnormal brain development. However, current views on maternal depression and child brain morphology were built upon region-of-interest analyses, cross-sectional studies, and clinical samples. In recent longitudinal prospective studies, brain imaging was completed predominantly one or two times only and precluded early childhood, when the brain structure undergoes tremendous change. We overcame these previous drawbacks using repeated structural brain imaging from age 4.5 to 10.5 years old (maximum of four time points measurements). Data of 217 children from the Growing Up in Singapore Towards healthy Outcomes cohort was analyzed. Maternal depression was measured with a questionnaire when children were 4.5 years old. After carefully considering outliers and conducting outcome imputation, linear mixed models were applied to repeated brain assessments to explore within-sample variations. First- and second-order age variables were included to consider the non-linear shape of the volumetric development. In the cross-sectional analysis, maternal depression was associated with left postcentral cortical volume at 6 years old (β = -0.216, 95%CI = -0.322 to -0.109, padj = 0.007). In the longitudinal analysis, we found that maternal depression was associated with curvilinear changes (/year2) in volumes of left pars triangularis (β = 0.017, 95%CI = 0.010 to 0.024, padj < 0.001), left supramarginal (β = -0.019, 95%CI = -0.027 to -0.011, padj < 0.001), left precentral (β = -0.020, 95%CI = -0.030 to -0.010, padj = 0.002), and left pars opercularis cortices (β = 0.019, 95%CI = 0.009 to 0.029, padj = 0.005). Graphically, regionally distinct patterns of the associations with developmental trajectories were observed. The frontal region (pars triangularis, pars opercularis, and precentral cortices) showed a steeper reduction in volumes or smaller volumes among children with depressed mothers compared to those with non-depressed mothers. In contrast, the parietal region (supramarginal cortex) showed an opposite pattern. In conclusion, exposure to maternal depression in early childhood was associated with cortical volumetric changes in several regions from frontal to parietal cortices throughout childhood.

Frontal cortex

Pars triangularis cortex volume [mm³]

Precentral cortex volume [mm³]

Pars opercularis cortex volume [mm³]

Parietal cortex

Supramarginal cortex volume [mm³]

Maternal depressive symptoms [SD]   -1   0   1
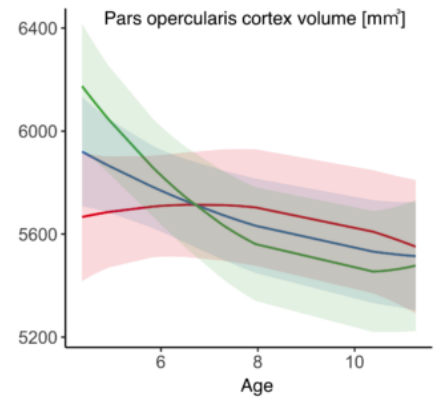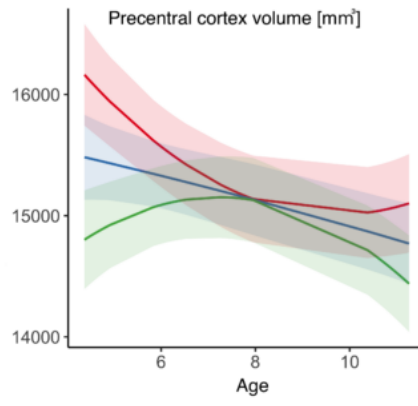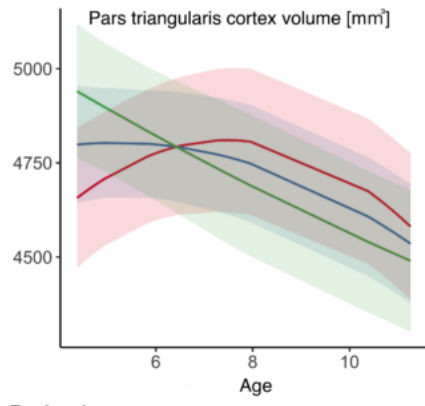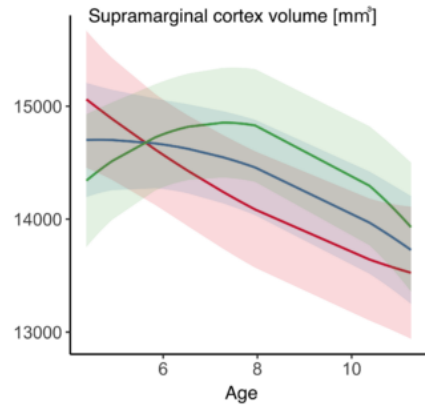
Paternal and Maternal Exposures to Per- And Polyfluoroalkyl Substances (PFAS) and Birth Outcomes: A Multi-Country Cohort Study

Pengfei Guo* Pengfei Guo Jiajun Luo Onyebuchi A Arah Gunnar Toft Zeyan Liew

Background Maternal prenatal exposures to per- and polyfluoroalkyl substances (PFAS) have been linked to adverse birth outcomes. However, few investigations have considered paternal PFAS exposure. We estimated the parent-specific associations of prenatal PFAS exposures with adverse birth outcomes.

Methods This study included 498 couples from the INUENDO cohort recruited at antenatal care visits in Greenland, Poland, and Ukraine during 2002-2004. We measured five major types of PFAS in matched parental serum during pregnancy (median week of gestation: 30). We analyzed three birth outcomes ascertained from medical records, including gestational age, birth weight, and birth length. We used weighted least square linear regression to evaluate parent-specific associations of serum-PFAS with the birth outcomes, adjusting for parental co-exposures and covariates. We also used quantile g-computation for mixture modeling of the birth outcomes of paternal and/or maternal exposures to multiple PFAS.

Results No associations were found between maternal and paternal PFAS exposures and gestational age. However, a higher level of maternal serum perfluorooctanoate (PFOA) was linked to a tendency towards lower birth weight and smaller birth length, after adjusting for paternal PFOA. Paternal exposure to four PFAS (except PFOA) was associated with lower birth weight or birth length, but the estimated effect sizes were small. The mixture analyses did not reveal apparent joint exposure effects.

Discussion Although we did not find conclusive evidence, some imprecise and parent-specific associations were noted for offspring lower birth weight or shorter birth length in relation to higher maternal serum PFOA or paternal serum PFOS, PFNA, PFDA, and PFHxS. Further investigations are needed to better understand parent- and sex-specific effects of prenatal PFAS exposures on offspring growth and development.

Fetal body composition in twins and singletons – are twins programmed to be smaller?

Jessica L. Gleason* Jessica Gleason Wesley Lee Zhen Chen Kathryn A. Wagner Daniel He William A. Grobman Roger Newman Seth Sherman Edward Chien Robert Gore-Langton Luis Goncalves Katherine L. Grantz

Background: Twins and singletons have different fetal growth trajectories, with twin growth significantly slowing beginning in the third trimester of gestation relative to singletons. These differences may represent normal physiological adaptation in otherwise uncomplicated twin pregnancies. However, there is a lack of information about the sequential progression of fetal soft tissue development in both singleton and twin pregnancies.

Methods: In the NICHD Fetal 3D Study, serial abdominal and thigh measurements were obtained using three-dimensional ultrasonography in dichorionic twins (n=306) and singletons (n=2,525). Using linear mixed effects models, we compared marginal means at each week of gestation (15-36) for the following fetal soft tissue parameters: abdominal area, maximum subcutaneous tissue thickness (MSCTT), fractional thigh volume (TVol), fractional fat thigh volume (FFTVol), fractional lean thigh volume (FLTVol) and a FFTVol/TVol ratio, adjusting for relevant covariates.

Results: Twin abdominal measures were slightly larger than singletons from 17-26 weeks for area (2.1-41.3 mm2) and 18-24 weeks for MSCTT (0.04-0.07 mm) and becoming smaller thereafter (area=24.1-303.1 mm2; MSCTT=0.04-0.35 mm). Beginning at 15 weeks, thigh volumes were smaller for twins (diffTVol= -0.09 cm3, 95% CI: -0.13, -0.05; and diffFFTVol= -0.07 cm3, CI: -0.12, -0.02) relative to singletons, persisting through 36 weeks (diffTVol= -6.77 cm3, CI: -10.0, -3.52 and diffFFTVol= -4.98 cm3, CI: -7.93, -1.71). FLTVol was also smaller for twins in all weeks of gestation. For the FFTVol to TVol ratio, twins still had a 1.3-3.2% smaller fat percentage for all weeks of gestation compared to singletons.

Conclusions: Despite third trimester twin growth deceleration, our discovery that twin thigh volumes consistently remain smaller from 15 weeks of gestation implies that twin growth adaptation may be predetermined in early pregnancy at a time when there is less competition for in-utero resources.

Smoking during pregnancy and second and third-generation health outcomes in a population-based multigenerational cohort Michelle Pearl* Michelle Pearl Kimberly Berger Alan Hubbard Peyton Jacob Gayle Windham Marty Kharrazi

Background: Smoking tobacco during pregnancy directly exposes the fetus (second generation [G2]) and their early reproductive cells (third generation [G3]) in addition to the pregnant person (first generation [G1]). Limited studies from mostly White cohorts have reported changes in G2 cardiometabolic health and G3 asthma, birthweight and neurodevelopment associated with *in utero* exposure to G1 smoking. We investigated the health effects of G1 smoking on pre-pregnancy obesity and chronic hypertension in G2, and very-preterm birth (<32 weeks gestation) and autism spectrum disorder (ASD) in G3, in White and Black cohorts.

Methods: Race-stratified case-cohort samples were drawn from all California birth records from 2007-2011 (G3) linked to mothers' California birth and newborn screening records since 1982 (G2; n=1,225 White; n=1,203 Black). G2 and G3 health outcomes were obtained from linked birth, screening, hospital discharge, and developmental services records. Stored G2 newborn blood spots were analyzed for the tobacco biomarker cotinine, with levels ≥ 10 ng/mL indicating *in utero* exposure to G1 smoking. Odds ratios were estimated with logistic regression adjusting for G1 neighborhood poverty, age, and parity.

Results: Thirty percent of White and Black G2 subjects were exposed *in utero* to G1 smoking. G3 very preterm birth was elevated among White G2 subjects exposed to G1 smoking, compared to those with cotinine <10 ng/mL (OR=1.41 [95% CI 1.13, 1.76]). This association was not observed among Black G2 subjects. No associations were observed for G2 pre-pregnancy obesity, G2 chronic hypertension or G3 ASD.

Conclusion: In this first study of multigenerational smoking effects to focus on Black women, no associations were found with selected second and third generation outcomes among Black women. The observation of increased very-preterm birth in the third generation in relation to *in utero* exposure to tobacco smoking within the White cohort warrants further investigation.

Short and long-term mortality after preterm birth: Evidence from a national population-based cohort Asma M. Ahmed* Asma Ahmed Sonia M. Grandi Eleanor Pullenayegum Sarah D. McDonald Jason Pole Shahirose S. Premji Marc Beltempo Fabiana Bacchini prakesh S. Shah Petros Pechlivanoglou

Background: Preterm birth (PTB) is a leading cause of neonatal mortality. However, evidence on mortality beyond the neonatal period is limited, especially in North America. We aimed to examine the effect of PTB on mortality from 1 to 36 years of age.

Methods: Using administrative data from Statistics Canada, we created a population-based cohort of children born in Canada in 1983-1996 (5 million births) and followed until 2019 (age 23-36 years) to ascertain deaths. We estimated RD and RR for all-cause mortality using log-binomial regressions, and HR for cause-specific mortality using Cox proportional hazards models (censoring individuals who died from other causes) within prespecified age intervals. We accounted for observed confounding using coarsened exact matching on baseline characteristics (e.g., birth year, parental demographics).

Results: During a median (IQR) follow-up of 29 (26-33) years, 72,662 individuals died (5,517 [1.7%] preterm and 49,034 [1.1%] term). PTB was associated with an increased risk of death in all age intervals (Fig 1), with the strongest association seen in early childhood (1-5 years) (RD 0.3%, 95% CI 0.3-0.4%; RR 2.8, 95% CI 2.6-3.0) and the weakest association in the 18-28 age group (RD 0.1%, 95% CI 0.0-0.1%; RR 1.1, 95% CI 1.1-1.2). For cause-specific mortality, PTB was associated with a higher risk of neurological and respiratory disease mortality across all age groups (HR 2.6 (2.2-3.0) and 2.2 (1.7-2.9) respectively, in the 18-36 age group). We also found increased risks of mortality due to cardiovascular, gastrointestinal, and endocrine-related causes and infections. Associations by gestational age (GA) categories showed higher risks with lower GA.

Conclusion: Individuals born preterm are at an increased risk of death from early childhood to their second and third decades of life, with higher risks as GA at birth decreased. These findings suggest the need to consider the long-lasting effects of PTB and may inform preventive strategies.

Figure 1. Risk differences (RD) and ratios (RR) for association between preterm birth and all-cause mortality in the matched cohort, stratified by age intervals

Note: RD and RR were calculated among individuals still alive at the beginning of the respective age range.
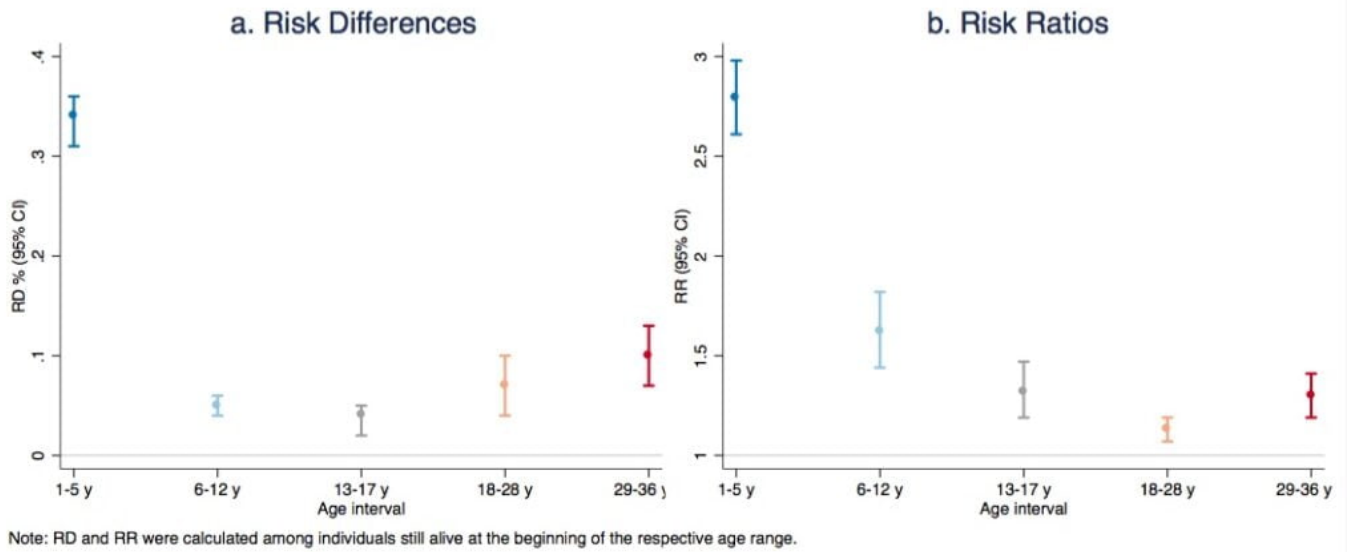
Sustained melatonin supplement use and the timing of pubertal onset in a diverse U.S. population. Ekaterina Sadikova* Ekaterina Sadikova Divyangana Rakesh Henning Tiemeier

Melatonin supplement use (MSU) is prevalent (12-20%) among U.S. youth, despite a debate about its effects on the timing of pubertal onset. Animal studies show that MSU can suppress gonadotropin releasing hormone secretion – the trigger of the pubertal cascade. The effect of MSU on pubertal onset is important to understand given adverse mental and physical health consequences of early puberty.

Using data from 5,933 prepubescent participants of the Adolescent Brain Cognitive Development study (baseline age 9-10 years, 28.6% female, 61.6% non-Hispanic white), we tracked MSU across 4 annual study visits. Pubertal onset was assessed using the parent-rated Pubertal Development Scale. All analyses were stratified by sex assigned at birth. Kaplan-Meier curves demonstrated unadjusted associations with any MSU. The parametric g-formula assessed the effect of sustained MSU on the timing of pubertal onset by accounting for confounding by constant and time-varying socioeconomic, parent, and child characteristics – including child sleep disturbances. An exploratory analysis looked at effect modification by race/ethnicity.

Unadjusted 4-year cumulative risk of pubertal onset was lower among melatonin users in both sex strata (log rank test p=0.09 for females and p=0.08 for males). The g-formula analysis showed no effect of sustained MSU on pubertal onset in either sex stratum (RR=1.00, 95%CI 0.98-1.01 among females and RR=1.04, 95%CI 0.97-1.09 among males). However, we found evidence of modification of MSU's effect by race/ethnicity among females (p=0.02 for interaction), with sustained MSU predicting modest delays in pubertal onset among minoritized females (RR=0.90, 95%CI 0.67-1.01).

Our analysis is the first to assess the causal effect of sustained MSU on pubertal timing in a diverse population. While no average effects were evident, more data is needed to confirm if MSU has potential to narrow racial/ethnic disparities in pubertal timing among children assigned female at birth.

Observed cumulative risk
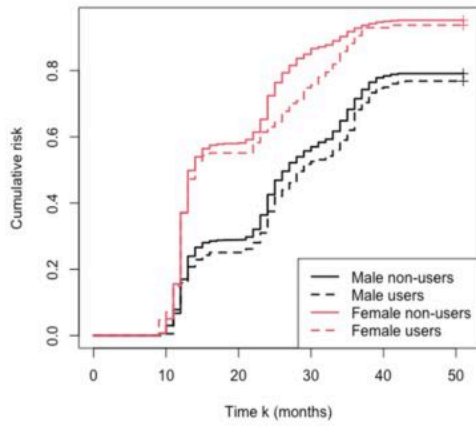
Kaplan-Meier curves capturing the comparison of cumulative probabilities of puberty onset across follow-up, stratified by any melatonin use and sex assigned at birth. Log rank tests assessed differences by melatonin use across follow-up: *p*=0.09 among females and *p*=0.08 among males.

Counterfactual cumulative risk
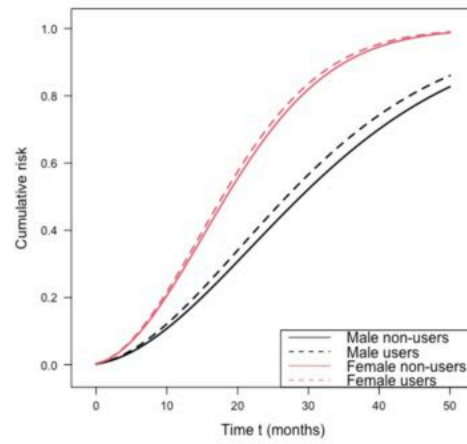
Counterfactual cumulative probability trajectories of pubertal onset given sustained MSU versus no use across follow-up, stratified by sex assigned at birth. Standardized across joint distributions of baseline income-to-needs ratio, parental marital status, parental somatic symptoms and mental health counseling, child age, race/ethnicity, and thought problems; baseline neighborhood privilege; time-varying child screen time, sleep disturbance symptoms, and BMI.

COVID-19 Vaccination and Ischemic Stroke in Adults ≥65 Years: Application of Rapid Safety Signal Assessment in Real-World Data Jenny Sun* Jenny Sun Susan Mather Michelle Iannacone Reema Mehta Heather Rubino Kofi Asomaning

Background: In Jan 2023, the US FDA and CDC announced a preliminary statistical signal for ischemic stroke in adults ≥ 65 years administered a booster dose of Pfizer-BioNTech (BNT) Bivalent (BA.4/5) COVID-19 vaccine. The statistical signal was seen in the CDC's ongoing surveillance but not in other safety systems. Additional real-world evidence was sought to rapidly assess the statistical signal.

Objective: To rapidly estimate the crude incidence of ischemic stroke after Pfizer-BNT Bivalent COVID-19 and comparator vaccinations using near real-time electronic health record (EHR) data.

Methods: Adults aged ≥65 years who received the Pfizer-BNT Bivalent (BA.4/5) COVID-19 vaccine, Moderna Bivalent (BA.4/5) COVID-19 vaccine, or a flu vaccine from 10/01/22-11/30/22 were identified from the Truveta database, which captures daily-refreshed EHR data from 14 US health systems. Individuals were followed from 1-21 days post vaccination for ischemic stroke. Follow-up continued 22-42 days post vaccination for use as a control window. Demographics and the crude incidence of ischemic stroke was summarized using descriptive statistics.

Results: 86,650 individuals received the Pfizer-BNT Bivalent COVID-19 vaccine, 38,342 received the Moderna Bivalent COVID-19 vaccine, and 406,707 received a flu vaccine. There was no difference in the crude incidence of ischemic stroke during the 1-21 day window vs. the 22-42 day window following administration of the Pfizer-BNT Bivalent COVID-19 vaccine (0.05% vs. 0.05%). The crude incidence of ischemic stroke in each window was similar for the other vaccine groups (Moderna: 0.06% vs. 0.07%; flu vaccine: 0.04% vs. 0.04%).

Conclusion: This rapid, large-scale assessment was planned, completed, and disseminated in <2 weeks, quickly providing additional data on the safety of the Pfizer-BNT Bivalent COVID-19 vaccine. Further development of similar infrastructure can provide faster investigation of future drug and vaccine safety signals.

Pharmacoepidemiology

Antiseizure medication use in pregnancy and adverse neonatal birth outcomes: a Canadian multisite population-based cohort study Alekhya Lavu* Alekhya Lavu Payam Peymani Silvia Alessi-Severini Chelsea Ruth Jamison Falk Karina Kowalec Christine Leong Shelley Derksen Roxana Dragan Marcus C. Ng Brandace Winquist Joseph Delaney Sherif Eltonsy

Introduction

Antiseizure medication (ASM) exposure in utero has been associated with an increased risk of adverse birth outcomes.

Objective

We aim to study the association between ASM treatment during pregnancy and adverse neonatal outcomes among pregnant people in two Canadian provinces.

Methodology

We conducted a multisite population-based retrospective cohort study of pregnant people in Manitoba from 1998 to 2021 and Saskatchewan from 1995-2023. We examined the association between ASMs and the risk of small for gestational age (SGA), low birth weight (LBW), preterm birth, NICU admissions, infants' length of hospital stays (LOS) (>3days), infant mortality (≤27), neonatal mortality (≤365 days), persistent pulmonary hypertension (PPHTN), neonatal respiratory distress syndrome (NRDS), severe neonatal morbidity (SNM) and neonatal readmissions among all pregnant people. Multivariate regression models were adjusted for various clinical covariates and confounders. We meta-analyzed the aggregated data from the two sites using random effects model.

Results

We included a total of 545,121 pregnancies in our analysis including 6874 exposed pregnant people. We observed a significant increase in the risk of SGA (adjusted odds ratio [aOR] 1.13, 95%CI 1.08-1.19), LBW (aOR 1.19, 95%CI 0.61-2.30), preterm birth (aOR 1.36, 95%CI 1.06-1.76), NICU admissions (aOR 1.30, 95%CI 1.08-1.57), LOS infant (aOR 1.18, 95%CI 1.05-1.31), infant mortality (aOR 1.21, 95%CI 1.02-1.44), neonatal mortality (aOR 1.23, 95%CI 1.07-1.43), PPHTN (aOR 1.38, 95%CI 1.20-1.57) and a non-significant increased risk of neonatal readmissions (aOR 1.10, 95%CI 0.94-1.29), SNM(aOR 1.08, 95%CI 0.81-1.44) and NRDS (aOR 1.06, 95%CI 0.79-1.43) when compared with unexposed pregnant people.

Conclusion

ASM exposure in pregnant people is associated with a significant increase in adverse birth outcomes. Therefore, future studies must investigate the safety of ASMs in epilepsy and non-epileptic conditions.

Policing/Incarceration

Syphilis on The Rise! Applied Epidemiology at The Federal Bureau of Prisons Enid Velez-Valle* Enid Velez-Valle Ellen Smith

Cases of syphilis and congenital syphilis are on the rise nationwide. Consistent with this pattern in the community, the Federal Bureau of Prisons has detected an increase in syphilis cases since 2018. Epidemiological analyses were performed to strategically implement efforts to decrease syphilis rates. Electronic medical records from 01/01/2018 to 12/31/2023 were used to identify and evaluate syphilis infections among Adults in Custody (AIC) in the federal prison system. Syphilis and comorbid health conditions were identified using ICD-10 codes. Laboratory information was included to identify average time-to-testing, and demographic and incarceration information from administrative records to assess subpopulations that may be at higher risk. Analyses included descriptive and regression analyzes using SAS Enterprise Guide (v8.3). The incidence of syphilis has reached an all-time high since 2018. There were 4 per 1000 AICs diagnosed with syphilis in calendar years 2022-2023. The average time-to-screening was 53 days. AICs diagnosed with syphilis were disproportionally female, AICs between 18-34 years old, White or Native American, Hispanic, residents of California, New York, or Florida, AICs primarily incarcerated for immigration crimes, and those who did not complete High School/GED. Females (OR=2.8, CI= 2.5, 3.1) and Native Americans (OR=1.9, CI=1.6, 2.3) had the highest odds of infection along with those with HIV (OR=19.5, CI=17.1, 22.2), Gonorrhea (OR= 9.2, CI=5.5, 15.5), and Chlamydia (OR=5.2, CI=3.7, 7.4). Prior to these analyses, many facilities were not conducting routine universal screening but instead risk-based screening, consistent with CDC recommendations at the time. These findings have helped push for universal screening, switching to a more sensitive reverse testing algorithm, an educational campaign for employees, and a new initiative to increase health education on sexual health that will be culturally competent for Native American subpopulations.

Impact of donation on perceived and actual health outcomes in living kidney donors in the western region of Saudi Arabia Emily L. G. Heaphy* Emily Heaphy Najib Kadi Eman A. Albishi Haneen Y. Al Omar Halal F. Alenizi Shatha A. Rahym Rasha M. Alderbi

Renal transplantation from a live donor can be done preemptively and is associated with a better rate of survival for the organ recipient compared to deceased donation. Donors, however, face risks of surgical complications and possible long-term health and psychological harm. Few prospective studies have examined these factors with conflicting results. Our hospital performs around 200 living kidney donor transplants yearly. We are conducting an observational prospective cohort study of living kidney donors (LKDs) aged 18 and older who are asked prior to nephrectomy about donating a kidney. The impact on their psychological and physical health is measured using the 36-item short form survey and clinical lab results. As of January 2024, 57 LKDs have undergone nephrectomy with a mean ± standard deviation age of 33.3 ± 7.2 years and 66.7% being male. Fourteen percent were donating to an unrelated recipient. More than two-thirds of the LKDs strongly agreed that: I feel free to do what I want about donating an organ (71.9%) and It was my idea to donate an organ (70.2%) and 87.5% self-reported being in excellent health. Among 41 patients completing six months follow-up, 70.7% self-reported excellent health. Creatinine levels (103.7 ± 16.0 vs. 74.1 ± 16.0 umol/L; t Value = -13.76, df = 39, p < 0.0001) and diastolic blood pressure (DBP) (78.8 ± 6.7 vs. 75.1 ± 9.0 mmHg; t Value = -2.85, df = 40, p = 0.0068) were significantly higher compared to baseline. There were no significant associations between donor's willingness to donate and their self-reported general health. There was no significant difference in patients' self-reported overall health between baseline and six months (Fisher's Exact Test p-value = 0.5071). There were no significant correlations between creatinine levels or DBP and donors' willingness to donate a kidney. Reaching our target enrollment of 100 LKDs is required to further expound on this relationship in the western region of Saudi Arabia.

The Impact of Unmeasured Confounding on the Association between Maternal Periodontitis and Adverse Birth Outcomes: Meta-Analyses of Observational Studies Abdullah Al-Taiar* Abdullah Al-Taiar May Salama Denise McKinney Sultan Alsullum Eric Mishio Bawa Anwar T. Merchant

Background and objectives: Maternal periodontitis has been consistently linked to adverse birth outcomes. However, a causal relationship is not established due to potential unmeasured confounding factors in observational studies and inconclusive results from randomized controlled trials. This study aimed to assess the impact of unmeasured confounding factors in meta-analyses examining the association between maternal periodontal disease and preterm birth or low birth weight.

Methods: We searched PubMed/Medline, the Cochrane database for systematic reviews, Embase, Google Scholar for articles published between 2002 and 2023. Systematic reviews with meta-analyses of observational studies were included if either preterm birth or low birth weight were the outcome and were published in English between 2002 and 2023. Search results were entered into Rayyan software after removing duplicates. Two researchers independently screened titles and abstracts, with a third reviewer resolving discrepancies. This study followed the Meta-analyses Of Observational Studies in Epidemiology (MOOSE) guidelines and was registered in PROSPERO under number CRD42023400331.

Results: There were 62 original studies from 9 meta-analyses meeting the inclusion criteria. In a random-effects meta-analysis of 19 cohort studies, more than 80% of the studies would have RR>2.00 even if an unmeasured confounder were three times more prevalent in the exposed group and raised the risk of preterm birth 3-fold. Similarly, in a meta-analysis of 10 cohort studies, if the association between an unmeasured confounder and maternal periodontitis as well as low birth weight were RR >3, 80% of the studies in that meta-analysis would have RR>2.00. Publication bias in these meta-analyses may have inflated the summary measures between maternal periodontal disease and preterm birth or low birth weight.

Conclusions: Associations between maternal periodontal disease and adverse birth outcomes in observational studies appear robust to unmeasured confounding factors, but publication bias may tend to inflate them. These findings support the hypothesis that maternal periodontal disease is causally related to adverse birth outcomes.

Reproductive

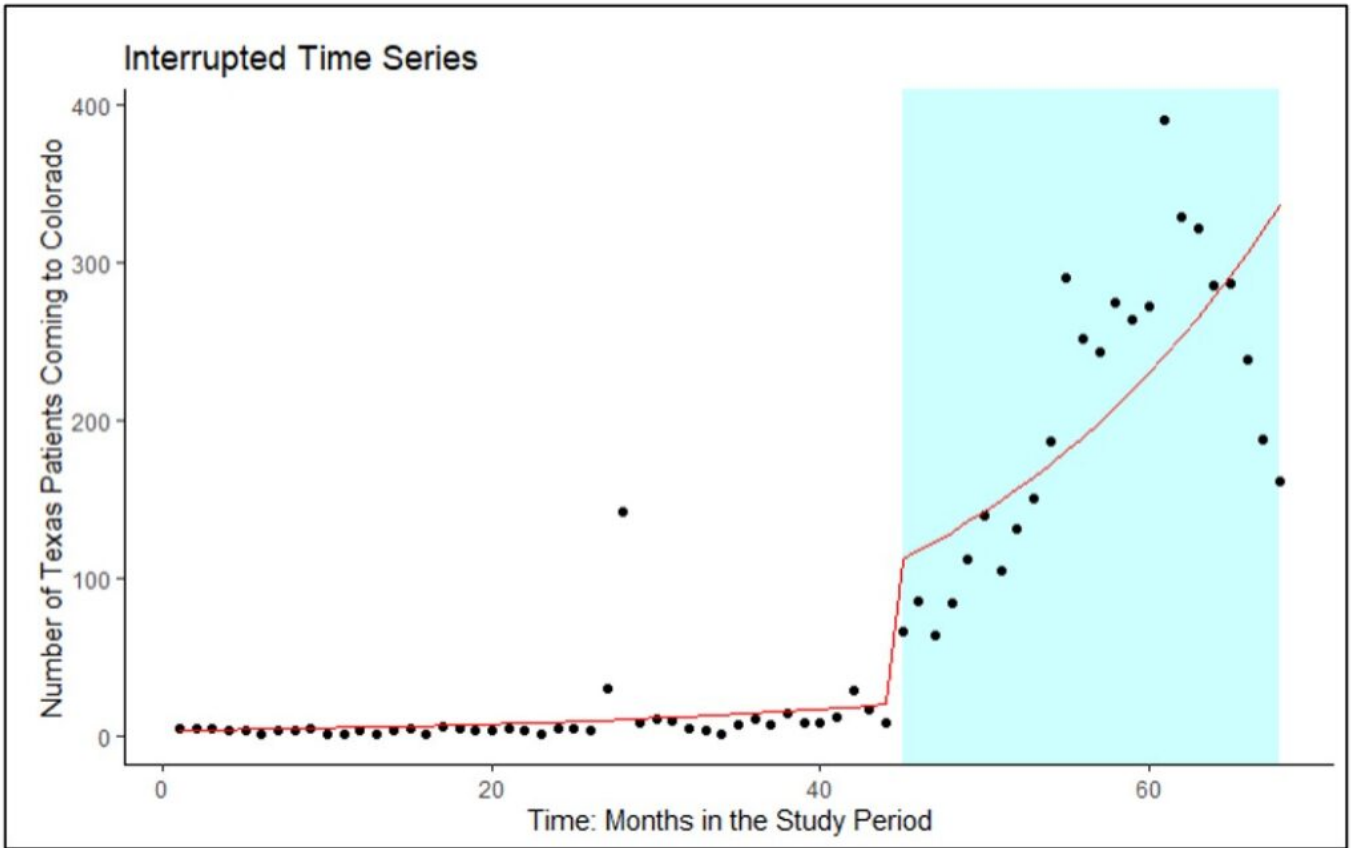**The Influence of Reproductive Access Restrictions on Out-of-State Abortion Care in Colorado, an Interrupted Time Series Analysis 2018-2023** Kelly DeBie* Kelly DeBie Andreas Neophytou Jennifer Peel Molly Gutilla Kayleigh Keller

Title: The Influence of Reproductive Access Restrictions on Out-of-State Abortion Care in Colorado, an Interrupted Time Series Analysis 2018-2023

Background: Abortion access in the United States has been shaped historically by Roe v. Wade, a case which created a Constitutional right to abortion. States seeking to challenge Roe passed laws more restrictive than Roe would permit. Texas' SB8 was passed in 2021 and forbids abortion after detection of cardiac electrical activity around six weeks. Roe was overturned in 2022 removing the right to abortion and leaving reproductive care access decisions to states.

Methods: Utilizing data from January 2018 to August 2023 on induced termination of pregnancies from the Colorado Department of Public Health and Environment, an interrupted time series analysis using Quasi-Poisson regression was used to assess the association between changes in law and monthly counts of patients from Texas traveling to Colorado for abortion services. The Texas SB8 enactment date was selected for the interruption point of the analysis.

Results: Texas residents were over 5 times more likely to travel to Colorado for abortion procedures after the enactment of SB8. Rate Ratio: 5.44, (95 % confidence interval: 1.81, 16.32).

Discussion: State restrictions on access to abortion may require patients to travel to other states for healthcare for abortion services. Changes observed here pre-date the repeal of Roe due to prior enacted Texas state law.

Conclusion: This study contributes evidence of changes in out-of-state patients seeking abortion in Colorado though these results may not be generalizable to other states. Here we can only account for those holding the privilege of having the ability and resources to travel to other states for these procedures, which may represent only a fraction of the total who would otherwise desire in-state services.

Interrupted Time Series

Number of Texas Patients Coming to Colorado (y-axis)

Time: Months in the Study Period (x-axis)

Birth spacing recommendations: a one-size-fits-all approach may not be appropriate Julie M. Petersen* Julie Petersen Mahsa Yazdy Anne Marie Darling Martha Werler National Birth Defects Prevention Study

Background: Guidelines strongly advise people who recently gave birth to wait 6 months before attempting the next pregnancy and consider interpregnancy intervals (IPI) of ≥18 months as optimal. We sought to evaluate whether age modifies associations between IPI and preterm birth.

Methods: We utilized data from the National Birth Defects Prevention Study (United States, 1997–2011) restricted to multiparas controls with livebirths in the two most recent pregnancies. IPI between the prior birth and the study pregnancy was categorized as <6, 6–11, 12–17, 18–23 (reference), 24–59, or ≥60 months. The study pregnancy was considered preterm if delivered at <37 0/7 weeks' gestation. We stratified by age at the prior birth, categorized as <25 (n=2484), 25–29 (n=1626), or ≥30 (n=1209) years. We estimated risk ratios (RR) between IPI and preterm birth using Poisson regression, adjusting for measured potential confounders. We conducted a multiple quantitative bias analysis to adjust for exposure-outcome dependent misclassification and selection bias. We computed e-values for any lower bounds of the RR 95% confidence intervals (LBCI) that were >1.0 after multiple bias adjustment.

Results: Preterm birth risk was highest with <6 months IPI (covariate-adjusted RR point estimates ≥1.3 in all age groups; 25–29 years had the strongest association). Preterm birth risk was lowest with 6–17 months IPI among ≥30 years. Associations tended to move downward but these patterns remained after adjustment for multiple biases, with the greatest attenuation among 25–29 years, although the LBCI for <6 months IPI remained >1.0 (e-value=2.4).

Conclusions: People ≥30 years may benefit from shorter IPI than currently recommended, possibly to avoid increased risks associated with advanced age (e.g., reduced fecundability, chronic health conditions, pregnancy complications). Residual confounding is unlikely to explain the <6 months IPI-preterm birth association among people 25–29 years.

Legend

Figure. Risk ratio point estimates for associations between interpregnancy interval category and preterm birth outcomes. Results stratified by maternal age at prior pregnancy: <25 years (panel A), 25 to 29 years (panel B), ≥30 years (panel C). Each model shown in a different color: unadjusted (yellow), covariate regression adjusted (fuchsia), adjusted for non-differential dependent misclassification (blue), adjusted for selection (green), and adjusted for multiple biases (dark purple). Results not computed due to too few exposed cases for individuals who were ≥30 years with an IPI of ≥60 months.

Coffee Consumption and Risk of Spontaneous Abortion in a Preconception Cohort Study

Martha Koenig* Martha Koenig Amelia Wesselink David Savtiz Kenneth Rothman Lauren Wise Elizabeth Hatch

Background: Coffee consumption during pregnancy has long been studied as a potential risk factor for spontaneous abortion (SAB, pregnancy loss at <20 weeks gestation). Nausea and vomiting in early pregnancy (NVP) may lead people to reduce coffee intake. Additionally, NVP is associated with a reduced risk of SAB. Previous research has underscored the role of reverse causation when measuring this association, as non-viable pregnancies may allow continuing coffee consumption, causing upward bias.

Methods: We analyzed data from Pregnancy Study Online (PRESTO), an online preconception cohort study, to examine associations between coffee intake and risk of SAB. We collected information on coffee consumption and NVP on the early pregnancy questionnaire (EPQ). We identified incident SABs on the late follow-up questionnaire. We fit multivariable-adjusted Cox models with weeks of gestation as the time scale to estimate hazard ratios (HRs) for the effect of coffee intake on SAB and 95% CIs. In our main analyses, we restricted our sample to those who completed the EPQ at ≥6 weeks gestation, the typical time of NVP onset, and ≤10 weeks gestation.

Results: The HR for ≥1 cups/day (vs. none) was 1.26 (CI: 0.92, 1.73). Among those with NVP, coffee intake was positively associated with SAB (HR for ≥1 cups/day [vs. none] 1.41 (CI: 0.95, 2.07)); for those without NVP, coffee intake was not associated with SAB (HR=0.97 (CI: 0.56, 1.68)). When results were stratified by gestational week at time of EPQ completion, HRs for ≥1 cups/day (vs. none) were 1.16 (CI: 0.86, 1.56), 0.96 (CI: 0.55, 1.67), 1.43 (CI: 0.79, 2.58), 1.03 (CI: 0.46, 2.28), 1.71 (CI: 0.74, 3.97) and 1.34 (CI: 0.53, 3.38) for <6, 6, 7, 8, 9 and ≥10 gestational weeks, respectively.

Conclusion: Coffee intake showed little consistent association with SAB incidence. Sustained coffee consumption beyond 7 weeks gestation may be influential to understanding associations.
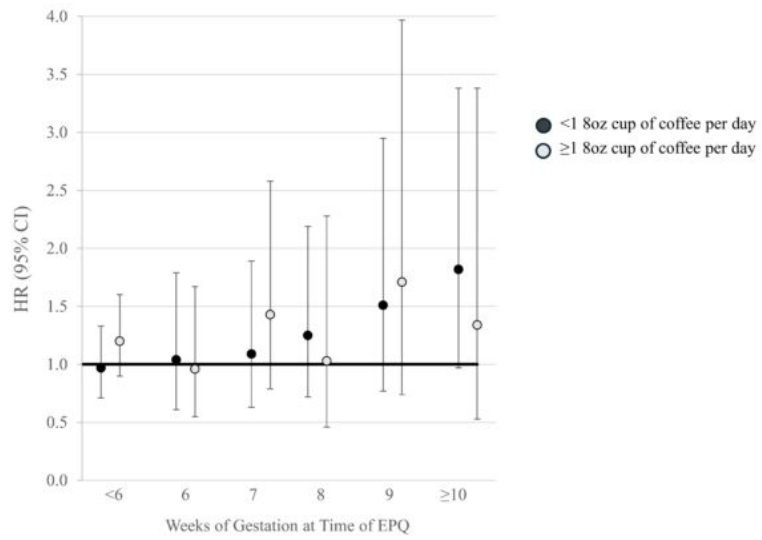
Figure. Hazards Ratios (HR) and 95% CIs for the association of cups of coffee per day and spontaneous abortion (SAB) stratified by week of EPQ (when exposure (coffee) and other covariates were ascertained), Pregnancy Study Online (PRESTO), 2013-2023.

Estimates are adjusted for age, parity, BMI, education, alcohol use, smoking, multivitamin intake, and symptoms of nausea and vomiting.

EPQ= Early Pregnancy Questionnaire

BMI= Body Mass Index

Reproductive

The Association Between Hemoglobinopathy Carrier States and Anemia During Pregnancy

Kimi Van Wickle* Kimi Van Wickle Stephanie Engel Achille Massougbodji Florence Migot-Nabias Anais Merckx Michel Cot Florence Bodeau-Livinec

Hemoglobinopathy carrier states, the presence of one abnormal copy of a hemoglobin variant, have largely unknown clinical manifestations during pregnancy despite their widespread regional frequency in sub-Saharan Africa due to their protection against severe malaria. We included 895 mother-infant dyads from MiPPAD, a randomized control trial in Benin that followed pregnant women less than 28 weeks' gestation through delivery, who received hemoglobin electrophoresis and had data collected on hemoglobin levels during antenatal visits and upon arrival for delivery. We investigated the extent to which trait status, including sickle cell trait and hemoglobin C trait, is associated with anemia over the course of pregnancy and at delivery and whether intrapartum malaria, as measured by placental parasitemia, mediates the association of carrier states with anemia at delivery (using gestational age-specific thresholds to account for physiologic hemodilution during pregnancy). We found that sickle cell trait, but not hemoglobin C trait, was associated with higher rates of anemia at delivery (OR = 1.59, 95%CI: 1.05, 2.40, p = 0.03). This relationship was exclusive to delivery and was not observed across the course of pregnancy (OR=1.05, 95%CI:0.80, 1,39, p = 0.70). Placental parasitemia did not substantially mediate the association between sickle cell trait and anemia at delivery: The odds of anemia amongst pregnant women with placental parasitemia did not differ by sickle cell trait status (OR = 1.00, 95%CI:0.99,1.01, p= 0.88). Likewise the odds of anemia through placental parasitemia among hemoglobin C trait carriers was not significant (OR = 1.08, 95%CI: 084, 1.40, p = 0.55). However, placental parasitemia was strongly associated with hemoglobin C trait (OR = 1.53, 95%CI: 1.09, 2.15, p = 0.01). Our findings demonstrate the distinct relationships that carrier traits have with anemia and malaria, two important predictors of maternal and neonatal outcomes, and suggest that sickle cell trait, but not hemoglobin C trait, is an important risk factor for maternal anemia with the highest risk period observed at delivery.
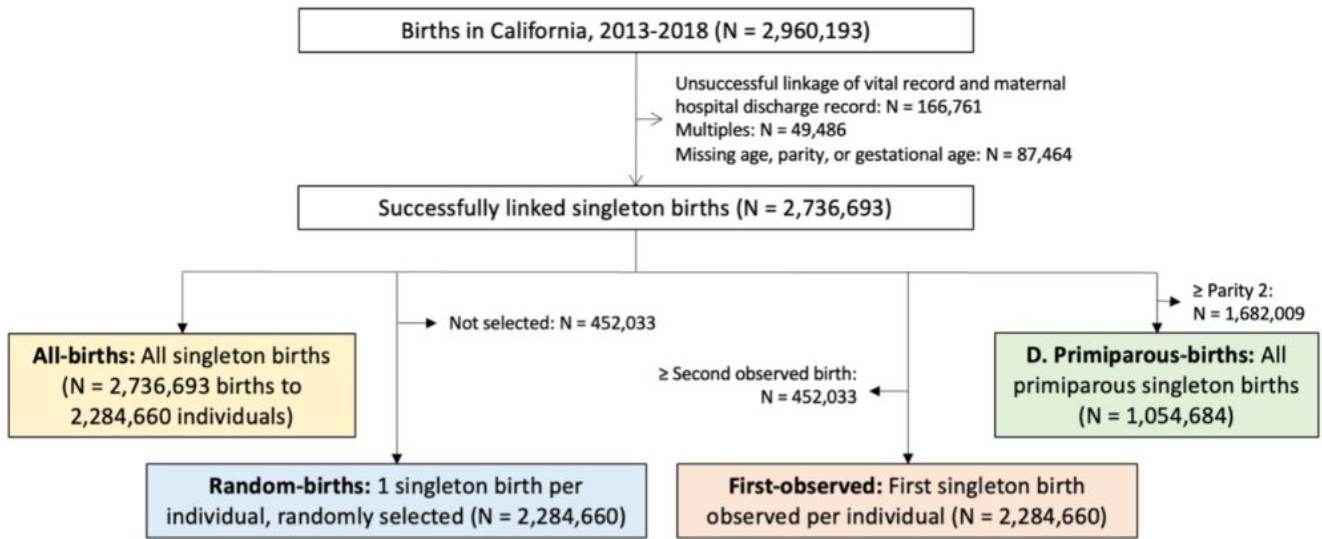
Reproductive

Considering pregnancies as repeated versus isolated events: An empirical comparison of common approaches across selected perinatal outcomes Shalmali Bane* Shalmali Bane Suzan Carmichael Julia Simard Maya Mathur

Despite published guidance on how to address repeated pregnancies to the same individual, a variety of approaches are observed. While some of these approaches are supported by the chosen research question, others are consequences of constraints inherent to a given dataset (e.g., missing parity). We compared common cohort selection and analytic approaches used for epidemiological research.

 Using vital records linked to hospital discharge records for singletons, we created four cohorts: (1) all births (2) randomly selected one birth per individual (3) first observed birth per individual (4) primiparous births. Sampling of births was not conditional on cluster. Study outcomes were severe maternal morbidity (SMM) and preeclampsia/eclampsia, and the independent variables were self-reported race/ethnicity (as a social factor) and systemic lupus erythematosus. We assessed the distribution of maternal characteristics, the prevalence of outcomes, overall and stratified by parity, and risk ratios (RRs). Among all births, we compared RRs from three analytic strategies: with standard inference, cluster-robust inference, and adjusting for parity.

Outcome prevalence was consistently lowest among all births and highest among primiparous births. RRs differed for study outcomes across all four cohorts, with the most pronounced differences between the primiparous-birth cohort and other cohorts. Robust inference minimally impacted the confidence bounds of estimates, compared to the standard inference, (e.g., lupus-SMM association: 4.01, 95% CI 3.54-4.55 vs. 4.01, 95% CI 3.53-4.56), while adjusting for parity slightly shifted estimates.

Researchers should consider the alignment between methods used, sampling strategy, and research question. This could include refining the research question to better match possible inference, considering alternative data sources, and acknowledging data limitations. If parity is an established effect modifier, stratified results should be presented.

Births in California, 2013-2018 (N = 2,960,193)

Unsuccessful linkage of vital record and maternal hospital discharge record: N = 166,761
Multiples: N = 49,486
Missing age, parity, or gestational age: N = 87,464

Successfully linked singleton births (N = 2,736,693)

Not selected: N = 452,033

≥ Second observed birth: N = 452,033

≥ Parity 2: N = 1,682,009

All-births: All singleton births (N = 2,736,693 births to 2,284,660 individuals)

D. Primiparous-births: All primiparous singleton births (N = 1,054,684)

Random-births: 1 singleton birth per individual, randomly selected (N = 2,284,660)

First-observed: First singleton birth observed per individual (N = 2,284,660)

Parity	N	%
1	1,054,684	38.5
2	901,412	32.9
3+	780,597	28.5

Parity	N	%
1	927,102	40.6
2	726,224	31.8
3+	631,334	27.6

Parity	N	%
1	1,054,684	46.2
2	655,053	28.7
3+	574,923	25.2

Parity	N	%
1	1,054,684	100

A Counterfactual Analysis of Impact of Cesarean Birth in a First Birth on Severe Maternal Morbidity in the Subsequent Birth Shalmali Bane* Shalmali Bane Suzan Carmichael Elliott Main Michelle Odden Julia Simard Peiyi Kan Jonathan Snowden

Severe maternal morbidity (SMM) is a sentinel outcome comprised of unexpected adverse outcomes (e.g., aneurysm) with significant short- and long-term consequences to maternal health. It is known that cesarean birth affects maternal outcomes in subsequent pregnancies, but specific effect estimates related to subsequent SMM are lacking. We sought to quantify the effect of cesarean birth reduction among nulliparous, term, singleton, vertex (NTSV) births (i.e., the most preventable cesarean births) on SMM in the second birth.

We examined birth certificates linked with maternal hospitalization data (2007-19) from California for NTSV births linked with second births (N = 779,382). The exposure was cesarean delivery in first birth and the outcome was SMM in the second birth. We used adjusted Poisson regression models to calculate risk ratios and population attributable fraction of SMM in the second birth and conducted a counterfactual impact analysis to estimate how lowering NTSV cesarean births could reduce SMM risk in second births (such that individuals with the lowest probability of cesarean delivery instead gave birth vaginally).

The adjusted risk ratio for SMM in the second birth given a prior cesarean birth was 1.68 (95% CI 1.50-1.89); 15.5% (95% CI 15.4%-15.5%) of this SMM may be attributable to prior cesarean birth. In a counterfactual analysis where 12% of the California population least likely to get a cesarean birth instead delivered vaginally, we observed 175 fewer SMM events in a population of individuals with a low-risk first birth and a subsequent birth.

 Lowering primary cesarean birth among a NTSV population is one mechanism to decrease downstream SMM events in subsequent births and overall. Additionally, our findings reflect the importance of considering the cumulative accrual of risks across the reproductive life-course.
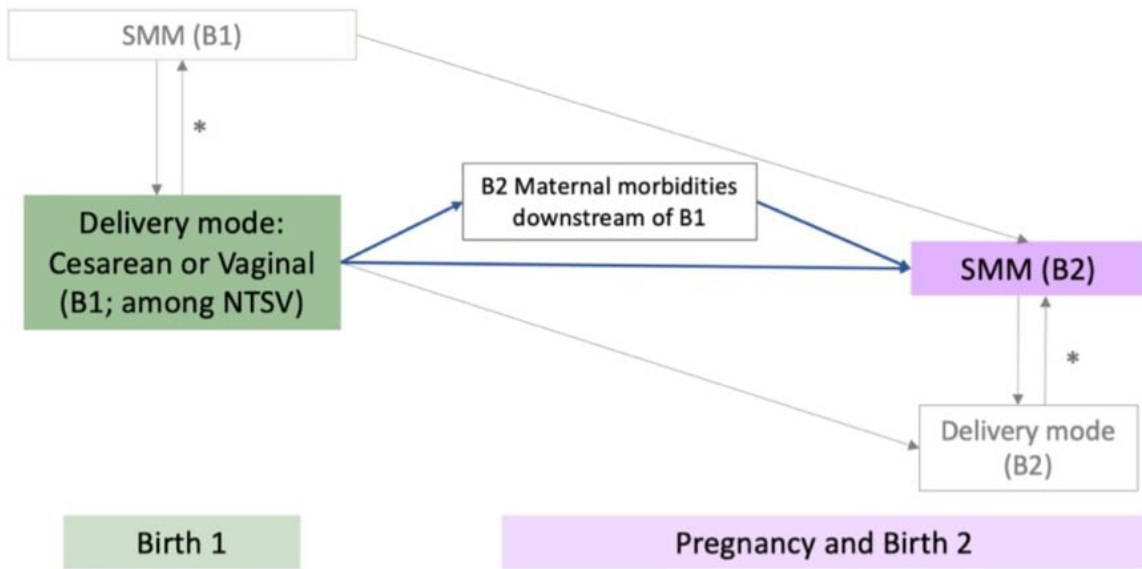
* Depending on timing of SMM relative to delivery, SMM could precede or follow delivery mode

Assessing the Validity of Public Web Search Data for Predictive Modeling of Epidemics

Marie-Laure Charpignon* Marie-Laure Charpignon Anika Puri Maimuna Majumder

Non-conventional data collected from public web searches, including Google Search Trends (GST), are increasingly used for predictive modeling of epidemics. Here, we investigated the validity of leveraging GST data to predict COVID-19 progression. Specifically, we examined the relationship between COVID-19-related morbidity-mortality (ie, case and death counts) and public interest in COVID-19 as ascertained through GST. We focused on the United States and analyzed data from Feb 2020 to May 2022, inclusive. We found that states with a larger share of Republican-leaning voters had lower levels of public interest in COVID-19 than those of COVID-19 morbidity-mortality. This pattern was most prominent during the Omicron wave. Further, we characterized the spatio-temporal dynamics of decoupling between Internet search interest and COVID-19 morbidity-mortality by state. Decoupling was defined as the point-in-time difference between the normalized GST value and the corresponding normalized COVID-19 morbidity-mortality; a negative value would indicate greater COVID-19 morbidity-mortality than the corresponding level of public interest. In Republican-leaning states, we found greater negative decoupling between Internet search interest and COVID-19 morbidity-mortality than in Democrat-leaning states, as the pandemic progressed. This result calls into question the effectiveness and generalizability of using GST to build epidemic forecasting models across locations. To account for confounders of the political leaning-Internet search interest relationship, we implemented a multivariable regression adjusting for local levels of social vulnerability, Internet penetration, and vaccine uptake. The presence of decoupling between COVID-19 morbidity-mortality and public interest suggests that GST information value may vary over time and by political leaning. Thus, caution is warranted when employing such data for spatio-temporal epidemic models of COVID-19 and other infectious diseases.
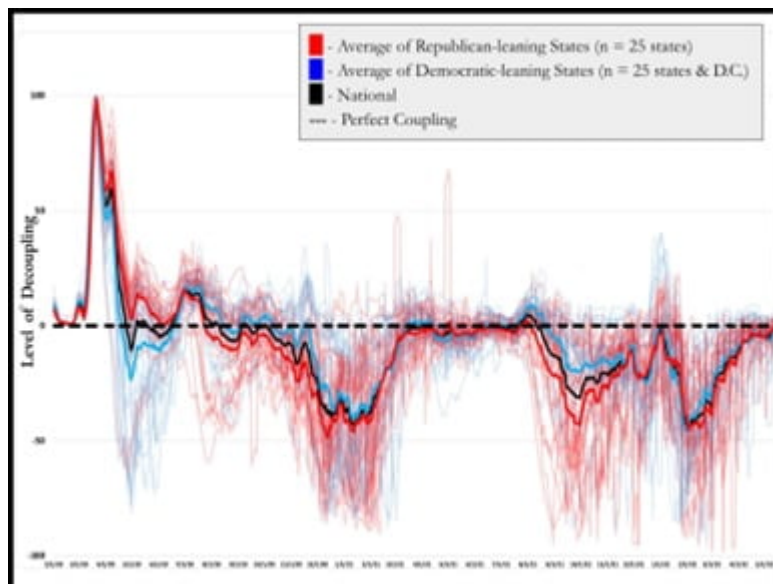
Proposal of a potential prevention model in preventive medicine Hideo Yamazaki* Hideo Yamazaki Soichi Sakabe Xiao Qing Hikaru Yamazaki Noriko Miyake

The textbook-based model is based on the three preventive categories as practical application stages in preventive medicine. The first category is a primary prevention included health promotion and specific prevention, the second is a secondary prevention included early detection and prompt treatment and the third is a tertiary prevention included prevention of deterioration and rehabilitation. In practical community health activity based on health promotion, the primary prevention is one of the most effective ways to prevent lifestyle-related diseases (LSRDs). In general, although the young-adults have a very low incidence rate in LSRDs, the cumulative exposure to behavioral disadvantage across stages of life may be strongly associated with predispose LSRDs. Therefore, it will be essential to subdivide primary prevention and identify a model that will provide alarm during the susceptibility phase on the natural history of diseases. However, an appraisal way for health conditions in a susceptibility phase based on the natural history of diseases has not been established yet. The purpose of this study is to propose a segmented model of primary prevention and to identify its thresholds.

Methods: A self-report questionnaire consisted of 54 items was administered to the young-adults and the elderly in Japan and linkage data were generated and analyzed in this study. Then the quantification method of the second type was applied to linkage data.

Results: The cutoff point based on the semi-health index (SHI) meant one's poor health condition in the susceptibility phase was 20.0 as a result of the application of the quantification method of the type second. SHI score was calculated by the norm eigenvectors of the first principal component derived from a principal component analysis (PCA). Furthermore, a distribution of the semi-health condition was determined by using this score. Cutoff points on the distribution were applied to the young-adults and the elderly, respectively.

Conclusions: This model has shown to be useful for evaluating the semi-health state for the young-adults and the elderly from a light of health promotion practice. Furthermore, it was suggested that the method could be applied as a screening test for the potential prevention.

Positive Development by Adversity: Conceptual Framework and Empirical Evidence using LONGSCAN study Takeo Fujiwara* Takeo Fujiwara

It is well known that adverse childhood experiences (ACEs) can lead to poor health. However, some children with less toxic ACEs showed positive development in adolescence under specific conditions, such as having supportive adults other than parents (i.e., outside adults). Here, we propose a new concept of child development, "positive development by adversity (PDA)."

The LONGSCAN, a nationwide longitudinal study based on child protection services, was used to test the concept of PDA. A combination of two inverse probability weighting for the allocation of hardships (i.e., poverty and neglect) at 6 years old and having a supportive adult during 12-16 years old using the covariates was applied. Social skills assessed by the Child Behavior Checklist (CBCL) from age 6 to 16 were used as the outcome variable. Multivariate linear regression analysis was performed comparing four groups, 1) children with hardship and supportive adults, 2) children with hardship but not having supportive adults, 3) children without hardship but having supportive adults, and 4) children without hardship and supportive adults.

In the results, it was found that children who experienced poverty and neglect and had outside adults showed greater social skills than children without poverty but with outside adults (coefficient: 2.28, 95% confidence interval: 0.14 to 4.42 to -0.14). These findings suggest that poverty and neglect in childhood may contribute to the positive development by adversity (PDA) of social skills, under specific conditions such as having outside adults.

LATEBREAKER

Social

Does choice of neighborhood disadvantage index matter? An application with preterm birth disparities Sarah C. Haight* Sarah Haight Kristen N. Cowan Jessie K. Edwards Thomas J. Luben Chantel L. Martin

Background: Epidemiologists often investigate the impacts of neighborhood disadvantage (ND) on health outcomes using indices created from publicly available data. However, it is not well known how choice of ND index can impact results. We (1) determined the most used ND indices in recent epidemiological research and (2) investigated how choice of ND index impacts the observed racial disparity in the relationship between ND and preterm birth (PTB).

Methods: We conducted a systematic scan of abstracts from 2020-2023 in 5 major epidemiology journals and conferences to determine the most used ND indices and assigned them to birth records for singleton live births with no birth defects to non-Hispanic (NH) Black and NH white birthing parents in North Carolina from 2016-2018. Linear binomial regression was used to calculate risk differences (RD) for PTB for a 1-standard deviation (SD) increase in each ND index, stratified by race.

Results: Our sample included 263,066 births (30.3% NH Black; 69.7% NH white). PTB was higher for NH Black than NH white deliveries (11.0% NH Black; 7.1% NH white). The most common ND indices were Neighborhood Deprivation Index (NDI), racial and economic Index of Concentration at the Extremes (ICE), Social Vulnerability Index (SVI), and Area Deprivation Index (ADI). Overall, the indices showed an increased risk of 13-15 more PTB per 1000 live births for a 1-SD increase in ND. RDs were higher for NH white (RD range: 8.2 – 11.2) compared to NH Black birthing parents (RD range: 8.1 – 9.0) for the NDI, ICE, SVI and ADI. As ND decreased, the PTB risk disparity between NH Black and NH white birthing parents widened with the NDI and ADI, indicating that the potential benefits of living in advantaged neighborhoods may not be equally shared; this gap was not observed with ICE or SVI.

Conclusions: The relationship between ND and health outcomes may vary depending on the index used, indicating the need for thoughtful consideration in their selection.

Figure 1. The risk of preterm birth associated with various measures of neighborhood disadvantage by birthing parent race - North Carolina, 2016-2018
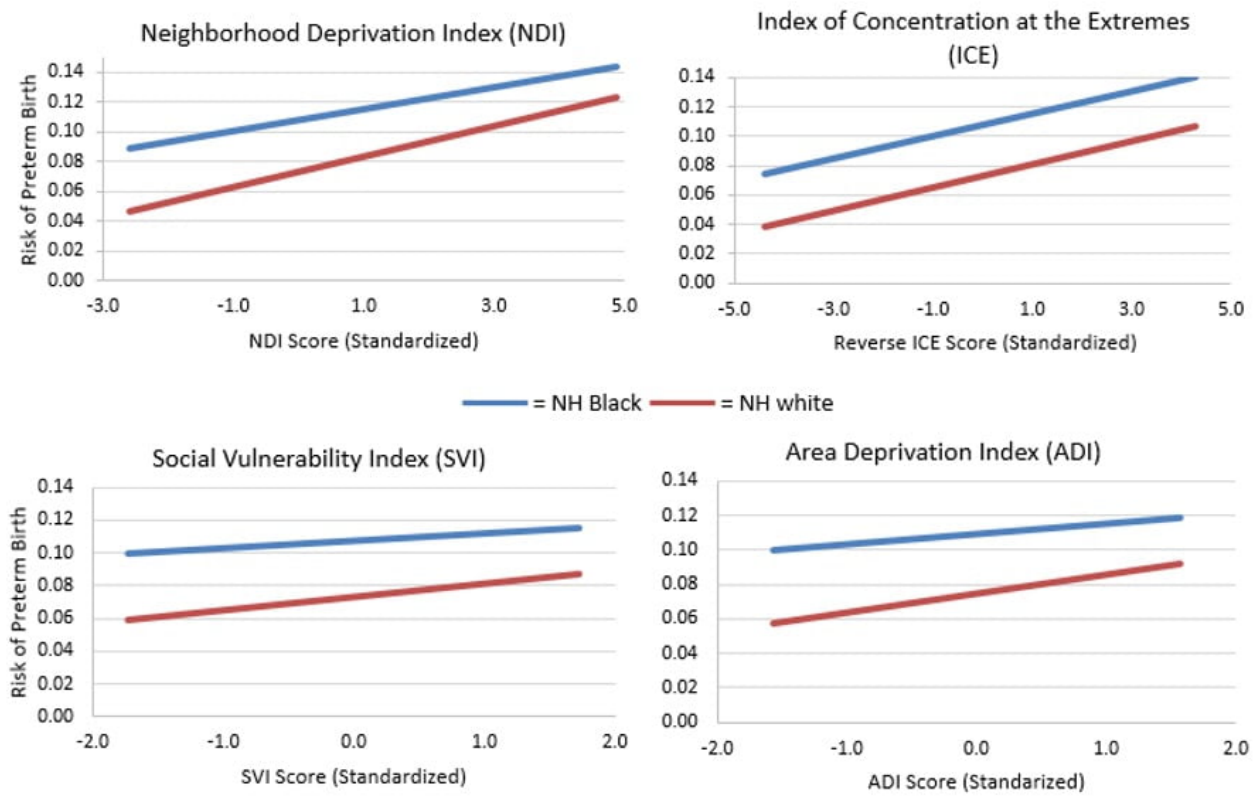
Social

Following the power: social class inequities in cause-specific mortality in the United States

Jerzy Eisenberg-Guyot* Jerzy Eisenberg-Guyot Audrey Renson

Introduction: Socioeconomic and racial health inequities in the US are vast, with sinking life expectancy propelled by excess mortality among poor and racially minoritized people. Hazardous working conditions, like low wages and poor job control, fuel the inequities. Underused relational theories suggest such hazards flow from structural power imbalances between workers, managers, and employers: social classes divisible by managerial authority and business ownership. However, while studies using relational theories have documented inequities in all-cause mortality in the US, none have investigated cause-specific mortality. We addressed this gap.

Methods: Our sample included respondents ages 18-64 to the 1986-2018 National Health Interview Survey with mortality follow-up through 2019 (n=1,067,193). Using data on business ownership, occupation, and employment status, we classified respondents as incorporated business owners (IBOs), unincorporated business owners (UBOs), managers, workers, and not in the labor force (NLF). Next, we used an inverse-probability-weighted Aalen Johansen estimator to estimate class inequities in mortality from 10 underlying causes, account for competing risks. In-progress analyses will test class-year, class-race, and class-gender interaction.

Results: We estimated considerable class inequities (Figure 1), with NLFs and workers, which are the largest classes across gender-races and disproportionately consist of women and people color, tending to be at greatest mortality risk. For example, the 34-year cancer-mortality risk among NLFs, workers, and UBOs was, respectively, 9.5% (95% CI: 9.2%, 9.8%), 8.0% (95% CI: 7.8%, 8.3%), and 8.2% (95% CI: 7.8%, 8.7%), greater than the risk among managers (7.0%; 95% CI: 6.7%, 7.4%) and IBOs (6.8%; 95% CI: 6.1%, 7.5%).

Discussion: We estimated large inequities in cause-specific mortality in the US, highlighting the urgency of building power among workers and other marginalized groups to promote public health.
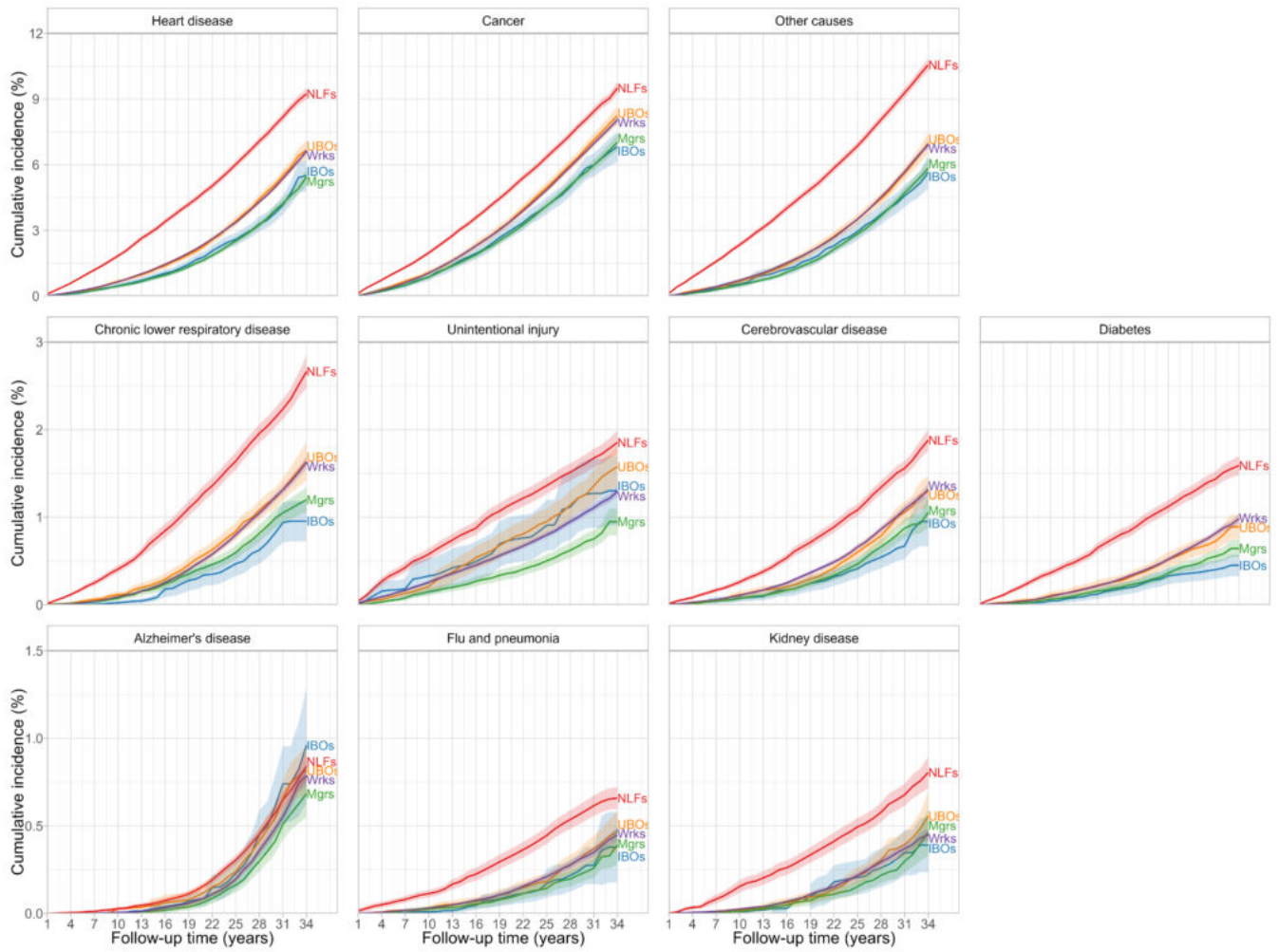
Measuring Human Mobility in Indoor Spaces: The MAPPING@Brown Study Jason R. Gantenberg* Jason Gantenberg Thomas A. Trikalinos Samuel F. Rosenblatt Guixing Wei Julia Netter Bradford Roarr Marta G. Wilson-Barthes Bryn C. Loftness Peyton B. Luiz Mark N. Lurie

Shortcomings in our understanding of disease transmission can hinder control of a circulating pathogen. Policymakers need detailed data on human mobility and interaction to inform decision-making and intervention design. During the SARS-CoV-2 pandemic, efforts to collect mobility data focused largely on the regional or national scale, but mounting effective responses to future pandemics will require supplementing these efforts with granular information on social mixing in indoor environments. We conducted the MAPPING@Brown study to explore the feasibility of collecting the relevant data. Specifically, we investigated the viability of using smartphone technology to infer individuals' movements and contact patterns indoors. In Fall 2023, we deployed a network of 2,121 Bluetooth transmitters across 8 floors of the Brown University School of Public Health (SPH) building. Transmitters resided at fixed spatial coordinates such that the approximate maximum distance between a given smartphone and a transmitter would be 2 meters. In November 2023 we enrolled a cohort of 197 SPH students, faculty, and staff, whom we asked to complete a demographic survey and to download a custom smartphone application. This app recorded which transmitters an individual phone observed, a timestamp, and the received signal strength indicators (RSSI). Over the 2-week data collection period, we collected 138,073,742 Bluetooth signal readings from 128 unique smartphones. We will infer participants' locations over time by estimating the distance between each smartphone and observed transmitter at a given time, based on a model for RSSI decay as a function of distance. Estimated distances will be used to derive devices' spatial coordinates via multilateration and other methods. The resulting map of individual trajectories—complemented by auxiliary environmental data on CO_2, temperature, and relative humidity—will inform high-resolution, spatially explicit agent-based models of indoor disease transmission.
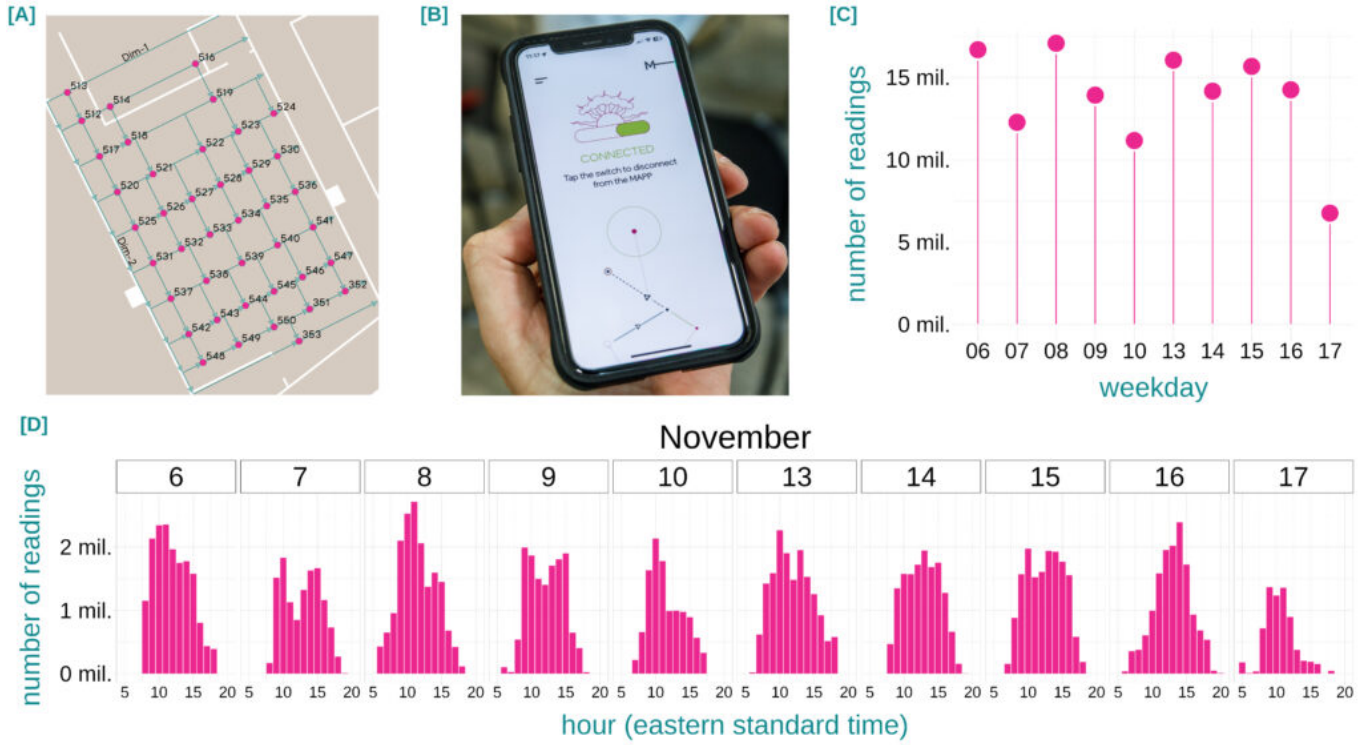
Figure. Overview of the MAPPING@Brown study. A) Bluetooth transmitter layout in a large classroom; B) The MAPPING@Brown smartphone app; C) Number of Bluetooth readings by day; D) Number of Bluetooth readings by hour.

Latino versus White Graduation Rates in Texas (2015-2021) Mireya Long* Emma Wood Mireya Long Chantel

Intro:
There is historical concern that persons of Hispanic/Latino ethnicity are graduating high school at lower rates in Texas than other groups. It is unclear if that is true across the state of Texas and if trends are changing over time.

Methods:
This cross-sectional geographic study looked at the percent of Latino US adults who graduated high school or completed the GED compared to the percent of White US adults within census tracts in Texas. Using available 5-year data from the American Community Survey in 2015, 2018, and 2021, we calculated the ratio of graduation percentages and ran a hot spot analysis for each year to compare change over time.

Results:
Each hotspot analysis showed that Houston, Austin, San Antonio, El Paso, and McAllen, Texas have a higher ratio of graduated Latino adults than White adults. Northeast Texas showed consistently higher rates of graduated White adults than Latino adults. Over time, the ratios in the Dallas area of graduated Latino adults to graduated White adults got closer to one, which means the percentages of graduated adults are closer to the same for both ethnicities.

Conclusion:
There is a general trend of equalizing percentages of high school attainment among Latinos and Whites. There are still areas of Texas (mostly in the Northeast) that have statistically significantly higher percentages of graduated White adults than graduated Latino adults. Therefore, the state should prioritize educational programs that target groups that are not reaching equal attainment.

Latino versus White Graduation Rates in Texas (2015-2021)
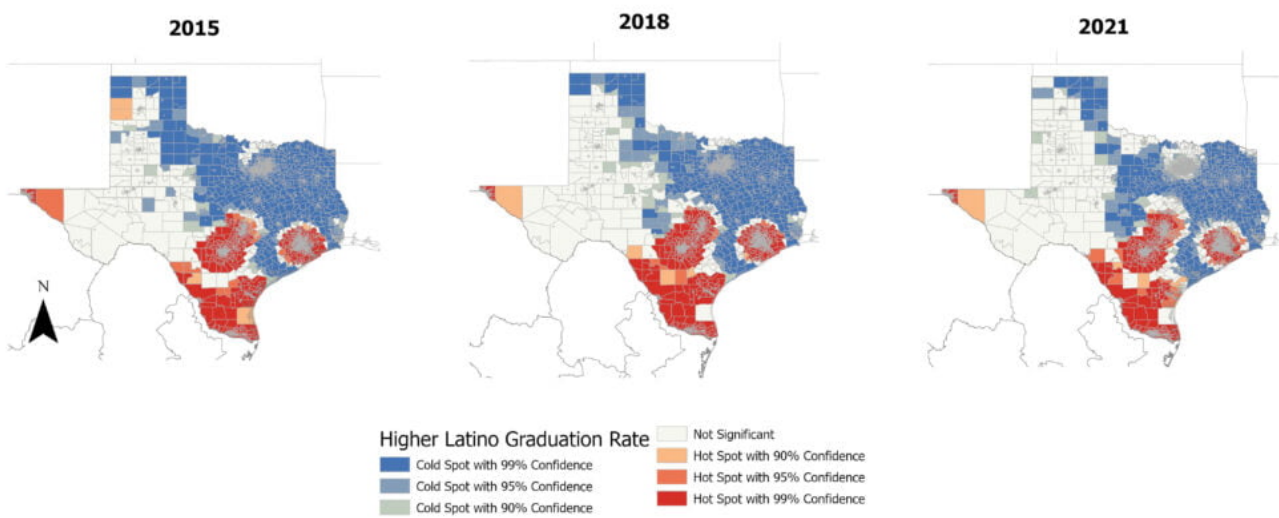
Housing matters: The impact of housing instability on all-cause mortality among people with HIV in British Columbia, Canada Megan Marziali* Megan Marziali Katherine Kooij Michael Budu Monica Ye Cassidy Tam Valerie Nicholson Taylor McLinden Scott Emerson Julio Montaner Robert Hogg

Aim: British Columbia (BC), Canada, is experiencing a housing crisis marked by a shortage of safe and affordable housing. We explore the impact of housing instability on all-cause mortality among a cohort of people with HIV (PWH) in BC.

Methods: Data are from the Longitudinal Investigation into Supportive and Ancillary Health Services (LISA) study, a cross-sectional survey (2007-2010) (n=998). Survey data are linked with prospective administrative health data from the BC Centre for Excellence in HIV/AIDS Drug Treatment Program (DTP) until March 31, 2020. Selection bias into LISA was potentially introduced through oversampling PWH marginalized by sociostructural inequities. We used inverse probability of participation weighting (IPPW) to address this bias. We constructed participation weights using information from the entire DTP database, which includes all known PWH in BC accessing antiretrovirals via the DTP (including respondents and non-respondents to the LISA survey). We modeled the association between housing instability and all-cause mortality using IPPW-weighted log-binomial regression, adjusting for confounders. Leveraging time-to-event data, we also estimated hazards of mortality associated with housing instability using an adjusted, IPPW-weighted Cox proportional hazards model.

Results: In this sample, 215 (22%) people reported housing instability. Overall, 239 people (24%) died from any cause between completion of the LISA survey until March 31, 2020; of those people, 94 (39%) experienced housing instability. We found experiences of housing instability were associated with an increased risk of mortality (aRR: 1.33; 95%CI: 1.18-1.50); similarly, housing instability was associated with an increased hazard of mortality (aHR: 1.46; 95%CI: 1.08-1.96).

Conclusion: PWH experiencing housing instability may have a greater risk of mortality. Our findings add to the literature supporting a need to expand access to safe and affordable housing.

Citizenship in Organ Procurement and Transplantation Network Data in 2022 Jesse Howell*
Jesse Howell Tamika Watkins Peter Stock Pramod Bonde

Background: The Organ Procurement and Transplantation Network (OPTN) Ad Hoc International Relations Committee (AHIRC) examines citizenship data for transplant candidates and recipients in their annual report. This report does not contain data on organ donors, and the committee expressed interest in examining donor data to supplement the report data.

Methods: We evaluated OPTN data collected in 2022 for waitlist (WL) registrations, transplanted recipients, and deceased organ donors (dd), and removed those with missing citizenship. Citizenship categories included: U.S. citizen, non-U.S. citizen/U.S. resident, and non-U.S. citizen/non-U.S. resident (NCNR), which was split into those who came to the U.S. for the purpose of transplant (NCNR-tx) and for a reason other than transplant (NCNR-oth). Those listed before 2012 used non-resident alien (NRA) rather than NCNR. Dd had an additional citizenship option of "unknown".

Results: In 2022, 68,099 adult and pediatric solid organ registrations were added to the WL. Of those, 1.5% were NCNR candidates, including 773 NCNR-oth and 225 NCNR-tx. There were 36,415 solid organ dd transplants in 2022 and 1.5% were to NCNR recipients, including 404 NCNR-oth, 125 NCNR-tx, and 4 NRA. Of all dd in 2022, 0.5% (n=81) were NCNR and 5.8% (n=865) had unknown citizenship.

Conclusion: There was no difference in the proportion of NCNR WL registrations and dd transplant recipients, but comparing to dd is difficult as almost 6% had unknown citizenship. In 2021, a proposal was released to remove the citizenship question from dd forms citing challenges in collecting this data from donor families. This was ultimately not pursued due to pushback, including from IRC, which suggested that the community needed to be better informed on why this data is collected and what it is used for. They also advised providing clarity on citizenship data elements to ensure less variation in how programs respond. These results support those recommendations.

Social

Association between social support and DNA methylation aging: an explorative study using NHANES 1999-2002 cohort Hanyang Shen* Hanyang Shen Nicole Gladish Belinda Needham David Rehkopf

Social support has been suggested by decades of research to be a consequential influence on health outcomes. Studies have reported a lack of social support increasing the risk of CVD, stroke, diabetes, cancer, and mortality. However, epigenetic aging, especially DNA methylation aging, has not been fully explored as outcomes, as it is a newly developed concept since 2013. This study examines the correlations between multiple social support measurements and a collection of DNA methylation biomarkers in a multiracial sample. The National Health and Nutrition Examination Survey (NHANES) is a national representative cohort of the noninstitutionalized US population. The sample with available DNA methylation data includes a random selection of one-half of eligible non-Hispanic white respondents aged 50 years and older (n=1,071) and all eligible non-Hispanic black (n=566), Mexican American (n=730), and other race (n=79) respondents aged 50 years and older from the 1999-2002 cohort. The Illumina Infinium Methylation EPIC Assay was used to measure DNA methylation sites per sample. Quality control steps include outlier removal, color correction, background subtraction, and normalization. The DNA methylation variables calculated include 13 clocks (Horvath, Hannum, SkinBlood, PhenoAge, telomere, Yang, Zhang, Lin, Weidner, VidalBralo, DunedinPoAM, GrimAge, and GrimAge2) and 10 mortality-related biomarkers (packyears, cystatin C, Adrenomedullin, Beta-2 microglobulin, logC-reactive protein, plasminogen activator inhibitor antigen, log HbA1C, leptin, TIMP metallopeptidase inhibitor 1, and growth differentiation factor 15). Social support exposures include perceived emotional support, perceived financial support, received support, and marital status. After controlling for covariates, we expect social support variables to be more related to clocks trained by morbidity and mortality and related to biomarkers of inflammation, a system more sensitive to psychosocial stress.

Social

Impact of Vietnam-era G.I. Bill Eligibility on the Distribution of HbA1c Among Older Americans: Evidence from the Vietnam Draft Lottery Natural Experiment Aayush Khadka*
Aayush Khadka Lucia Pacca Abigail Arons Anusha M. Vable

Diabetes complications risk increases non-linearly with increasing glycosylated hemoglobin (HbA1c) levels. Structural interventions that reduce fundamental causes of disease (e.g., low education) may reshape the HbA1c distribution by having larger protective effects at higher HbA1c levels. We assessed this theory in the context of the Vietnam-era G.I. Bill, a structural intervention that subsidized college education for 6 million veterans. Using the Vietnam draft lottery natural experiment, we estimated the causal impact of G.I. Bill eligibility on the HbA1c distribution among Health and Retirement Study respondents. Eligibility depended on length and manner of discharge from military service. Our analytic sample included men born between 1947-1953 with one valid outcome measure (N=1,639). We proxied G.I. Bill eligibility using lottery-defined draft eligibility (intention-to-treat [ITT] analysis) and self-reported veteran status (instrumental variables [IV] analysis; instrument: draft eligibility). HbA1c measured from blood spots was our primary outcome. We estimated ITT effects using linear and quantile regressions and IV effects using two-stage least squares and IV quantile regression estimators. We adjusted for year-and-month-of-birth fixed effects and estimated heteroskedasticity robust standard errors in all models. Draft eligibility lowered mean HbA1c (b=-0.09, 95% confidence intervals (CI) -0.23,0.05), had negligible impact on lower HbA1c quantiles, and had protective effects at higher quantiles (e.g., 10th quantile: b=0.00 [95%CI -0.08,0.08]; 90th quantile: b=-0.25 [95%CI -0.51,0.01]). IV results were generally in the same direction as the ITT effects, but standard errors were larger (e.g., 10th quantile: b=-0.13 [95%CI -1.30,1.03]; 90th quantile: b=-1.39 [95%CI -31.44,28.66]). Results suggest that G.I. Bill eligibility reshaped the HbA1c distribution to one of lower diabetes risk by being more effective in the high-risk right tail of the HbA1c distribution.

Effect of lottery-defined draft eligibility on mean and quantiles of HbA1c (intention-to-treat effect)
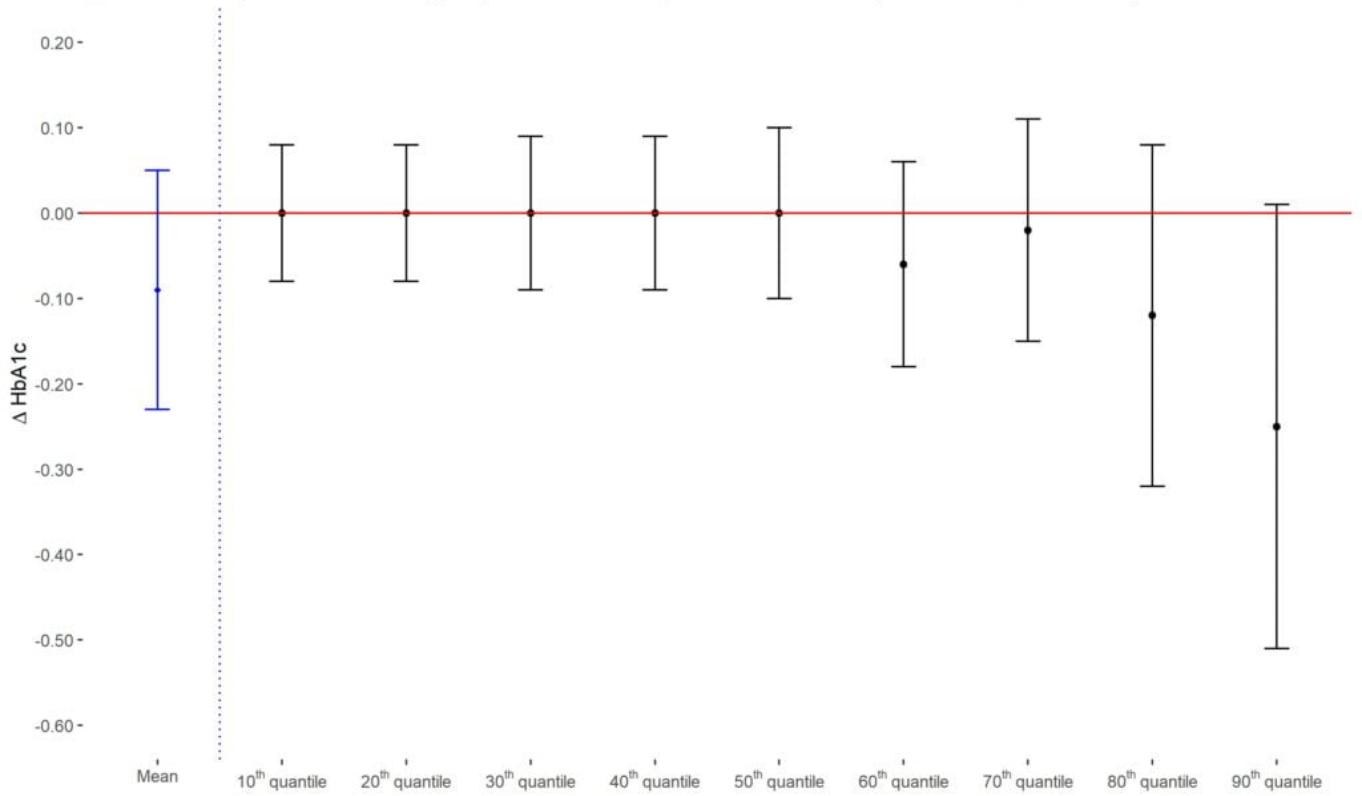
Notes: Effect at the mean estimated using linear regression while effect at the quantiles estimated using quantile regression.
We adjust for year-and-month-of-birth fixed effects and estimate heteroskedasticity robust standard errors in all models.

Differential associations between early-life education and dementia risk by childhood socioeconomic status, race, and sex Whitney Wells* Whitney Wells Jilly Hebert Anusha Vable

Early-life education plays a key role in child development, which influences later cognitive health. However, access to early education varies widely in the US. Two common pre-K educational options are paid preschool and Head Start (free preschool for families with low income). To inform policy related to pre-K access, this study evaluates if attendance at preschool or Head Start is associated with dementia risk.

We used the National Longitudinal Survey of Youth 1979 (NLSY) to examine the relationship between self-reported attendance at preschool or Head Start and dementia risk. We used results from a prediction model that extends on a previously validated algorithm estimating dementia risk from cognition measures (mid-life memory, attention, and mental status) and mid-life demographics and health conditions. We adjusted for demographic factors and proxies for childhood SES (cSES), and examined subgroup differences by race/sex and father's employment status as a marker of cSES with interaction terms.

There was little relationship between preschool and dementia risk in all models, or for Head Start and dementia risk overall; however, in stratified models, we found differential relationships for Head Start by father's employment status and race/sex. While individuals whose fathers were employed showed no association, attending Head Start was associated with lower dementia risk for individuals whose fathers were not present in the household (-0.01; 95% CI: -0.02, -0.001). Head Start was associated with higher dementia risk for White men (0.02; 0.003, 0.03) but lower dementia risk for Black men (-0.01; -0.02, -0.001), with limited evidence for an association for Hispanic men and women, White women, or Black women.

The Head Start program may have reduced socioeconomic and Black-White dementia inequities by lowering dementia risk for individuals who grew up in single-mother households and for Black men.

Association between Head Start attendance and later-life dementia risk, by subgroup:
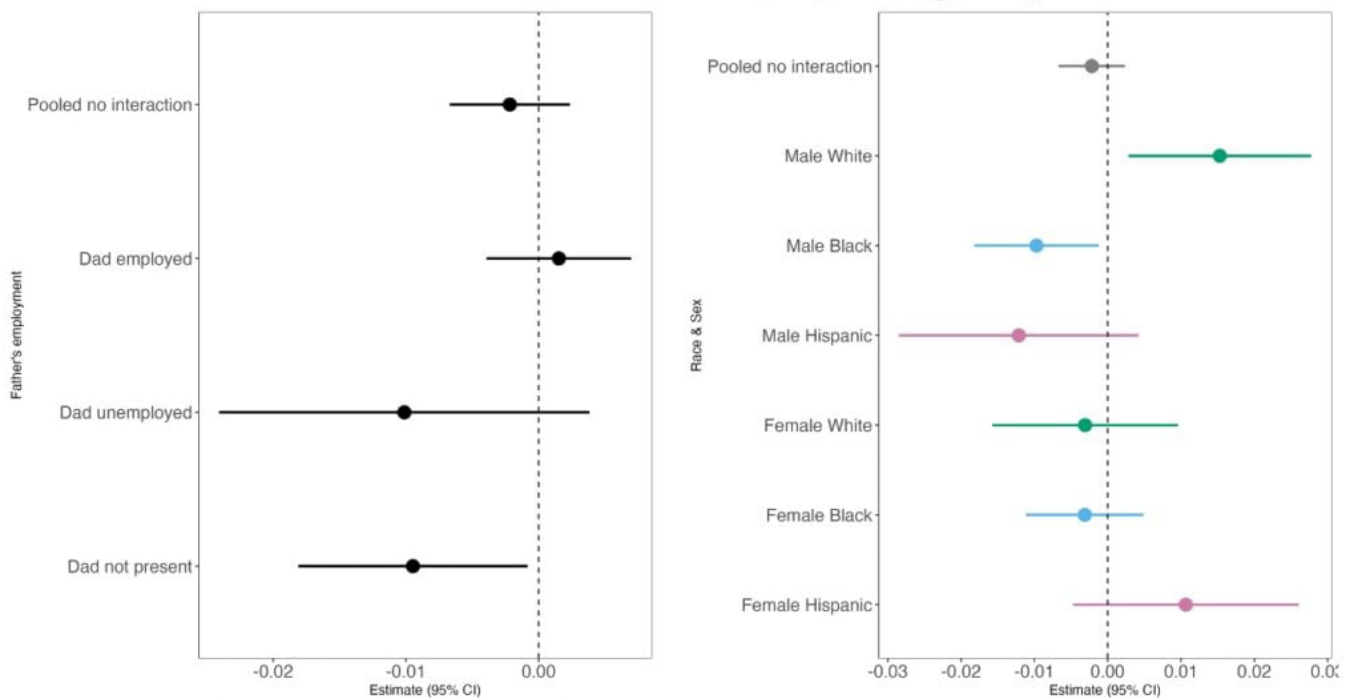
Figure 1a&b. Association between Head Start attendance and later-life dementia risk by father's employment (as proxy for childhood SES) and race/sex. Subgroup-specific estimates were obtained using rotating reference groups to estimate subgroup effects. Models adjusted for all covariates.
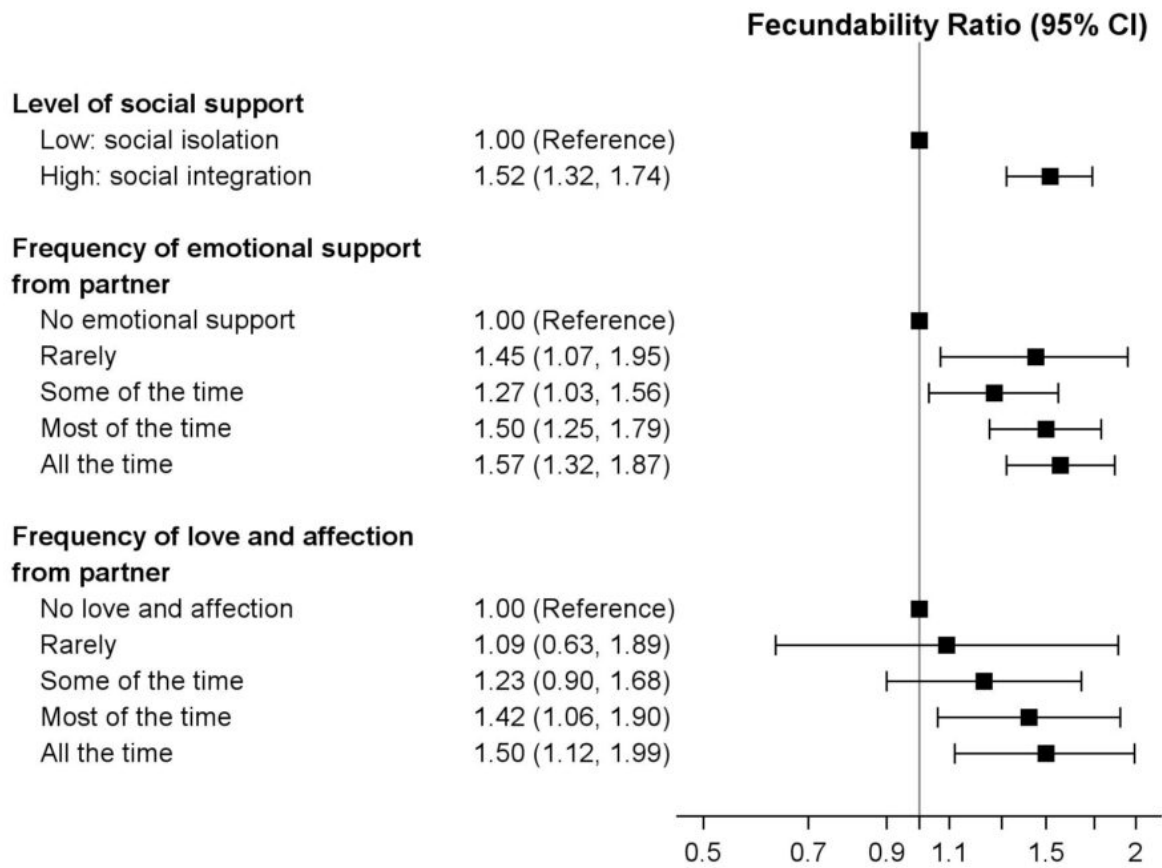
Social

Association of social and partner support with fecundability Molly N. Hoffman* Molly Hoffman Collette N. Ncube Sharonda M. Lovett Julia C. Bond Renée Boynton-Jarrett Lauren A. Wise

Background: Social connection is a key determinant of health and a priority area for the U.S. Surgeon General.

Methods: We used data from Pregnancy Study Online, a North American preconception cohort study (N=6,866). Eligible female participants completed a supplemental questionnaire (SQ) on psychosocial factors at baseline. We assessed past-year social support with an adapted 8-item version of the Berkman-Syme Social Network Index (SNI) and fecundability (per-cycle probability of conception) from bimonthly follow-up questionnaires. Summed SNI scores were categorized as <5 (socially isolated) and ≥5 (socially integrated). We assessed past-year partner support using 2 questions: "To what extent could you count on your partner to provide you with emotional support?"; "To what extent did your partner show you love and affection?" (response options: never, rarely, some of the time, most of the time, all the time). We used proportional probabilities regression to estimate fecundability ratios (FR) and 95% CIs, adjusted for age and history of infertility or miscarriage and weighted by the inverse probability of SQ completion.

Results: Social integration was common (93%) and associated with fecundability (FR 1.52; CI 1.32-1.74). Most participants reported "all the time" to questions about partner emotional support (53%) or love and affection (61%). Relative to those with no partner emotional support, fecundability was higher for those with support rarely (1.45; CI 1.07-1.95), some of the time (1.27; CI 1.03-1.56), most of the time (1.50; CI 1.25-1.79), and all the time (1.57; CI 1.32-1.87). Relative to those with no partner love and affection, fecundability was higher for those with partner love and affection rarely (1.09; 95% CI 0.63-1.89), some of the time (1.23; CI 0.90-1.68), most of the time (1.42; CI 1.06-1.90), and all the time (1.50; CI 1.12-1.99).

Conclusions: Social integration and partner emotional support and affection may have positive effects on fecundability.
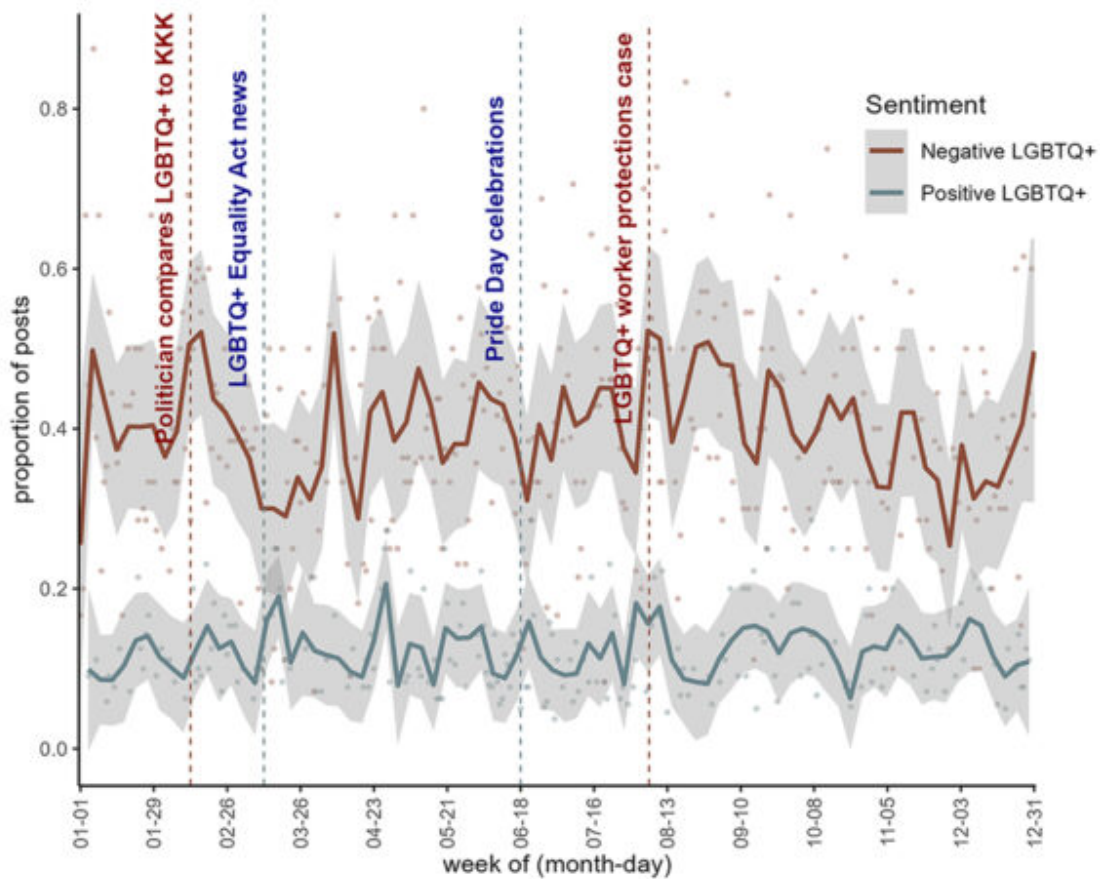
Fecundability Ratio (95% CI)

Level of social support

Low: social isolation	1.00 (Reference)
High: social integration	1.52 (1.32, 1.74)

Frequency of emotional support from partner

No emotional support	1.00 (Reference)
Rarely	1.45 (1.07, 1.95)
Some of the time	1.27 (1.03, 1.56)
Most of the time	1.50 (1.25, 1.79)
All the time	1.57 (1.32, 1.87)

Frequency of love and affection from partner

No love and affection	1.00 (Reference)
Rarely	1.09 (0.63, 1.89)
Some of the time	1.23 (0.90, 1.68)
Most of the time	1.42 (1.06, 1.90)
All the time	1.50 (1.12, 1.99)

0.5   0.7   0.9   1.1   1.5   2

Note: Models are weighted with inverse probability of selection weights and adjusted for age and history of infertility or miscarriage

Social

Social media-derived LGBTQ+ sentiment and teen mental health Junaid S Merchant* Thu T. Nguyen Heran Mane Xiaohe Yue

The proliferation of state-level policies targeting LGBTQ+ youth reflects growing divisions in public attitudes and raises concerns about the psychological impacts of these trends amidst historical lows in teen mental health. This study utilized social media data to measure public sentiment about LGBTQ+ issues and examined associations with mental health outcomes of US teens in the 2019 release of the Youth Risk Behavior Surveillance System (YRBSS). X (formerly Twitter) posts (N=18,000,000+) from 2016-2022 were collected for an ongoing study. Posts were filtered for LGBTQ+ keywords, classified for positivity or negativity using a machine learning sentiment model, and averaged at geographic and temporal scales to quantify LGBTQ+ sentiment as the proportion of posts classified in each category. Time-series of nationally averaged LGBTQ+ exhibit sensitivity to LGBTQ+-relevant historical events, like the rise in positivity during Pride events and spikes in negative sentiment following anti-LGBTQ+ policy discussions in 2019 (Figure 1a). We evaluated the relationship between state-level LGBTQ+ sentiment and self-reported suicidal ideation in the past 12 months (yes/no binary responses) among high school students (N=160,112) across 44 states. Results show that state-level negative LGBTQ+ sentiment is associated with slightly elevated risk for suicidal ideation (odds ratio = 1.014 [1.00, 1.027]) even when adjusted for individual- and state-level factors. We uncovered novel patterns of disparities when disaggregating identity dimensions across 5 races, 3 sexual orientations, and 2 genders (=30 intersecting strata; Figure 1b) indicating stronger associations between LGTBQ+ sentiment and health among homo- and bisexuals compared to heterosexual teens. Our findings highlight the utility of social media data for examining the ongoing challenges of LGBTQ+ health and the importance of considering intersecting identities in health disparities research.

A) LGBTQ+ Sentiment Timelines 2019

Sentiment
- Negative LGBTQ+
- Positive LGBTQ+

Politician compares LGBTQ+ to KKK
LGBTQ+ Equality Act news
Pride Day celebrations
LGBTQ+ worker protections case

proportion of posts

week of (month-day)

B) Predicted Probabilities of Suicidal Ideation

gender = female

Homo | Hetero | Bi

gender = male

Homo | Hetero | Bi

race
- Asian
- Black
- Hispanic
- Other/Multi
- White

state-level negative LGBTQ+ sentiment (% negative posts)

Social
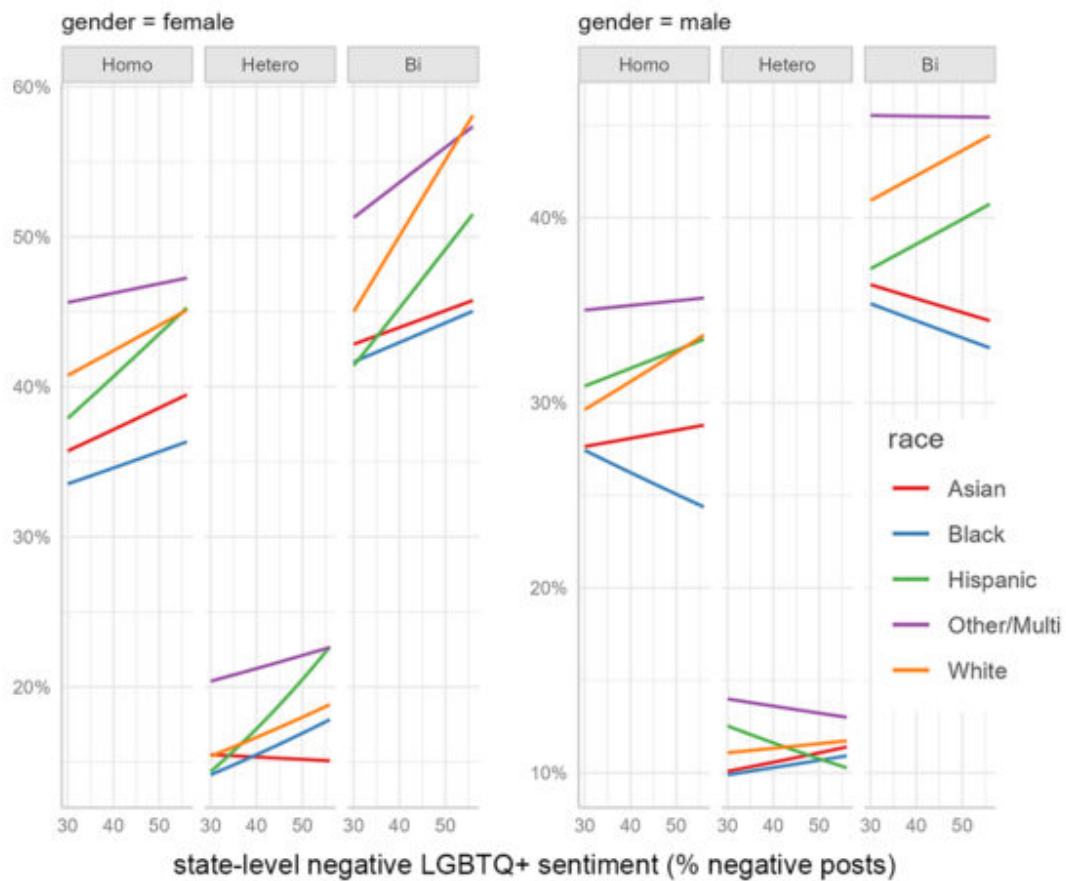
Assessing the Relationship Between Place-Based Economic Connectedness and Health in the United States Stephen Uong* Stephen Uong Nadav Sprague Katherine Keyes Andrew Rundle

Introduction

Economic connectedness, connections between people of different socioeconomic status, is related to higher economic mobility but its relationship with health is uncertain. In a US-nationwide analysis, we aim to assess our hypothesis that economic connectedness is protective against adverse health outcomes and positively associated with preventive service utilization, with stronger associations in areas experiencing more poverty.

Methods

We merged zip code tabulation area (ZCTA)-level data from the Social Capital Atlas (economic connectedness), CDC PLACES 2023 release (health indicators), US Census American Community Survey 2014-2018 estimates (sociodemographics). Economic connectedness was defined as the share of high-SES friends among low-SES people (72.2 million Facebook users aged 25-44 active within last 30 days from May 28, 2022). Across 18,074 ZCTAs, we fit adjusted linear models to determine the association between economic connectedness with A) 5 adverse health indicators: no insurance access, poor health status, health diagnosis/condition, disability, health behavior and B) preventive service utilization. We further stratified models by poverty, <5%, 5-20%, and >20% (% households with incomes lower than the federal poverty level) and assessed whether hypotheses were met (p-association < 0.05).

Results

Overall, 89% (n=33) of models showed protective associations for adverse health outcomes and positive associations for preventive service utilization. In poverty-stratified analyses, 76% (n=28) of models had stronger associations with higher poverty (>20% vs. <5%).

Conclusion

Our findings suggest that economic connectedness is beneficial for health, especially in high poverty areas. This emphasizes the potential of community-level interventions, such as designing public library programs and parks to foster cross-class interactions and friendships, to contribute to improved community health.
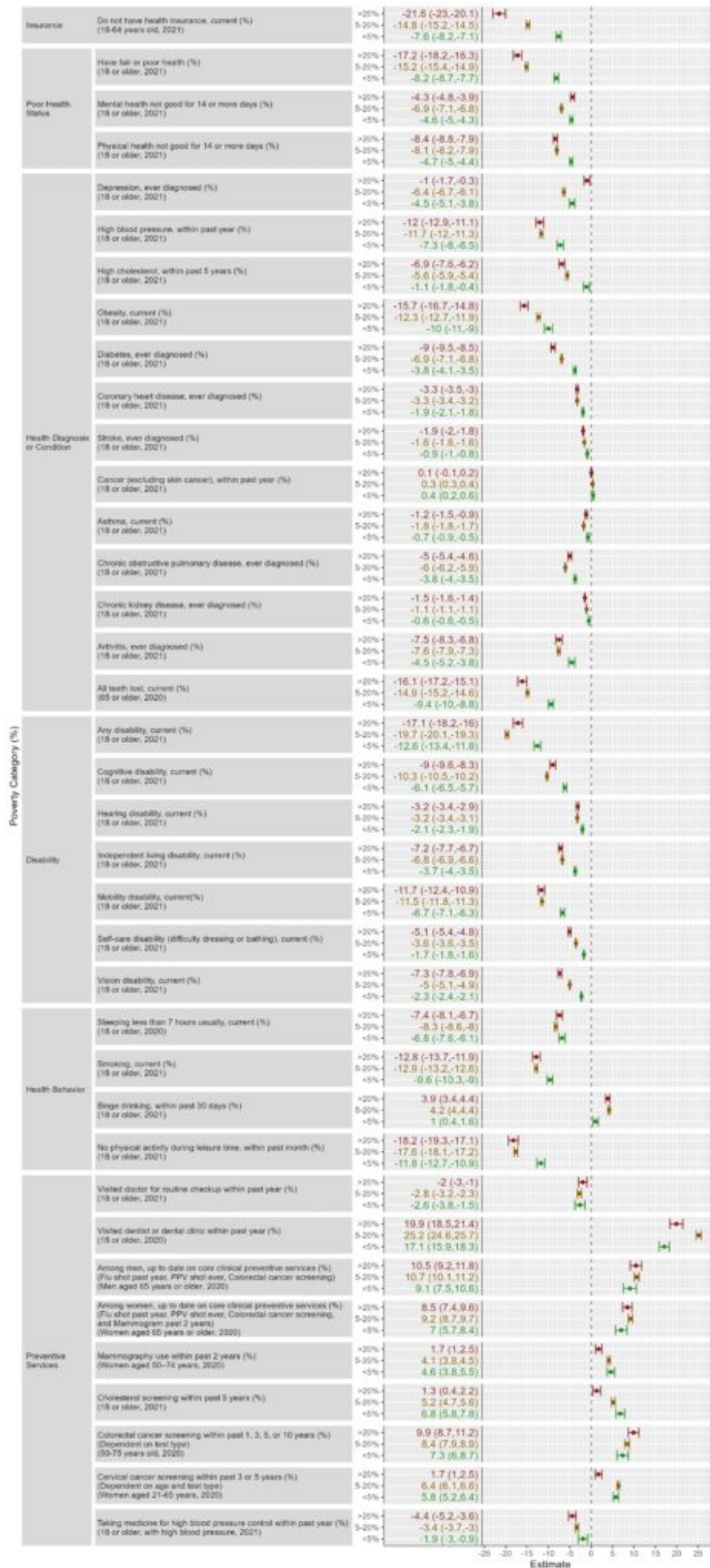
Whose assets? The relation between individual and household level income and savings with mental health Catherine Ettman* Catherine Ettman Emma Dewhurst Ben Thornburg Brian Castrucci Sandro Galea

A growing literature has established a link between financial assets (e.g. income and savings) and mental health. However, it is unclear whether the mental health benefits of financial assets differ across personal versus household ownership of the asset. Using four waves of the nationally representative COVID-19 and Life Stressors Impact on Mental Health and Well-being (CLIMB) survey collected in Spring 2020, 2021, 2022, and 2023 (n=1,271 participants), we estimated the odds of elevated symptoms of depression (PHQ-9) and anxiety (GAD-7) across individual and household level income and savings in separate and pooled models with time fixed effects, clustering standard errors at the individual level to account for repeated measures over time. Post-stratification weights were constructed for this sample such that estimates are consistent with nationally representative statistics from the Current Population Survey. All models adjusted for age, race and ethnicity, sex, education and employment status, and geographic region. Having personal savings below the median category ($10,000-$14,999) was associated with 1.76 times the odds of depression (95% CI: 1.19, 2.59; p = 0.005), and 1.53 times the odds of anxiety (95% CI: 1.01, 2.32, p = 0.045) relative to having $15,000 or over in savings. Having personal annual income below the sample median category ($35,000-$44,999) was associated with 1.67 times the odds of depression (95% CI: 1.23, 2.28; p = 0.001), and 1.75 times the odds of anxiety (95% CI: 1.24, 2.47, p = 0.001) relative to having $45,000 or over in income. After adjusting for demographic and socioeconomic status, personal-level financial assets were significantly associated with mental health but household-level assets were not. The mechanisms by which savings and income protect mental health may differ, informing different potential policy interventions to address well-being. It is possible that focusing interventions on the individual, rather than the household, may be a more direct way to address the mental health risks associated with having fewer financial assets.

Study Design

Sampling based on Milestones (SMile): A potential alternative study design Ian Shrier* Ian Shrier Tibor Schuster Yi Li Zachary Vernec Russell Steele

Some authors suggest simulating data to evaluate potential biases prior to starting a study. We wanted to evaluate a current hypothesis that concussion causes symptoms through decreases in binocular vision near point convergence (NPC). Because symptom resolution ranges from days-months, sampling at fixed timepoints is inefficient. Rather, if the NPC vs. symptom relationship is time-independent, we expect no bias with sampling based on milestones (SMile design): time of concussion, 50% improved symptoms, and healed. We created Oracle data (comprehensive Monte Carlo simulation study) using the same healing rate and linear slope for NPC vs. symptom for each participant. Bias was the difference of the average slope and the Oracle data slope (= 1). There was never bias when there was no measurement error. With multiplicative measurement error up to 50%, the overall bias was <5%. Grouped by initial symptom score, the slope was underestimated by ~30% for the mild (low symptom score) group, and overestimated by ~8% for the severe group (high symptom score). Bias increased in the mild group when we excluded participants who healed quickly. Bias decreased when measurement was delayed by days after the milestone. All these biases completely depend on observed error measurement. The SMile design may be useful when, within the same individual, two linearly related characteristics (ie. NPC and symptom scores) can be precisely measured over time. Further work will explore other assumptions.

Substance Use

Relative effectiveness of cigarillo warning themes in text and pictorial formats: An experimental study among a nationally representative sample of US young adults Rime Jebai* Rime Jebai Erin L. Sutfin Alexandra R. Zizzi Beth A. Reboussin Jennifer Cornacchione Ross

Significance: Health warning labels (HWLs) are an effective tool to communicate the health risks of cigar use and can decrease use when applied on cigar packages. This study aims to assess the relative effectiveness of the themes of the six FDA-proposed cigarillo warnings in text and pictorial format by cigarillo smoking status.

Methods: A nationally representative sample of cigarillo users and susceptible nonusers ages 18-29 were randomized to a text or study-developed pictorial warning condition. Within each condition, participants viewed all six of the FDA-proposed HWLs in random order. The warning themes were lung cancer and heart disease; cancers of the mouth and throat; nicotine/addiction; not a safe alternative; harm to baby; and secondhand smoke. We assessed negative affect, cognitive elaboration, and perceived message effectiveness (PME) for each warning. ANOVA for repeated measures followed by Bonferroni adjustment for multiple comparisons were used to test the equality of outcome means between the HWLs themes within text and pictorial format for current (past 30 day) cigarillo users and susceptible nonusers.

Results: Of the 348 participants, 62.0% were current users, and 37.9% were susceptible nonusers. The sample was 46.5% female; mean age 23.9. There were significant differences between the 6 pictorial HWLs' themes for negative affect (F=2.35;p=0.04). Among current users, the pictorial HWL cancers of the mouth and throat (M±SD=2.98±1.13) elicited the lowest negative affect compared to the nicotine/addiction (3.35±1.27;d=0.29), harm to baby (3.31±1.26;0.25), and not a safe alternative pictorial HWLs (3.30±1.24;0.26). The nicotine/addiction pictorial HWL (3.35±1.27) evoked higher negative affect than lung cancer and heart disease (3.04±1.25;0.27). No significant differences were found among pictorial HWL themes for susceptible nonusers. No differences were observed among the text HWL themes for current or susceptible nonusers.

Conclusions: Differences among the 6 HWL themes emerged within the pictorial format. Except for cancers of the mouth and throat and lung cancer and heart disease, the pictorial HWLs depicted people, displaying the full face or the entire person. Pictorial HWLs depicting people to represent health effects may be more effective than images of diseased organs or body parts. The FDA should consider adding such images to the text warnings on cigarillo packages to better convey the health risks of cigarillo smoking and reduce its rates among young people.

Substance Use

Association Between State Cannabis Laws and Opioid Outcomes: A Systematic Review David Fink* David Fink Lauren Gorfinkel Sarah Gutkind Diana Bachowski Zachery Mannes Andrew Saxon Deborah Hasin

AIM: Individuals and communities in the US are increasingly devastated by opioid-related morbidity and mortality. During the same time period these increases occurred, paralleling these increases in opioid-related morbidity and mortality, state medical cannabis laws (MCL) and recreational cannabis laws (RCL) have become increasingly widespread. This study aimed to examine whether cannabis legalization is associated with changes in the prevalence of opioid outcomes.

METHODS: We systematically reviewed the literature in 5 databases (EconLit, EMBASE, MEDLINE, PsycINFO, Web of Science Core Collection) and Google Scholars for titles and articles. We included observational studies published in English that examined the association between state MCL or RCL and opioid-related health outcomes.

RESULTS: Of 1536 articles, 45 met the inclusion criteria. Of these, 17 examined MCL only, 11 examined RCL only, and 8 examined both MCL and RCL. Opioid-related outcomes included opioid prescriptions dispensed (n=14), opioid overdose deaths (n=13), opioid use (n=11), opioid use disorder (n=4), opioid use disorder treatment (n=2), and opioid-related hospital or emergency department visits (n=4). Overall, the current literature is mixed. However, studies using data from 2010 and earlier tended to support an association between MCL and opioid outcomes, but this relationship often became neutral or even negative in more recent years.

CONCLUSIONS: The shift in direction of results from positive to neutral or negative in more recent years may indicate that earlier results involving only MCL were spurious, i.e., the result of unrelated temporal trends in opioid outcomes and cannabis laws, or that the current situation, with cannabis increasingly legalized for recreational purposes, is different from the earlier one. As the number of states legalizing cannabis for recreational use continue to increase, further research on cannabis legalization and opioid outcomes is crucial.

Substance Use

Examining gender disparities in health and COVID-19 pandemic impact among those with substance use disorders: National Survey on Drug Use and Health, 2021 Brandi Moore*
Brandi Moore Farzana Kapadia

Background: Despite growing attention to the overall health and wellbeing of people with substance use disorders (SUD), there has been limited focus on understanding potential gender-based health disparities among this population. Thus, we examined the extent of such gender-based disparities among persons with SUD, particularly after the COVID-19 pandemic.

Methods: Employing 2021 National Survey on Drug Use and Health data restricted to n=10,311 adults meeting DSM-5 criteria for past-year drug and/or alcohol use disorder, weighted prevalence estimates of key substance use, health, and COVID-19 pandemic-related outcomes were calculated by gender. Further, using multivariable logistic regression models, we examined the relationship between gender and these outcomes while controlling for key sociodemographic variables.

Results: In 2021, 14.20% of women and 19.06% of men met DSM-5 criteria for SUD. Compared to men, women were more likely to report: recent STI (AOR=1.88; 95%CI:1.22-2.89), recent emergency department visits (AOR=1.26, 95%CI:1.02-1.55), recent unmet need for mental healthcare (AOR=2.05; 95%CI:1.68-2.50), serious/moderate mental illness (AOR=2.08; 95%CI:1.78-2.44), and presence of ≥1 chronic health condition (AOR=1.33; 95%CI:1.13-1.57). Also, compared to men, women were more likely to report negative impacts from the COVID-19 pandemic including: frequent, serious financial worries (AOR=1.53; 95%CI 1.28-1.83), increased alcohol intake (AOR=1.51; 95%CI:1.26-1.82), declines in mental health (AOR=2.12; 95%CI:1.78-2.52), and moderate/severe impacts on health due to a lack of access to mental healthcare (AOR=1.42; 95%CI:1.08-1.89) or medical care (AOR=1.83, 95%CI:1.31-2.56).

Conclusion: Persistent gender-based health disparities exist among those with SUD. Future research on the health/wellbeing of persons with SUD should account for and further investigate such disparities, especially during periods of social and economic shocks such as the COVID-19 pandemic.

Substance Use

Promethazine Use, Abuse, and Related Harms in the United States Saranrat Wittayanukorn Conrad* Saranrat Conrad Henry Appiah Sara Karami Celeste Mallama Sheheryar Muhammad Rajdeep Gill Rose Radin

Background: Promethazine, an antihistamine, is widely used in the U.S. and indicated for several conditions. There have been reports of promethazine-containing products (PP) abuse with/without other substances.

Objectives: To quantify dispensing of selected PP (promethazine single-entity [SE], promethazine-codeine combination [CC], and promethazine combination [CO] products, excluding codeine) and harms associated with their abuse.

Methods: We used the IQVIA U.S. Launch Edition database (2010-2022) to estimate annual prescriptions dispensed for PP from U.S. outpatient retail pharmacies. We examined the frequency and utilization-adjusted rates of poison center (PC) cases and emergency department (ED) visits associated with PP abuse by using the National Poison Data System (2010-2022) and National Electronic Injury Surveillance System-Cooperative Adverse Drug Event Surveillance (2016-2021).

Results: The estimated total prescriptions dispensed for PP decreased 41% from 20.8 million (M) in 2010 to 12.3M in 2022. Promethazine SE was the most commonly dispensed PP (55%). Overall, PC abuse cases involving PP declined from 2010 (n=232) to 2022 (n=99); 2,383 PC abuse cases involving PP were observed. Promethazine CC had higher utilization-adjusted annual rates of PC abuse cases (18.9-26.1 per 1M prescriptions dispensed) than promethazine SE (10.4-14.7) or promethazine CO (2.4-5.0). Among single-substance PP PC abuse cases, minor effect was the most common medical outcome category. Annual national estimates of ED visits involving promethazine SE (1,772 visits) and promethazine CC abuse (1,411 visits) usually involved additional substances. The annual utilization-adjusted rate of ED visits involving abuse of promethazine CC (93.1) was higher than for promethazine SE (40.6).

Conclusions: Amid declining retail dispensing of PP in the U.S., national PC and ED visit data suggest that PP abuse-related harms are relatively uncommon, declining, and often involve promethazine CC.

Patterns of Alcohol Misuse Screening in a Nationally Representative Sample of Older Adults Samantha Brown* Samantha Brown Iva Magas Jennifer Hoenig

Background: Alcohol misuse among U.S. older adults is a growing concern. Alcohol screening is a crucial intervention point for older adults given their frequent contact with healthcare. This study examines national patterns in alcohol screening among adults aged 65 or older who had outpatient medical visits.

Methods: The 2021-2022 National Surveys on Drug Use and Health were analyzed. Alcohol misuse screening was defined as having been asked by a healthcare provider about the amount or frequency of alcohol use or presence of problematic alcohol use. The prevalence of past-year alcohol misuse screening, alcohol use disorder (AUD), and past-month binge drinking were examined by population characteristics. Analyses were conducted in SUDAAN.

Results: Among past-year alcohol users 65 or older, 91.9% had an outpatient medical visit, of whom 48.1% were screened for alcohol misuse. Screenings were more prevalent among those who were younger (ages 65-69: 53.5%, 70-79: 48.3%, ≥80: 33.7%), male (52.8%, female: 43.6%), veterans (54.7%, non-veterans: 46.5%), or had higher income (≥$75K: 53.4%, $50K-$74,999K: 50.0% vs $20K-$49,999: 41.7%, <$20K: 40.5%). Additionally, 8.5% of alcohol users 65 or older with an outpatient medical visit had AUD and 18.6% were binge drinkers, of whom 67.6% and 56.1% were screened, respectively. While older adults with lower income were less likely to be screened, they were more likely to have AUD (<$20K: 13.7% vs $50K-$74,999K: 6.1%, ≥$75K: 8.0%) or binge drink (<$20K: 24.9% vs $50K-$74,999: 15.3%, ≥$75K: 17.4%).

Discussion: Despite guidelines for universal substance misuse screening in older adults, less than half of older adults examined were screened for alcohol misuse and a third of those with AUD were not screened. Screening was lowest among adults 80 or older, who suffer more severe health consequences from alcohol. Further research is needed to understand the screening gap among low-income older adults, who were more likely to have alcohol misuse.

Substance Use

National Online Survey of People Who Use Drugs: Challenges and Potential Solutions

Winston Luhur* Winston Luhur Cristina Chin Czarina Navos Behrends

The majority of surveys of people who inject drugs (PWID) are limited in reach and access to the full population of PWID, both in geography and diversity, due to limitations of reaching this hidden population through usual recruitment methods. People of color, LGBTQIA+ people, people residing in rural areas and/or harm reduction deprived areas, and people who rarely connect with harm reduction services are the least surveyed and understood PWID populations. Online-based recruitment and surveys may be a pathway to reach these hidden populations of PWID. As the use of technology and internet access becomes more ubiquitous, research using online-based recruitment and survey techniques are growing in the field of substance use. While there is great promise for using these methods to obtain larger and more diverse samples of PWID, the methods for implementing online methods for recruitment and survey administration are not well established in the field of substance use and pose various challenges, including determining best practices for online recruitment in order to maximize data validity, prevent fraudulent responses, and minimize sampling biases. With the HOME (Harm reduction services Offered through Mail-delivery Expansion) study, we aim to determine the acceptability and use of mail-based harm reduction services for PWID across the United States, with an emphasis on PWID who are not connected to existing harm reduction services. We will describe the successes and challenges of recruiting PWID using online approaches in the HOME study, such as successful advertising approaches and the optimal online settings for recruitment that reaches diverse populations of PWID. Best practices for detecting fraud and maximizing data validity as well as issues of bias throughout the data collection process will be detailed using our initial sample. These strategies will inform subsequent large-scale, nationwide efforts that aim to use this methodology in the future.

Socio-demographic disparities in e-cigarettes and cigarette use among adults with epilepsy in the United States, findings from the 2021 National Health Interview Survey Miranda Ellen Gehris* Miranda Gehris Mohammad Ebrahimi Kalan

Introduction: Smoking cigarettes among US adults has declined since the mid-1960s, however, disparities persist; declines have not been consistent across some populations including epileptic adults. This study examined socio-demographic disparities in e-cigarettes and cigarette use among people living with epilepsy (PLWE).

Methods: Data were drawn from the 2021 National Health Interview Survey. Our analytic sample included 511 PLWE (extrapolated 4.5 million US PLWE) who participated in 2021 NHIS. We performed weighted multivariable regression models to explore the sociodemographic disparities in current use of e-cigarettes and cigarettes. All analyses were weighted to adjust for non-response and to be representative of PLWE in the US. Adjusted odds ratios and 95% confidence intervals are reported.

Results: Current adult epileptic smokers were more likely to be male (AOR=1.4; 95%CI:1.2-1.5), older (vs 18-24, AOR range=2.1-5.1), less educated (vs. graduate degree, AOR range=2.3-5.8), and live beneath the poverty threshold (vs above, AOR range=1.8-2.3) (all ps<0.0001). They were less likely to be non-white (vs. white, AOR range=0.3-0.6) and have health insurance (vs. none, AOR=0.6; 95%CI: 0.5-0.7)(all ps<0.0001).

Current adult epileptic e-cigarette users were more likely to be male (AOR=1.5; 95%CI:1.4-1.7), gay, lesbian, or bisexual (vs straight, AOR=2.1; 95%CI:1.6-2.7), less educated (vs graduate degree AOR range=1.7-2.8, all p<0.0001), and live beneath the poverty threshold (vs. above, AOR= 1.2; all ps<0.05). They were less likely to be older (vs 18-24, AOR range=0.1-0.5), non-white (vs. white, AOR range=0.4-0.7) and have health insurance (vs. none, AOR=0.8, 95%CI0.7-1.0; p<0.05).

Conclusions: Sociodemographic disparities exist in e-cigarette and cigarette use among US PLWE, reflecting the uneven distribution of interventions among this population. It is crucial to design, develop, and implement tobacco cessation preventive measures to address the needs of PLWE.

Prospective Association of Tobacco Retail Density with Youth Vaping Initiation Alyssa F. Harlow* Alyssa Harlow Laura K. Thompson Sandrah P. Eckel Adam M. Leventhal Myles G. Cockburn Jessica L. Barrington-Trimis

Background: Restricting density of tobacco retailers may prevent youth vaping via reduced access and fewer marketing exposures. However, studies on tobacco retailer density and youth vaping are scant and limited by cross-sectional designs or outdated timeframes.

Methods: We used 4 semi-annual data waves (Fall 2021-Spring 2023) of a prospective cohort study of Southern California youth who never vaped at baseline (n=3,248; mean baseline age=15y[range=12-17y]). Participant geocoded addresses at baseline (Sept-Dec 2021) were merged with spatial data on tobacco retailers from state registries (Sept 2021). We calculated the number of retailers within circular buffers surrounding participant homes (400m, 800m, 1600m buffers) and the density of retailers/KM2 within home census tracts (n=427 unique census tracts). Cox models estimated associations of tobacco retailer exposures at baseline with vaping initiation over 1.5 years of follow-up, adjusting for individual-level sociodemographic factors and neighborhood disadvantage and walkability.

Results: The mean number of tobacco retailers within home buffers was 0.6 for 400m (range=0-8), 2.6 for 600m (range=0-18), and 9.2 for 1600m buffers (range=0-37), with a mean census-tract density of 1.2 retailers/KM2 (range=0-13.8). The incident rate for vaping initiation was 3.9% per semi-annual study wave. There was little evidence for an association of number of tobacco retailers within buffers surrounding participant homes with vaping initiation. However, tobacco retailer density within home census tracts was positively associated with vaping initiation (adjusted HR for one-unit increase in density/KM2=1.08, 95%CI=1.01-1.16).

Conclusion: Tobacco retailer density near adolescent homes was associated with vaping initiation. Findings highlight the potential role of regulations that restrict retailer density in preventing youth vaping, and a need for further research to explore mechanisms underlying inconsistencies across exposure measures.

The Association Between Outcomes of Naloxone Administration and Class of Substance Use
Sunghyun* Sunghyun Chung

The Association Between Outcomes of Naloxone Administration and Class of Substance Use

Sunghyun Chung, MPH

Introduction
Point West Syringe Service Program is a harm reduction program based in Jefferson County, Colorado. Participants in this program may obtain new injection supplies, have access to safer sex supplies, counseling, and education materials, referrals for substance use and/or mental health support, and naloxone. This study conducted a descriptive analysis and cross-sectional investigation using the Point West Tracking System Data to examine the differences in outcomes of naloxone administration among participants based on the class of substances used.

Methods
A total of 311 naloxone administrations were examined who completed annual demographic and injection questionnaires and naloxone use reports. Outcomes of naloxone administration were classified as either mild ("survived, woke up with or without help) and severe ("paramedics came to naloxone user, or did not survive"). Drug classifications were opioids; opioid/stimulant combinations; opioid/depressant combinations; stimulants; or depressants. Logistic regression analysis was conducted to assess the relationship between substance class, poverty level, and Outcomes of naloxone administration.

Results
The majority of participants were males aged 30-39, predominantly White, followed by Hispanic/Latinx. Logistic regression showed that using opioid/depressant combinations ($p=0.0243$) and stimulants ($p=0.0031$) significantly predicted severe outcomes of naloxone administration, as did higher poverty levels ($p=0.0073$).

Conclusion
The class of substances used by participants significantly impacts the success of naloxone administrations. Opioid/Depressant Combination and Stimulant use, and a higher poverty level were identified as a significant factor contributing to severe outcomes of naloxone administration. This underscores the importance of tailoring harm reduction strategies to substance classes and addressing socioeconomic factors to enhance the effectiveness of Naloxone interventions.

Expert knowledge from living experience: Applications to Directed Acyclic Graphs Megan Marziali* Megan Marziali Peggy Frank Kathleen Inglis Wayne Campbell Sandy Lambert Patience Magagula Silvia Guillemi Catherine Worthington Robert Hogg Valerie Nicholson Michael Budu Melanie Murray

Aim: Causal inference is not possible without background knowledge and relies on the background knowledge being correct, as it is encoded in identifiability assumptions. It is generally understood this knowledge comes from academic subject matter experts; people with living experience should also be considered experts, providing unique and novel insights to causal questions. Our study blends living experience with scientific domain knowledge to construct the directed acyclic graph (DAG) underpinning our research question about aging and HIV, challenging the notion of what constitutes "expert" knowledge.

Methods: We assembled a team of quantitative and qualitative, including diverse peer researchers (i.e., People Living with HIV). To train peer researchers and other team members unfamiliar with DAGs, we organized a retreat where peer researchers watched short tutorials on building a DAG. Quantitative research team members created these tutorials to define types of bias (e.g., confounding, selection bias) and outline DAG rules. The team worked together to create a DAG illustrated by a peer researcher-artist, combining the living experience of peer researchers with scientific and medical knowledge from quantitative researchers. The DAG was then refined with input from epidemiologists. Qualitative researchers transcribed the process of learning about and drawing the DAG to understand how peer researchers engaged with this tool.

Results: Peer researchers found drawing DAGs intuitive. Visualizing the temporal ordering of variables was a crucial moment in understanding the causal structure for peer researchers. The complexity of the DAG enmeshed with temporal ordering humanized the research; seeing the web of covariates resonated as a reflection of a person's life journey.

 Conclusion: Constructing DAGs incorporating living experience is feasible, ethical, and strengthens epidemiologic studies by reconceptualizing our definition of background knowledge and humanizing research.

Lower estradiol concentrations are associated with knee-specific pain in postmenopausal women Emily Ha* Emily Ha Jennifer Brooks Peter M Smith Andy Kin On Wong

Background: Knee osteoarthritis is a major source of knee pain in postmenopausal women, and evidence suggests a link between sex hormones and chronic pain. However, the relationship between estrogen concentrations and the development of knee pain in postmenopausal women is underexplored. The study aimed to determine the cross-sectional and longitudinal associations between estradiol concentration and knee pain in postmenopausal women.

Methods: Data on postmenopausal women in the United Kingdom (UK) Biobank were used. Baseline serum estradiol (E2) was measured using a two-step competitive assay (range: 73–17,621 pmol/L). For 155,341 out of 192,532 postmenopausal women, estradiol concentrations were below the detection limit. Thus, quantifiable estradiol was categorized into tertiles, with an additional undetectable category. Knee pain was measured via questionnaires at baseline and the five-year follow-up. Modified Poisson models, adjusted for potential confounders, were used to estimate the cross-sectional and longitudinal associations.

Results: Among 192,532 postmenopausal women (mean age=60.4, SD=5.4), 16.4% reported knee pain and the median estradiol concentration was 289.0 pmol/L (IQR=217.0 pmol/L–443.8 pmol/L). Those with lower estradiol concentrations had a significantly higher risk of knee pain at baseline and 5 years later (18–28% higher risk) compared to the highest tertile. Postmenopausal women with undetectable concentrations had 1.18 times the prevalence of knee pain at baseline (95% CI=1.10–1.27) and 1.87 times the risk of knee pain 5 years later (95% CI=1.70–1.95) compared to the highest estradiol tertile.

Discussion/Conclusion: Lower estradiol concentrations were significantly associated with an increased risk for knee pain in postmenopausal women. Estradiol may play a role on influencing the degree of knee pain. Specific mechanisms of how low estradiol levels could translate to more knee pain should be investigated as future mitigation strategies.

Women's Health

Hysterectomy patterns and trends in Mexico, 2010-2019 Britton Trabert* Britton Trabert Lina Sofia Palacio Mejia Juan Eugenio Hernández Ávila Jorge Salmerón Liliana Gómez Flores Ramos Martín Lajous

Hysterectomy is the most common surgical procedure among reproductive age women. More than 50% of hysterectomies are performed for benign reasons, while gynecologic cancers account for ~10% of hysterectomies in the United States (US) and other high-income countries. Global cancer reporting does not correct for the proportion of the population who have undergone hysterectomy, which increases with age but has also demonstrated recent temporal declines in many countries. These changes have important implications for the interpretation and comparison of uterine cancer rates worldwide. The uncorrected uterine cancer rate in the US is more than triple the rate in Mexico. Given the lack of information on hysterectomy patterns in Mexico and marked differences in uterine cancer incidence when comparing Mexico and the US, we set out to describe recent hysterectomy trends in Mexico. We utilized data from the automated system of hospital discharges (including ambulatory care) that is curated and validated by the Ministry of Health and covers ~57% of the population. Age-standardized rates (ASRs) were calculated through the direct method using the US 2010 female population. The current analysis included 267,245 individuals 20+ years of age who had a hysterectomy from 2010-2019. The most common indication was fibroids (n=147,936, 55.4%), while gynecologic cancer represented only 5.8% of procedures (n=15,490). The overall ASR of hysterectomy was 137.6 per 100,000 woman-years (95% CI: 137.1-138.1). The ASR was stable from 2010-2015 (annual percent change: 0.8%; 95% CI: -1.3, 2.9) followed by a substantial decrease from 2015-2019 (-7.1%; -9.9, -4.4). There was wide geographic variation in hysterectomy rates across Mexico (Figure). While the declining hysterectomy rate observed in Mexico is consistent with recent decreases observed in many countries, the ASR of hysterectomy was much lower in Mexico than the US and does not explain the large difference in uterine cancer rates.
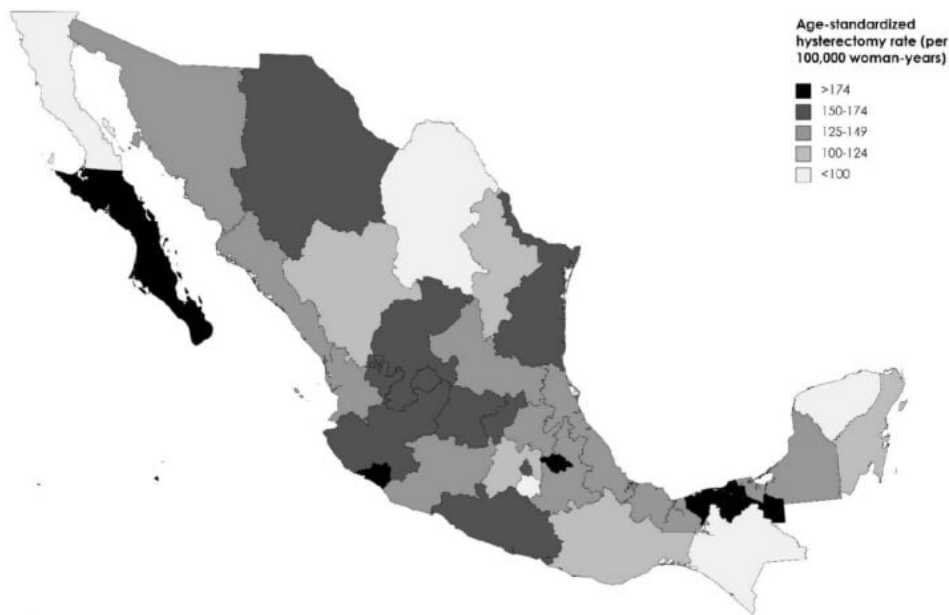
Figure. Geographic distribution of age-standardized hysterectomy rates by state, Mexico (2015-2019).

Footnote: Rates reported per 100,000 woman-years; age-standardized to 2010 US female population. Shading corresponds to the magnitude of age-standardized hysterectomy rates which range from light grey for the lowest rate (<100 per 100,000 woman-years) to black for the highest rate (>174 per 100,000 woman-years). Data from Mexico's Automated Subsystem of Hospital Discharges (or SAEH, *Sistema Automatized de Egresosos Hospitalarios*). Figure generated using https://www.mapchart.net/mexico.html.

LATEBREAKER

Women's Health

Antenatal Depression and its Associated Factors: Findings from Kuwait Birth Cohort Study
Abdullah Al-Taiar* Abdullah Al-Taiar Reem Al-Sabah Ali H. Ziyab Saeed Akhtar Majeda S. Hammoud

Background and objectives: Pregnant and postpartum women are at high risk of depression due to hormonal and biological changes. Antenatal depression is understudied compared to postpartum depression and its predictors remain highly controversial. The aim of this study was to estimate the prevalence of antenatal depression and investigate factors associated with this condition including vitamin D, folate and Vitamin B12 among participants in the Kuwait Birth Cohort Study.

Methods: Data collection occurred as part of the Kuwait birth cohort study in which pregnant women were recruited in the second and third trimester during antenatal care visits. Data on antenatal depression were collected using the Edinburgh Postnatal Depression Scale (EPDS), considering a score of ≥ 13 as indicator of depression. Logistic regression was used to investigate factors associated with antenatal depression.

Results: Of 1108 participants in the Kuwait Birth Cohort study, 1070(96.6%) completed the EPDS. The prevalence of antenatal depression was 21.03%(95%CI:18.62-23.59%) and 17.85%(95%CI:15.60-20.28%) as indicated by an EPDS ≥13 and EPDS ≥14, respectively. In the multivariable analysis, passive smoking at home, experiencing stressful life events during pregnancy, and a lower level of vitamin B12 were identified as predisposing factors. Conversely, having desire for the pregnancy and consumption of fruits and vegetables were inversely associated with antenatal depression.

Conclusion: Approximately, one fifth of pregnant women had depression indicating the need to implement screening program for depression in pregnant women, a measure not systematically implemented in Kuwait. Specifically, screening efforts should focus on pregnant women with unintended pregnancies, exposure to passive smoking at home, and recent stressful live events.

Women's Health

Endometriosis and midlife circulating biomarkers of inflammation and total cholesterol

Leslie V. Farland* Leslie V. Farland William J. Degnan, III Holly R. Harris Kathryn M. Rexrode Stacey A. Missmer

Introduction: Mounting evidence suggests that women with endometriosis are at greater risk for cardiovascular disease (CVD). Endometriosis may influence CVD through a detrimental impact on circulating inflammatory biomarkers and lipids. However, there is a paucity of research on endometriosis and these biomarkers in midlife.

Methods: We used generalized linear models adjusted for potential confounding factors to determine the association between history of laparoscopically-confirmed endometriosis and log-transformed plasma C-reactive protein (CRP) (n=3,935), interleukin-6 (IL-6) (n=3,495), tumor necrosis factor-alpha (TNF-a) (n=2,967), high-density lipoprotein (HDL) (n=1,533), low-density lipoprotein (LDL) (n=1,324), and total cholesterol (n=4,898) among participants with existing blood measurements in the Nurses' Health Study II. We investigated heterogeneity by body mass index (BMI; <25 kg/m2 vs. > 25 kg/m2), infertility history, parity, and history of gynecologic surgery (oophorectomy and/or hysterectomy).

Results: On average, participants were 44 years old at blood draw. We did not observe associations between endometriosis and inflammatory biomarkers (CRP % difference:-4.6, 95% CI [-15.7,7.8]; IL-6: -0.4% [-7.2,7.1]; TNF-a:-1.3% [-4.1,1.6]). Nor did we observe associations between endometriosis and HDL (0.8% [-3.7,5.6]), LDL (-0.2% [-5.2,5.0]), or total cholesterol (1.0% [-0.7,2.7]). However, the association between endometriosis and total cholesterol varied by BMI (P-value, test for heterogeneity:0.05). Among women with a BMI > 25 kg/m2, those with endometriosis had 2.7% higher total cholesterol (0.2,5.2) than those without endometriosis.

Discussion: History of endometriosis diagnosis was not associated with levels of inflammation, HDL, or LDL midlife. Endometriosis was modestly associated with total cholesterol among those with a BMI > 25 kg/m2. These findings suggest that endometriosis may be associated with CVD through other mechanisms

Is This My Period? Defining Menses in Epidemiological Research Maegan E. Boutot* Maegan Boutot Brian W. Whitcomb Elizabeth R. Bertone-Johnson

Introduction: Menses length is a reproductive health indicator but has no standard definition. Two often used definitions are from the International Federation of Gynaecology and Obstetrics (FIGO) and the World Health Organization (WHO); the primary difference between them being that FIGO considers one day of low-intensity bleeding (spotting) prior to heavier bleeding as the start of menses. No definition addresses spotting after heavy bleeding, and it is unclear what to do with mid-menses spotting. This ambiguity leave researchers, clinicians, and people with menses at risk for misunderstanding what is "typical" menses length, impacting research and clinical care.

Methods: We applied the WHO, the FIGO and a modified FIGO definitions to menstrual diaries from the Effects of Aspirin in Gestation and Reproduction (EAGeR), a pre-pregnancy cohort with no birth control use. Daily bleeding was recorded as 0 (none), 1 (spotting), or 2-5 (light to heavy flow). We examined how definitions and inclusion of spotting impacted mean, median, and clinical categorization of length into short (3 day), typical (4-8 days), and long cycles (9+ days).

Results: Participants (n=1,039, mean age 28.7 years) contributed 55,078 days with bleeding scores of 0-5. Participants defined 39.3% of any bleeding as spotting; 96.3% of participants reported spotting. WHO and FIGO definitions had similar median (4 days) and mean (about 4.3 days) menses lengths; including post-bleeding spotting days increased the median and mean to greater than 5 days. One in three (36.3%) menses would have different clinical categorizations based on definition, largely due to how spotting following heavier bleeding was categorized.

Discussion: Spotting was commonly reported by EAGeR participants, and meaningfully impacts the distribution of clinical cycle lengths. Additional consideration of spotting is needed to develop definitions for research and clinical care and to investigate associations with clinical outcomes.

Daily bleeding data from an EAGeR participant, categorized by three potential definitions of menses.
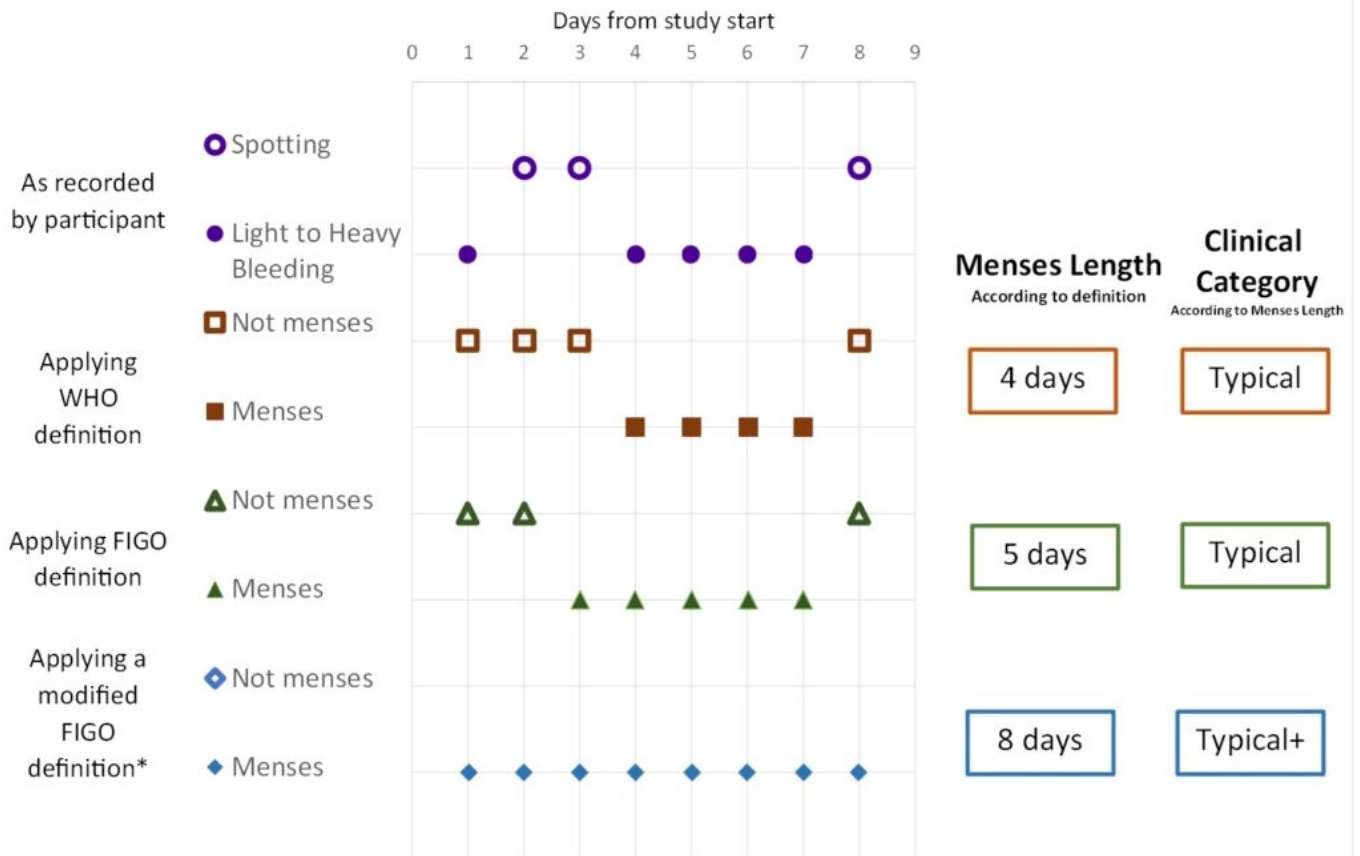
*Under this third definition, all bleeding days for this participant could be considered as part of menses
+According to FIGO, up to 8 days of bleeding is typical. According to the American College of Obstetricians and Gynecologists, this would be atypically long menses.

Women's Health

Sex differences in posttraumatic pain development after acute physical trauma Rachel Gaither* Rachel Gaither Nina Joyce Sarah Linnstaedt Samuel McLean Francesca Beaudoin

Chronic pain impacts >50 million US adults, with women about twice as likely to report chronic pain as men. Acute physical trauma (e.g. motor vehicle crash) is a common catalyst for chronic pain, and its defined time origin is useful for investigating pain development. Few analyses have investigated sex differences in posttraumatic pain despite evidence that adverse symptoms are more common in female trauma survivors. We used the AURORA cohort (n=3789) to assess whether female sex assigned at birth is associated with increased likelihood of chronic pain development after trauma exposure. Participants were enrolled in the emergency department (ED) after presenting with non-life-threatening physical trauma and followed serially for one year. Sex was defined as sex assigned at birth, and pain was assessed in the ED and at 2-weeks, 2-, 3-, 6-, and 12-months post-trauma using the 0-10 Numeric Rating Scale (score ≥4 indicating moderate/severe pain). Log-binomial regression models with inverse probability of censoring weights were used at each timepoint to determine the association between sex and pain severity while accounting for potential selection bias due to differential loss to follow-up by sex. Baseline characteristics were similar across sex and posttraumatic pain was common overall, with 77.8% and 55.7% of participants reporting moderate/severe pain at 2 weeks and 3 months, respectively. Prevalence of pain pre-trauma and in the ED was similar across sex, but individuals assigned female at birth had increased risk of moderate/severe pain compared to those assigned male by 2 weeks (RR [95% CI]: 1.20 [1.16-1.25]). This elevated risk persisted throughout follow-up (3-month: 1.28 [1.20-1.37], 6-month: 1.32 [1.22-1.41]). Overall, female sex at birth was associated with higher risk of posttraumatic chronic pain, and subsequent work should investigate the impact of sex on pain recovery trajectories over time while incorporating specific measures of sex characteristics.

Removals and more invasive treatments following insertion of a hormonal intrauterine device to treat benign gynecological conditions Michael J Green* Michael Green Mollie E Wood Erin T Carey Joacy G Mathias Lauren G Anderson Kemi M Doll Whitney R Robinson

Introduction: Hormonal intrauterine devices (IUDs) are recommended first-line treatments for symptomatic benign gynecological conditions, but little is known about prognosis following insertion. We describe frequency and timing of IUD removal and more invasive follow-up treatments and assess whether this differed by race or ethnicity.

Methods: With records from a healthcare system in the US South (2014-2019), we established a cohort of 779 pre-menopausal patients (aged 18-45 years; Non-Hispanic White n=455; Non-Hispanic Black n=204; Hispanic n=120) who had IUDs inserted with associated diagnostic codes for a benign gynecological condition. Additional treatments were tracked over a median follow up time of 1.9 years (707 days). We abstracted data on symptoms in the 4 months prior to insertion, constructing scores for severity of bulk, bleeding, and gynecological pain. Cox regression models assessed how race/ethnicity was associated with time to removal or more invasive treatment, with adjustment for age at insertion, symptom severity, prior IUD use and insurance status.

Results: 34 patients (4%) had their IUD removed, an average of 275 days following insertion. 78 patients (10%) received a more invasive treatment (75 hysterectomies, 3 endometrial ablations) at an average of 382 days later. Compared to White patients and after adjustment for covariates, Hispanic patients were more likely to have had the IUD removed (HR: 2.9[1.1-7.8]), while removal rates for Black patients were similar to those of White patients (HR: 1.5[0.6-3.4]). Rates of receiving more invasive treatments were lower for Black (HR: 0.7[0.4-1.1]) and Hispanic (HR: 0.7[0.3-1.4]) patients but confidence intervals over-lapped the null.

Conclusion: Within ~2 years following insertion of a hormonal IUD for a benign gynecological condition, rates of IUD removal and receiving more invasive treatment were both low. There were no clear racial differences in rates of receiving more invasive treatment.

Association between birthweight and cognitive function in middle-aged adults: the Bogalusa Heart Study Eunsun Gill* Eunsun Gill Soo Jung Kang David J Libon Ileana De Anda-Duran Lydia A Bazzano Wei Chen Camilo Fernandez Alonso Emily W Harville

Introduction: Although the relationship between low birthweight and impaired global cognitive function (CF) before midlife has been demonstrated, the relationship between birthweight and cognition after midlife and potential racial disparities remain inconclusive. This study examined the association between birthweight and midlife CF stratified by race.

Methods: 1,032 subjects from the Bogalusa Heart Study (67% Whites, 33% Blacks, mean age 48.1 ± 5.3 years) were studied. Cognition was assessed with tests measuring verbal episodic memory, working memory, attention, graphomotor information processing speed, language, and global CF. Each test was standardized by sex and age, then averaged. The global CF was computed by averaging all cognitive test scores. Standardized scores from the Wide Range Achievement Test-III (WRAT-III)–Reading subtest and the Wechsler Adult Intelligence Scale-III (WAIS-III)–Vocabulary subtest measured achieved education. Multiple linear regression was used to estimate the association between birthweight (per 100 grams) and CF, adjusting for age, sex, personal achieved education, smoking, drinking, parental education, maternal age at birth, and maternal hypertension and diabetes, with multiple imputation used to address missing covariates.

Results: For Whites, each 100 gram decrease in birthweight was associated with a reduction of 0.008 standardized units in the global CF (SE: 0.005; p=0.016), but this association was not observed in Blacks (beta (SE): 0.009 (0.005); p=0.084). In Whites, lower birthweight was associated with worse graphomotor information processing speed (beta (SE): 0.014 (0.006); p=0.014), but not in Blacks (beta (SE): 0.005 (0.008); p=0.561).

Conclusions: By midlife, lower birthweight appears to convey vulnerability with respect to global CF and graphomotor information processing speed in Whites but not in Blacks. Importantly, the impact of birthweight on selected cognitive abilities in midlife may vary by race.
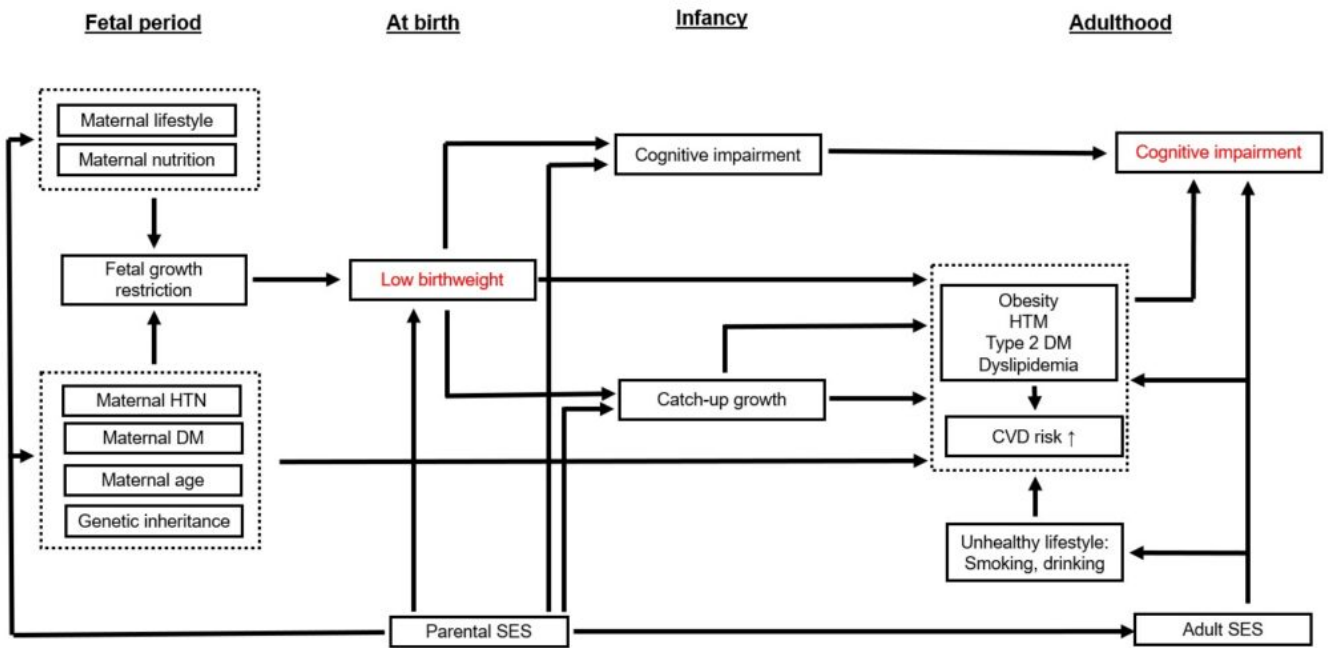
Figure 1. Conceptual Model

Abbreviations: HTN, hypertension; DM, diabetes mellitus; SES, socioeconomic status; CVD, cardiovascular disease

LATEBREAKER

Aging

Examining the Associations of Social Support and Chronic Stress on ADRD Plasma Biomarkers in the Health and Aging Brain Study-Health Disparities (HABS-HD) Cohort

Jillian Lee* Jillian Lee Leigh Johnson Sid E. O'Bryant Michelle M. Mielke

Background: There is limited research examining how modifiable risk factors of Alzheimer's disease and related dementias (ADRD) impact plasma biomarker levels. Therefore, in a large diverse cohort, we cross-sectionally examined the association between social support and chronic stress on plasma biomarkers levels and whether gender modified these associations.

Methods: Participants included 2,830 older adults (mean [SD] age, 64.98 [8.5] years; 63% women) enrolled in the Health and Aging Brain Study-Health Disparities (HABS-HD). Perceived social support was measured using the Interpersonal Support and Evaluation List. Chronic stress was measured using the Chronic Burden Scale. Plasma ADRD biomarkers were assayed using the Simoa platform. Linear mixed-effect models evaluated the associations between social support and chronic stress on plasma biomarkers, adjusting for age, education, gender, and race/ethnicity.

Results: Higher social support was associated ($p<0.05$) with lower levels of total tau (b=-0.00931), pTau181 (b=-0.0106), and NfL (b=-0.290). With increasing social support, males had lower levels of IL-6 (b=-0.0395) and NfL (b=-0.341) whereas females had lower levels of total tau (b=-0.00998). Higher chronic stress was associated with higher levels of total tau (b=0.0116), NfL (b=0.156), and lower levels of Aβ42/40 ratio (b=-0.0000888). With increasing chronic stress, males had higher levels of Aβ42/40 ratio (b=-0.000143), total tau (b=0.0122), and pTau181 (b=0.0181), compared to females.

Conclusions: In the cross-sectional study, higher social support was associated with lower levels of plasma biomarkers associated with ADRD pathology and higher chronic stress was associated with higher biomarker levels; results differed by gender. Future research is needed to evaluate the longitudinal associations of social support and chronic stress on changes in plasma biomarker trajectories overtime and to further examine gender differences.

LATEBREAKER

Aging

Loneliness and Social Isolation among Older Asian Indian Immigrants in the United States
RoiSan Nhpang* RoiSan Nhpang Malinee Neelamegam

Background: Loneliness and social isolation (SI) are common issues among older adults in the United States, particularly among immigrants, with these conditions being associated with significant health and mental health issues. This mixed method explorative study aims to describe loneliness and SI among older Asian Indian immigrants in the United States.

Method: Survey and semi structured in-depth interviews were conducted among 31 older Asian Indian immigrants aged 55 years or older in the Dallas-Fort Worth (DFW) area. Loneliness was determined based on the DeJong Gierveld Loneliness Scale and SI was determined based on the Revised Lubben Social Network Scale (LSNS-R). T-tests were conducted to explore the association between the duration of immigration, loneliness and social isolation. Qualitative data were analyzed thematically with a priori and emergent codes.

Result: Majority of the participants (74%) were women, and 55% of the participants were aged 65 years or older. Among them, 26% reported feeling moderately lonely or more with 3% reported feeling severely lonely, while 23% reported experiencing SI. On average, participants have been living in the US for 34.6 years. T-test results indicate that, although not statistically significant, participants expressing loneliness had, lived in the US for an average of 30.6 years, compared to 36.0 years for those without loneliness. In contrast, significant differences (p-value <0.05) were found in the mean years living in the US between participants reporting SI (21.0 years) and those who did not (37.4 years). Emerging themes included concern about support in caregiving, and navigating illnesses alone.

Discussion: As loneliness and social isolation pose serious health conditions among older adults, the findings underscore the importance of understanding and examining factors contributing to these feelings among older Asian Indian immigrants in the US.

Aging

Title: Association of perceived neighborhood social characteristics with cognitive function and decline in the Health and Retirement Study Xu Zhang* Kendra Sims Xu Zhang M. Maria Glymour

Background: Perceiving lack of neighborhood cohesion or limited social ties may reduce later-life cognitive function and accelerate decline. We hypothesized that adverse neighborhood context harms cognitive health for men more than women. Methods: We analyzed 14119 Health and Retirement Study participants (aged 51-101, 74% Non-Hispanic White, 58% women) who responded to scales on neighborhood social cohesion and social ties in 2006 or 2008. Data on our outcomes of interest, biennial scores on immediate and delayed word recall batteries, were collected from 2006 through 2018. With gender-stratified linear regressions and linear mixed-effect models adjusted for social determinants of health, we evaluated the association of each neighborhood characteristic with standardized recall scores at baseline and 12 years. Results: The baseline mean neighborhood social cohesion score was 0.59 (SD=0.23); and mean social ties score was 0.53 (SD=0.32). Neighborhood social cohesion was positively associated with baseline memory performance for both genders: e.g., scoring higher on social cohesion was associated with a 0.13-SD (95% CI: 0.10; 0.16) increase in immediate recall. Women reporting more social ties had higher baseline immediate recall scores (β: 0.04; 95% CI: 0.01, 0.06), but this association was reversed among men (β: -0.03; 95% CI: -0.05, 0.00). Over 12 years, neighborhood characteristics were not associated with cognitive trajectories: e.g., the per-visit change in delayed recall for those reporting more social ties was 0.01 (95% CI: -0.03; 0.04) for women and -0.02 (95% CI: -0.07; 0.02) for men. Conclusions: Unexpected associations between perceived social ties and cognitive function indicate future need to evaluate differential reporting on psychosocial scales, selection bias, and gender-specific strategies to retain older adults when evaluating neighborhood determinants of cognitive health.

Cognition function and its relationship with cerebral ageing signs detected by high-resolution magnetic resonance: preliminary findings from the ELSA-Brasil Alessandra C Goulart* Alessandra C Goulart Isabela M Benseñor Claudia C Leite Claudia k Suemoto Maria CG Otaduy Arão B Oliveira Itamar S santos Paulo A Lotufo Isabela M Benseñor

The brain aging process, which is highly heterogeneous and multifactorial, determines structural differences that can influence cognitive status. Therefore, in a preliminary analysis of an ongoing large neuroimaging sub-study in the Brazilian Longitudinal Study of Adult Health (ELSA-Brasil), it was assessed the integrity of brain structures by 3 Tesla magnetic resonance imaging (MRI) (ongoing since April 2023) and its association with, the performance in ELSA-Brasil cognition tests (the Consortium to Establish a Registry for Alzheimer's Disease – Word List, semantic and phonemic verbal fluency and the Trail-Making Test B), occurred 4 years (Wave 3) before MRI. We performed an exploratory analysis by partial correlation (adjusted by sex, age, educational level, and estimated total intracranial volume for volumetry analyses) between cognition function and brain structural regions of interest (ROI) related to cortex thickness and volume analyzed by volumetry (FreeSurfer® version 7.3.2) in both hemispheres. Among 89 participants (60.7% women, median age 63 years), cognitive performances at Wave 3 were diversely associated with structural brain markers of aging. White matter hypointensities (WMH) were inversely associated with global memory z-score ($r = -0.274$, $p = 0.023$), while the cortical thickness in the right superior frontal lobe was positively associated with verbal fluency (semantic and phonemic) ($r = 0.261$, $p = 0.02$) but not left ($r = 0.188$, $p = 0.096$). Other ROIs were not significantly associated with cognitive function. Preliminary data revealed some brain structural markers related to brain aging, such as the degree of WMH and frontal cortical thickness associated with worse memory and better verbal fluency scores, respectively. A larger sample and longer follow-up time with upcoming data on cognition, mental health, and risk factors will help to unravel the meaning of high-resolution cerebral markers findings in the aging process.

Aging

The Effects of The South African Older Person's Grant on Food Expenditure Among Rural Older Adults: Findings from The Population-based HAALSI Study Haeyoon Chang* Haeyoon Chang Ryan G. Wagner Kyle L. Grazier Lindsay C. Kobayashi

Food insecurity is common among rural South African older adults and associated with a range of adverse health outcomes. The South African Government's Older Person's Grant (OPG) may enhance household income and alleviate food insecurity. We used a regression discontinuity design to examine changes in self-reported monthly household food expenditure at the OPG age-eligibility threshold, age 60, and effect modification by country of birth. Country of birth is an indicator of social stratification in the study region, as those born outside South Africa in this context are largely former refugees from Mozambique with lower education and literacy, who have historically lived segregated from their South African-born peers. Data were from 1,318 adults within five years of the pension age-eligibility threshold (age 60) in the population-representative "Health and Aging in Africa: A Longitudinal Study in Rural South Africa" (HAALSI; 2014/15). We identified a statistically non-significant decrease of 70.98 Rand (95% CI= -147.69, 5.72) in monthly food expenditure with OPG eligibility. When stratified, older adults born outside of South Africa, experienced no significant changes in food expenditure with OPG eligibility, while South African-born older adults had a significant decrease of 108.40 Rand (95% CI= -194.79, -21.70) in food expenditure. This decrease represents 9% of the food insecurity threshold in South Africa where an average monthly food expenditure of <1,200 Rand for households of 3-4 members signals food insecurity. Results suggest potential variations in spending patterns may be influenced by country of birth in this setting. South African adults may have greater means and access to public benefits, leading to a more conservative approach to pension spending. These findings contribute to understanding how exogenous changes in income induced through pension eligibility may shape food security in resource-constrained settings.
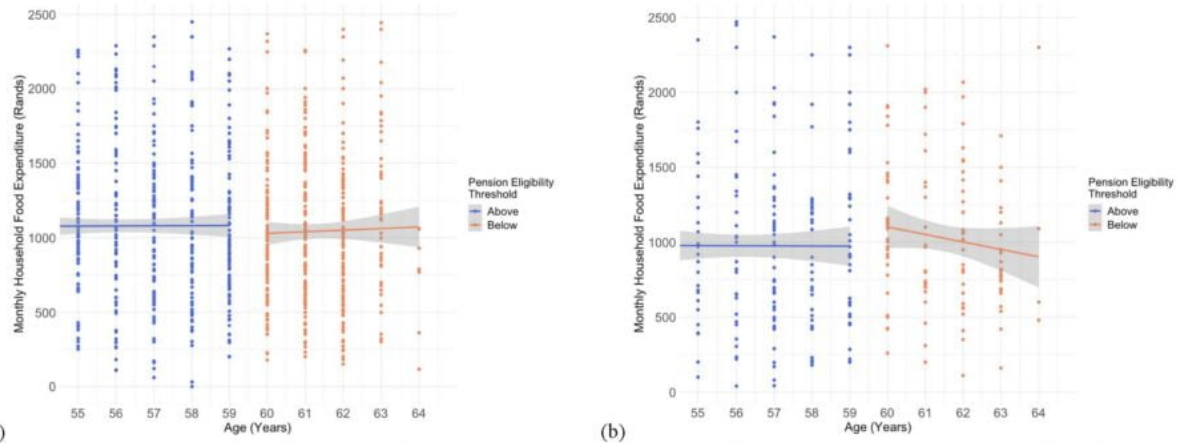
Figure 1. Plot of self-reported monthly household food expenditure in Rands and age stratified by country of birth: (a) country of birth in South Africa (n=957), (b) country of birth outside of South Africa (n=361), HAALSI 2014/15, men and women aged 55 to 64 years (n= 1,318). Linear regression lines represent the average trend in monthly household food expenditure above (blue) and below (orange) the Older Person's Grant threshold.

Table 1. Older Person's Grant eligibility on monthly household food expenditure stratified by country of birth, +/- 5 years from eligibility threshold at age 60, HAALSI 2014/15 (n= 1,318)

		Estimates	95% CI	P-value
	Full sample (n= 1,318)	-70.98	-147.69, 5.72	0.070
Stratified by county of birth*	Born in South Africa (n= 957)	-108.40	-194.79, -21.70	0.014
	Born outside of South Africa (n= 361)	16.80	-138.96, 172.57	0.833

Full sample adjusted for gender, number of household members, marital status, education status, employment status, country of origin, household asset index, household wealth index, and household consumption quintiles.
*Adjusted for gender, number of household members, marital status, education status, employment status, household asset index, household wealth index, and household consumption quintiles.

Association between Midlife Intake of Ultra-processed Food and Later-life Subjective Cognitive Complaints among Older Women Kejia Zhang* Kejia Zhang Fen Wu Karen L Koenig Yian Gu Anne Zeleniuch-Jacquotte Yu Chen

Almost two-thirds of cases of Alzheimer's disease (AD), the most common form of dementia, are women. Subjective cognitive complaints (SCCs) are predictors of mild cognitive impairment and AD. Research into risk factors for SCCs may offer insight into the etiology and prevention of AD. Ultra-processed foods (UPFs) contain many ingredients including food additives that improve palatability and processed raw materials. Evidence is limited on the role of mid-life UPFs intake in late-life SCCs.

We included 5,119 participants who responded to the 2018 or 2021 follow-up from the New York University Women's Health Study, a prospective cohort of 14,274 women recruited in 1985-90. Data on diet were collected at baseline using the validated Block food frequency questionnaire. Energy-adjusted total intake of UPFs and subgroups of UPFs, defined following the NOVA guidelines, were estimated using the residual method. SCCs were assessed by six self-reported questions at follow-up. We estimated ORs for ≥ 2 SCCs in relation to quintiles of UPFs intake, controlling for potential confounders including total calories, demographic and lifestyle factors, and comorbidities.

The ORs (95% CI) for ≥ 2 SCCs were 1.15 (0.94-1.39), 1.06 (0.87-1.30), 1.20 (0.99-1.46), and 1.24 (1.02-1.51), comparing women in 2nd, 3rd, 4th, and 5th quintile of energy-adjusted UPFs intake with those in the bottom quintile (p-trend = 0.02), respectively. The association was similar with multiple imputation and inverse probability weighting to account for potential selection bias. Among UPF subgroups, the OR for ≥ 2 SCCs was 1.24 (1.02-1.51), 1.20 (0.98-1.47), and 1.19 (0.97-1.46) comparing women in top quintile of energy-adjusted intakes of dairy, meats, and fast food, respectively, with those in the bottom quartile.

Higher levels of UPF intakes in midlife was associated with higher odds of late-life SCCs in women.

Does healthy behaviour make you look good? Zhu Liduzi Jiesisibieke* Zhu Liduzi Jiesisibieke Zhu Liduzi Jiesisibieke C Mary

Background: Motivations to improve health may vary; improving personal attractiveness could be a powerful motivator. We investigated whether health-related behaviours commonly mentioned by the World Health Organization also affected appearance (facial aging) in men or women using Mendelian randomization.

Methods: We identified independent (r2<0.001) genetic variants strongly (p<5e-8) predicting body mass index, smoking, alcohol use, diet (omega-3, omega-6) and to allow for differences by sex testosterone and estrogen; we then considered their impact on facial aging. We used inverse variance weighted estimates with sensitivity analysis and assessed sex differences using a z-test.

Results: Body mass index (per standard deviation (SD)) was positively associated with facial aging in both men (beta 0.07, 95% confidence intervals (CI) 0.05 to 0.08) and women (0.04, 95% CI 0.02 to 0.05) (p value for sex-difference 0.002). Smoking status (cigarettes per day) was also associated with facial aging (beta 0.02, 0.01 to 0.04, p value for sex-difference 0.89), but not smoking initiation with little evidence of a sex difference. Alcohol use was unrelated to facial aging. In men, omega-3 (per SD), but not omega-6, was positively associated with facial aging (beta 0.02, 95% CI 0 to 0.03), but less clearly in women (p value for sex-difference 0.20). Among men, testosterone was associated with facial aging (beta 0.03 per SD, 0.01 to 0.04), while no such association was found in women (p value for sex-difference 0.02). In women, estrogen (pmol/L) protected against facial aging (beta -0.01, -0.03 to -0.001), although this was not evident in men (p value for sex-difference 0.41).

Conclusions: Adiposity, smoking, omega-3 fatty acids and testosterone may adversely affect appearance, but estrogen may enhance appearance. Whether these insights could be utilized as additional motivators for healthy behaviour, such as weight loss and smoking cessation, could be investigated.

Aging

Unraveling the Nexus: Social Isolation, Loneliness, and Pain Outcomes in Older Adults

Yulin Yang* Yulin Yang Jacqueline Torres Ashwin Kotwal

Social isolation and loneliness pose a pressing public health challenge and are linked to many health conditions in older adults; however, little is known about the role of social isolation and loneliness in shaping pain outcomes and management. This study aims to understand how social isolation and loneliness are associated with pain and the use of non-opioids or opioids pain medications. We analyzed data from 14,118 Americans aged 50 and above from the Health and Retirement Study (HRS 2016-2020; 31,130 person-wave observations). We fitted generalized estimating equation (GEE) log-binomial models to evaluate how social isolation (household and core contacts, social Network Interactions, and community Engagement) and loneliness (3-item UCLA Loneliness Scale) are associated with the prevalence of high-impact pain (moderate-to-severe pain, or pain limiting usual activities), taking over-the-counter pain medications (e.g., Advil, Aleve, Tylenol) in the past three months, and taking opioids pain medications (e.g., Vicodin, OxyContin, codeine) in the past three months. We stratified our analyses by sex and race/ethnicity. All models applied survey weights and controlled for age, sex, race/ethnicity, education, household wealth, nursing home status, and Medicaid enrollment. Overall, both social isolation and loneliness were associated with higher risks of high-impact pain (Social isolation Prevalence Ratio [PR]: 1.12, 95% confidence interval [CI]: 1.02, 1.23; loneliness PR: 1.45, 95% CI: 1.35-1.56). Social isolation was associated with a lower risk of using OTC pain medications (PR: 0.87, 95% CI: 0.78, 0.96), while loneliness was associated with greater risk of using OTC pain medications (PR: 1.09, 95% CI: 1.02, 1.18). We found limited evidence that social isolation was associated with self-reported opioids use, but loneliness was associated with greater risk of opioids use (PR: 1.25, 95% CI: 1.12, 1.39). In stratified models, there was some variation by gender, race, and ethnicity. Our findings demonstrate important associations between social isolation, loneliness, and high-impact pain among older adults, revealing nuanced patterns in the use of non-opioids or opioids medications. Addressing social connectedness may be relevant to comprehensive pain management strategies for older adults.

Aging

How do discrepancies between subjective and objective health predict the risk of injurious falls in older Swedish adults? Bill Calvey* Bill Calvey Anna-Karin Welmer Amaia Calderon Larrañaga Joanna McHugh Power Rebecca Maguire

Objectives

Previous studies demonstrated that discrepancies between subjective and objective health measures are associated with physical and mental health-related outcomes in older adults. However, the extent to which they relate to risk of injurious falls remains unclear. We investigate whether such discrepancies are associated with risk of injurious falls in community-dwelling Swedish older adults.

Method

A prospective, observational cohort study, using data from the Swedish National Study on Aging and Care in Kungsholmen followed a sample of 2,222 older adults, aged 60+ years at baseline (2001 – 2011). A 'health asymmetry' metric classified older adults into four categories, based on the level of agreement between their subjective and objective health scores ('health pessimist', 'health optimist', 'poor health realist' and 'good health realist'). Time-varying Cox proportional hazard and Laplace regressions were used to investigate whether these health asymmetry categories were associated with risk of injurious falls, i.e. falls leading to inpatient or outpatient care.

Results

Over a ten-year follow-up, 23.5% of the sample experienced an injurious fall. Health optimists had the greatest risk of experiencing an injurious fall (HR: 2.16, 95% CI: 1.66, 2.80), when compared to good health realists. Poor health realists (HR: 1.77, 95% CI: 1.50, 2.11) and health pessimists (HR: 1.66, 95% CI: 1.21, 2.29) also had increased risk of experiencing injurious falls, compared to good health realists. Being health pessimist was only associated with the risk of injurious falls within the younger cohort (HR=2.43, 95% CI=1.63, 3.64), and among males (HR=1.95, 95% CI=1.14, 3.33).

Conclusions

Older adults with similar objective health levels may differ in terms of their injurious fall risk, depending on their subjective health. Interpreting subjective health alongside objective health is clinically pertinent, when assessing injurious fall risk.

Redlining, race, and cognition within the Health and Retirement Study Jenna Rajczyk* Jeffrey Wing Jenna Rajczyk Julie Strominger Helen Meier

Introduction: Cognitive impairment and dementia burdens in the US are projected to rapidly increase with the growing aging population yet may not be equally shared for all race/ethnic groups. Differential distributions of resources and income by race/ethnicity may influence cognitive outcomes, where these unequal distributions attributed to structural racism have had major impacts on Black Americans.

Methods: Using Health and Retirement Study data, we evaluated the association between historic redlining index (calculated from Home Owners' Lending Corporation security maps) and race on cognitive status cross-sectionally in 2016 and 2-year incident dementia or cognitive impairment not dementia (CIND). Weighted binary logistic regression modeled odds of dementia/CIND (Langa-Weir classification) compared to normal cognitive status, with the combination of race and redlining included in the model as a 4-level factor (reference: white-no redlining). Models were adjusted for age in 2016, education, gender, multimorbidity, marital status, and 2012-2016 neighborhood poverty level.

Results: Twenty percent of participants in 2016 (575/2133) had dementia or CIND. The association of redlining alone among white participants was negligible compared to white participants in non-redlined areas (OR: 0.86; 95% CI: 0.55, 1.34). However, Black participants in both non-redlined and redlined areas had more than twice the odds of having dementia/CIND compared to white participants in non-redlined areas (OR: 2.27; 95% CI:1.29, 3.97; OR: 2.23; 95% CI: 1.38, 3.63, respectively). Similar associations were observed with incident dementia/CIND.

Conclusions: Our findings elucidate the combined influence of individual-level race and residence in a historically redlined area on prevalent CIND/dementia, and the likely impact of redlining alone on incident CIND/dementia. The impact of historic redlining from nearly a century ago still has negative consequences on present day cognitive status.

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Aging

Social integration and subsequent disability in older adults from California

L. Paloma Rojas-Saunero* L. Paloma Rojas-Saunero Ryo Ikesu Natalie Gradwohl Ruijia Chen Rachel A. Whitmer Paola Gilsanz M. Maria Glymour Elizabeth Rose Mayeda

Background: Understanding the benefits of social integration on health among older adults is important for informing the design of future interventions to prevent isolation and promote healthy aging. The aim of this study is to estimate the association between social integration and subsequent disability in older adults in California. **Methods:** We used longitudinal data from the Kaiser Healthy Aging and Diverse Life Experiences (KHANDLE) study and the Study of Health Aging in African Americans (STAR) and included all participants free of instrumental activities of living (IADL) limitations at baseline. Social integration was defined by the Berkman-Syme Social Network Index (SNI) at baseline and was categorized as least integrated (SNI: 0-2), moderately integrated (SNI: 3-4), and most integrated (SNI: 5-6). The outcome corresponds to having any (versus no) IADL limitations [managing money (keeping track of expenses, paying bills); doing chores at home (vacuuming, sweeping, dusting, straightening up); preparing own meals] on the follow-up visits over 4 years. We fit generalized estimating equation models to estimate the risk of incident disability by social integration category, adjusting for baseline age, sex, and educational attainment. **Results:** We included 1702 participants (n = 349 "least integrated", n = 947 "moderately integrated", n = 406 "most integrated"). Mean baseline age was 73 (SD: 7) years, 60% were women. Median follow-up was 2.3 years. The adjusted risk ratio for newly reported IADL limitations was 1.17 (95% CI: 0.90, 1.52) for participants moderately integrated and 0.65 (95% CI: 0.46, 0.93) for most integrated participants, compared to those least integrated. **Discussion:** These findings suggest that social integration is associated with lower risk of developing disability in later life. Future work needs to expand on how changes in social integration impact incident disability.

Mortality Risk Reduction and Smoking Cessation among Older Population with Long-term Smoking History Shimin Chen* Shimin Chen

Background: There is limited evidence on the benefits of smoking cessation among older populations with long-term smoking history. To quantify the association between smoking cessation and mortality by years since quitting among older populations with long-term smoking history.

Design: Data from Beijing Healthy Aging Cohort Study (BHACS), which was conducted among communities aged over 55 years old at recruitment and collected via questionnaire between July 2009 and September 2015, were utilized in this large representative prospective cohort study of older population. Participants were followed up for all-cause and cancer mortality until March 2021. All the participants from BHACS were included in current analyses. Self-reported smoking status and years since quitting were collected at recruitment, and all-cause mortality was followed up. Cox proportional hazards models were used to examine the association of smoking cessation with mortality.

Results: A total of 11 235 individuals were included, with age at recruitment was 70.35 (7.71) years, 4 930 (43.9%) were males. 3 561 (31.7%) were former smokers, with medians (quartiles) years of smoking 43 (34, 50) years. There were 1 617 (14.4%) deaths among 71 573 person-years of follow-up (872 [17.7%] in males). Compared with never smokers, HR (95%CI) for participants who current smoked was 2.898 (2.092-4.013); quit smoking less than 10 years (medians [quartiles] 4 [1, 7] years) before recruitment was 2.738(1.972-3.802); 10 to 20 years (16 [13, 20] years), 1.807(1.286-2.540); and 20 years or more (30 [25, 37] years), 1.293(0.981-1.705). The risk of all-cause and cancer mortality decreased gradually over years since quitting. Quitting less than 10 years, 10 to 20 years and 20 years or more, former smokers avoided an estimated 8.4%, 57.5% and 84.6% of excess all-cause mortality associated with current smoking, respectively. An association of smoking cessation with decreased mortality existed among former smokers regardless of smoking history.

Conclusions: Current smoking was related with almost triple the mortality risk of never smoking in this study. Smoking cessation, even with long-term smoking history, was related with significant decreases in the relative excess mortality associated with continuing smoking.

Behavior

Mutual causal relationship between food intake and regular meal behaviors among socioeconomically disadvantaged children and youth: An evidence-based longitudinal study from 2009 to 2017 in Taiwan Yueh-Ting Lai* Yueh-Ting Lai Yueh-Ting Lai Yun-Hsuan Wu

Introduction

Evidence has showed that children's food intake and regular meal behaviors influenced childhood obesity and these behaviors exhibited mutual associations. Moreover, children from disadvantaged families exhibit worse forms of these behaviors. However, there are limited studies that use longitudinal data to investigate the mutual causal relationship between food intake and regular meal behaviors, especially among socioeconomically disadvantaged children in Taiwan.

Methods

Data from the five waves (2009, 2011, 2013, 2015, 2017) of the Taiwan Database of Children and Youth in Poverty (n=1400) were used. Food intake behaviors were assessed using two variables: 1) the frequency of fruit and vegetable intake (FVI) and 2) the frequency of snack and beverage intake (SBI). Regular meal behaviors were captured by two variables: 1) the frequency of breakfast (BF) and 2) meal pattern, which classified individuals into four patterns based on having regular main meals (MM) and non-main meals (nMM). Ordinal and multinominal mixed logistic regression were applied to examine the mutual causal relationship.

Results

There were mutual causal relationships between food intake and regular meal behaviors. Children with more frequent FVI were more likely to have BF and less likely to have irregular MM, while those with higher frequency of SBI were more likely to have nMM. On the contrary, children having more frequent breakfast were more likely to have FVI. Irregular MM was associated with a lower likelihood of FVI, while nMM was linked to a higher likelihood of SBI. Furthermore, children who had both MM and nMM were more likely to have higher FVI and SBI.

Conclusion

Based on our findings, we suggest that children should consider adopting both improved food choice and regular meal behaviors, rather than concentrating on just one behavior, to develop healthy eating behaviors. Further studies are needed to explore the underlying mechanism of these mutual effects on children's health.

Use of generative adversarial networks to create synthetic data Hayden Smith* Hayden Smith

Background: Generative adversarial networks (GANs) consist of two competing models (e.g., neural networks), a generator and discriminator. The generator creates synthetic data from random noise while the discriminator attempts to distinguish between real and generated data. The networks optimize generation and discrimination of synthetic data via an iterative competitive training process using a defined value function. This approach can be used to generate data for teaching, research, and sharing of sensitive information. Objective: to describe two processes for creating synthetic data using GANs.

Methods: Two generative examples were constructed. The first example consisted of simulating data based on a simple function (e.g., Var1 ~ N(0, 1), Var2 = Var1^2 + U(-0.9, 0.9)). This example served to introduce the basic process using a GAN. Next, an available version of the Framingham Heart Study data was used to generate a synthetic dataset using a conditional tabular GAN (CTGAN). Synthetic and real data were then evaluated and contrasted.

Results: The top panel of the Figure shows the model building progress for the simple example overlaid on real data. The last pane on the top panel shows the benefit of using drop out to regularize network output. The bottom panel of the Figure shows some summary displays for the second example's generated synthetic data. Also presented at the conference will be statistical model comparisons based on synthetic and real data as well as a basic attempt to use synthetic data to augment a power analysis.

Conclusions: The presented processes can be used to create synthetic data based on supplied data files. Different types of GANs, value functions, and hyperparameter tuning can be explored to attempt to meet project goals. For example, if data appear to be too deterministic or overfit, approaches like dropout can be incorporated. Future work may include exploring GAN applications for power analysis, outcome imbalance, and imputation.
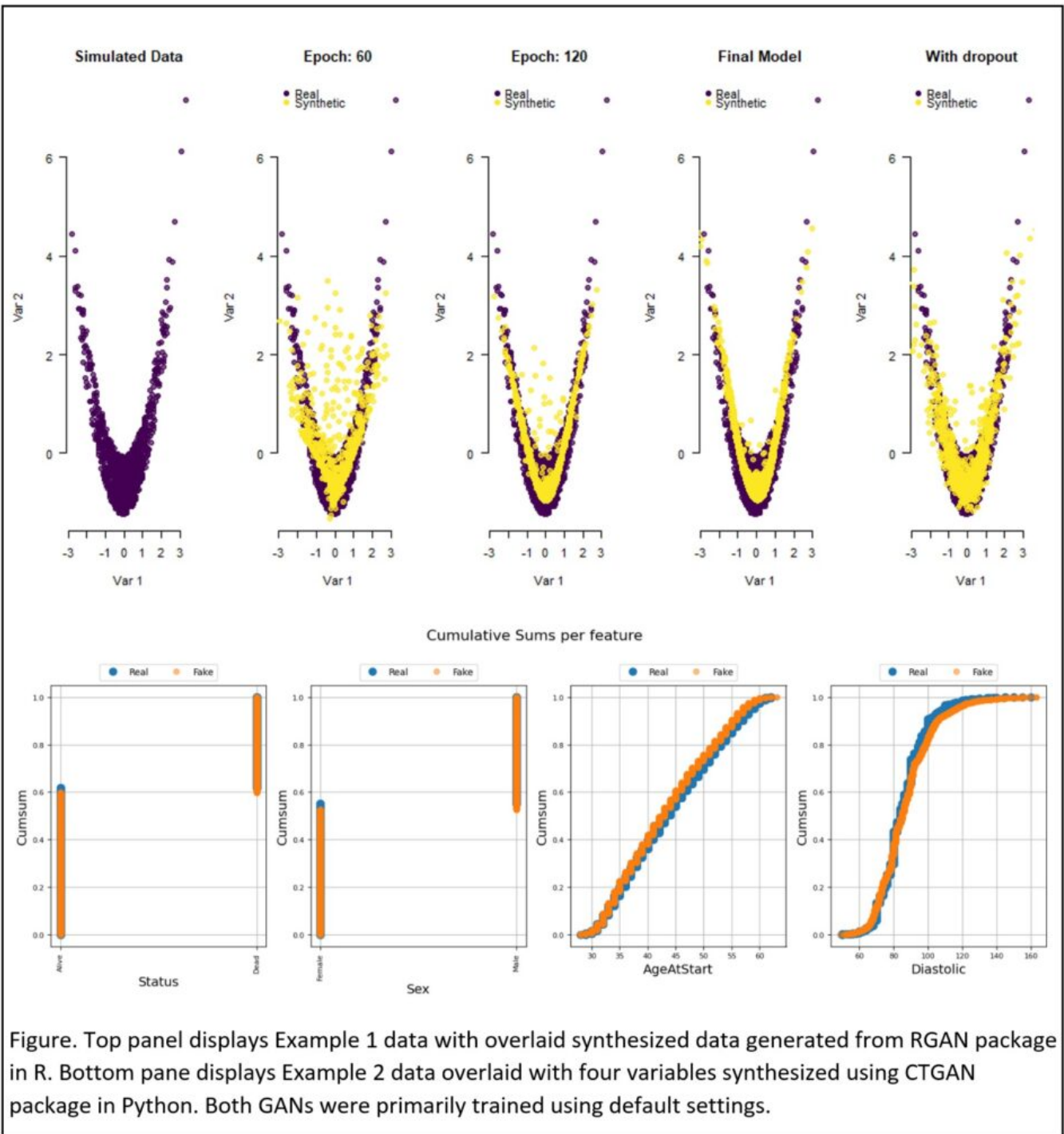
Figure. Top panel displays Example 1 data with overlaid synthesized data generated from RGAN package in R. Bottom pane displays Example 2 data overlaid with four variables synthesized using CTGAN package in Python. Both GANs were primarily trained using default settings.

Big Data/Machine Learning/AI

Neural Networks for the prediction of neonatal mortality in Rio de Janeiro State, Brazil

RENAN MORITZ VARNIER R ALMEIDA* Renan Renan Moritz V R Almeida Renan Moritz V R Almeida Nubia Karla de Oliveira Almeida

Objective: To predict neonatal mortality using hospital administrative data by means of Logistic Regression (LR) and Multilayer Perceptron (MLP) models.

Methods: Records of 167.928 singleton births in Rio de Janeiro State hospitals (Brazil), 2019-2020, were obtained from a national administrative information system (Datasus). Fifteen variables pertaining to characteristics of the mother, the pregnancy and the newborn were identified and used as predictors for neonatal mortality. Data were randomly split in two sub-sets: a training (70% of data) and a testing set, and two models were developed in the training set: An LR and a one hidden layer MLP. Given the relative rarity of the outcome variable, the training set was also "balanced": a new dataset was created with proportions 30/70% for the minority/majority classes of the outcome, and the models were also developed for this set. The SMOTE-N (Synthetic Minority Oversampling Technique-Nominal), RO (Random Oversampling) and RU (Random Undersampling) algorithms were used for data balancing. Model performance was evaluated in the testing sub-set by the metrics: *Accuracy, Precision, Recall (Sensitivity), F1-score, Specificity,* and *AUC*. The analyses were done with the *R* and *Python* languages. LR models adopted a significance level of 5%.

Results: Overall, neonatal mortality rate was 0.6%, and all predictors could be retained in the LR models for SMOTEN and RO approaches (most important predictors: Apgar at birth, gestational age and birthweight). Whatever the model, both the LR and the MLP had AUCs close to 0.88. Sensitivity displayed low values for the unbalanced data, with significant improvements when balanced (0.12/0.09 for LR/MLP unbalanced to 0.59/0.33 balanced with SMOTE-N; 0.72/0.62 balanced with RO and 0.73/0.69 with RU).

Conclusions: Both the Logistic Regression and the Multilayer Perceptron were good classifiers for the studied data. Balancing training data helped improving model's sensitivity.

Big Data/Machine Learning/AI

BMI polygenic risk score as a tool for quantifying the magnitude of bias in the association between cross-sectional measures of BMI and osteoarthritis in the UK Biobank Patrick Carry* Patrick Carry Jyothi Lokanadham Mike Zuscik Cheryl Ackert-Bicknell

Osteoarthritis (OA) is associated with long-term disability and reduced quality of life. Due to lack of preventative interventions, there is a critical need to identify modifiable risk factors. Obesity has been hypothesized as a risk factor but, associations between BMI and OA are often measured in cross-sectional studies that are prone to bias due to residual confounding and reverse causation. Genetic measures of BMI may provide an unbiased estimate of the association between BMI and OA. The purpose of this study was to quantify differences in the strength of association between genetic measures of BMI and OA vs cross-sectional measures of BMI and OA.

We queried the UK Biobank (UKB) to identify individuals with health outcome and genetic data. Cross-sectional BMI was based on BMI at enrollment. Genetic BMI was based on a BMI polygenic risk score (PRS) from prior meta-analyses. Multivariable logistic regression models, adjusted for genetic batch, ancestry, age, prior joint injury, sex, and community economic deprivation (Townsend index) were used to test the association between BMI and OA. We also included interaction terms between BMI and covariates. We compared odds ratios (ORs) representing OA and cross-sectional BMI (biased) vs OA and PRS BMI (unbiased). All ORs represent odds of OA per 1 standard deviation increase, facilitating direct comparisons between the BMI measures.

There was a significant association between the BMI PRS and knee OA (OR: 1.22, 95% CI: 1.20-1.24) and hip OA (OR: 1.13, 95% CI: 1.11-1.32). Cross-sectional BMI ORs were higher than PRS BMI for knee OA (OR: 1.81, 95% CI: 1.78-1.84, +48%) and hip OA (OR: 1.27, 95% CI: 1.25-1.30, +13%). In the subgroup analysis, ORs for cross-sectional BMI were consistently higher for knee OA (range: +29% to +52%) and hip OA (range: +6% to +22%, Figure 1).

There was a strong interrelationship between BMI, affected joint, and demographics. Cross-sectional BMI consistently overestimated the association between BMI and OA. Bias, as represented by percent difference in genetic vs cross-sectional BMI, was highest in relation to knee OA, older age, male sex, and higher affluence. Genetic based measures of exposures are a useful tool for quantifying the magnitude of bias in the strength of the association between environmental risk factors and disease in cross-sectional studies.
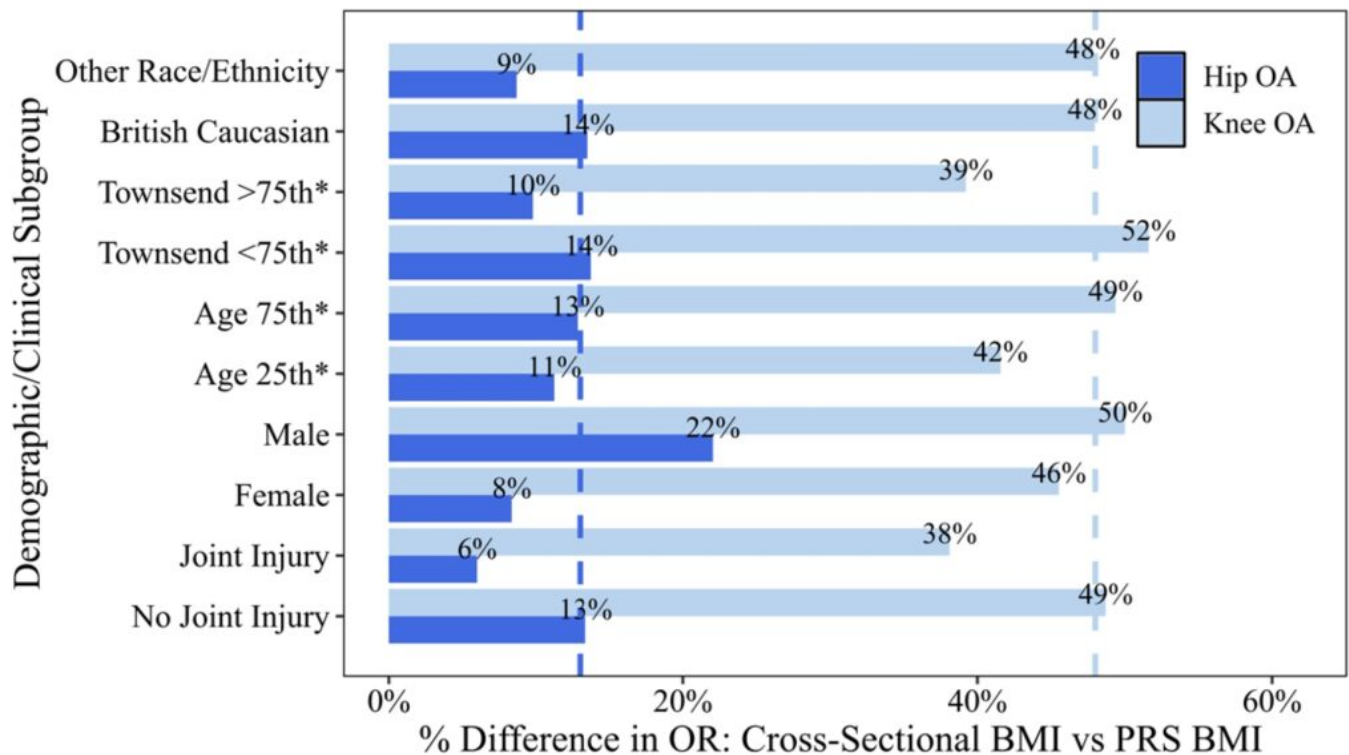
Figure 1. Percent difference (bias) in odds ratios (OR) representing the association between osteoarthritis (OA) and BMI based on a polygenic risk score (PRS) vs BMI based on a cross-sectional measure. ORs were estimated within subgroups defined based on race/ethnicity (British Caucasian vs Other), sex, age, prior knee/hip joint injury, Townsend deprivation index (community level measure of material deprivation, high levels represent deprivation while low levels indicate affluence). All ORs are reported as odds of OA per 1 standard deviation increase in BMI, facilitating direct comparison between the BMI measures. The light blue vertical line represents average percent difference in cross-sectional BMI vs PRS BMI (+48%) for knee OA, the dark blue vertical line represents average percent difference in cross-sectional BMI vs PRS BMI (+13%) for hip OA. *Represents percentiles within the UK Biobank.

Text Classification Models for Natal Sex Identification from Electronic Health Records of Transgender Population Qi Zhang* Qi Zhang Yuting Guo Timothy L. Lash Abeed Sarker Michael Goodman

Transgender and gender diverse (TGD) people assigned at birth (natal) male or female sex are often referred to as transfeminine (TF) and transmasculine (TM), respectively. TF and TM persons may have health outcomes related to gender affirming therapy. Electronic health records (EHR) allow systematic identification of TGD people in large health systems, but the EHR administrative designation of sex/gender is unreliable for TGD people because it may designate gender or natal sex. In this study, we developed natural language processing (NLP) models to distinguish TF from TM based on free-text clinical notes. The Study of Transition Outcomes and Gender (STRONG) cohort includes TGD members enrolled in Kaiser Permanente healthcare plans from 2006 through 2022. We used text strings containing relevant keywords among 6150 members with gold standard labels for model development. Data were divided into training (64%), validation (16%), and test (20%) sets. We first applied support vector machines (SVM), random forests (RF), shallow neural networks, and k-nearest neighbor models. In addition, two deep learning models, BiLSTM and Transformer (RoBERTa), were also used. Models were evaluated based on micro F1-score, precision (positive predictive value) and recall (sensitivity) metrics. An ongoing adaptive validation study is being conducted using data on 40,305 new TGD candidates from multiple sites based on manual review of text strings. We first validate the natal sex of 100 subjects with predicted scores above 0.98 and below 0.02, respectively, from each site. Our results show that SVM produced the highest F1-score (0.97, 95% CI: 0.96, 0.98) with a recall of 0.97 and a precision of 0.97, and RF yielded comparable performance (F1-score: 0.96, 95% CI: 0.95, 0.97), followed by RoBERTa (F1-score: 0.95, 95%: 0.94, 0.97). The NLP models can provide an efficient way for automated EHR-based identification of natal sex in the TGD population, with SVM achieving the optimal performance.
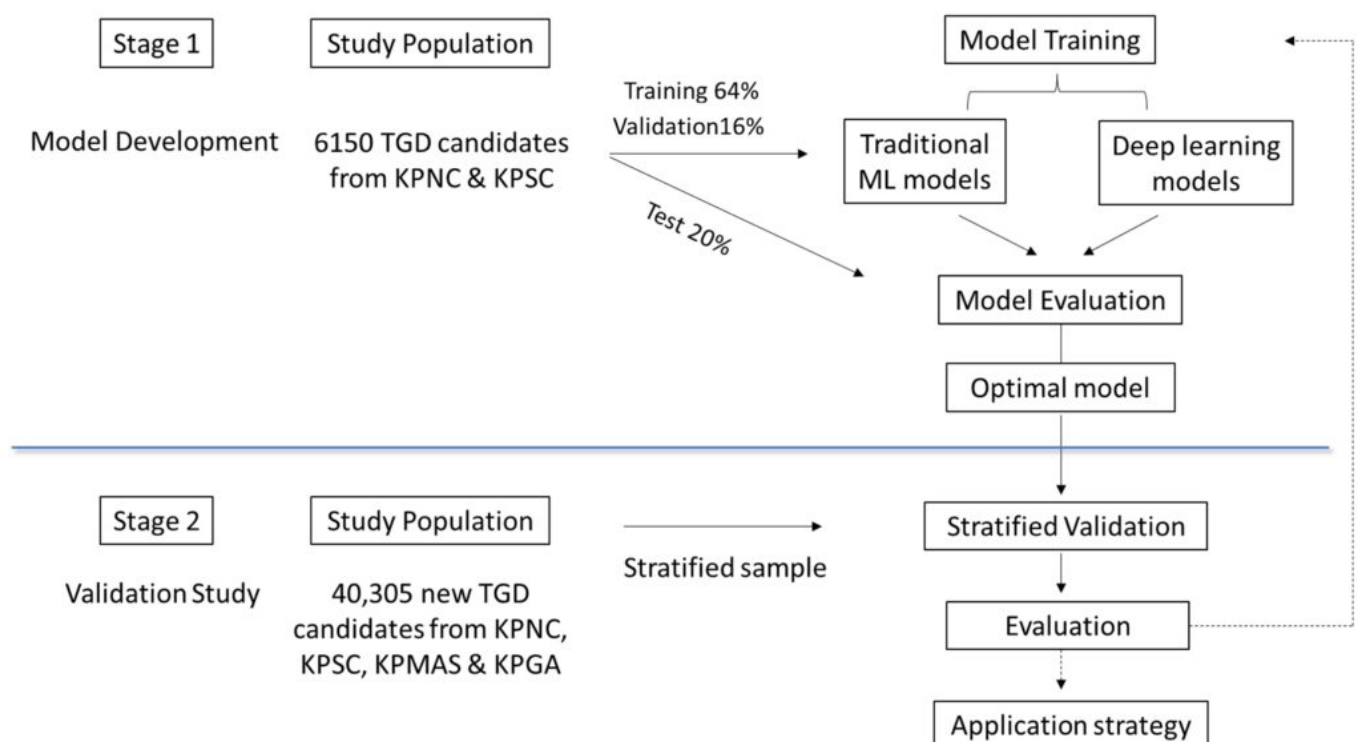
Figure 1. Schematic of study design

Big Data/Machine Learning/AI

Machine Learning and racial disparities in health Keisyanne de Araujo Moura* Keisyanne Araujo Moura Letícia Gabrielle Souza Augusto César Ferreira de Moraes Alexandre D. P. Chiavegatto Filho

Background
Machine learning (ML) models are increasingly being developed to predict health outcomes. The implementation of ML algorithms in healthcare has proven to be increasingly promising. However, the use of algorithms can introduce biases inherent in datasets, leading to issues such as algorithmic discrimination and presenting a potentially far-reaching threat to equity in healthcare.

Methods: Systematic literature review through the evaluation and synthesis of published articles, registered in PROSPERO. Searches were conducted in major databases, including articles that tested the use of ML, presented algorithm performance criteria, were original research with a focus on racial disparities. Well-defined inclusion and exclusion criteria.

Results: The initial search yielded 3,204 potentially eligible information titles, which were refined after applying inclusion and exclusion criteria, resulting in the selection of 13 articles for evaluation. Regarding the training-test division, six articles used k-fold cross-validation and seven studies carried out a complete division strategy between training and testing, with training percentages ranging between 60 and 88.15% and tests between 20 and 31.2 %. The main algorithms used were XGboost, Random Forest, and MSE, with AUCs ranging from 0.71 to 0.94. Studies have identified a wide range of issues related to racial disparities in machine learning, including different predictive accuracy for racial minorities, inequalities due to performance metric selection, and the presence of large racial imbalances in training data.

Conclusions: A central concern lies in training algorithms with data that mirrors societal biases. This scenario can lead to unfair outcomes and racial disparities in healthcare. Therefore, it is crucial to conduct a thorough analysis of biases embedded during the development of artificial intelligence models, taking into account sensitive variables such as race and ethnicity.

Figure 1: Flowchart

Big Data/Machine Learning/AI
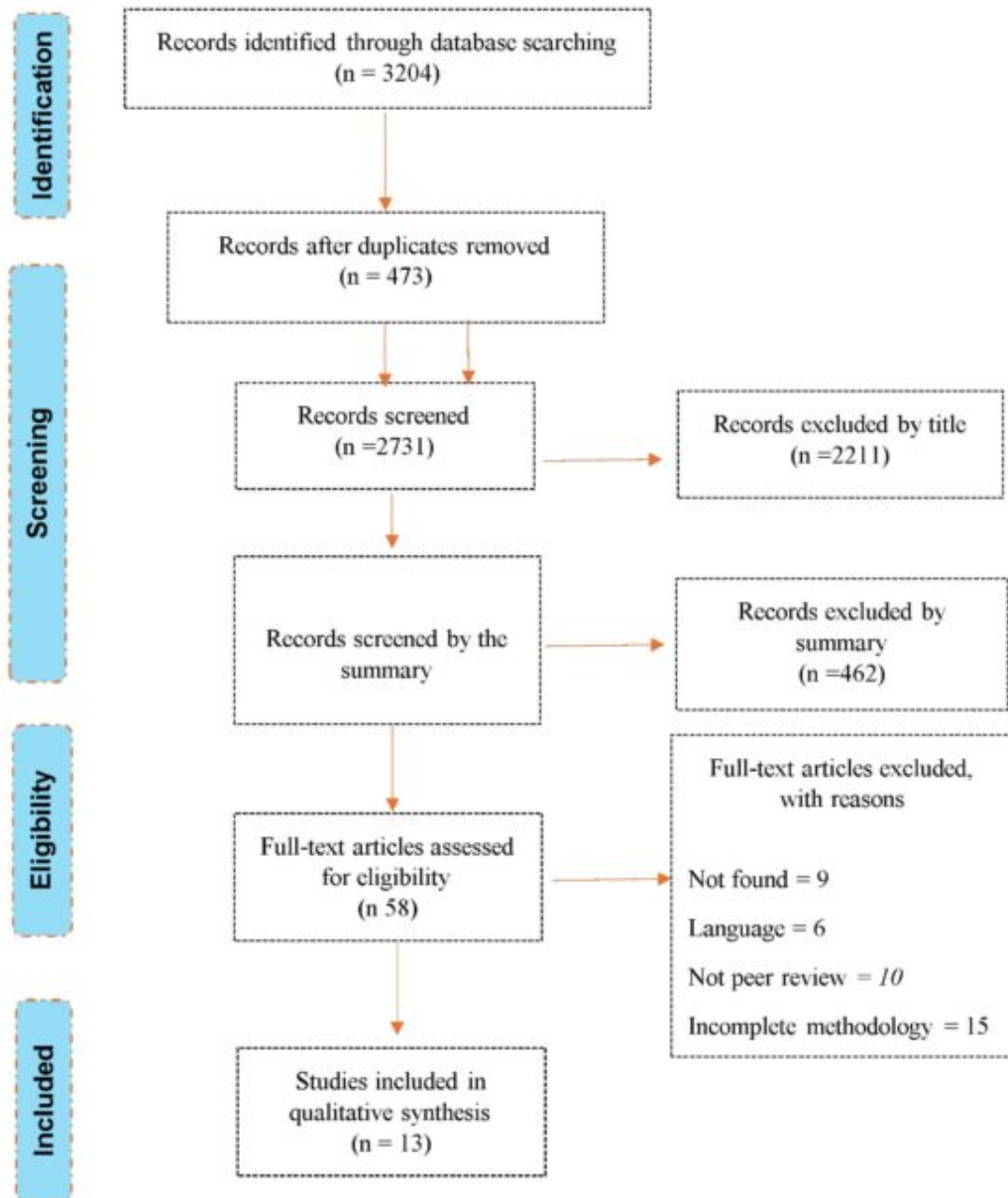
What if we had built a prediction model with a survival super learner instead of a Cox model 10 years ago? Arthur Chatton* Arthur Chatton Héloïse Cardinal Kevin Assob Feugo Robert W Platt Mireille E Schnitzer

Classical approaches to prediction were mainly based on parametric models, but there is a current trend towards using more flexible machine learning approaches. Indeed, many machine learning approaches do not rely on parametric assumptions about the underlying data-generating process and have the potential to predict more accurately. Nevertheless, there is still no free-lunch method, even with machine learning. Their improved flexibility is at the cost of an increased risk of over-fitting, needing more data to converge, and the final performance still depends on the particular data-generating process. Ensemble methods aim to overcome these issues by combining a diverse and rich set of algorithms or "learners" into one final prediction. For instance, the super learner takes a weighted sum of the individual predictions from each incorporated learner to produce a final prediction that is theoretically as accurate as the best-performing candidate learner.

However, both the patients' characteristics and the guidelines to treat them evolve over time. As a result, the performance of a prediction model decreases over time with this population shift, and a prediction model performing well when developed (even externally validated) can become useless later.

Little evidence exists about the performance drift occurring over time for machine learning-based prediction models. But ensemble methods were not considered, nor were time-to-event outcomes. Therefore, the present study aims to fill this gap in the literature.

The KTFS is a prediction score developed in the early 2000s in France to predict the return to dialysis eight years after kidney transplantation. We develop a KTFS-like score with a survival super learner on the same learning data as the KTFS used, and we validate their performance (discrimination, calibration and net benefit at 8 years) on patients transplanted between 2010 and 2015 from the same open cohort and other European or Canadian external cohorts.

Big Data/Machine Learning/AI

Federated learning for health outcomes predictions in a multicentric sample of hospitals

Murilo Bigoto* Murilo Bigoto Alexandre Dias Porto Chiavegatto Filho

Employing patient data in healthcare for predictive algorithms raises technical and ethical challenges in privacy and security. Despite the growing use of Federated Learning (FL) to protect patient privacy, significant hurdles persist. Our study aimed to develop COVID-19 mortality risk prediction algorithms across 21 Brazilian hospitals, using diverse FL structures. Twenty-two predictors, including age, gender, vitals, and hematological data, were assessed in two scenarios. The first scenario evaluated Logistic Regression (LR) and Multilayer Perceptron (MLP). A global model was created by averaging coefficients from each hospital. The second scenario involved Random Forest (RF) and XGBoost (XGB), aggregating local trees into a global model. All models showed similar metrics (AUC-ROC: LR 0.80, RF 0.79, XGB 0.78, MLP 0.80). FL outperformed local learning in both scenarios, maintaining the same hyperparameter space. In local learning, RF gained 6.5%, LR 7.2%, XGB 5.5%, and MLP 12.8%. Lower gains for RF and XGB indicated superior local performance. Clear predictive enhancement was seen for hospitals with fewer patients. Hospital data aggregation by five Brazilian regions showed increased AUC-ROC in FL (0.838) compared to local models (0.835), a 0.34% improvement. Our study highlights the potential of FL in predicting health outcomes from diverse hospital sources, ensuring patient privacy and security. It emphasizes FL not only for local predictive enhancement but also for generalization gains across different contexts.

LATEBREAKER

Cancer

Sociodemographic Factors and Financial Toxicity among Cancer Patients and Survivors: A Nationwide Study in Japan Kaori Suga* Kaori Suga Yuri Ito Kosuke Inoue Yuichi Ichinose Takahiro Higashi Naoki Kondo

Background: Financial toxicity (FT) refers to increased risk of treatment discontinuation and anxiety experienced in daily life due to the cost burden of cancer treatment. FT is reportedly linked to decreased quality of life and increased mortality, but few studies have thoroughly examined patient demographics among different age groups, especially in countries with Universal Health Coverage (UHC). We aimed to explore patient demographics and living conditions associated with FT, among adult cancer patients in Japan, which has UHC, and identify factors strongly linked to FT.

Methods: We analyzed responses from the Patient Experience Survey, a self-administered questionnaire conducted by the National Cancer Center in 2018. Patients were categorized as "have FT" if they agreed with one or both statements: "Changed or discontinued treatment" or "Impact on treatment and life (10 items)" due to treatment cost. We used weighted analysis to ensure representation of the target population—patients who started cancer treatment in 2016, used a modified Poisson regression model to analyze the association between patient demographics and FT, estimated the Prevalence Ratio (PR) and conducted subgroup analysis by sex.

Results: Of 6,783 valid responses (3,529 men, 3,254 women) 29.2% of men and 32.2% of women reported FT. Results of the multivariate analysis among both sexes showed a high PR of FT was associated with younger age, malignant lymphoma/leukemia, during treatment, chemotherapy, taking leave or retiring due to treatment, absence of consultants, feeling alienated, and experiencing prejudice. Age at diagnosis was higher for under 39s (vs 65+) PR= 1.82 [95% CI, 1.48-2.23] for men and PR= 1.41 [95% CI, 1.20-1.65] for women.

Conclusion: These results show the need for counseling support and a better work-treatment balance for cancer patients. They also highlight the importance of improving the social environment to help patients and survivors maintain connections with society.

Carcinogenic Metals and Colorectal Cancer Incidence: Pilot Results from the Louisville Environmental Assessments Pilot Study (LEAPS) in Colorectal Cancer Natalie DuPre* Natalie DuPre Lu Cai Jason Xu Allie Jin Olufunmilayo Babarinde Jeevan Adhikari Sandy Kavalukas

Background: Colorectal cancer (CRC) is the 3rd most commonly diagnosed cancer in the US, with the CDC recently reporting that Kentucky has the highest age-standardized CRC rate despite high CRC screening. Cadmium (Cd) and arsenic (As) are known human carcinogens for certain cancers. However, most epidemiologic studies on As and Cd with CRC are within occupational settings considering CRC mortality outcomes and not CRC incidence.

Methods: The Louisville Environmental Assessments Pilot Study (LEAPS) in CRC is a clinical case-control initiated in August 2023. We consented CRC cases and controls who were undergoing procedures related to CRC or screening from an urban hospital. Participants completed a detailed questionnaire and provided urine and blood samples. As and Cd were measured in biospecimens of eight non-smoking participants using inductively coupled plasma mass spectrometer (ICP-MS). We compared metal concentrations (ng/mL) in 3 cases and 5 controls with unequal variance t-tests.

Results: Within the LEAPS-CRC population (28 CRC cases; 52 controls), CRC risk factors were more prevalent in CRC cases than controls. The standard deviations (SD) were 0.32 ng/mL for urinary Cd, 0.16 for blood Cd, 6.8 for urinary As, and 0.46 for blood As. On average, urinary Cd was 0.16 ng/mL higher in CRC cases (i.e. 0.46 vs 0.30 ng/ml) than controls, corresponding to half of a SD. Blood Cd concentrations were 0.155 ng/mL higher in CRC cases than controls (i.e. 0.28 vs 0.12 ng/ml), that corresponds to ~1.0 SD. Urinary As was 0.9 ng/mL higher in CRC cases than controls (i.e. 6.64 vs 5.69 ng/ml). As expected, differences were not statistically significant due to small sample sizes. Conclusion: Preliminary data suggests that carcinogenic metals in biospecimens may be associated with CRC incidence in non-occupationally exposed and non-smoking populations. The ongoing LEAPS-CRC investigation holds the potential to determine whether carcinogenic metals may be novel CRC risk factors.

Spectrum of cancer risk in Asian American, Native Hawaiian, and other Pacific Islander Populations After Solid Organ Transplantation in the United States Jun Tao* Jun Tao Jaimie Z. Shing Kelly Yu Aimée R. Kreimer Mei-Chin Hsieh Karen Pawlish Jie Li Baozhen Qiao Eric A Engels

Background: Solid organ transplantation (SOT) is a lifesaving therapy for patients with end-stage organ disease; however, immunosuppressive agents used to prevent graft rejection increase cancer risk. While this has been well described among White, Black, and Hispanic SOT recipients in the United States, cancer risk in Asian American (AA), Native Hawaiian, and other Pacific Islander (NHPI) SOT recipients is ill-defined. We aim to describe and compare cancer risk among AA and NHPI SOT recipients in the US.

Methods: Cancer cases in AA and NHPI SOT recipients during 1990-2019 were obtained from the Transplant Cancer Match study, a linkage of the US transplant registry with 34 population-based cancer registries in the US. For each cancer type, we calculated a standardized incidence ratio (SIR) comparing incidence among SOT recipients with incidence in the general US population, by race (AA and NHPI). Expected cancers in the general AA and NHPI populations were calculated using rates from the Surveillance, Epidemiology, and End Results program. Among SOT recipients, incidence rate ratios (IRRs) for each cancer type were calculated, comparing risk between NHPI and AA populations.

Results: During 1990-2019, a total of 22,971 AA and 1,793 NHPI individuals received SOT (57.9% male, median age of 51 at transplantation). Compared to the general AA population, AA SOT recipients had a higher risk of overall cancers (SIR=1.7, 95%CI=1.6-1.8) and several cancers, most notably Kaposi sarcoma (15.3, 6.6-30.2), non-epithelial skin cancer (9.8, 5.4-16.5), anal cancer (7.9, 3.6-15.1), renal pelvis cancer (7.4, 3.7-13.2), non-Hodgkin lymphoma including chronic lymphocytic leukemia (NHL/CLL, 6.4, 5.6-7.3), and Hodgkin lymphoma (6.1,2.8-11.7). Other elevated SIRs among AA SOT recipients were cancers of the stomach, bladder, thyroid, and kidney, and leukemia (SIR range=1.8-5.3). Compared to the general NHPI population, NHPI SOT recipients had a higher risk of total cancers (SIR=1.3, 95%CI=1.0-1.5) and NHL/CLL (4.5, 2.3-7.9). Compared with AA SOTs, NHPI SOTs had a higher risk of pancreatic cancer (IRR=3.7, 95%CI=1.6-8.6) and skin melanoma (6.7, 1.2-36.4).

Conclusion: This study highlights the elevated cancer risk among AA and NHPI SOT recipients compared with the general AA and NHPI populations. The spectrum of cancer risk resembles what has been observed in other racial/ethnic SOT recipients, with an elevated risk for virus-related cancers due to immunosuppression during SOT therapy.

LATEBREAKER

Cancer

Characteristics of women with metastatic HR+/HER2+ breast cancer in a Kaiser Permanente observational cohort Sheila Weinmann* Sheila Weinmann Debra P. Ritzwoller Marilyn Kwan Reina Haque Stella Stergiopoulos Ashley Cha-Silva Eric Gauthier Daniel Sapp John Dickerson Weiming Hu Nikki Carroll Lie Hong Chen Valerie Lee Ravi Zalavadi Kathryn Richert-Boe Maureen O'Keeffe-Rosetti

Background: Approximately 10% of female breast cancer tumors express hormone-receptor positive/human epidermal growth factor receptor 2 positive (HR+/HER2+) molecular subtype. This study of the HR+/HER2+ metastatic breast cancer (mBC) patient population describes demographic/clinical characteristics, treatment patterns, and outcomes in a racially diverse, insured, population-based cohort, drawn from four regions of the Kaiser Permanente health system.

Methods: Eligible subjects were women age ≥18 years with HR+/HER2+ invasive breast cancer who were either initially diagnosed with Stage IV disease or were diagnosed at an earlier stage and experienced recurrence with distant metastasis from 2012-2021 with data collected through 2021. Information from electronic health records (EHR) was combined with manually abstracted data to create the analytic dataset.

Preliminary Results: We identified 473 racially and ethnically diverse women with HR+/HER2+ mBC, 46% with de novo Stage 4 breast cancer (D) at diagnosis and 54% with recurrent mBC (R). Median age at mBC diagnosis was 59 years for D cases and 62 years for R cases. Major sites of metastases, including bone, liver, lung, brain, and distant lymph nodes, were similar in D and R groups.

15% of patients received no systemic treatment for their mBC (9% D, 20% R), For those with systemic treatment, 75% received anti-HER2 agents (88% D, 62% R) and 75% received hormone therapy (83% D, 67% R). Of the R cases, 56% received anti-HER2 therapy in the adjuvant setting. Of women who initiated first-line treatment, 68% progressed or died (66% D, 74% R). Median first line progression-free survival was 16 months (23 D, 11 R).

Conclusion:

In this population-based study, 85% of women received systemic therapy, and the majority of those received anti-HER2 therapy per current treatment guidelines.

The impact of Medicaid expansion on non-small cell lung cancer diagnosis, survival, and disparities Lu Zhang* Lu Zhang Marvin Okon Jingxuan Zhao K. Robin Yabroff Rachel Mayo Khoa Truong Xuesong Han

Background

Medicaid Expansion (ME) under the Affordable Care Act increased insurance coverage among low-income populations. We examined the associations of ME with changes in early stage at diagnosis and 3-year overall survival among individuals with non-small cell lung cancer (NSCLC), by race/ethnicity and residential segregation status.

Methods

Patients aged 18-64 newly diagnosed with NSCLC in 2010-2013 (pre-expansion) and 2015-2019 (post-expansion) from 22 states that expanded Medicaid eligibility before 12/31/2014 and 16 states that had not expanded Medicaid by 12/31/2019 were identified from the North American Association of Central Cancer Registries CiNA database. Outcomes included diagnosis at localized stage and 3-year overall survival. Residential racial and economic segregation was measured by the Index of Concentration at Extremes (ICE) at the county level. The Difference-in-differences (DD) approach was used. Linear probability regressions were fitted for early-stage diagnosis and flexible parametric survival models were fitted for survival, , and stratified by race and ethnicity and ICE tertile.

Results

A total of 215,854 patients from expansion and 167,180 patients from non-expansion states were included. ME was associated with significant increases in local stage diagnosis (aDD=1.55ppt, P<.0001) and 3-year survival (aDD=2.28ppt, P<.0001). The pattern was consistent across racial/ethnic groups and ICE tertiles, though the net increase in early-stage diagnosis associated with ME was most prominent among non-Hispanic White patients (aDD=1.82ppt, P<.0001).

Conclusion

ME was associated with an increase in early diagnosis and 3-year overall survival of NSCLC in a nationwide population-based database. The improvements were seen in all segments of populations in terms of race/ethnicity and residential segregation status.

Domain-specific physical activity across the life course on the risk of ovarian cancer

Jennifer Ritonja* Jennifer Ritonja Sreenath Madathil Belinda Nicolau Lisa Leung Vikki Ho Michal Abrahamowicz Anita Koushik

Past studies examining moderate-to-vigorous physical activity (MVPA) and ovarian cancer risk have focused on recreational MVPA and have found inconsistent results. Most studies measured MVPA during older adulthood, which may not represent pertinent exposure. To-date, no study has examined how timing of MVPA across the lifetime from all four primary domains (recreation, occupation, housework and transportation) impacts risk. Using the life course approach, we sought to identify if ovarian cancer risk is influenced by total (from all four sources) and domain-specific MVPA during certain critical or sensitive life periods or accumulated over adulthood. In a population-based case-control study in Montreal (2011-2016), MVPA was determined using recalled information on the frequency and duration across adulthood of physical activities from all domains. We used the Bayesian relevant life course exposure model to estimate the relative importance of MVPA exposure during 3 life periods (early childbearing years [ages 20-29], late childbearing years/perimenopause [ages 30-49], and postmenopause [ages $\geq$50]) on ovarian cancer risk. In preliminary results among 344 cases and 668 controls aged $\geq$52 years, the domain with the largest contribution to total MVPA was housework (between 65-70% for the 3 life periods). Increasing cumulative exposure to MVPA across the adult life course was associated with a reduced ovarian cancer risk for both total and housework MVPA, with ORs for each additional 50 metabolic equivalent (MET)-hours/week of: OR=0.91; 95% credible interval (CrI)=0.78-1.04 for total MPVA, and OR=0.85; 95% CrI=0.67-1.02 for housework MVPA. For both, the posterior distributions for importance of the three life periods were similar. ORs for other physical activity domains did not support a reduced risk. Our findings support the life course hypothesis of an accumulation effect in the association between MVPA and ovarian cancer risk, mainly driven by housework MVPA.

Cancer

The association between protein biomarkers and thyroid cancer in a racially and socioeconomically diverse population in New-York: A nested case-control study Gary Joseph*
Gary Joseph Maaike van Gerwen Seunghee Kim-Schulze Zhihong Chen Girish N. Nadkami Haibin Guan Elena Colicino Eric M. Genden Lauren M. Petrick

Background: Inflammation is a hallmark of cancer. However, there is a lack of studies exploring the association between inflammation protein biomarkers and thyroid cancer (TC) in humans. We assessed the association between inflammation protein biomarkers and TC risk, using plasma samples collected at or before the TC diagnosis.

Methods: We identified 88 patients with TC and matched them with 88 controls based on sex, age, race/ethnicity, body mass index, smoking status, and year of sample collection in BioMe, a medical record-linked biobank at the Icahn School of Medicine at Mount Sinai. Ninety-two proteins measured by the Inflammation Olink Target 96 were included in the analysis. We assessed the association between the proteins and TC using logistic regression, Cox regression (for TC cases diagnosed ≥ 1 year after plasma samples collection and their matched controls) and generalized weighted quantile sum (gWQS) regression models.

Results: Eight proteins were negatively and nominally associated with TC including CCL19 (ORadj, 0.67, 95%CI: 0.47-0.94), CDCP1 (ORadj, 0.48, 95%CI: 0.25-0.88), CST5 (ORadj, 0.42, 95%CI: 0.21-0.78), CXCL6 (ORadj, 0.73, 95%CI: 0.53-0.99), FGF-21 (ORadj, 0.73, 95%CI: 0.56-0.93), IL7 (ORadj, 0.55, 95%CI: 0.31-0.96), MMP-1 (ORadj, 0.72, 95%CI:0.54-0.95), and OPG (ORadj, 0.34, 95%CI: 0.15-0.72), many of which belong to the pathway of proinflammatory and profibrotic mediators (WikiPathways, WP5095, FDR=9.68e-05). Similar associations were noted in subgroup analysis for TC cases diagnosed ≥ 1 year after plasma samples collection. Additionally, we observed a negative TC association with the proteomic mixture (β=-1.17, p=0.022).

Conclusion: Negative associations were found between the proteins and TC risk, which suggests a potential protective role of these proteins in the context of TC. Large-scale prospective studies are needed to better understand these biomarkers' contribution in TC development.

Cancer

Age-period-cohort modeling of esophageal carcinoma risk in a middle eastern country:1980–2019 Saeed Akhtar* Saeed Akhtar Ahmad Al-Shammari Mohammad Al-Huraiti Fouzan Al-Anjery

Background: Esophageal cancer is the eighth most common cancer and the sixth leading cause of cancer-related deaths worldwide. Owing to disparity in epidemiology of esophageal cancer across different populations, monitoring the esophageal cancer trends is crucial. Therefore, this cross-sectional cohort study examined the contributions of age, period, and cohort effects in the temporal trends of esophageal cancer in Kuwait.

Methods: The data on incident esophageal carcinoma cases from January 1980 through December 2019, from Kuwait Cancer Control Center Registry and reference population were obtained. Age-period-cohort (APC) analysis was conducted using a loglinear Poisson regression model. Descriptive statistics were complemented with APC parameters' estimates. Age effect was presented as IRs (per 105 person-years), whereas period and cohort effects as adjusted RRs.

Results: Over the study period**,** a total of 496 esophageal carcinoma cases in 12.8 million person-years at risk were diagnosed. Of these, 269 (54.23%) were esophageal squamous-cell carcinoma, 147 (29.64%) adenocarcinoma and 80 (16.13%) cases were histopathological unspecified. Subsequently, all histopathological types were grouped as esophageal cancer. Overall age-standardized incidence rate (per 105 person-years) of esophageal cancer during study period was 10.51 (95% CI: 6.62-14.41). APC analysis showed that age and birth cohort effects were significant ($p < 0.05$) determinants of declining, and subsequently stabilizing esophageal carcinoma incidence rates in all three temporal dimensions (Figure1).

Conclusions: A substantial decline in esophageal carcinoma incidence rates was recorded, which significantly varied in all three temporal dimensions. The observed birth cohort patterns suggest changing lifestyle and dietary patterns seem to be responsible for decreasing esophageal cancer risk in Kuwait. Future studies may examine the biological basis for temporal decline in esophageal cancer risk.
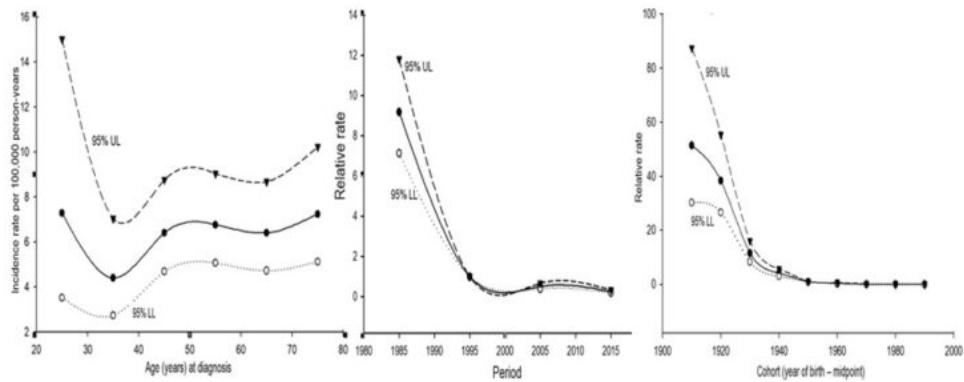
Fig. 3. APC-fitted temporal trend (**a**) expected oesophageal cancer incidence rates in the reference age group (a_0) adjusted for cohort deviations: 1980–2019; (**b**) APC-fitted period effect on the oesophageal cancer incidence rate – the period relative rate adjusted for age and nonlinear cohort effects in each period relative to the reference period 1980–2019; (**c**) Birth cohort effect on the incidence rates of oesophageal cancer – cohort relative rates adjusted for age and nonlinear period effects in each cohort relative to the reference cohort of 1950–1959

Application of a Maternal Comorbidity Index to Predict Childhood Cancer Risk: A Population-Based Case-Control Study in Denmark (1977-2013) Tobiloba Adanma Adenekan*

Tobiloba Adanma Adenekan Julia Heck Cheng Yin Johnni Hansen

Background

A mother's health conditions before and during pregnancy could have important consequences for her child's health, including cancer development, as was observed in some prior studies.

Objectives

This study aimed to identify the impact of varying maternal comorbidities on the development of childhood cancers. This study applied an Obstetric Comorbidity Index (OCI) (Bateman, 2013) to examine maternal comorbid conditions in childhood cancer risk.

Methods

We conducted a population-based case-control study using the Danish National Patient Registry to obtain maternal health conditions and the Cancer Registry for child outcomes, at two time periods: cases (n=2578) and controls (64450) with ICD-10 diagnoses from 1994-2013, and the second population included cases (n=8339) and controls (n=208475) with ICD-8 and 10 diagnoses from 1977-2013. We estimated the risk of childhood cancer using conditional logistic regression.

Results

Multiple gestation pregnancy (OR=1.17, 95% CI 1.05, 1.30), maternal pre-existing diabetes (OR=1.68, 95% CI 1.14, 2.48), congenital heart disease (OR=2.62, 95% CI 1.13, 6.09) and previous cesarean delivery (OR=1.35, 95% CI 1.03, 1.75) showed an increased risk of childhood cancers (all types combined). In the 1977-2013 population, there was an increased risk of acute lymphocytic leukemia (ALL; OR=1.08, 95% CI 1.04, 1.13) and rhabdomyosarcoma (OR=1.13, 95% CI 1.01, 1.27) for each unit of increase on the OCI. Examining mothers that had a score of at least one in the OCI, there was a higher risk of ALL (OR=1.43, 95% CI 1.26, 1.62), non-Hodgkin lymphoma (OR=1.50, 95% CI 1.17, 1.91), Burkitt lymphoma (OR=1.71, 95% CI 1.12, 2.61), and rhabdomyosarcoma (OR=1.58, 95% CI 1.10, 2.26).

Conclusion

The results of the study show varying effects of exposure to one or more maternal comorbidities on individual pediatric cancer types, and an overall increased risk of several cancers in children with mothers who have 1 or more comorbidities.

Table 3: Crude and Adjusted Odds Ratios (ORs) with 95% Confidential Intervals for maternal comorbidity as a continuous variable and risk of individual childhood cancers

Cancer type	N (%)	ICD 10 Odds Ratio (OR) (95% CI)	Adjusted OR[a] (95% CI)	N (%)	ICD 8 and 10 Odds Ratio (OR) (95% CI)	Adjusted OR[a] (95% CI)
Acute lymphocytic leukemia	173 (31.7)	1.05 (0.99, 1.11)	1.05 (1.00, 1.11)	384 (24.5)	1.38 (1.17, 1.62)	1.08 (1.04, 1.13)
Acute myeloid leukemia	31 (27.7)	1.01 (0.88, 1.16)	1.01 (0.88, 1.17)	70 (21.7)	1.46 (1.03, 2.07)	1.00 (0.90, 1.12)
Hodgkin lymphoma	18 (16.7)	0.96 (0.80, 1.14)	0.94 (0.78, 1.13)	71 (15.3)	0.86 (0.59, 1.27)	0.97 (0.87, 1.08)
Non-Hodgkin lymphoma	45 (36.6)	1.07 (0.96, 1.20)	1.07 (0.96, 1.20)	101 (24.3)	1.83 (1.36, 2.46)	1.07 (0.98, 1.17)
Burkitt lymphoma	19 (40.4)	1.08 (0.90, 1.30)	1.08 (0.91, 1.30)	35 (28.2)	2.12 (1.29, 3.51)	1.08 (0.93, 1.25)
CNS tumors	152 (24.6)	0.99 (0.93, 1.05)	0.99 (0.93, 1.05)	374 (18.8)	0.91 (0.77, 1.08)	1.01 (0.96, 1.05)
Astrocytoma	41 (24.3)	0.98 (0.86, 1.11)	0.98 (0.86, 1.11)	118 (18.8)	0.82 (0.59, 1.12)	1.01 (0.93, 1.10)
Medulloblastoma	20 (29.9)	1.02 (0.85, 1.21)	1.02 (0.85, 1.21)	39 (17)	1.01 (0.64, 1.61)	0.95 (0.82, 1.11)
Intracranial cancer	63 (27.3)	1.03 (0.94, 1.13)	1.02 (0.93, 1.13)	172 (19.6)	1.31 (1.04, 1.66)	1.03 (0.96, 1.10)
Glioma	63 (26.6)	1.01 (0.92, 1.11)	1.01 (0.92, 1.11)	185 (17.9)	0.90 (0.71, 1.15)	1.01 (0.94, 1.07)
Neuroblastoma	30 (22.9)	1.05 (0.94, 1.16)	1.05 (0.95, 1.17)	70 (19.1)	0.87 (0.58, 1.29)	1.05 (0.96, 1.15)
Retinoblastoma	21 (29.6)	1.15 (1.00, 1.31)	1.16 (1.01, 1.32)	35 (19.4)	0.91 (0.52, 1.57)	1.09 (0.96, 1.24)
Rhabdomyosarcoma	15 (25.9)	1.05 (0.88, 1.25)	1.06 (0.88, 1.27)	47 (25.4)	1.44 (0.89, 2.33)	1.13 (1.01, 1.27)
Wilms' tumors	26 (28.3)	0.80 (0.62, 1.03)	0.81 (0.64, 1.04)	60 (20.5)	1.29 (0.89, 1.88)	1.00 (0.89, 1.13)
Bone cancer	23 (24.7)	0.99 (0.84, 1.15)	0.98 (0.84, 1.15)	65 (18.4)	1.18 (0.81, 1.70)	0.97 (0.87, 1.09)
Germ Cell Tumors	25 (26.0)	1.00 (0.85, 1.16)	1.00 (0.86, 1.17)	84 (17.4)	1.04 (0.74, 1.48)	0.99 (0.89, 1.09)

Note:

[a] The adjusted model was adjusted for birth order and urbanicity of residence

Abbreviations: OR, odds ratio; CI, confidence interval

Cancer

Association between premenopausal breast density and body composition measures Sable Fest* Sable Fest Colette P. Davis Thomas W. Kensler John Shepherd Holly R. Harris

Background: Breast density is a strong risk factor for premenopausal breast cancer. Body mass index (BMI) is inversely associated with breast density and premenopausal breast cancer risk. However, BMI does not account for body fat composition, which may be more associated with breast density. Moreover, few predictors of premenopausal breast density are known since screening mammography is not recommended for individuals below age 40. Our objective was to examine the association between premenopausal breast density and body composition measures using dual-energy X-ray absorptiometry (DXA).

Methods: We recruited menstruating persons aged 18-45 years and measured breast density and body composition with DXA scans (n=92). Breast fibroglandular volume (cm3) and total breast volume (cm3) were used to calculate percent breast density. Android and gynoid regions and visceral adipose tissue (VAT) were examined as body composition measures. Correlations and linear regression were used to examine the associations between breast density and body composition measures. The residual method was used to obtain a measure of android adiposity independent of VAT.

Results: Percent breast density was inversely correlated with all body composition measures with the strongest association for android fat (R=-0.85; p<0.0001). When accounting for all body composition measures in regression models, only android fat remained significant. However, when VAT-adjusted residuals of android fat were examined, both android fat and VAT remained significant.

Conclusion: Body composition measures were more strongly associated with premenopausal breast density than BMI, particularly android fat. Android fat is a combination of visceral and subcutaneous fat, the former of which is more metabolically active. Future research investigating the role of inflammatory biomarkers in this association may help us further understand the relation between body composition measures and breast density.

Cancer

Adherence to the WCRF/AICR Guidelines Among Cancer Survivors and Mortality: A Cohort Study Based on the KoGES-HEXA Donghyun Won* Donghyun Won Jeeyoo Lee Sooyoung Cho Aesun Shin

The growing number of cancer survivors is a global concern, with over 32 million estimated worldwide. The World Cancer Research Fund/American Institute for Cancer Research (WCRF/AICR) has suggested that all cancer survivors follow cancer prevention recommendations to improve quality of life and survival. This study aims to investigate the effect of adherence to the guidelines among cancer survivors on mortality. The scoring logic incorporates two body fatness, physical activity and six dietary factors, yielding a total score ranging from 0 to 7, where higher scores refer to the better adherence. All eight factors are self-reported, and participants were categorized into five groups (<3, 3-4, 4-5, 5-6, >6). A chi-squared test was conducted to identify features associated with the adherence. Hazard ratios (HRs) with 95% confidence intervals (CIs) were calculated to estimate the association between adherence scores and all-cause mortality using a Cox proportional hazards model. Among 173,195 individuals who recruited between 2004 and 2013 in the Health Examinees study, 3,967 participants at baseline and 1,518 participants at the follow-up were identified as cancer survivors. Over a median follow-up of 10.5 years, 443 deaths occurred. Women, older age, non-smoker, lower education level, lower income and diabetes patients were more likely to adhere to guidelines. Overall, higher adherence did not show an association with mortality among the cancer survivors. However, among survivors with diabetes, adherence was associated with the lower mortality after adjusting for age and sex (3-4: HR = 0.28, CI: 0.11-0.70; 4-5: HR = 0.24, CI: 0.10-0.59; 5-6: HR = 0.58, CI: 0.24-1.37; >6: HR =0.41, CI: 0.13-1.31) when compared to the lowest score group (<3). Adherence to the WCRF/AICR guidelines is advised for cancer survivors, with a specific focus on those who also have diabetes.

Cancer

Longest held occupation, pesticide occupation employment and prostate cancer aggressiveness among Black and White men in the North Carolina-Louisiana Prostate Cancer Project (PCaP) Carolyn Eberle* Carolyn Eberle Laura Farnan Jeannette T. Bensen James L. Mohler, Eboneé N. Butler

Background: Black US men experience higher incidence of aggressive prostate cancer (PCa) compared with White US men; modifiable risk factors for the PCa are largely unknown. We examine overall and race-specific associations between longest held occupation, employment in a pesticide occupation, and PCa aggressiveness. Methods: We used data from PCaP, a population-based study of Black and White men diagnosed with PCa. We classified longest held occupation using International Standard Classification of Occupations; ever employment was reported for five pesticide occupations. We defined PCa aggressiveness as low, intermediate, or high, based on clinical characteristics linked to risk of progression (Gleason grade, clinical stage, and prostate-specific antigen value). To describe the association between occupation and aggressive PCa, we used logistic regression models to calculate ORs and 95% CIs and examined potential effect-measure modification (EMM) by race. Results: Among 2,111 men, "Managing Directors and Chief Executives" (OR=1.85, 95%CI 1.03-3.35), "Plant and Machine Operators and Assemblers" (OR=1.31, 95%CI 1.00-1.71), and "Agricultural, Forestry, and Fishery Laborers" (OR=3.87, 0.85-17.6) had higher odds of high/intermediate aggressive PCa. Pesticide occupations, landscaping (OR=1.44, 95%CI 1.01-2.04), and garden shop work (OR=1.95, 95%CI 1.16-3.28) had higher odds of high-aggressive PCa. Employment ≥ 30 years among "Plant and Machine Operators and Assemblers", "Heavy Truck and Lorry Drivers", and "Agricultural, Forestry, and Fishery Laborers" was positively associated with high-aggressive PCa. We observed substantial heterogeneity of occupation by race (see figure), but not consistent evidence of EMM. Conclusions: Employment as plant/machine operators, agricultural laborers, and in pesticide occupations may increase odds of aggressive PCa; disproportionate employment of Black men in these jobs may contribute to Black-White disparities in PCa aggressiveness.
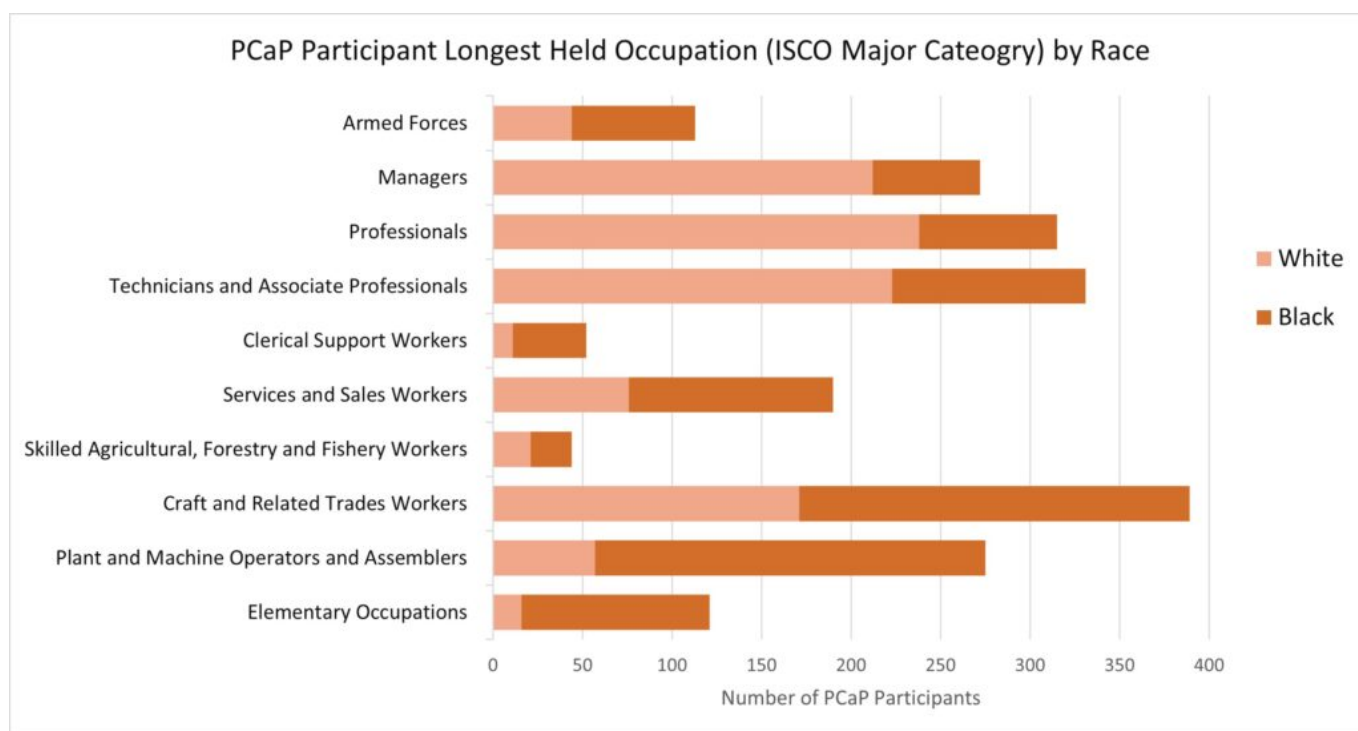
Cancer

Night shift work and risk of colorectal cancer: results from a prospective cohort study among 56,490 female nurses in the Netherlands Linske de Bruijn* Linske de Bruijn Nina E. Berentzen Jelle J. Vlaanderen Roel C.H. Vermeulen Hans Kromhout Katarzyna Flora E. van Leeuwen Michael Schaapveld

Introduction: Shift work that involves night shifts has been classified as probably carcinogenic to humans, possibly related to the suppression of melatonin secretion. Although experimental studies suggest that melatonin inhibits intestinal tumor proliferation, epidemiological evidence for a relationship between night shift work and colorectal cancer (CRC) risk is lacking.

Methods: We prospectively examined the association between night shift work exposure and CRC in the Nightingale study. In 2011, 59,947 Dutch female nurses completed a questionnaire, including lifetime occupational history with detailed information on night shift work. Up to July 2021, 312 incident CRCs were recorded. Age-adjusted hazard ratios (HRs) and 95% confidence intervals (CIs) for associations between night shift work exposure variables and CRC risk were estimated using Cox regressions.

Results: The analysis included 56,490 nurses of whom 81% ever worked night shifts for a mean duration of 11.8 (SD=8.4) years. Compared with nurses who never worked night shifts, the risk of CRC for nurses who ever worked night shifts was slightly above the null (HR=1.15; 95%CI=0.85-1.54). A longer duration of working night shifts (≤9, 10-19, ≥20 years) and lifetime cumulative number of night shifts (tertiles in cases: 1-432; 433-1080; >1080 shifts) were not associated with CRC risk. Chronotype did not affect the associations of CRC risk with any shift work variable.

Conclusion: Our results suggest that exposure to longer durations of night shift work, as well as exposure to different measures of cumulative lifetime night shift work, are not associated with CRC risk. Our study does not provide further evidence for an association between night shift work and CRC.

Cancer

Historical redlining and risk of breast cancer in the NIH-AARP Diet and Health Study Aleah Thomas* Aleah Thomas Jonguen Rhee Rena R. Jones Lauren M. Hurwitz Jared A. Fisher Jessica M. Madrigal

Background: The 1930's federal Home Owners' Loan Corporation (HOLC) enacted residential racial segregation through 'redlining.' This historical practice may contribute to modern residential segregation and social inequities, potentially increasing cancer risk. However, evidence of the association between redlining and cancer is limited. We investigated the association between historical redlining and incident breast cancer in a large prospective cohort.

Methods: We linked georeferenced HOLC grading data (1937-1940) from the University of Richmond to enrollment (1995-1996) addresses for the NIH-AARP Diet and Health Study. A total of 25,944 women (86% of women in the cohort) were included. Multivariable Cox models estimated HRs and 95% CIs for HOLC grade at participant address (best, still desirable, definitely declining, redlined) in relation to incident breast cancer overall (2,341 cases) and by estrogen (ER) and progesterone (PR) receptor status, after adjusting for breast cancer risk factors, census tract level median household income, and ambient air pollution at the residence.

Results: Redlined neighborhoods (vs. other HOLC grades) had lower median household income and had larger proportions of participants from racial and ethnic minority groups and those with lower educational attainment. We found no association between HOLC grade and breast cancer risk overall (HR [redlined vs. best or still desirable]=0.90, 95% CI=0.80, 1.03). We observed suggestive positive associations for hormone receptor-negative tumors [ER-, HR=1.25, 95% CI=0.85, 1.84; PR-, 1.14 (0.85, 1.52)] and inverse associations for hormone receptor-positive tumors [ER+, 0.82 (0.69, 0.97); PR+, 0.78 (0.65, 0.95)].

Conclusion: We did not find evidence that residence in historically redlined neighborhoods is associated with overall breast cancer risk. Possible associations by hormone receptor status warrant further evaluation.

Cancer

Lung cancer risk update in the US Radiologic Technologists Cohort: Can we revise sex-specific radiation-related risk estimates at low dose-rates? Cato M Milder* Cato Milder
Elizabeth K Cahoon Martha S Linet Dale L Preston Bruce H Alexander Cari M Kitahara

NASA risk projections show female astronauts are more likely than males to die from radiation-induced cancer. This finding stems from studies of Japanese atomic bomb survivors, which estimated greater radiation-related risk of lung cancer in females than males, though other cohorts have not replicated this sex-specific difference. The US Radiologic Technologists (USRT) cohort provides an opportunity to assess sex-specific lung cancer risk in a large occupational cohort with detailed smoking information.

Included were 72,238 female and 22,293 male US radiologic technologists who responded to a baseline survey and were alive and cancer-free at follow-up start. Lung cancer incidence from 1999-2013 was obtained from linkages with 43 state/regional cancer registries. Cumulative lung doses (mean=13.4 mSv for females, 17.9 mSv for males) were estimated through 1997. We used Poisson regression to estimate excess relative risk (ERR) of lung cancer per 100 mGy, stratified on age, birth year, and sex, adjusting for time-varying smoking status (ever/never/former) and pack-years. We tested dose-response effect modification by sex.

A total of 865 and 372 lung cancers occurred in females and males, respectively, during follow-up (median 14 years). We observed increased lung cancer risk with greater cumulative lung dose [ERR/100 mGy: 2.00, 95% CI: 0.51, 5.31]. In sex-specific models, the male ERR (3.92, 95% CI: 0.71, 10.28) was higher than the female ERR (0.11, 95% CI: -0.33, 2.26) (p-interaction: 0.45).

We did not observe a stronger positive association between cumulative lung dose and lung cancer incidence in females than males. However, this analysis contains considerable uncertainty, particularly as doses are only estimated through 1997, and these results could not be replicated in USRT lung cancer mortality analyses. Nonetheless, our results challenge NASA's assumptions of elevated lung cancer risk in females, suggesting the need to combine multiple cohorts for risk projection.

Cancer

No Elevated Risk of Cancer in Women of Southeastern Louisiana 12 Years after the Deepwater Horizon Oil Spill Tyler Prusisz* Tyler Prusisz Ariane Rung Mei-Chin Hsieh Evrim Oral Edward Trapido Elizabeth Levitzky Edward Peters

Background: Oil spills are reoccurring ecological disasters that cause extensive damage not only to the environment, but also to physical and mental health. However, as demand for oil continues to increase, critical gaps exist in our understanding of how these spills affect cancer risk.

Methods: We linked the Women and Their Children's Health Study (WaTCH), which recruited women between the ages of 18 and 80 in southeastern Louisiana following the 2010 Deepwater Horizon oil spill (DHOS), the largest in marine history, to the Louisiana Tumor Registry to examine the affect of economic, physical, and overall oil spill exposure on in-situ and malignant cancer. We compared age-adjusted cancer incidence rates of the 2,847 women in the WaTCH cohort to Louisiana-wide rates. Adjusted Cox proportional hazard and Poisson regression models estimated the risk of cancer from oil spill exposures.

Results: The age-adjusted cancer incidence rates for the WaTCH cohort and all of Louisiana were 609.8 (95% Confidence Interval [CI]: 482.9 – 762.6) and 652.3 (95% CI: 648.8 – 655.8) cases per 100,000 women per year, respectively. The calculated hazard ratio for time to cancer (199 cases) from total oil spill exposure was 0.945 (95% CI: 0.855 – 1.043). Findings were similar for site-specific cancer and economic and physical oil spill metrics.

Conclusions: Our findings indicate that there is no increased risk of cancer in the women of southeastern Louisiana 12 years after the DHOS.

Impact: Our study is the first to prospectively examine the association between oil spill exposure and cancer incidence.

Cancer

Pre-diagnostic circulating resistin concentrations and mortality among individuals with colorectal cancer: Results from the European Prospective Investigation into Cancer and Nutrition study Thu Pham* Thu PHAM Katharina Nimptsch Tobias Pischon Krasimira Aleksandrova Mazda Jenab Veronika Fedirko Kana Wu Anne Kirstine Eriksen Anne Tjønneland Gianluca Severi Joseph Rothwell Rudolf Kaaks Verena Katzke Alberto Catalano Claudia Agnoli Giovanna Masala Maria Santucci De Magistris Rosario Tumino Roel Vermeulen Amaia Aizpurua Camino Trobajo-Sanmartín María-Dolores Chirlaque Maria-Jose Sánchez Sai San Moon Lu Amanda J. Cross Sofia Christakoudi Elisabete Weiderpass

Resistin is a protein involved in inflammation and angiogenesis processes and may play a role in the progression of colorectal cancer (CRC). However, it remains unclear whether resistin is associated with increased mortality after CRC diagnosis. We examined pre-diagnostic serum resistin concentrations in relation to CRC-specific and all-cause mortality among 1343 incident CRC cases from the European Prospective Investigation into Cancer and Nutrition cohort. For CRC-specific mortality as the primary outcome, hazard ratios (HRs) and 95% confidence intervals (95% CI) were estimated from competing risk analyses based on cause-specific Cox proportional hazards models and further in sensitivity analyses using Fine-Gray proportional subdistribution hazards models. For all-cause mortality as the secondary outcome, Cox proportional hazards models were used. Subgroup analyses were performed by sex, tumor subsite, tumor stage, body mass index and time to CRC diagnosis. Resistin was measured on a median of 4.8 years before CRC diagnosis. During a median follow-up of 8.2 years, 474 deaths from CRC and 147 deaths from other causes were observed. Resistin concentrations were not associated with CRC-specific mortality (HRQ4vsQ1 = 0.95, 95% CI: 0.73-1.23; Ptrend = .97; and HRper doubling of resistin concentration = 1.00; 95% CI: 0.84-1.19; P = .98) or all-cause mortality. Results from competing risk (sensitivity) analysis were similar. No associations were found in any subgroup analyses. These findings suggest no association between pre-diagnostic circulating resistin concentrations and CRC-specific or all-cause mortality among persons with CRC, and the potential insignificance of resistin in CRC progression. [In Press]
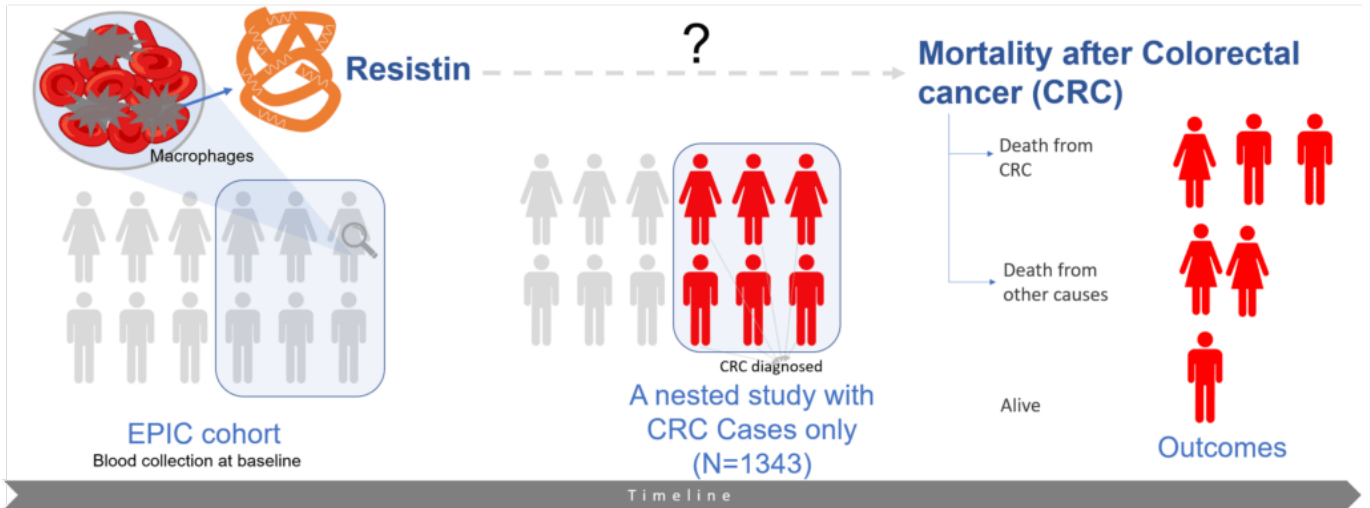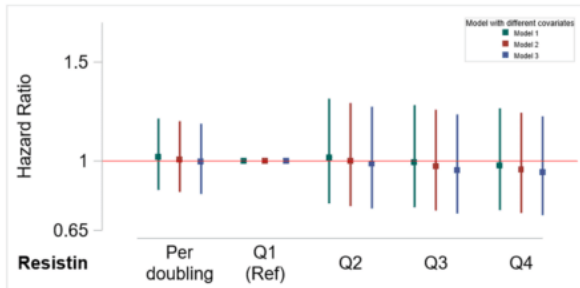
Fig. 1 Hazard ratios & 95% confidence intervals for CRC-specific mortality
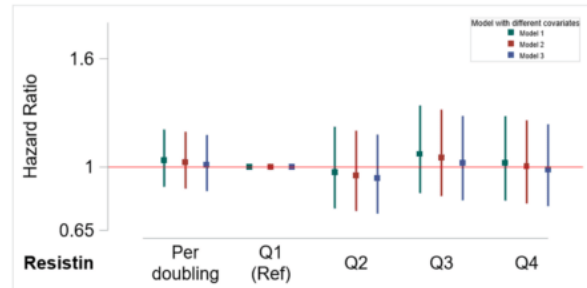
Fig. 2 Hazard ratios & 95% confidence intervals for all-cause mortality

Model 1: Adjusted for age at CRC diagnostis and sex. Model 2: Model 1 with additional adjustment for year of CRC diagnosis, and tumor subsite. Model 3: Model 2 with additional adjustment for body mass index and residuals of waist circumference in a linear model with BMI.

Clinical Consequences Post-Implementation of a 5th Generation Cardiac Troponin Assay at an Academic Medical Center in Western Pennsylvania Brent Willaims* Teigan Dwyer Tyson Barrett Amber Shergill Indu Poornima

Background: High-sensitivity troponin testing (Hs-trop) was introduced in the United States in 2017 and has been adopted in American hospitals. Recent guidelines endorsed transition to Hs-trop to appropriately triage patients with chest pain. This study investigates differences in patient testing, myocardial infarction (MI) diagnoses, and health care utilization after transitioning to Hs-trop within 6 hospitals in a blended health system.

Methods: Patients 18 years or older presenting to the emergency department (ED) with chest pain during the study interval were included in the retrospective study if at least one troponin level was measured. A blended data approach was used – testing and health outcomes information was drawn from electronic health records while utilization information was procured from claims data. Downstream testing of echocardiograms, stress testing, coronary computed tomography angiography (CCTA), and invasive coronary angiography as well as diagnosis of MI types 1 and 2 were recorded and compared between patients before the implementation (N=7668) of Hs-trop and patients after the implementation of Hs-trop (N=7347). Multiple health care utilization and cost metrics were tracked following discharge for patients who were members of the Highmark Health Plan. Comparisons were done via weighted means and weighted standard deviations and weighted least squares regression.

Results: 15,015 patients were included in the study with a median age of 55 years, mostly white (77%) and female (54%). The post-implementation group had fewer troponin tests completed (2.2 vs 2.4); more elevated troponins (24.1% vs 13.6%); less likely to receive any subsequent cardiac diagnostic testing, including echocardiography (OR = 0.85), stress testing (OR = 0.76), or CCTA (OR = 0.69); more likely to be directly discharged from the ED (OR = 1.6); and less likely to return to the ED within 30 (OR=0.74) or 90 (OR=0.74) days post-discharge. Health care costs were not different between the two groups, but the post-implementation group utilized healthcare 9.7% less than the pre-implementation group (p<.0001)

Conclusion: Implementation of Hs-trop resulted in fewer tests and more ED discharges, and was associated with less healthcare utilization, indicating value for both patients and payors.

Cardiovascular

Thyroid peroxidase antibodies are associated with incidence, but not progression, of coronary artery calcification: ELSA-Brasil study Vandrize Meneghini* Vandrize Meneghini William R. Tebar Giuliano Generoso Carolina CPS Janovsky Paulo A. Lotufo Márcio S. Bittencourt Alexandre C. Pereira Isabela M. Benseñor

Introduction: Coronary artery calcification (CAC) is an established risk factor for cardiovascular diseases and early mortality. Recent studies have shown the thyroid peroxidase antibodies (TPOAb) as a marker of chronic low-grade inflammation. Still, little is known regarding the impact of TPOAb levels on CAC incidence and progression.

Objective: We explore the association of TPOAb levels with CAC incidence and progression in an ethnically diverse cohort.

Methods: We included individuals with no prior cardiovascular disease and two CAC measurements in ELSA-Brasil. Fasting plasma TPOAb levels were used as continuous data (log-transformed), categorized in quartiles and as positive TPOAb. We defined incident CAC as a baseline CAC=0 followed by CAC>0 on the second visit. CAC progression was defined according to Berry and Hokanson methods. We performed Cox and logistic regression models to investigate the association of TPOAb levels with CAC incidence and progression, respectively.

Results: A total of 3015 individuals (57.2% women, 49.3±8.1 years, 55.2% white) were included. The mean interscan period was 5.0 ± 1.0 years. CAC incidence occurred in 333 (14.5%) of 2292 individuals with baseline CAC of 0. Among the 723 participants with CAC > 0 at baseline, 328 (45.4%) and 434 (60%) had progression of CAC according to Berry and Hokanson criteria. The highest quartile of TPOAb was associated with a higher risk of CAC incidence when compared to the lowest quartile, even after multiple adjustment (HR: 1.53 95%CI: 1.11-2.11). Similar result was observed for euthyroid participants (HR: 1.62 95%CI: 1.11-2.37); which also showed that higher levels of TPOAb, as a continuous variable, were associated with a higher risk of CAC incidence (HR: 1.23 95%CI: 1.05-1.44). There was no significant association between TPOAb titers and CAC progression (p=NS).

Conclusions: We found that higher levels of TPOAb were associated with higher risk of CAC incidence, but did not affect CAC progression.

Association of the adequacy of hypothyroidism treatment with the metabolic vulnerability index Vandrize Meneghini* Vandrize Meneghini Carolina Castro Porto Silva Janovsky William R. Tebar José Augusto Sgarbi Patrícia de Fatima dos Santos Teixeira Steven R. Jones Michael J. Blaha Peter P. Toth Paulo A. Lotufo Isabela M. Benseñor

Introduction: A novel mortality biomarker for cardiovascular risk, the Metabolic Vulnerability Index (MVX), has recently emerged but is still unexplored in the context of thyroid disorders. MVX integrates inflammation and malnutrition markers measured by metabolomics.

Objective: We investigated the association of the adequacy of hypothyroidism treatment with MVX scores in participants from the ELSA-Brasil study.

Methods: Cross-sectional study using baseline data of São Paulo Research Center (N=4666). Individuals with normal thyroid function and clinical and subclinical hypothyroidism were included. Thyroid function and adequacy of treatment were classified according to thyrotropin, free thyroxine levels, and levothyroxine use. GlycA and small high-density lipoprotein particles (7.4-8.7nm) are markers of inflammation, while branched-chain amino acids (valine, leucine, and isoleucine), and citrate are markers of malnutrition and were measured by NMR spectroscopy (LipoProfile® 4 test spectra, LabCorp). Sex-specific MVX scores were calculated and transformed in standard values. Generalized linear regression models were adjusted for sociodemographic and lifestyle factors, chronic diseases, cardiovascular history, and glomerular filtration rate.

Results: Participants were 51.5±9 years old, and 2,522 (54%) were female. The prevalence of euthyroidism and untreated, inadequately and adequately treated hypothyroidism were 82.7%, 10.0%, 2.8%, and 4.5%, respectively. Participants untreated (β:1.12 95%CI:1.02-1.23) and inadequately treated (β:1.41 95%CI:1.19-1.68) for hypothyroidism had higher MVX scores than the euthyroid group. After adjustment for potential confounders, participants with untreated hypothyroidism had higher MVX scores (β: 1.10 95%CI: 1.01-1.21), than the euthyroid participants.

Conclusion: The findings suggest that individuals inadequately treated and untreated for hypothyroidism present with a higher metabolic vulnerability and possibly higher cardiovascular risk.

The role of epigenetic aging in physical activity and cardiovascular mortality Judy Fan* Judy Fan Hanyang Shen David H. Rehkopf

Background:

DNA methylation (DNAm) clock, a DNAm-based measure of biological age, has been shown to reflect vascular aging that could lead to cardiovascular (CV) diseases. Although exercise-modulated CV protection has been well-studied, there is a lack of nationally representative population-based studies that examine the role of epigenetic aging in this relationship.

Objective:

This study aims to evaluate the association of physical activity and CV mortality mediated through epigenetic aging in US adults.

Methods:

US adults aged 50 years and older from NHANES 1999-2002 with available DNA specimens (n=2446) and self-reported physical activity data will be included. The intensity of physical activity will be assessed as metabolic equivalents (METs) and categorized into minimal, moderate, and vigorous according to NHANES guidelines. Heart disease specific mortality, followed through December 2019, was obtained from linked National Death Index files. To evaluate DNAm clock, DNAm assay on peripheral blood was first performed using the Illumina Infinium MethylationEPIC BeadChip. The 'Horvath' DNAm clock, measuring the accumulation of methyl groups to DNA, was then computed using DNAm data after quality control steps, background subtraction, and color correction, imputation, and normalizations. It was compared with chronological age to predict epigenetic aging. We will perform causal mediation modelling to assess direct and indirect effects of physical activity after considering DNAm clocks as mediator. Control variables in our analysis include age, sex, body mass index, total and HDL cholesterol, systolic and diastolic blood pressure, glycosylated hemoglobin, c-reactive protein, creatinine, race and ethnicity, occupational category, income, and education.

Results/Conclusion:

We hypothesize that epigenetic aging from DNAm clock has a moderate effect on the physical activity-CV mortality association.

Cardiovascular

Mortality Burden of Atherosclerotic Cardiovascular Diseases and Associated Risk Factors in Taiwan: 2000-2020 Fang-Wen Nora Lu* Hsien-Ho Lin Fang-Wen Nora Lu Bo-Chen Liu Wen-Kai Yang April Hill Wei-Cheng Lo Hsien-Ho Lin

Study Aim: We estimated the patterns of Atherosclerotic Cardiovascular Diseases (ASCVD)-related mortality over an extended timeframe (2000-2020) in Taiwan and the impact of major risk factors.

Methods: We analyzed the multiple cause of death data in the vital registry of Taiwan and used a verified naïve Bayes classifier algorithm to redistribute the garbage codes to the underlying causes of death. We used the redistributed mortality data in adults (>=20 years) to calculate the age-standardized mortality rate of ischemic heart disease (IHD) and ischemic stroke (IS), and estimated years of life lost (YLL) using the life table of Taiwan. Data from the National Health Interview Survey (2001, 2005, 2009, 2013, 2017) and the Nutrition and Health Survey in Taiwan (2013-2016) were used to estimate the prevalence and population attributable fraction (PAF) of five major ASCVD risk factors: high systolic blood pressure, high LDL cholesterol, high fasting plasma glucose, high body mass index, and smoking.

Results: During the past two decades, there was a notable decline in the age-standardized mortality rate and YLL rate due to ASCVD (Figure 1). The decline was faster in the first than the second decade, with an average annual percent change of the mortality rate being 2.58% and 0.77% in the first and second decade respectively for IHD (Figure 1A) and 16.11% and -3.04% respectively for IS (Figure 1B). The analysis of risk factor revealed that in 2013, high systolic blood pressure accounted for the largest proportion of the ASCVD mortality burden, with a PAF of 48.51%. This was followed by 20.10% for high LDL cholesterol, 20.08% for high fasting plasma glucose, 10.03% for high body mass index and 9.47% for smoking.

Conclusions: Our analysis revealed an alarming deceleration of the decline of ASCVD mortality burden in Taiwan. Interventions targeting high systolic blood pressure, high LDL cholesterol, and high fasting plasma glucose are needed to alleviate the ASCVD burden.
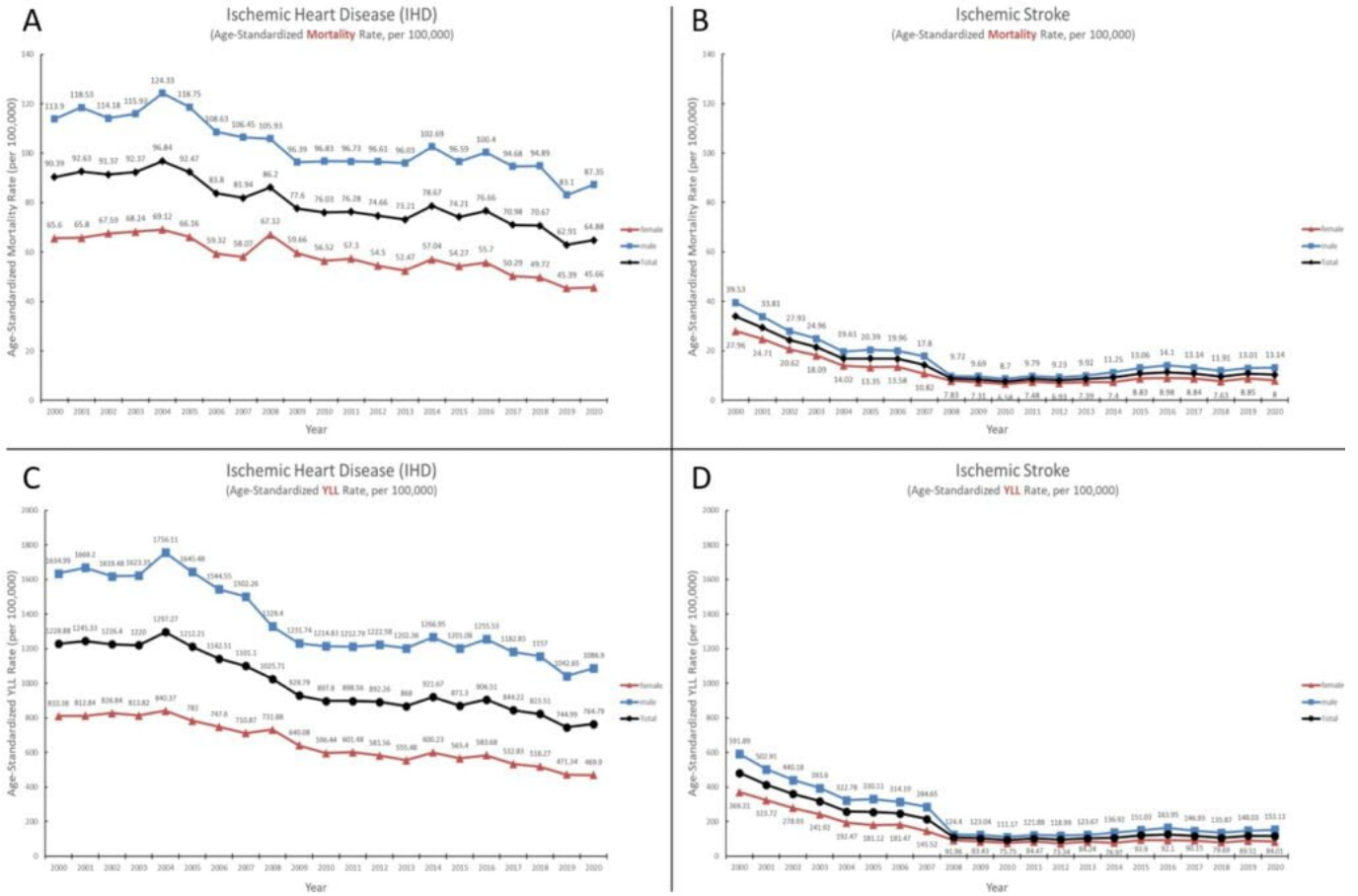
Figure 1: Age-standardized mortality rate and years of life lost (YLL) rate per 100,000 adult population for ischemic heart disease (Figure 1A and 1C) and ischemic stroke (Figure 1B and 1D), respectively

Cardiovascular

Cardiovascular health is positively associated with a higher total whole brain cortical volume in US adolescents – ABCD Study Augusto César F. De Moraes* Augusto César Ferreira De Moraes Marcus Vinicius Nascimento-Ferreira Ethan H. Hunt John Virostko Susan S. Tapert Harold W. Kohl

Aim: This study aimed to test the associations of components of cardiovascular health with brain health development in US adolescents.

Methods: This was a cross-sectional analysis from 2nd year follow-up of the Adolescent Brain Cognitive Development study. We included adolescents aged 11 to 12 years old recruited in 21 US cities with complete questionnaire data for dietary intake, physical activity, nicotine exposure, sleep health; health evaluation for body mass index, blood lipids, glycated hemoglobin, or blood pressure; and covariate data. **Exposure – cardiovascular health:** Life's Essential 8 (LE8) 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. **Outcome – brain development indicators:** mean cortical thickness, total whole brain cortical volume in mm2 and mm3, measured by functional magnetic resonance imaging.

Results: A total of 978 individuals were analyzed. The mean (SD) age was 11.9 (0.2) years; 44.9% were girls, 53.4% were White, and 62.6% of parents had at least a college degree. Sleep health LE8 score was directly associated with total whole brain cortical area in mm3 ($\beta = 294.9$; CI 95%, 82.8–506.9) and mm2 $\beta = 94.2$; CI 95%, 24.7–163.7). The BMI LE8 score was directly associated with mean cortical thickness ($\beta = 0.008$; CI 95%, 0.004–0.011). Individuals with more favorable cardiovascular health behaviors showed total whole brain cortical area in mm3 ($\beta = 365$; CI 95%, 36.6–693.4) and mean cortical thickness. LE8 overall scores were directly associated with total whole brain cortical area in mm3 ($\beta = 738.5$; CI 95%, 247.9–1,229.2) and mean cortical thickness in mm3 ($\beta = 0.0015$; CI 95%, 0.006–0 .0023).

Conclusions: Adequate sleep, healthy height, cardiovascular health behaviors, and overall cardiovascular health were directly linked to higher total whole brain cortical volume in US adolescents, supporting potential public health advances to promote these behaviors for their potential benefits to brain development.

Cardiovascular

Comorbidities and healthcare utilization among young adults with congenital heart defects by Down syndrome status – Congenital Heart Survey to Recognize Outcomes, Needs, and wellbeinG (CH STRONG), 2016-2019 Vanessa Villamil* Vanessa Villamil Karrie F Downing Jennifer G Andrews Matthew E Oster Maureen Galindo Jenil Patel Wendy N. Nembhard Sherry L Farr

Background: About 50% of live births with Down syndrome (DS) have congenital heart defects (CHD). Yet little is known about the health and healthcare needs of adults with DS and CHD. Our aim was to examine comorbidities and healthcare utilization of adults with DS and CHD.

Methods: From 2016-2019, the Congenital Heart Survey to Recognize Outcomes, Needs, and well-beinG (CH STRONG) surveyed adults with CHD, ages 19-38 years, or a proxy (e.g. parent), identified from active birth defects registries in Arkansas, Arizona, and Atlanta. Multivariable Poisson regression generated adjusted prevalence ratios (aPR) and 95% confidence intervals for associations between DS and comorbidities and healthcare utilization, adjusting for covariates; prevalence estimates for these associations were standardized to the 9,312 CH STRONG eligible individuals by site, sex, race/ethnicity, birth year, and CHD severity.

Results: Among 1,500 respondents, 9.1% had DS. Compared to adults with CHD without DS, adults with CHD and DS were more likely to be male (55.5% vs 45.0%), <25 years old (51.8% vs 42.7%), non-Hispanic white (72.3% vs 69.3%), and have public insurance (77.4% vs 22.8%) (all p<0.05), but less likely to report cardiac comorbidities (5.5% vs 14.2%; aPR=0.27 [0.12-0.58]), emergency room (ER) visits (19.3% vs 32.5%, aPR=0.57 [0.40-0.83]), hospitalizations (6.2% vs 13.2%; aPR=0.56 [0.32-0.99]), cardiac-related hospitalizations (0.7% vs 5.3%; aPR=0.16 [0.04-0.67]), and delays in care due to cost (1.2% vs 19.6%; aPR=0.14 [0.04-0.43]) in the last year. Adults with CHD and DS compared to those without DS had no detectable differences in severe CHD (38.7% vs 33.8%; p=0.25) or receiving cardiology care in the last 2 years (52.6% vs 44.7%; aPR=1.05 [0.82-1.36]).

Conclusions: Adults with DS and CHD may have better access to care, resulting in fewer cardiac comorbidities and use of ER and inpatient care. However, all adults with CHDs may benefit from improvements in receipt of cardiology care.

Cardiovascular

Individual- and school-level factors associated with adolescent metabolic syndrome: A multilevel structural equation modeling study Yu-Ting Chin* Yu-Ting Chin Wei-Ting Lin Pei-Wen Wu Sharon Tsai Chien-Hung Lee

Underlying pathophysiological mechanisms contribute to the aggregation of abnormal cardiovascular factors that form metabolic syndrome (MetS). This phenomenon is influenced by factors at various levels, highlighting the importance of adopting a multilevel perspective when investigating its determinants in adolescents. This study used a multilevel structural equation modeling to assess the effects of individual- and school-level factors on the confirmatory factor analysis-derived score for MetS (csMS) in adolescents. A representative cohort of 2,727 adolescents was randomly selected from 36 schools in three economically diverse areas in Taiwan. The participants' individual- and school-level factors, as well as their cardiovascular profiles, were evaluated. In terms of individual factors, adolescents with the intake of >500 mL/day of SSB had a direct effect on csMS score (a 0.17 elevation) after accounting for covariates. Mediation analysis indicated that higher levels of uric acid mediated 5.2% of the association, while body mass index (BMI) mediated 51.3%. Regarding school-level factors, students in schools with >11 sports venues within a 600 m radius had a 0.25 lower csMS score compared to those in schools with ≤11 sports venues. In the cross-level assessment, the number of sports venues was found to modify the association between SSB consumption and BMI in the multilevel structural equation modeling. This study presents data that demonstrate the multilevel structural association between SSB intake and the latent MetS construct in adolescents.

Causal Inference

Studying the effectiveness of firearm policies in reducing firearm harms using causal inference Roni Barak Ventura* Roni Barak Ventura Maurizio Porfiri James Macinko Manuel Ruiz Marín

Firearm violence is a significant threat to public health in the U.S., where more than 200 people sustain a nonfatal firearm injury and more than 100 people die from it every day. In spite of these unsettling figures, Americans still seek to hold guns for protection of their homes and families. In order to prevent firearm-related harms without limiting citizens' right to bear arms, one must identify the policies that minimize firearm harms. To this end, we study the causal relationships between firearm laws, firearm ownership, and firearm deaths. Specifically, we investigate whether permissive and/or restrictive laws promote and/or discourage firearm ownership and deaths.

We collate data about firearm-related laws from RAND's State Firearm Law Database, where each law is classified as restrictive or permissive. We also collect the monthly numbers of accidents, homicides, and suicides committed with firearms reported on CDC's Wonder database. Lastly, we obtain monthly estimates of firearm ownership from an econometric spatiotemporal model we have previously developed. We generate two monthly time series: one that reflects the restrictiveness of the firearm-related legal environment, and another that measures "Deaths Per Gun". We apply the information-theoretic notion of transfer entropy to infer a causal link from the former to the latter.

We uncover a causal link for delays ranging from zero to three months, suggesting that restrictive laws can effectively reduce "Deaths Per Gun" in the short term. This analysis is the first to demonstrate a causal effect of firearm laws on firearm harms and firearm ownership. It serves as a stepping stone for analyses that could guide future legislation to effectively reduce regional firearm harm rates.

Errors and Their Visualization in the Calculation of the Population Attributable Fraction
Etsuji Suzuki* Etsuji Suzuki Eiji Yamamoto

The population attributable fraction (PAF) has been widely used to assess the potential impact of health interventions in epidemiology. One of the common errors in the calculation of the PAF is the use of an "adjusted" risk ratio in the Levin formula (i.e., the "partially adjusted" Levin formula). Although previous studies have addressed the "bias" in this approach, there is some confusion because of the lack of a clear definition of the PAF, and it is important for researchers to understand the concept of the PAF in the counterfactual framework. In this presentation, we discuss the errors in the "partially adjusted" Levin formula and illustrate them visually in wireframes by varying the standardized mortality ratio (SMR) and associational risk ratio (aRR) when the prevalence of exposure is fixed. When SMR > 1, both the true PAF and the "partially adjusted" Levin formula become positive; when SMR = 1, they both become 0; and when SMR 1. When SMR > aRR, the absolute bias is positive and relative bias is larger than 1. Their magnitudes increase as the difference between SMR and aRR increases. By contrast, when SMR < aRR, the absolute bias is negative and the relative bias is smaller than 1. Their magnitudes are relatively small. The patterns of the wireframes did not substantially change when the prevalence of exposure varied. Although the bias of the "partially adjusted" Levin formula may be much smaller than that of the (crude) Levin formula, this does not necessarily justify the use of the "partially adjusted" Levin formula. A comprehensive understanding and accurate interpretation of the PAF requires a clear grasp of its definition in the counterfactual framework. Improper calculations of the PAF frequently occur in the absence of this understanding, and confusion persists regarding the condition under which the Levin formula is valid.

Causal Inference

Assessing Stochastic Positivity with Convex Hulls Mark Klose* Mark Klose Tim Feeney

Positivity is a fundamental causal identification condition that ensures inferences are drawn only among individuals with a counterfactually treated counterpart. Positivity consists of deterministic positivity (structural characteristics preventing treatment receipt) and stochastic positivity (random chance preventing a comparable person from receiving the opposite treatment). Methods to assess stochastic positivity violations include comparing distributions stratified by treatment in descriptive tables, and non-overlap of model-estimated propensity scores. Each of these methods has its faults: descriptive tables are unable to assess violations in high dimensional scenarios and propensity score models rely on strong parametric assumptions. To avoid these limitations, we approach positivity from a geometric point of view. From this perspective, each covariate combination can be plotted in k-dimensional space as a point. These points can be stratified by treatment and summarized by a convex hull, the smallest k-dimension enclosure that contains all points and any convex combinations between points. The intersection between both hulls represents all plausible covariate combinations without stochastic positivity violations.

We demonstrate the convex hull using data from a trial comparing estrogen versus placebo for treatment of prostate cancer. When comparing by age and weight index only (n=505), we find 41/505 (8%) individuals were outside the hull intersection. Some characteristics of these individuals are they were over the age of 85 or their weight index is less than 74 or greater than 140.

By assessing positivity with convex hulls, we only require that any valid future observation is a convex combination of observed data. This framework generalizes to any dimension and works with continuous and discrete variables. This allows epidemiologists to assess high-dimension positivity violations without relying on parametric models.

Constructing Convex Hulls for Positivity
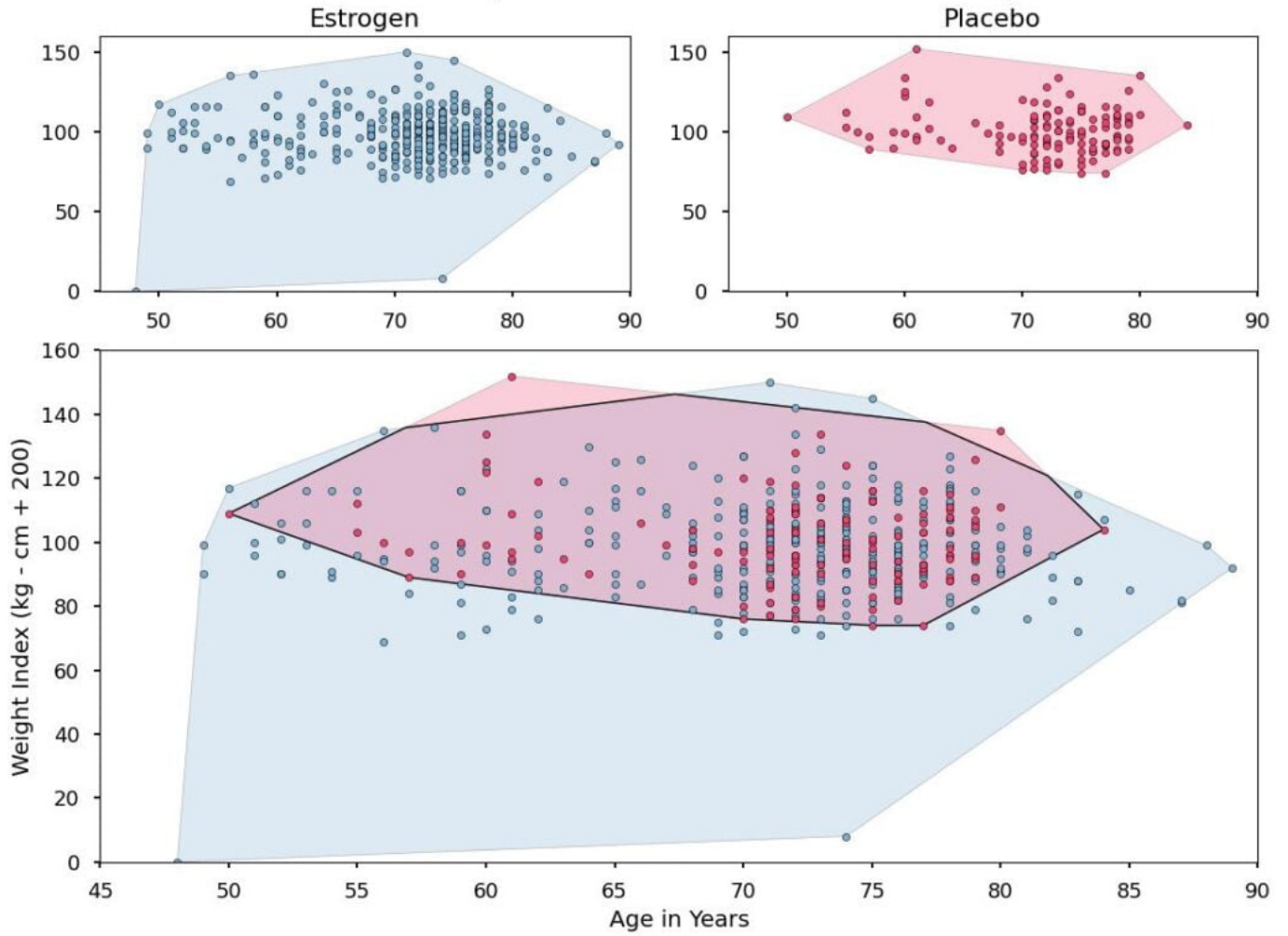
Causal Inference

Formal causal inference in experimental N-of-1 trials Marco Piccininni* Marco Piccininni
Stefan Konigorski Mats Julius Stensrud

Recent interest in precision medicine has challenged the relevance of average treatment effects estimated from randomized control trials (RCTs). Experimental N-of-1 trials aim at assessing the response to an intervention in a single individual.

N-of-1 trials are often characterized by a multiple cross-over design, multiple measurements of the outcome, random allocation of the treatment sequence, and blinding. Results are generally analyzed using standard statistical methods and claims that causal inference is not needed for experimental N-of-1 trials can be found in the literature, where confusion exists around concepts such as time-varying confounding and the guarantees given by randomization.

The aim of this work is to ground experimental N-of-1 trials in a formal potential outcomes framework for causal inference.

This allows us to define a conditional average treatment effect (CATE) that represents a natural target in the N-of-1 setting, termed the U-CATE. We discuss the assumptions needed for its identification and estimation under different data generation mechanisms. We consider settings in which carryover effects, trends over time and outcome autocorrelation are present, with emphasis on scenarios of particular relevance. We show how the simple mean difference may be a valid estimator of the U-CATE when interventions have effects limited in time and address symptoms of a stable medical condition. More complex scenarios require the g-formula to identify the U-CATE. We clarify the role of randomization in experimental N-of-1 trials, the link between RCTs and N-of-1 trials, and more generally, formalize intuitive claims from the N-of-1 trial literature. While the idea behind N-of-1 trials might seem simple, only causal thinking and approaching the problem rigorously can unveil the complex methodological aspects of this design.

Interpretation of Associational Language in Research Noah Stovitz* Noah Stovitz Ian Shrier
Jake Quilty-Dunn Jennifer Hill

Researchers often use ambiguous language, and even clearly written non-causal language may be misinterpreted as causal. The purpose of this study is to evaluate the effect of language on the interpretation of causality in research articles. We surveyed under- or recently graduated university students. We randomized them to see one of 5 different "linking words" between variables that might represents causes and outcomes (ordered by perceived level of causal implication: affects, increases, predicts, increased with, correlated with) within three different contexts which varied by a priori level of perceived causal relationship (exercise and dehydration: likely causal, study abroad and graduation: possibly causal or non-causal, born early in week and intelligence: likely non-causal). In the first 60 respondents with complete data, the proportion of respondents who reported the claim as having a strong causal implication was only 25% for affects (our a priori strongest causal implication), 53% for increases, 35% for predicts, 38% for increased with, and 22% for correlated with. The context affected the interpretation for 45% (27/60) of the participants. Among those participants, 19% (5/27) interpreted the claim as being more causal even though the context shifted from likely causal to likely non-causal. We conclude that interpretations of linking words are complex, with the likelihood of a true causal effect affecting the interpretation.

Association between referral to specialty care and patient-centered outcomes among patients with Alzheimer's disease and related dementias: an analysis leveraging physician preference instruments

Erin Ferguson* Erin Ferguson Silvia Miramontes Katherine Possin Justin S White Anna Chodos Fan Xia Alexander Smith Eva Raphael M Maria Glymour

Background: Primary care providers (PCPs) must often decide whether to refer patients with Alzheimer's disease and related dementias (ADRD) to specialists. It is unclear whether specialist care improves patient outcomes. Leveraging random variation in PCPs' preference for specialty referral, we evaluated whether referrals are associated with patient-centered outcomes using observational and instrumental variable (IV) methods.

Methods: Analyses included 3,577 individuals diagnosed with ADRD by San Francisco Bay Area PCPs from 1998 to 2022. Referral to specialists (neurologists and memory care) was determined from electronic health records. The instrument (PCP preference) was defined as the proportion of prior patients a PCP referred to specialists. We identified 9 outcomes using ICD codes: hip fractures, depression, urinary or fecal incontinence, weight loss, hospitalizations, falls, and benzodiazepine or antipsychotics use. We modeled observational associations between referral to care and cumulative incidence of outcomes 5 years post-diagnosis using linear regressions adjusted for age, sex, race, and insurance type; two-stage least squares models were used for IV analyses.

Results: The sample was an average of 79 years (SD: 6.6) at ADRD diagnosis; 8.9% received a referral. Preference strongly predicted actual referral (F=183.7). At 5 years, referral was observationally associated with worse outcomes in every domain except fecal incontinence (**Figure 1**). In IV estimates, referral was associated with absolute increases in antipsychotics use (overall risk=17%; RD associated with referral=0.25, 95% CI:0.06-0.56), depression (overall risk=24%; RD=0.27, 95% CI:0.07-0.48), and falls (overall risk=30%; RD=0.31, 95% CI:0.06-0.56) (**Figure 1**).

Discussion: Referral to specialty care was adversely associated with some patient-centered outcomes. However, this IV has limitations to interpretation and viability, which we will discuss and explore in our future work.

Figure 1. Fully adjusted associations between observed referral status or physician preference for referral (2SLS) and 9 outcomes observed 5 years after ADRD diagnosis: hip fractures (hip fx), fecal incontinence (FI), prescriptions for benzodiazepines (BZs), weight loss (Wt loss), hospitalizations, urinary incontinence (UI), prescriptions for antipsychotics (APs), depression, and falls.
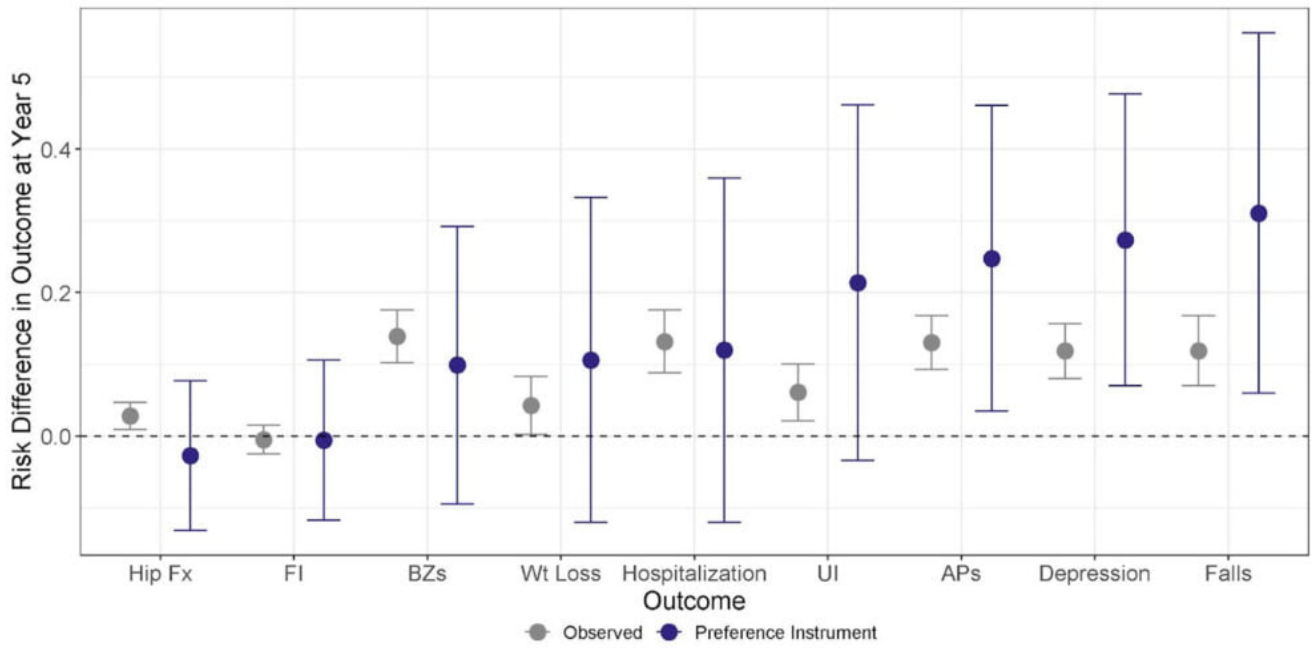
The Utility of Missing Data Graphs in Recovering Causal Effects from Selection Bias

Haidong Lu* Haidong Lu Maya Mathur Fan Li

Selection bias remains a central concern in methodological research in epidemiology and other social sciences. Traditional causal diagrams, featuring a single selection node, are sufficient for assessing the presence of many forms of selection bias, and work fine when only considering complete-case estimation. However, this approach falls short in elucidating the recoverability of causal effects from selection bias due to missing data in more general settings, because a single selection node does not distinguish between variables that are fully observed and those that are partially missing. For instance, in scenarios of selection bias due to differential loss to follow-up, it is often required that the information on the exposure and covariates connecting the selection node and the outcome is fully observed for both selected and unselected samples, such that the causal effect in the entire sample can be recovered. To address this limitation, we review the link between selection bias and missing data and introduce the use of missing data graphs (as known as m-graphs), a form of causal diagram, to better characterize selection bias scenarios. Furthermore, we demonstrate the utility of missing data graphs for selection bias scenarios within several special causal structures, and describe simple identification rules to specify which variables' full distribution is necessary for recovering causal effects from selection bias.

Arrests, Policing, and COVID-19 Vulnerability Index by Community Area within Chicago, IL

Allison Boretsky* Allison Boretsky Aveline Roderick Victoria Fisher Nadia N. Abuelezam

Background: Police presence and arrests in marginalized communities have led to increased distress, general distrust towards police, and negative health outcomes in citizens. Police have been used to enforce COVID-19 social distancing policies and other COVID-19 related interventions, despite most not being trained public health professionals. We aim to assess the relationship between police enforcement and subsequent community COVID-19 vulnerability and outcomes in Chicago between 2019 and 2020.

Methods: The Chicago COVID-19 Vulnerability Index (CCVI) ranks communities on 10 variables to assess social vulnerability to COVID-19 (i.e. socioeconomic status) and COVID-19 impact (i.e. incidence and mortality). Higher CCVI scores indicate a higher COVID-19 vulnerability. Using 2019 and 2020 arrest data, we compared total arrests per community area with the community's CCVI score. We used Pearson's correlation test to determine the correlation between CCVI scores and 2019 and 2020 arrests, respectively.

Results: In both 2019 and 2020, the greatest number of arrests occurred in Austin and North Lawndale (categorized as "high COVID-19 vulnerability" areas). The Pearson's correlation coefficient between 2019 total arrests and CCVI score was 0.28 (95% CI: 0.06, 0.47) with a p-value of 0.01. The Pearson's correlation coefficient between 2020 total arrests and CCVI score was 0.30 (95% CI: 0.08, 0.49) with a p-value of 0.007.

Conclusion: The most policed communities in 2019 were considered highly vulnerable on the CCVI index in 2020. Communities most heavily impacted by COVID-19, including by COVID-19 mortality, were more heavily policed in 2020 than communities with lower CCVI scores. This suggests that in addition to worse COVID-19 outcomes, the pandemic disproportionately exacerbated the inequities marginalized communities faced.

Evaluating the Use of Event Metadata Extracted from Online News Media for Disease Outbreak Detection Yannan Shen* Yannan Shen David Buckeridge Russell Steele Philip Abdelmalik

Digital disease surveillance (DDS) uses internet-based data to detect and monitor health threats. DDS leverages advanced techniques to extract structured event metadata of event entities such as whether an event was caused by an unclassified pathogen. Our study aims to understand the data properties of event metadata and explore the use of a self-controlled case series design to assess the temporal association of event entities and the emergence of the Omicron variant. We obtained COVID-19 event metadata between October 1 and December 31, 2021, from a DDS system, BioCaster, and daily counts of Omicron-positive genome samples for the same period from the Global Initiative on Sharing All Influenza Data. Countries with detected change points in at least one entity were included. For each country, the emergence of the Omicron variant was identified based on genome counts using Bayesian change point analysis. We defined a risk period of 9 days following each emergence and included an 18-day pre-exposure period to address potential assumption violation, as more genome samples may be collected after news reporting a new variant. Conditional Poisson regression was used to estimate the relative incidence (RI) and its 95%CI. Given the significant media attention garnered by the World Health Organization's announcement regarding the identification of the Omicron variant, we conducted a secondary analysis with a truncated study period until November 25, 2021, to eliminate the potential impact of the announcement. During the study, 67 countries were included. The number of changes detected from different entities varied from 19 to 419. No increasing incidence of changes in any entity was identified. However, after shortening the study period, increased RIs were found for the entity indicating events caused by unclassified pathogens (2.24 95%CI 1.03, 4.84). These findings highlight the potential of online news media for signalling the emergence of significant infectious diseases.

Risk of Incident Rheumatoid arthritis in Post COVID-19 Infection: A Systematic Review and Meta-analysis of Cohort Studies Amarit Tansawet* Parkin Paramiraksa Metavee Boonsiri Poramin Patthamalai

Objective
Increasing evidence has reported the incident of autoimmune disease including rheumatoid arthritis (RA) following COVID-19 infection. However, the inconsistencies remain among studies. Our study aim to determine the risk of incident RA in post COVID-19 infection.

Methods
A comprehensive search of PubMed, EMBASE, Scopus, Cochrane library, and medRxiv was independently conduct by two reviewers to identify cohort studies reporting the risk of incident RA in patients with post COVID-19 infection, compare to controls who were not diagnosed with COVID-19 throughout the follow-up period. Eligible studies will be further extracted key characteristic. Quality assessments were performed according to the Newcastle-Ottawa Scale (NOS). The PRISMA and Meta-analysis of Observational Studies in Epidemiology (MOOSE) reporting guidelines were followed. To ensure the minimize effect of confounder, only the adjusted hazard ratio (aHR) were pooled using the random-effects meta-analysis. Publication bias was assessed by funnel plot.

Results
A total of 5 studies with 5 cohorts (n = 20,113,294 participants) were eligible for inclusion and were pooled in the meta-analysis. A significant association was found between post COVID-19 infection and risk of incident RA (pooled aHR, 2.80; 95% CI, 1.60-4.88). Subgroup analysis by age revealed that no association was found in patient aged < 40 years (pooled aHR, 0.96; 95% CI, 0.21-4.47). Nevertheless, patients age ≥ 40 years were at significantly increased risk of developing RA following COVID-19 infection (pooled aHR, 3.75; 95% CI, 1.83-7.69). No evidence of publication bias was observed. Quality assessments of the included studies were high.

Conclusion
Patients with post-COVID-19 infection have a significant increase risk of incident RA, particulary in the age group of ≥ 40 years. The possible risk of RA needs to be considered when managing patients with post COVID-19 infection, especially in the case with RA risk at baseline.

LATEBREAKER

COVID-19 Pandemic

Influenza Vaccination Rates Before and During the COVID-19 Pandemic in the USA Lasata Shrestha* Lasata Shrestha Mahima Joshi Shivani Paudel McKenna Eastment Alyson Littman

The United States Centers for Disease Control (CDC) estimated that influenza (flu) contributed to 4900– 52000 deaths annually between 2010 and 2022. Despite annual vaccination being the most effective preventive measure, flu vaccination rates in the US for the last decade have been lower (less than 65%) than the Healthy People 2020 Initiatives' desired target of 70%. The lower flu vaccination could be related to disparities in access to vaccine and vaccine coverage, health literacy, race, geographical location, and differences in healthcare decision-making, which the COVID-19 pandemic further exacerbated. Using the Behavioral Risk Factor Surveillance System (BRFSS) dataset, we compared the flu vaccine uptake rates before the COVID-19 pandemic (unexposed: 2018-2019) to those during the pandemic (exposed: 2020-2021). Flu vaccine uptake prevalence ratios (PR) were calculated using generalized linear models, adjusted for household income, self-reported health, age, insurance coverage, sex, and education. Additionally, effect modification by Medicaid expansion, race/ ethnicity, and urbanicity/rurality was examined, but since there were no meaningful differences in the during vs. pre-pandemic associations by these factors, they were instead adjusted for in the final analyses. The prevalence of flu vaccination before the pandemic was 44.4% compared to 52.6% during the pandemic (aPR= 1.19, 95%CI 1.18, 1.19). Associations were similar after adjustment for potential confounders (aPR = 1.19, 95%CI 1.18, 1.19). This study highlights the pandemic-driven difference in flu vaccination rates and the importance of understanding the impact of the COVID-19 pandemic on health-seeking behaviors in various communities.

A novel method for the classification of medical environment features in COVID-19 research Edwin McCulley* Edwin McCulley Usama Bilal Gina Lovasi Brisa Sanchez Alinan Schnake-Mahl Jana Hirsch

The COVID-19 pandemic disproportionately affected vulnerable populations worldwide. Some faced greater risk of severe COVID-19 outcomes due to individual factors like preexisting medical conditions, while others were affected by environmental factors such as the presence or absence of medical facilities that provide lifesaving care. Despite investigations into the individual factors that predispose individuals to severe COVID-19, less attention has been paid to the contextual effects of place-based environmental factors on COVID-19 outcomes. We aimed to compare 4 methods of measuring COVID-19-relevant features in the nearby medical environment (ME). We utilized individual mortality data on COVID-19 deaths from the National Center for Health Statistics to compute rates of COVID-19 deaths in US counties from 2020-2021. We obtained local ME features from the National Establishment Time Series, grouped into 23 categories. We then used Quasi-Poisson Generalized Linear Models to predict COVID-19 death rates using four approaches: a theory-driven approach based on expert knowledge of three reviewers, a backwards stepwise approach, a Least Absolute Shrinkage and Selection Operator (LASSO) approach, and a synthesized approach which included predictors that were relevant across two or more models. Each model identified several COVID-19-relevant ME features (Figure 1), with the stepwise and LASSO approaches providing the best-fit models based on qAIC. Furthermore, pharmacies/drug stores, emergency medical transport, and urgent care emerged as important predictors of COVID-19 death rates across models, suggesting a critical role in the screening, treatment, and prevention of COVID-19 during year 1 of the pandemic. This novel classification method can help identify ME factors that are predictive of population-level COVID-19 impacts and can guide public health research aimed at reducing or eliminating inequities in COVID-19 outcomes, especially among vulnerable populations.

Figure 1) Medical Environment Features and Candidate Models

NETS Category	Abbrev.	# Models	Theory Model	Stepwise Model	LASSO Model	Synthesized Model
Behavioral Health Hospitals	BHH	0				
Behavioral Health Outpatient and Continuous Care	BHO	2		✓	✓	
Acupuncture and Biofeedback	BIO	1			✓	
Pediatric Dental Care	CDS	3		✓	✓	✓
Chiropractors	CHR	1			✓	
Children Hospitals	CHS	1		✓		
Offices or Clinics of Pediatric Health Practitioners	CPC	1			✓	
Dental Care	DDS	3		✓	✓	✓
Pharmacies/Drug Stores – SIC Code based definition	DRG	4	✓	✓	✓	✓
Pharmacies/Drug Stores – Chain name based definition	DRN	4	✓	✓	✓	✓
Hearing Aids Retail and Testing Locations	EAR	1		✓		
Emergency Medical Transport	EMT	4	✓	✓	✓	✓
Hospitals and Major Medical Centers	HOS	1	✓			
Offices or Clinics of Health Practitioners	HPC	2	✓	✓		
Kidney Centers	KCT	0				
Mental Health Hospitals	MHH	0				
Mental Health Outpatient and Continuous Care	MHO	0				
Optical	OPT	2		✓	✓	
Physical and Occupational Therapy	PHT	0				
Residential Facilities with Health Care	RES	2	✓		✓	
Residential Care	RSC	1	✓			
Retail Clinics	RTC	1	✓			
Urgent Care	URG	4	✓	✓	✓	✓

Influenza vaccination in adults with and without COPD before and after the COVID-19 pandemic in the US: a national-level study (2017-2022) Marissa Wold* Marissa Wold S. Cristina Oancea

Introduction: The current literature has limited information regarding influenza vaccination (IV) among chronic obstructive pulmonary disease (COPD) patients prior to the COVID-19 pandemic, and no information on the topic assessing the years following the pandemic. The majority of the literature prior to the pandemic assesses the safety and efficacy of the IV in COPD patients, rather than focusing on an examination of actual vaccination behavior. Little is known about IV behavior in COPD patients in the years prior to and following the pandemic.

Methods: This cross-sectional study used Behavioral Risk Factor Surveillance Survey (BRFSS) data from the years 2017 to 2022 (n=1,471,405, 51% males). The exposure was COPD diagnosis and outcome was IV in the last year. Confounders were chosen based on previous literature and included in a directed, acyclic graph (DAG) for analysis. Weighted and adjusted logistic regression models were conducted overall and by the significant effect modifiers sex and year.

Results: Having COPD significantly increases the weighted adjusted odds (WAO) of IV when compared to not having COPD, overall, by sex, and by year. For the years 2017-2022, among men with COPD (6%), and among women with COPD (7.5%), the WAO (95% CI) of IV were:

1.33(1.18,1.48);1.24(1.11,1.38);1.53(1.37,1.71);1.51(1.29,1.75);1.22(1.07,1.38);1.30(1.16,1.46) and

1.27(1.16,1.40);1.36(1.23,1.49);1.26(1.15,1.39);1.07(0.95,1.20);1.23(1.10,1.37);1.22(1.11,1.35)

when compared to men, and women, without COPD, respectively.

Conclusions: Study findings suggest males had significantly greater WAO ratios of receiving IV than females in 2019 and 2020, the year immediately pre- and then during-Covid 19 pandemic. Understanding the potential barriers for IV receipt by sex, especially during a pandemic, and especially for individuals impacted by COPD, is essential for better health interventions in times of a national crisis such as a pandemic.
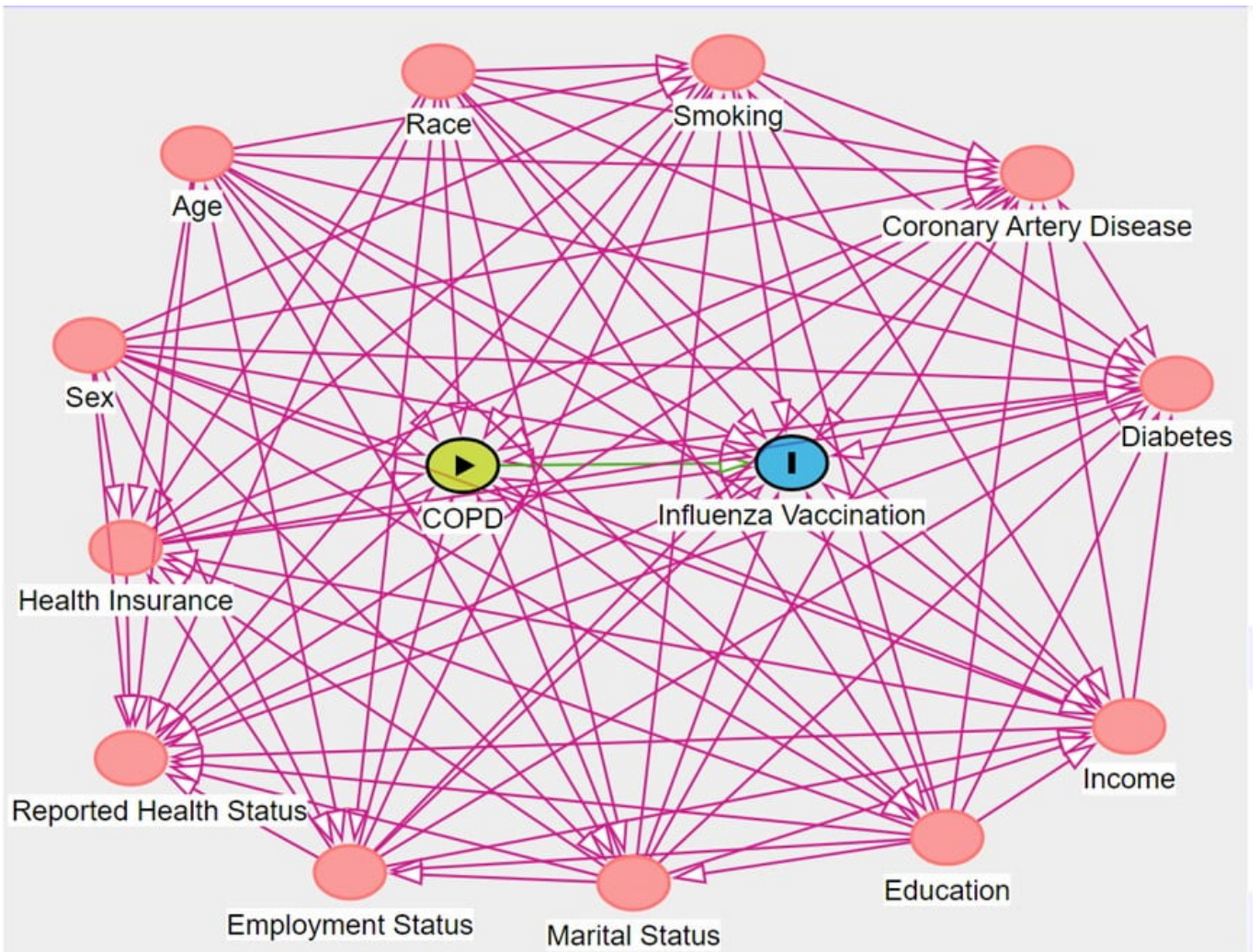
COVID-19 hospitalizations and hospitalization outcomes among children with immunocompromising conditions, MarketScan Commercial Database, 2020-2022 Regina M. Simeone* Regina Simeone Emilia H. Koumans Angela P. Campbell

People who are immunocompromised are at increased risk for infections compared with those who are not. Our objectives were to assess the association between presence of immunocompromising conditions (IC) in children and COVID-19 hospitalization, and whether hospitalization outcomes occurred more frequently in children with IC compared to those without. Using the MarketScan® Commercial Databases from January 1, 2020–December 31, 2022, eligible children were 0–17 years, continuously enrolled in participating insurance plans for ≥2 years, with ≥1 outpatient encounter. We identified children with IC as having ≥1 IC ICD-10-CM code(s) during a hospitalization, or ≥2 outpatient encounters with IC ICD-10-CM codes. Age, sex, and geographic region of residence were included in all models. We used Poisson regression with robust standard errors, additionally adjusted for non-COVID-19 hospitalizations to estimate the risk ratio (RR) and 95% confidence interval (CI) for any COVID-19 hospitalization. For models of COVID-19 hospitalization outcomes, we additionally adjusted for year and non-COVID-19 hospitalizations before first COVID-19 hospitalization. A negative binomial distribution was used to model hospital length of stay. We included 3,116,239 children; 90,043 (2.9%) had IC and 78,855 (2.5%) had ≥1 hospitalization. Among 3,193 COVID-19 hospitalizations, 1,000 (31.3%) had an IC diagnosis. Compared to those without, children with IC were 5.8 times more likely to have a COVID-19 hospitalization (CI: 5.2, 6.4); among children with ≥1 hospitalization, those with IC were 1.3 times more likely to have a hospitalization with COVID-19 (CI: 1.2, 1.4). Among children with a COVID-19 hospitalization, those with IC were more likely to be admitted to the intensive care unit and be re-admitted within 30 days of COVID-19 hospitalization (RRs=1.2) (Figure). Future work should assess drivers of COVID-19 hospitalization, specific IC, and hospitalization outcomes among children with IC.

Figure. Risk ratios[a] comparing COVID-19 hospitalization outcomes[a] among children with a hospitalization with COVID-19 with and without immunocompromising conditions, MarketScan Commercial Claims and Encounters, 2020-2022
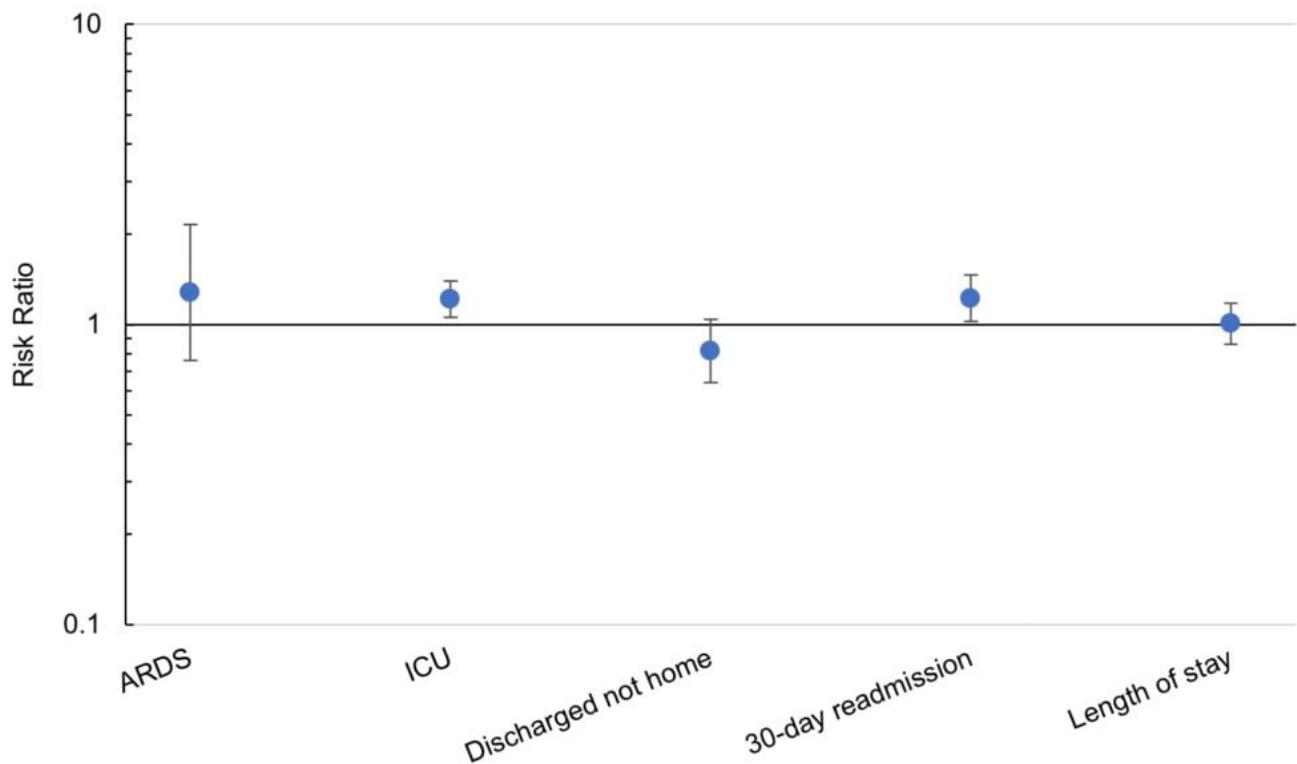
Abbreviations: ARDS: Acute respiratory distress syndrome; ICU: Intensive care unit

a.   Poisson regression models with robust standard errors were used to estimate risk ratios, accounting for within-child correlation. Models were adjusted for child age, sex, geographic region of residence, year of hospitalization, and number of hospitalizations without a COVID-19 diagnosis before initial COVID-19 hospitalization.

Economic Context, Schooling Modality, and Mental Health in U.S. Adults Living with Children During the COVID-19 Pandemic Catherine Ettman* Catherine Ettman Elena Badillo Goicoechea Elizabeth A. Stuart

The COVID-19 pandemic upended contexts for families; relatively little work has studied the influence of pandemic-era context on the mental health of adults living with children. We aimed to assess the relation between economic context and schooling modality with the mental health of adults living with school-age children during the pandemic. Using a large, national sample from the COVID-19 Trends and Impact Surveys collected in partnership with Meta (CTIS; N=1,485,072 responses from November 2020 through June 2022), the sample included over one million responses from adults living with children under the age of 18 years old during the COVID-19 pandemic who were active Facebook users. We used weighted multiple logistic regression to estimate the association of frequent feelings of depression and anxiety, respectively, with economic context and schooling modality, controlling for demographics, state, and COVID-protective behaviors (e.g., mask wearing). We found that financial worry was most strongly associated with reporting frequent feelings of depression and anxiety across all time periods, and the association significantly increased over time (p<0.001) from aOR 2.25 (95%CI 2.19, 2.32)/aOR 2.63 (95%CI 2.54, 2.73) in Fall 2020 to aOR 3.11 (95%CI 3.01, 3.22)/aOR 3.79 (95%CI 3.64, 3.95) in Spring 2022 for anxiety and depression symptoms, respectively. Living with children in fully online schooling (vs. fully in-person schooling) was associated with worse mental health in all study periods, increasing from aOR 1.08 (1.05, 1.11)/aOR 1.06 (1.02, 1.10) in Fall 2020 to aOR 1.20 (1.10, 1.32)/aOR 1.28 (1.16, 1.42) in Spring 2022 for anxiety and depression symptoms, respectively. Financial worry and schooling modality were associated with mental health of adults living with children in the household during the COVID-19 pandemic and the strength of the association grew over time. These findings suggest a need to focus on economic context of families during largescale events. Future policy decisions around schooling modality–or of how to support families and communities during periods of school closure–may consider parental mental health an additional factor worth weighing.

Figure 1. Adjusted odds ratio for frequent feelings of anxiety and of depression by economic factors and schooling modality
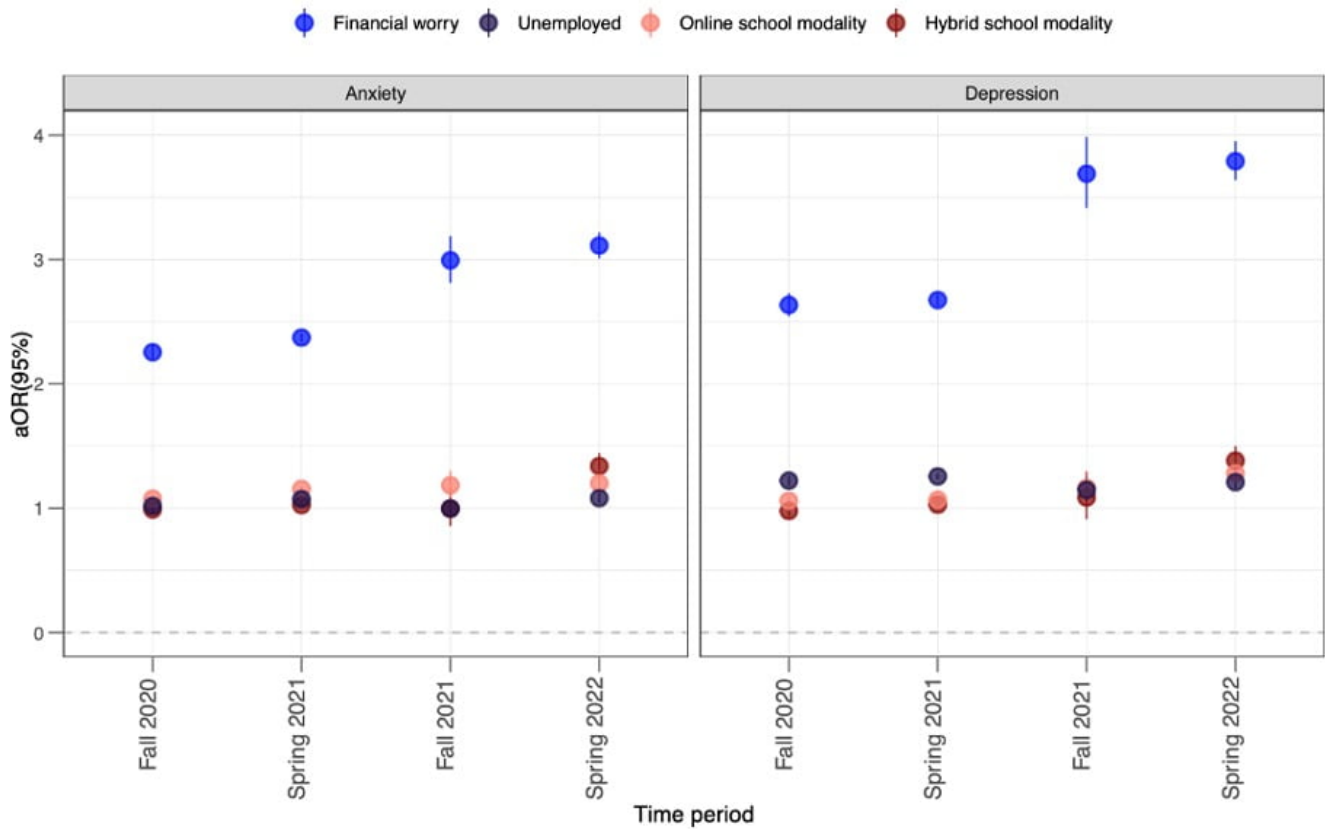
Note: CTIS data used: Fall 2020 collected November 24, 2020 - December 19, 2020 (N=245,079); Spring 2021 collected from January 3, 2021 - May 1, 2021 (N=995,497; Fall 2021 collected August 29, 2021 - December 19, 2021 (N=49,631)); Spring 2022 collected January 3, 2022 - May 15, 2022 (N=194,865). All models control for age, gender, education, race and ethnicity, state, and COVID-protective behaviors.

Chronic Lung Disease and Long Covid Syndrome in Postmenopausal Women from the Women's Health Initiative

Patrick Montine* Patrick Montine Danielle J Harvey Lorena Garcia Christian Sandrock John Robbins

Abstract: We analyzed the cross-sectional association between pre-existing chronic lung diseases (CLD), namely asthma and chronic obstructive pulmonary disease (COPD), and the manifestation of Post-COVID Conditions (PCC) symptoms in postmenopausal women. The background highlights the increased risk of asthma development in women before menopause due to estrogen's impact on airway inflammation and its potential to intensify the oxidative stress caused by cigarette smoke, a significant contributor to COPD. The study aims to assess whether pre-existing CLD is linked to PCC in postmenopausal women with COVID-19. Excluding participants who tested negative for COVID-19 and those who developed CLD after December 31, 2019, the study employs the WHO PCC definition for outcome measurement and evaluates CLD history using bivariate and multivariable logistic regression models. Among 37,289 participants responding to COVID-19 Survey 2, 1237 reported positive COVID-19 results with 413 (33%) participants having PCC. The participants who reported positive COVID-19 predominantly comprising White (90%), Non-Hispanic (96%) individuals residing in urban areas (90%), with a median age of 83.79 ± 5.52. Preliminary bivariate results indicate a significant association between COPD (OR 1.51, 95% CI: 1.10-2.06, P < .01) and PCC, while asthma (OR 1.36, 95% CI: 0.99-1.86, P = .05) demonstrates a borderline association with PCC. The discussion underscores the implication that women with pre-existing CLD may be more predisposed to PCC, offering valuable insights for a deeper understanding of PCC mechanisms.

Assessment of four South American countries' COVID-19 pandemic preparedness, responses, and lessons learned Andrea Ramirez Varela* Andrea Ramirez Varela Michael Touchton J. Jaime Miranda Juliana Mejía Grueso Rachid Laajaj Gabriel Carrasquilla Martha Vives Florez Ana María Vesga Gaviria Ana María Ortiz Hoyos Alejandra Velásquez Morales Nubia Velasco Silvia Restrepo Restrepo

Background: The COVID-19 pandemic emerged in a context that lacked adequate prevention, preparedness, and response (PPR) activities, and global, regional, and national leadership. South American countries were among world's hardest hit by the pandemic, accounting for 10·1% of total cases and 20·1% of global deaths. This study aims to explore how pandemic PPR were affected by political, socioeconomic, and health system contexts. We explore how PPR may have shaped pandemic outcomes in Argentina, Brazil, Colombia, and Peru, lessons learned and advance an agenda for improving PPR capacity at regional and national levels. **Methods:** Mixed-methods sequential explanatory study in four South American countries based on structured interviews and focus groups with elite policy makers. **Findings:** Structural and contextual barriers limiting PPR activities were identified at the political, social, economic levels, and health care system. The perception was that top-level government officials had insufficient political will for prioritizing pandemic PPR and post-COVID-19 recovery programs in their countries' health agendas. **Interpretation:** To place pandemic PPR at the highest level of South American national public health agendas, we recommend the development of a regional task force on COVID-19, post-pandemic recovery, and emerging disease threats in the next two years, social and economic protection for vulnerable groups, improved primary health care and surveillance systems, and investing in risk communication strategies and community engagement. **Funding:** Open Society University Network OSUN Fellowship, Queen Elizabeth II Academy for Leadership in International Affairs, Chatham House, UK; Universidad de los Andes, Fundación Santo Domingo, and Asociación Nacional de Empresarios, Colombia.

Temporal Trends in Hyperinsulinemia and Insulin Resistance Prevalence among Nondiabetic Adults in the U.S., NHANES, from 1999 to 2018

Chuyue Wu* Chuyue Wu Yixun Ke Roch A. Nianogo

Background:

Hyperinsulinemia and insulin resistance are strong predictors for future cardiometabolic diseases.

Objective:

Our aim is to estimate and test the temporal trends in hyperinsulinemia and insulin resistance prevalence by race/ethnicity and poverty level, among non-diabetic adults in the United States from 1999 to 2018.

Methods:

We used data from the National Health and Nutrition Examination Survey (NHANES) from 1999 to 2018. Hyperinsulinemia was defined as people with serum fasting insulin levels $\geq$ 10 U/ml (the median). Insulin resistance was defined by using the Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) index $\geq$ 2.6 (the 66th percentile). We assessed nonlinearity by evaluating cubic terms in polynomial logistic regression models. Logistic regression models were fitted to test the sample weighted and age-standardized time trends.

Results:

We included 17,310 men and nonpregnant women, aged 20 years or older, and free of diagnosed diabetes. The prevalence of hyperinsulinemia and insulin resistance rose by about 40% from 1999 to 2018 (Figure 1). Non-Hispanic (NH) White people and those with higher family income (i.e., higher ratio of family income to poverty level) were more likely to have lower prevalence of hyperinsulinemia and insulin resistance. The prevalence of hyperinsulinemia and insulin resistance among NH Black and Hispanic individuals was consistently higher compared to NH White people. NH Asian people had a rapid increase in hyperinsulinemia and insulin resistance prevalence since 2013. We found the presence of temporal trends for each subgroup defined by race/ethnicity and poverty level (P for trend < 0.01).

Conclusions:

There was an increased time trend in the prevalence of hyperinsulinemia and insulin resistance among nondiabetic adults in the US from 1999 to 2018. This underscores the need for targeted interventions, particularly addressing disparities across racial and income subgroups.

Figure 1: Prevalence and 95% Confidence Interval (CI) of Hyperinsulinemia and Insulin Resistance among Nondiabetic Adults in the US by Poverty Levels and Race/Ethnicity, NHANES, from 1999-2000 through 2017-2018
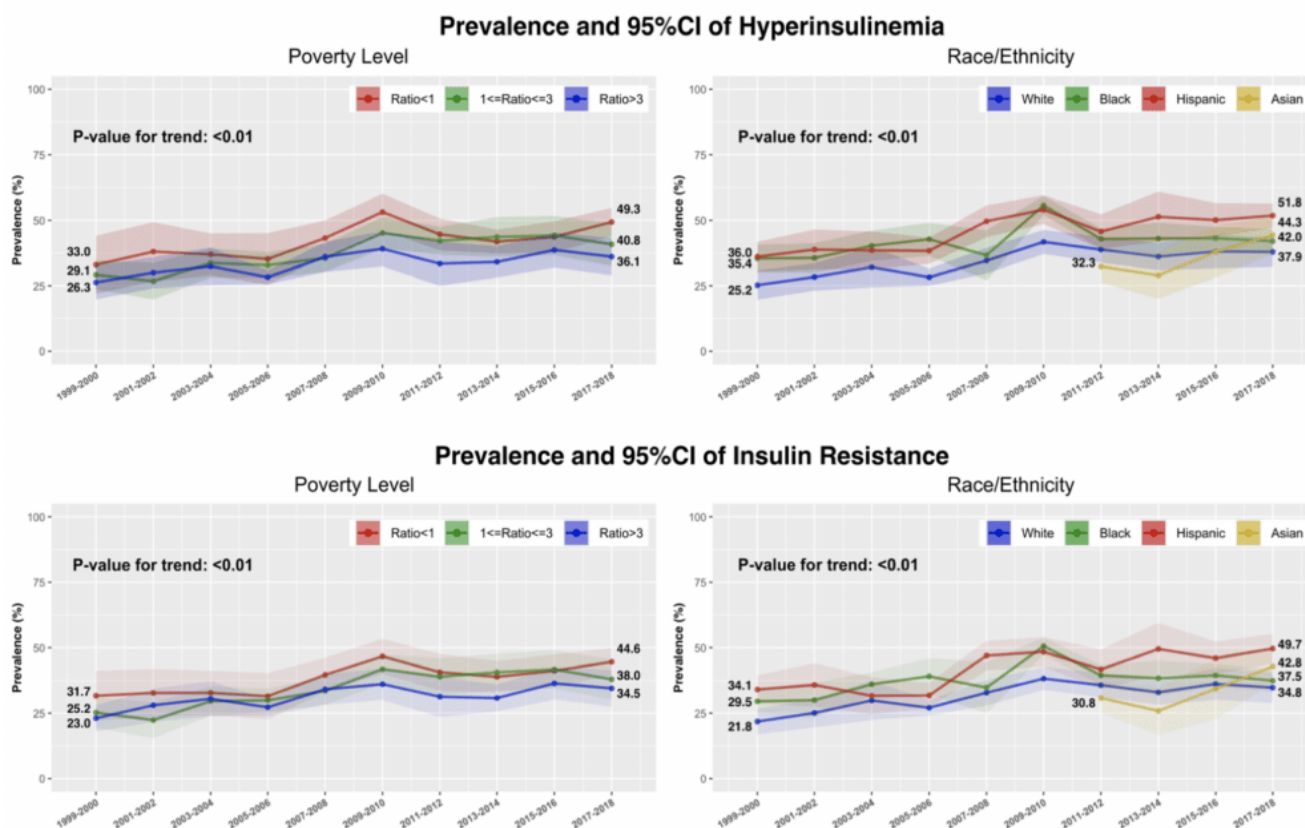
Note: data for non-Hispanic Asian Americans was available in the NHANES only from 2011 through 2018.

Association between Urinary Arsenic and Selenium and Self-Reported Diabetes Sarah Mayberry* Sarah Mayberry Namvar Zohoori Lora J. Rogers Shelbie D. Stahr L. Joseph Su

Diabetes is one of the most common chronic conditions in U.S. adults, with its burden only projected to increase. Arsenic and selenium exposure may contribute to diabetes development, elements not typically considered in prevention efforts. Although inconclusive, early research suggests environmental arsenic exposure may increase diabetes risk. In trace amounts, selenium functions as an antioxidant; however, U.S. observational studies have shown a positive association between selenium and diabetes risk, possibly from overconsumption. Many studies have hypothesized antagonistic and synergistic pathways between these elements, yet their exposure and interaction regarding diabetes status is largely unstudied. Data from the Arkansas Cardiovascular Health Examination Survey, a cross-sectional probability sampling of Arkansas adults, was used to examine these element exposures in relation to self-reported diabetic status. Self-reported data and spot urine samples were collected from 1,385 individuals. Urinary arsenic and selenium concentrations were measured using an inductively coupled plasma mass spectrometer and adjusted for creatinine concentration. Post-sampling weight and stratum were used to account for the survey design and final response rate (28%). 1,187 subjects (85.7%) were included in the logistic regression analysis to assess trace element exposure associated with self-reported diabetes status, adjusting for confounding factors. Selenium exposure appears more strongly associated with diabetes (OR:4.05, 95%CI:1.05-15.66) compared to arsenic (OR:1.96, 95%CI:0.84-4.54), with synergistic interaction between the elements observed, albeit insignificant (OR:1.22, 95%CI:0.98-1.52). These findings coincide with existing observational studies and may underscore the concern for selenium overconsumption's deleterious effects. While further research is required, these results suggest the importance of monitoring these elemental exposures to minimize diabetes' burden.

Diabetes

Evolution of type 2 diabetes over 20 years and subsequent dementia incidence: an application of sequence and cluster analysis Scott C Zimmerman* Scott Zimmerman Jingxuan Wang Lucia Pacca Hyelee Kim Paola Gilsanz Sarah F Ackley Whitney Wells Anusha M Vable Melinda C Power Rachel Whitmer Catherine Schaefer M Maria Glymour

Type 2 diabetes (T2D) onset age, glucose control, treatment, and sequelae may be associated with dementia incidence. Electronic health records (EHRs) contain detailed histories of individuals' diagnoses, labs and treatment over time, enabling analysis of complex T2D trajectories.

Using EHR and survey data from the Kaiser Permanente Northern California Research Program on Genes, Environment and Health measured 1996-2020, characterized individuals' annual states as one of 14 states defined by KPNC membership, T2D diagnosis, and combinations of glucose control, treatment, and kidney dysfunction. Among T2D-free individuals at age 50, we characterized individuals' state trajectories from age 50-69 and calculated clusters of similar trajectories using sequence and cluster analysis. Among individuals without dementia by age 70 we used Cox models to estimate associations between these clusters and subsequent dementia incidence after age 70, compared to individuals without a T2D diagnosis by age 70.

We summarized the 16,970 unique T2D-related trajectories experienced by 20,424 eligible individuals diagnosed with T2D by age 70 into 9 clusters (**Figure**). Clusters varied by T2D diagnosis timing and duration, HbA1c control, treatment, and kidney dysfunction. Dementia incidence over an average follow-up of 9.5 years varied across clusters relative to the group of 173,852 individuals without T2D at age 70, which had the lowest incidence. The lowest incidence for those with T2D was in a cluster characterized by long-term Kaiser membership, T2D onset typically after age 60, and moderate control of HbA1c with few drugs (cluster 6, HR=1.59 95%CI=(1.04, 2.42)). The highest risk cluster was characterized by onset of T2D typically before age 60 and chronic high HbA1c with low-to-moderate use of antihyperglycemic drugs (cluster 9, HR=4.26 95%CI=(3.13, 5.80)).

In these real-world data, dementia incidence varied substantially based on timing of T2D diagnosis, duration and treatment trajectories.
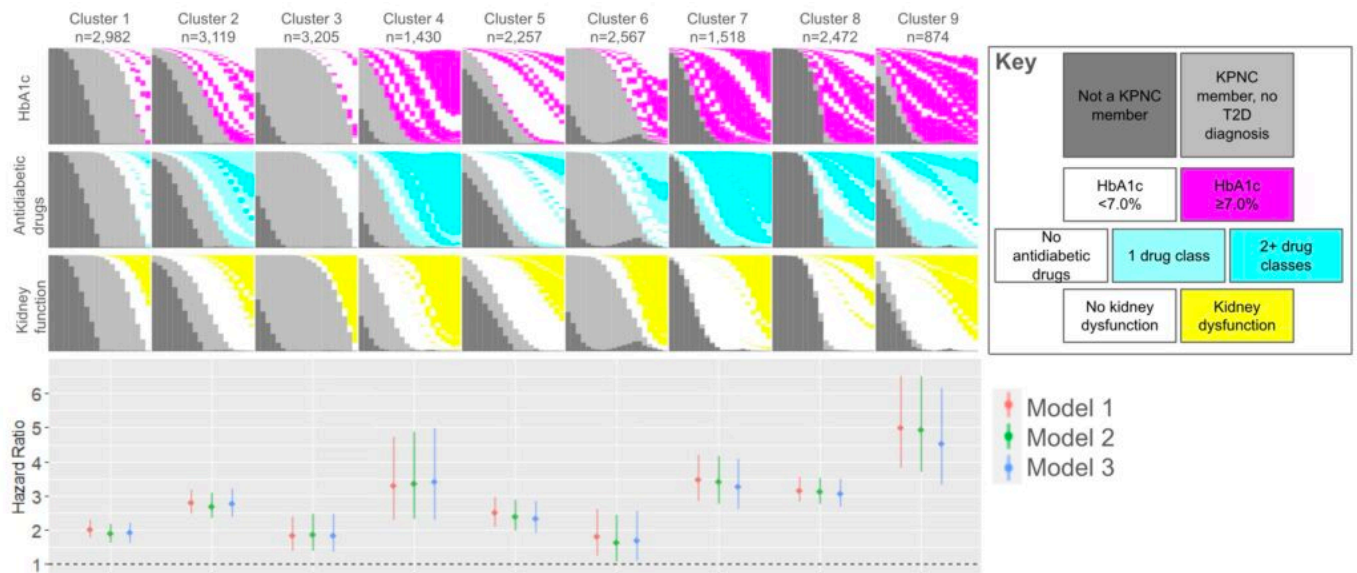
Figure: Clusters identified by sequence and cluster analysis: Variable-specific state density plots for each cluster from age 50 to 70 for HbA1c control (magenta, row 1), number of antidiabetic drug class prescriptions (cyan, row 2) and kidney dysfunction (yellow, row 3), and cluster-specific hazard ratios (row 4) relative to diabetes-free group at age 70 (dashed black line) . Model 1 adjusted for basic demographics (sex, race/ethnicity). Model 2 additionally adjusted for time-invariant survey measures (foreign birth, parents' foreign birth, education, survey language). Model 3 additionally adjusted for income and marital status at the survey date.

DNA Methylation Biomarkers for Cumulative Lead Exposures and Cognitive Impairment

Kanghong Shao* Kanghong Shao Yu Yu Beate Ritz Kimberly C Paul

Background Recent evidence suggests that cumulative low-level lead exposure has adverse effects on cognitive function in the elderly. To date, the few studies that examined it measured bone lead exposure with K-X-ray fluorescence (KXRF), methods that are mostly unavailable in large community-based studies. Here, we explore the use of a methylation measures for bone lead in the Alzheimer's Disease Neuroimaging Initiative (ADNI) cohort.

Methods Tibia and patella bone lead levels were measured using blood DNA methylation biomarkers in 643 participants from the ADNI cohort. Cognitive function was assessed using the Montreal Cognitive Assessment (MoCA) test. Longitudinal analyses of bone lead and cognitive decline were conducted using linear mixed-effect regression models.

Results DNAm derived tibia and patella lead levels were negatively associated with MoCA scores over time. With increasing tibia lead, there was a decrease in MoCA scores (per interquartile range (IQR): β=-0.25; 95%CI: -0.44, -0.05), while the MoCA decrease for patella lead was smaller (per IQR: β=-0.16; 95%CI: -0.38, 0.07). When stratifying by sex, women showed a stronger decrease in cognitive function with increasing tibia lead (per IQR β=-0.35; 95%CI: -0.65, -0.04) than in men (per IQR β=-0.19; 95%CI: -0.44, 0.07). The estimated decrease in MoCA scores per tibia lead IQR increase was strongest among participants with two APOE4 alleles (per IQR β=-0.85; 95%CI: -1.63, -0.08), while for those with one or zero alleles we estimated weaker effect sizes (per IQR one allele: β=-0.27; 95%CI: -0.62, 0.08; zero allele: β=-0.13; 95%CI: -0.37, 0.11).

Conclusion These findings strengthen the evidence that cumulative long-term lead exposures at environmental levels are associated with decreased cognitive function in the elderly, especially women and carriers of two APOE4 alleles. These findings based on whole blood methylation data align well with previous epidemiologic studies that used KXRF for measuring bone lead.

Short Term Exposure to Air Pollution is Associated with Hospital Admissions and Emergency Department Visits for Individuals with Sickle Cell Disease Kelsey M. Maclin, MS*

Kelsey Maclin Kristina M. Zierold, PhD, MS

Introduction

Sickle cell disease (SCD) is a genetically inherited blood disorder affecting people of African descent and Hispanics. SCD is characterized by painful episodes and acute lung injury known as acute chest syndrome (ACS). Patients with SCD have a life expectancy 20 years less than those without SCD. The health complications of SCD may be affected by environmental factors, particularly air pollution. There is minimal research investigating air pollution and SCD.

Methods

This review included SCD articles related to respiratory and pain complications associated with air pollution. Six databases were used to identify articles. We excluded articles without human subjects and articles that did not have air pollution effects. There were five articles that were included in this review.

Results

There were hospital admissions and emergency department (ED) visits associated with the criteria air pollutants. When higher concentrations of ozone were present, there was an increase in hospital admissions for pain. Elevated concentrations of nitrogen dioxide were associated with an increase in hospital admissions for pain and ACS. Additionally, higher concentrations of particulate matter were associated with an increase in ED visits for ACS and pain. There were conflicting results for the effect of carbon monoxide exposure on SCD as well as for the effect of sulfur dioxide on SCD.

Discussion

SCD is often a debilitating disease for Black and Hispanic individuals. This review found associations between air pollution exposure and SCD hospitalizations or ED visits. This negatively impacts the quality of life for patients with SCD and shortens their life expectancy. Being aware of increased air pollution, SCD patients may take steps to protect themselves.

Conclusion

With mixed research findings and minimal literature to date on the association between air pollution and SCD complications, future research needs to be conducted to add to the knowledge of environmental impacts on SCD.

Environment/Climate Change

The association between short-term wildfire smoke exposure and hospitalization among older adults with Alzheimer's disease and related dementias Vivian Do* Vivian Do Joan A. Casey Marianthi-Anna Kioumourtzoglou Marissa Childs Jennifer J. Manly Francesca Dominici

Under climate change, wildfire smoke exposure has increased nationally in the US. Wildfire smoke-related health effects may be worse for older adults (≥65 years) due to underlying physiology and pre-existing conditions. In particular, older adults living with Alzheimer's disease and related dementias (ADRD) may be at special risk as air pollution can trigger inflammatory responses in the brain and exacerbate other conditions. No studies have considered the impact of wildfire smoke on older adults with ADRD. We evaluated the relationship between wildfire fine particulate matter (PM2.5) and cause-specific hospitalizations among Medicare enrollees with ADRD and investigated possible effect modification by urbanicity. We identified 2,768,845 Medicare enrollees with an ADRD hospitalization between 2000-2016 and classified their zip code of residence as urban or rural based on Rural-Urban Commuting Area codes. We assigned exposure in the zip code of residence using 2006-2016 daily wildfire smoke PM2.5 predictions. We used a case-crossover design and distributed lag nonlinear models to estimate associations of wildfire PM2.5 and hospitalizations across 0-6 day lags. We observed null relationships for our main analyses but found effect modification by urbanicity. In rural zip codes, a 10g/m3 increase in wildfire smoke over a 7-day lag (lag0-lag6) was associated with an increased risk for respiratory hospitalizations (RR: 1.05, 95%CI: 1.00-1.10). In urban areas, we found a negative association for same day (lag0) depression-related hospitalizations (RR: 0.93, 95%CI: 0.88, 0.98). Adults living with ADRD, especially those in rural locations, may have elevated risk of hospitalization during wildfire smoke events. Wildfire smoke events may have also led to delayed care-seeking for mental health services among urban residents living with ADRD. Such findings are important for future strategies to protect population health in a changing climate.

Investigating the relationship between ambient temperature and reproductive hormonal changes among women attempting pregnancy Kaniz Rabeya* Kaniz Rabeya Neil J. Perkins Lindsey M. Russo Pauline Mendola Timothy P. Canty Karen C. Schliep Carrie J. Nobles

Background: High ambient temperatures have been associated with adverse reproductive and pregnancy outcomes, however, the role of hormones has been understudied. We investigated the association between ambient temperature and reproductive hormones among women trying to get pregnant.

Method: A prospective time-to-pregnancy study (EAGeR trial, 2006-2012) enrolled 1228 women from Buffalo, Scranton, Denver, and Salt Lake City. Daily temperature was collected from weather monitoring stations and averaged across an early-to-mid follicular phase window (1-10 days after menses) and ovulation window (11-16 days). Daily diaries and fertility monitors tracked timing of menstrual cycles and ovulation. Estrone-3-glucuronide, estradiol, follicle-stimulating hormone (FSH), luteinizing hormone (LH), progesterone, and pregnanediol glucuronide were measured in urine at ovulation and in the luteal phase (8 days after ovulation) in the first menstrual cycle. Generalized linear models estimated the association between temperature and hormones by warm (Apr. 1-Sept. 30) vs. cold (Oct. 1-Mar. 31) seasons adjusting for fine particulate matter and ozone.

Result: During the warm season, women exposed to 1°C higher ambient temperature in the early-to-mid follicular phase and ovulation windows had -0.03 (95% CI, -0.14, 0.08) ng/mL lower FSH and -0.12 (95% CI, -0.23, -0.01) ng/mL lower LH, respectively, at ovulation. Conversely, a 1°C increase of temperature in the cold season during the early-to-mid follicular phase and ovulation windows was associated with 0.15 (95% CI, 0.02, 0.28) ng/mL higher FSH and 0.12 (95% CI, 0.004, 0.24) ng/mL higher LH, respectively, at ovulation. Higher estradiol at ovulation was observed with higher temperatures in both seasons. Few associations were found during the luteal phase.

Conclusion: Both higher and lower temperatures were associated with lower FSH and LH at ovulation, suggesting hormones may be a sensitive pathway for impacts on reproductive health.

Perfluoroalkyl substances and childhood immunity to measles, mumps, rubella and varicella Jillian Ashley-Martin* Jillian Ashley-Martin Elizabeth McLachlan Clarissa Klenke Alberto Severini Susan MacPherson Yashika Handa Mandy Fisher Michael Borghese Robin Shutt Kavita Singh Joseph Braun Isabelle Boucoiran Michael Luster Victor Johnson Tye E Arbuckle Janice Hu

Perfluoroalkyl substances (PFAS), a class of persistent chemicals used in consumer products for their heat, water and stain repellant properties, have been associated with reduced responses to child vaccines. Existing studies have not focused on immunity to measles, mumps, rubella or varicella (MMRV) in young children. Our objective was to quantify associations between prenatal PFAS concentrations and levels of MMRV antibodies in preschool aged children.

Our study population was 402 singleton children enrolled in the Canadian Maternal-Infant Research on Environmental Chemicals study with complete PFAS and MMRV data. We measured second trimester plasma concentrations of 6 PFAS and serum concentrations of total MMRV IgG antibodies in MIREC children age 2-5. Using multivariable linear regression models adjusted for key covariates, we quantified the percent change in IgG levels for each doubling of prenatal PFAS concentrations. To account for vaccination status, we conducted a sensitivity analysis restricted to participants classified as seropositive.

The majority of children were seropositive to measles (94%), mumps (88%), and rubella (96%); fewer (35%) were seropositive to varicella. Median PFAS concentrations ranged from 0.15 to 4.3 μg/L. Perfluorodecanoic acid, perfluorononanoic acid and perfluorohexane sulfonate were associated with up to 50% higher rubella, mumps and measles IgG concentrations; these estimates were attenuated or null in seropositive models (Figure 1). Perfluorooctanoic acid was positively associated with higher rubella IgG concentrations in seropositive models (13% (95% CI: 2.8,23)) but not in the main analyses (11%, 95: CI: -33,39).

Prenatal PFAS were not associated with reduced child MMRV immunity in this population. Restriction to seropositive participants may mitigate some potential bias related to lack of vaccination history data. Future MIREC research will investigate lactational and concurrent childhood PFAS exposure in relation to MMRV.

Figure 1. Adjusted[1] percent change (95% CI) in serum MMRV IgG concentrations per doubling in prenatal plasma PFAS concentrations
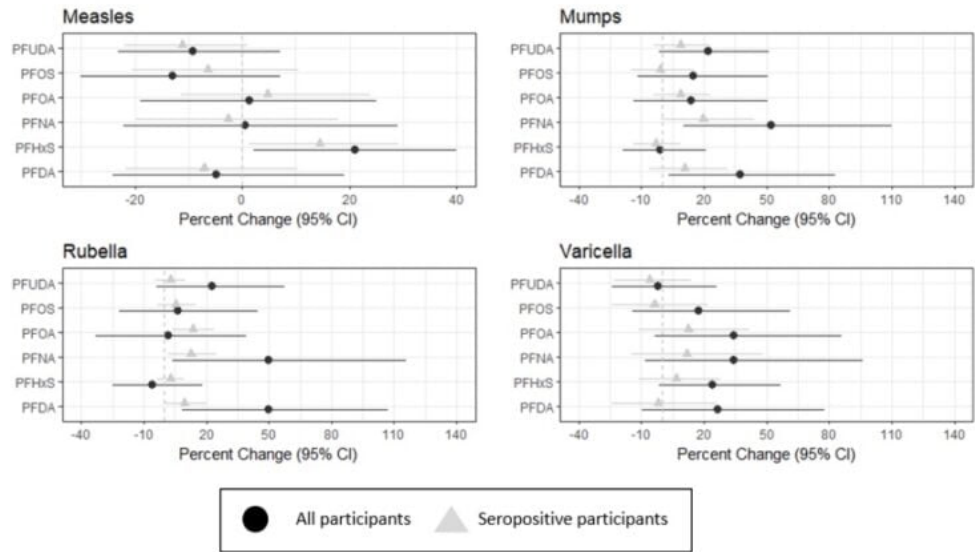
Abbreviations: MMRV measles, mumps, rubella, varicella; PFDA Perfluorodecanoic acid, PFHxS Perfluorohexane sulfonate, PFNA Perfluorononanoic acid, PFOS Perfluorooctane sulfonate, PFOA Perfluorooctanoic acid, PFUDA Perfluoroundecanoic acid; Beta coefficients from linear regression model were back-transformed to calculate % change per log2 unit increase in PFAS.
[1]adjusted for maternal age, parity, maternal education, maternal race, maternal smoking, pre-pregnancy body mass index, study site, and child age using complete case analysis. Vertical dashed line represents the null value. Sample size was 391 for all participants and between 133-364 for seropositive participants.

Neighborhood Socioeconomic Conditions and Disparities in Birth Weight: Investigating Mediation by Prenatal Exposure to Multiple Air Pollutants

Nan Ji* Nan Ji Erika Garcia Rima Habre Shohreh F. Farzan Theresa M. Bastain Carrie V. Breton

Background: Despite the strong evidence that prenatal air pollutant exposure is impacted by neighborhood socioeconomic (NSES) and associated with downstream birthweight (BW), the mediating role of prenatal exposure to multiple air pollutants in the NSES and BW relation has not been examined. Our study examined the mediation effect of multiple air pollutants during pregnancy in the association between NSES and BW. **Methods**: BW were abstracted from medical records for women participating in the Maternal and Developmental Risks from Environmental and Social Stressors (MADRES) study—a pregnancy cohort of predominantly low-income Hispanic/Latina women in Los Angeles. One-year averaged Child Opportunity Index overall and from the social and economic domain (COI and COI-SE) before pregnancy were obtained based on participant's residential address. Primary mediators were pregnancy-averaged concentrations of 10 air pollutants. Mediation effects of these pollutants were examined using a regression-based approach (cmest R package) and adjusting for potential confounders (N = 702). **Results**: Compared to those exposed to the lowest quartile, women exposed to the 4th quartile of COI and COI-SE had heavier babies at birth, with increased BW of 41.9 grams (g ; 95%CI: -5.8 g, 89.6 g) and 34.4 g (-11.4 g, 80.2 g), respectively. Nitrogen dioxides (NO_2) exposure during pregnancy was found to mediate 10.0 g (0.1 g, 19.9 g) and 8.5 g (0.1 g, 16.9 g) of the observed NSES-BW association. **Conclusions**: Women living in high-opportunity neighborhoods (high COI and COI-SE) before pregnancy delivered infants with higher BW. These positive associations were partially mediated by NO_2 exposure during pregnancy. Our next steps include (1) using structural equations modeling to assess the mediation effect of trimester-specific air pollutants; (2) using dimension-reduction approaches to assess the mediation effect of air pollutant mixtures.
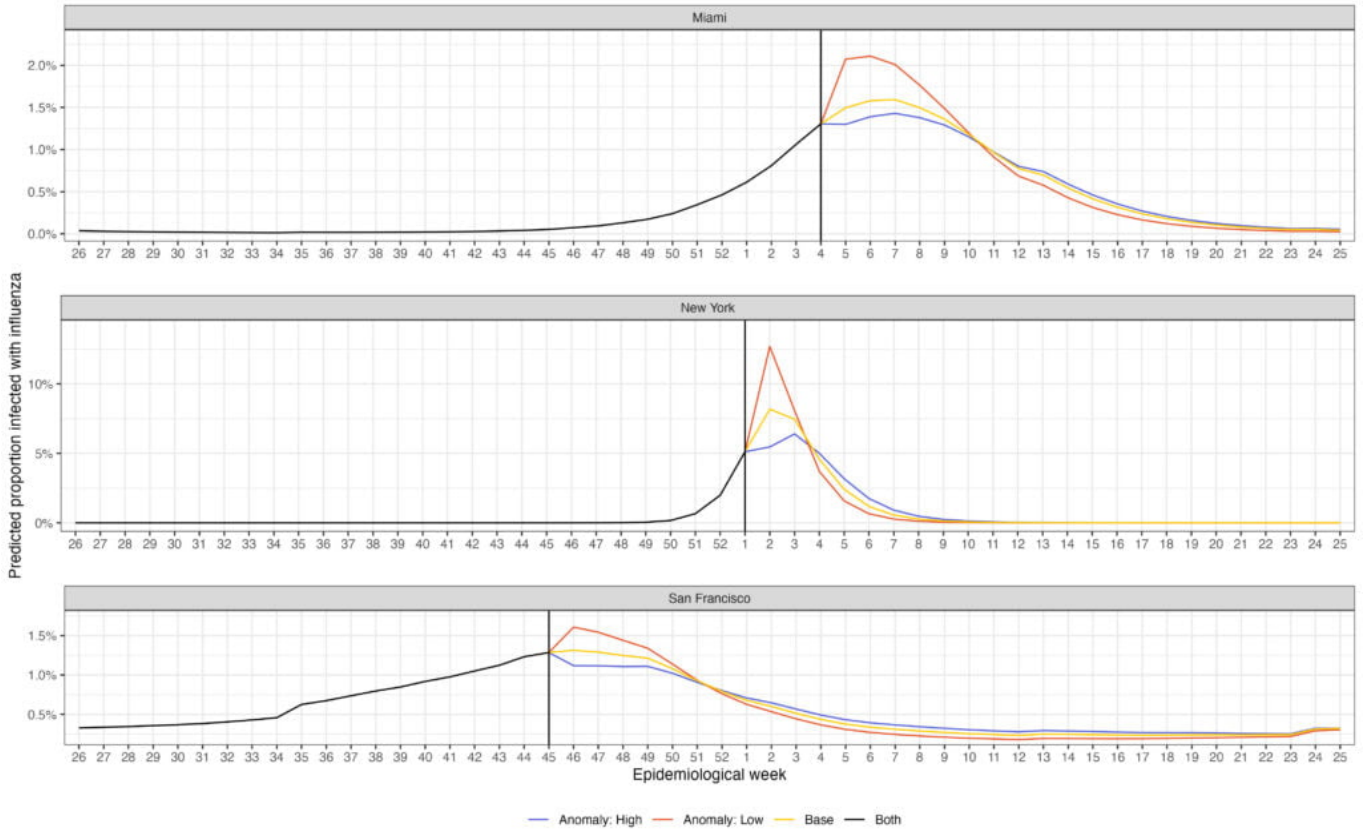
Environment/Climate Change
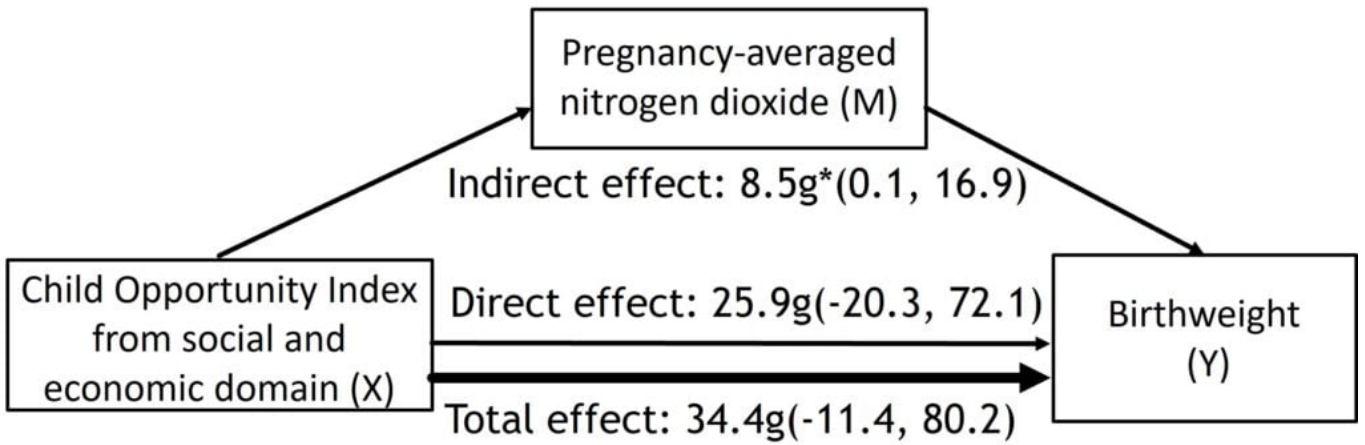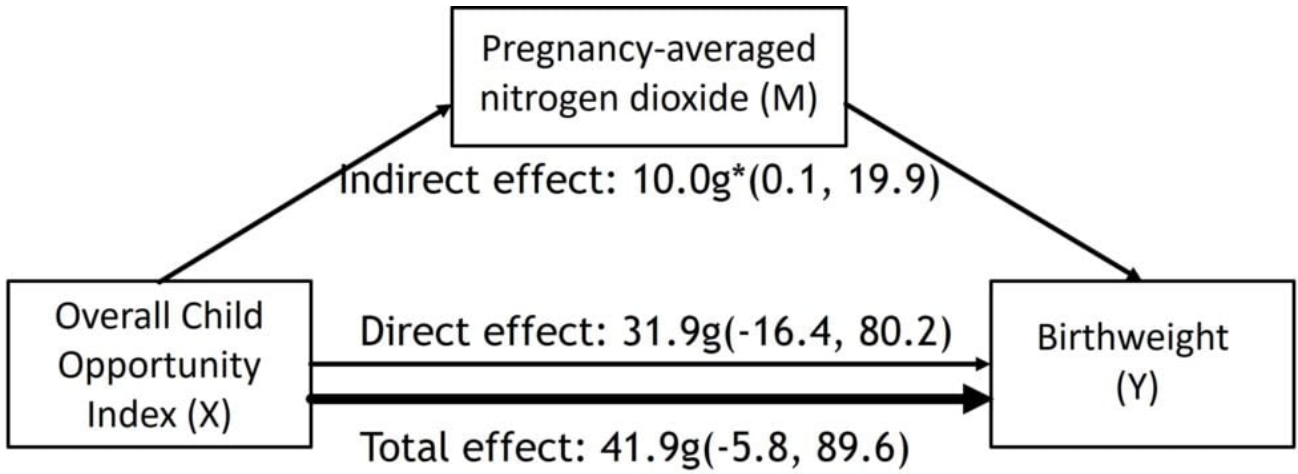
Impact of climate variability on projected influenza outbreaks Aleksandra Stamper*
Aleksandra Stamper Rachel Baker

Wintertime influenza epidemics consistently account for substantial morbidity and mortality in temperate regions around the globe. The timing of an influenza outbreak is closely tied to seasonality, with epidemics occurring during the winter months in temperate areas. These regions typically experience lower absolute humidity (AH) of the ambient air during winter, creating conditions that previous studies demonstrate to enhance influenza virus survival and transmission. Climate change is expected to alter patterns of extreme weather events, including AH and temperature; however, it remains uncertain how these extremes could affect the timing and severity of the seasonal influenza outbreak. Here, we used a mechanistic epidemiological influenza model, fitted to observational data, to examine the impact of weather extremes on the influenza season.

We adapted the Susceptible-Infected-Recovered model and applied it to Miami, New York, and San Francisco. The model for each location was calibrated using historical weekly influenza incidence and AH data, with the relationship between AH and transmission based on prior experimental data. By introducing a single week of unusually high or low humidity (1st and 99th percentile) at different times during the influenza season, we calculated the projected differences in peak size, timing, and overall magnitude of the anomalous model compared to the base model.

Our findings, presented in the figure, indicate that while abnormally low AH during winter may starkly increase the influenza peak (a projected increase of 18.3% to 35.6% in the proportion of infected individuals), anomalously high wintertime AH may result in a lower peak of infected individuals but a prolonged outbreak period. The framework developed here provides insights into the potential impacts of extreme climate variables on influenza outbreaks, informing public health preparedness and guiding the development of effective mitigation strategies for future epidemics.

Association between fine particulate matter (PM2.5) and severity of acute respiratory infections among young US children in the major cities in the United States: a claims-based cohort study Damien Foo* Damien Foo Annette K. Regan Seulkee Heo Eric B. Schneider Joseph Canner Michelle L. Bell

Background: Acute respiratory infections (ARIs) are a leading cause of morbidity and mortality among young children. Air pollution may play a role in the exacerbation of ARIs via inflammation, immunosuppression, and oxidative stress, yet this effect has been infrequently evaluated among young children.

Objectives: To evaluate the impact of short-term exposure to fine particulate matter (PM2.5) to ARI severity among children aged <5 years.

Methods: We analyzed data from a claims-based cohort of US children aged <5 years enrolled in a private health insurance plan who were diagnosed with an ARI between January 2018 and March 2020. We use daily monitored PM2.5 concentrations at the metropolitan statistical area level to estimate the short-term weekly exposure to PM2.5. We evaluated the association between short-term exposure to PM2.5 and the risk of hospital admissions and readmissions with an ARI, intensive care unit (ICU) admission, mechanical ventilation, prescription claim for antiviral medication, and length of stay using generalized linear models adjusting for individual-, ecological-, and community-level covariates.

Results: Of the 598,164 unique ARI episodes, we observed 3,511 antiviral prescription claims, 5,081 hospital admissions, 1,486 ICU admissions, 129 mechanical ventilations, and 61 hospital readmissions. The risk of an antiviral prescription claim increased by 11% (95% confidence interval [CI]: 1.07,1.15) per interquartile range increase in exposure to PM2.5 (3.37 μg/m3); this association was consistent irrespective of age group or influenza vaccination status. We observed a 6% and 11% increased risk of ICU admission (95% CI: 1.01, 1.10) and mechanical ventilation (95% CI: 1.06, 1.18), respectively, among children not vaccinated against influenza and no increase among vaccinated children.

Discussion: Short-term exposure to PM2.5 may contribute to ARI severity among young children. Influenza vaccination may modify the risk of severe ARI-associated outcomes.

Sleep Health among Communities Placed at Risk of Climate Change-Related Disaster

Chandra L. Jackson* Symielle A. Gaston Kaitlyn Lawrence Steve B. Ampah W. Braxton Jackson II Marina R. Sweeney Casey Zuzak Melanie Gall Christopher Emrich Dale P. Sandler Chandra L. Jackson

Climate change-related disasters resulting from natural hazards (e.g., hurricanes) can disrupt sleep environments, negatively impact sleep, and potentially exacerbate sleep disparities. However, data are sparse. To investigate sleep health among communities at risk of natural hazards, overall and by race/ethnicity and gender, we used data from the US Gulf Long-term Follow-up Study. Geocoded residential addresses at enrollment were linked to census tract-level National Risk Index (NRI) percentile data, which quantifies and ranks the risk of negative impacts of natural hazards (e.g., heat waves) in an area compared to other geographical areas in the US. Multiple sleep dimensions self-reported in 2017-2021 included short workday and non-workday sleep duration (<7 hours); insomnia symptoms; excessive sleepiness; Pittsburgh Sleep Quality Index scores for sleep disturbances, sleep medication use, and daytime dysfunction; sleep disordered breathing; and healthcare provider-diagnosed sleep apnea. We determined PRs using modified Poisson regression or mean differences and 95% CIs between NRI quartiles (Q4-Q2 vs. Q1 [lowest risk]) and each sleep dimension, adjusting for sociodemographic, health, and environmental exposure characteristics. We tested interaction terms by race/ethnicity and gender. Among 9,534 adults (mean age±SD of 44±13 years; 81% men, 69% White, 19% Black, 12% another race/ethnicity), participants in NRI Q4 vs. Q1 had a higher prevalence of short non-workday sleep duration (PR=1.21 [95% CI:1.02-1.44]) and insomnia symptoms (PR=1.19 [1.09-1.31]) as well as higher sleep medication use and daytime dysfunction. A non-monotonic association between NRI Q2 vs. Q1 and a higher prevalence of sleep apnea occurred only among participants identifying as another race/ethnicity than White or Black (PR=1.52 [1.02-2.24]; p-interaction=0.02). NRI was not associated with other sleep dimensions. Higher climate-related disaster vulnerability was associated with poorer sleep.
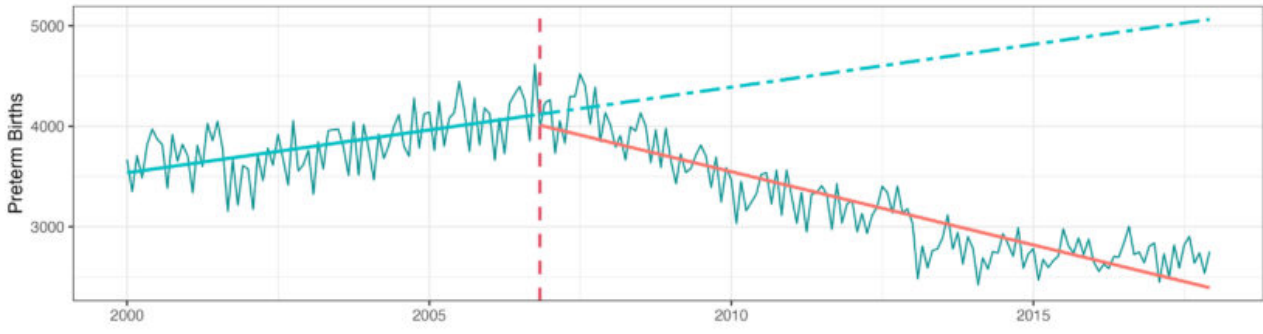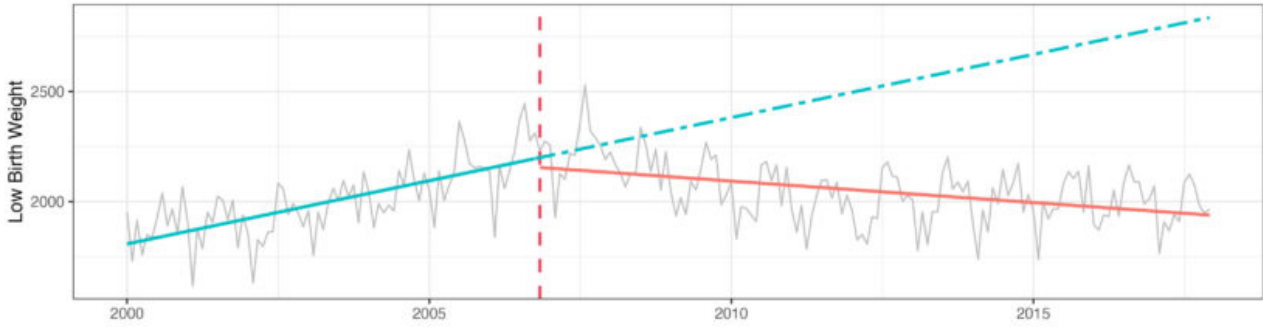
LATEBREAKER

Environment/Climate Change

National regulatory change in drinking water arsenic standards and adverse birth outcomes in the state of California, 2000-2017 Ilan Cerna-Turoff* Ilan Cerna-Turoff Madison Stoms Robbie M. Parks Joan A. Casey Julie Herbstman Anne E. Nigra

The 2006 US Environmental Protection Agency's Final Arsenic Rule (FAR) reduced federal public water arsenic regulatory standards from 50 to 10 µg/L. We examined adverse birth outcomes plausibly associate with arsenic in drinking water (preterm, low birthweight, very low birthweight, and small-for-gestational-age births) and estimated the number averted in California from the FAR implementation. We analyzed electronic birth records from January 1, 2000 to December 31, 2017 (N=9,429,344) and assigned ZIP Code water arsenic concentrations to birth parent residential addresses. We applied an interrupted time series design, with November 1, 2006 as the intervention (~nine months after FAR implementation for gestation length). We used seasonal autoregressive integrated moving average (SARIMA) models to evaluate the difference between observed trends and hypothesized linear slope increases. We stratified analyses by child sex and birth parent's Hispanic ethnicity, race, ability to pay for prenatal care—a proxy for socioeconomic status—and education level. Sensitivity analyses further estimated adverse births among birth parents who resided in ZIP Codes that reduced water arsenic below 5, 2, and 1 µg/L. We estimated California-wide monthly reductions in preterm births (-21.7, 95% CI -10.2, -33.2), low birth weight (-13.0, 95% CI -6.8, -19.3), and small-for-gestational age births (-22.6, 95% CI -12.3, -32.8). Overall, we estimated the largest effects in infants with birth parents who were Hispanic, white, or had low socioeconomic status. Reductions in preterm births were observed for ZIP Codes that reduced water arsenic below 1 and 2 µg/L. The FAR was associated with reductions in adverse birth outcomes in California (~9888 total from 2006-2017). Greater declines in areas that reduced water arsenic below 1 and 2 µg/L suggests more preterm births may be averted with lower regulatory standards. Federal water regulations are a tool in advancing environmental justice.
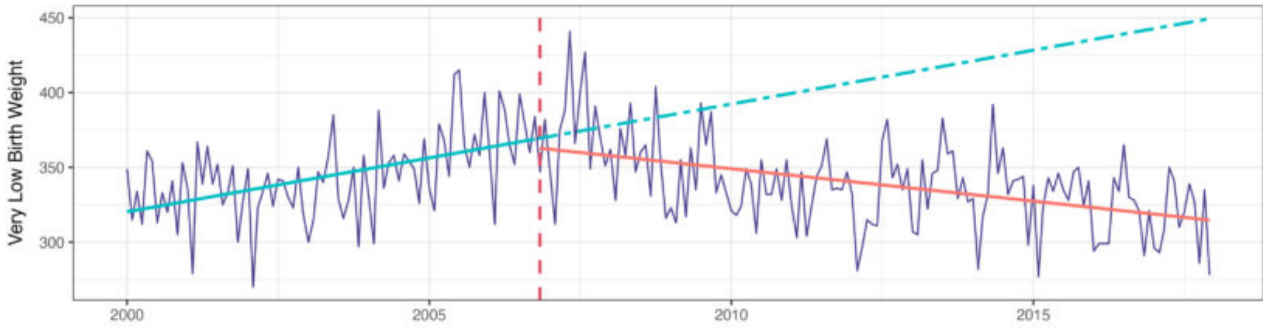
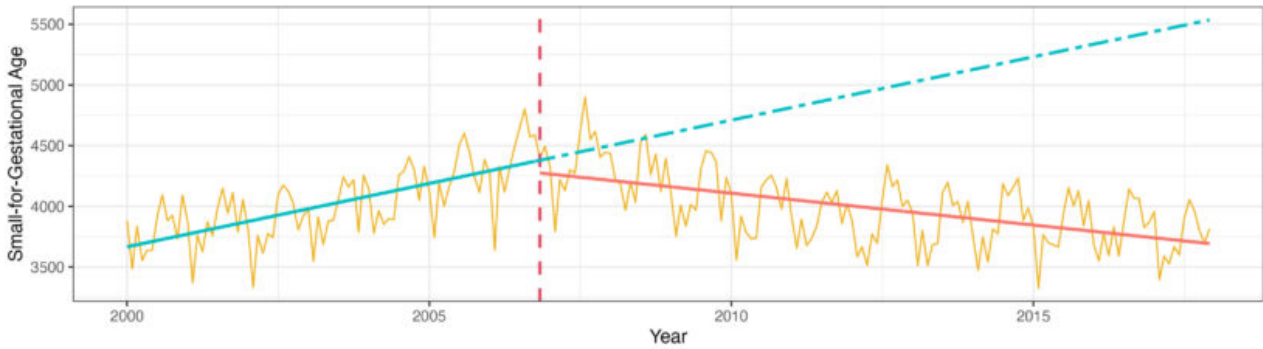Monthly Adverse Birth Outcomes in California from 2000 to 2017, Contrasted with Hypothesized Linear Increases

LATEBREAKER

Environment/Climate Change

Neighborhood features related to child physical activity, sleep, and mental health during the COVID-19 pandemic: Results from the All Our Families Study Tona Pitt* Tona Pitt Gavin McCormack Maria Ospina Suzanne Tough Sheila McDonald

During the COVID-19 pandemic, governments implemented public health measures to reduce disease transmission by restricting individuals to homes and area. As well, incidence of mental health issues increased among children. Since activities were restricted to neighborhoods, features of the neighborhood (i.e., greenspace, walkability) may have contributed to protecting child mental health by promoting healthy behaviors like physical activity and sleep.

This study aims to describe urban form features associated with health behaviors and mental health symptoms during the COVID-19 pandemic.

This study will use data from the All Our Families Cohort (Calgary, Canada). A subsample of this pregnancy cohort participated in three surveys on pandemic experiences (May 2020, March 2021, and November 2021) and a child development survey completed in August 2023.

Descriptive statistics of health behaviors and mental health symptoms will be calculated over those four surveys. As well, we will compare neighborhood features for children who did and did not experience clinically relevant mental health symptoms, who did and did not accumulate recommended levels of physical activity and who did and did not accumulate levels of sleep recommended by the Canadian Paediatric Society.

At the first COVID-19 survey (n=893), 42.0% of children met the recommended guidelines for physical activity. At the third survey (n=1,021), this percentage reduced to 19.4%. The prevalence of clinically significant mental health symptoms among children increased over time. Initially, 5.8%, 5.2%, 2.3%, and 3.7% of children displayed symptoms indicative of anxiety, depression, hyperactivity, and inattention, respectively. By the third survey, these numbers increased to 9.6% for anxiety, 9.9% for depression, 4.4% for hyperactivity, and 8.4% for inattention.

As we have just recently received these data, next steps will describe the neighborhood features for children by health behaviors and symptoms over the pandemic.

Tree canopy, socioeconomic status, and cardiovascular disease in Durham County, North Carolina: A descriptive study using census tracts Sophie Ravanbakht* Sophie Ravanbakht Emily D'agostino Christine Gray

Cardiovascular disease (CVD) is the leading cause of death in the U.S., and the prevalence of diseases and related comorbidities such as stroke and high blood pressure are especially high in the American South. Disparities in access to care and community amenities make poor outcomes sharper in communities of color and lower-income communities. Climate change is increasingly understood to be exacerbating both poor CVD outcomes, and CVD disparities. Land features such as tree canopy may help protect against poor CVD outcomes. The Durham Neighborhood Compass (DNC) is a community resource designed to democratize data and enable local community assessment. We linked census tract data on tree canopy coverage (TCC) in 2016 and race/ethnicity and median income in 2021 from the DNC to census tract prevalence of stroke and high blood pressure from the CDC's 500 cities 2022 data. Our goal was to explore CVD, race/ethnicity, and income as related to TCC in Durham, North Carolina. We defined high TCC as >=43% and low TCC as <43% based on a natural threshold in the distribution across tracts. Mean race/ethnicity population in tracts with high TCC was 46% White, 12% Hispanic, and 31% Black, and in tracts with low TCC was 37% White, 17% Hispanic, and 41% Black. We found median income in high TCC tracts was $73,772 and in low TCC tracts was $49,570. These preliminary results suggest no difference in CVD among high vs low TCC; however, tracts with higher percentage minoritized populations and lower income have much lower TCC. As more data are available, future analyses should consider more granular levels of geography, change over time, and modification by race/ethnicity and income.

Environment/Climate Change

Quantifying extreme rainfall events as health-related exposures in HIV care populations: an analysis using precipitation and flood data at 382 sub-Saharan Africa HIV clinics in 20 countries, from 1981-2022 Avantika Srivastava* Avantika Srivastava

Extreme weather events (EWE) can disrupt access to HIV care and related services and shift patient priorities, but little is known of how EWEs shape HIV care engagement and treatment outcomes. Understanding these associations can help elucidate how climate change impacts HIV care utilization and outcomes now and in future decades. With this in mind, we developed measures for EWE exposures using events captured in global precipitation and flood databases.

We integrated high spatiotemporal resolution rainfall and flood data with HIV clinic data from 1981-2022 for 382 clinics across 20 countries in sub-Saharan Africa (SSA). Variables were developed based on gridded daily precipitation, available at 0.05° spatial resolution from Climate Hazards InfraRed Precipitation with Station data (CHIRPS) that combine satellite imagery with weather station data, and on the Global Active Archive of Large Flood Events (GALFE), which uses government reports, news, and remote sensing to capture timing and characteristics of large flood events.1,2 Exposures were defined as days with: flood events, precipitation over site-specific thresholds of the top percentile of historical 10-day rolling averages, and precipitation over 50mm.

From 1981-2022, there were 2,366 periods (62,460 days) of flood-based extreme wet weather, averaging 26.4 days. Floods increased in frequency and duration, with 58 events averaging 5.4 days from 1990-1994 and 267 events averaging 12.9 days from 2015-2019. CHIRPS covered 13,377 EWEs (57,551 days), with 1,281 EWEs (4,759 days) from 1990-1994 and 1,899 EWEs (8,136 days) from 2015-2019. EWEs increased in intensity, with mean total precipitation of 69.6mm from 1990-1994 and 83.7 from 2015-2019.

Extreme wet weather burden at SSA HIV clinics is substantial and has steadily increased in frequency, duration, and intensity. Assessing EWE exposure impact on short- and long-term HIV care outcomes is an important next step to inform climate change adaptation strategies.

Environment/Climate Change

Prenatal Ambient Air Pollutant and Climatic Factors Mixture Exposure and Fetal Growth

Stefania Papatheodorou* Stefania Papatheodorou Katie Senechal Michael Leung Anna Modest Michele Hacker Antonella Zanobetti

Introduction: Research linking prenatal ambient air pollution and climatic factors with fetal growth has largely considered one factor at a time. Real-life exposure involves exposure to mixtures of pollutants and climatic factors; not considering joint effects/effect modification by co-exposures contributes to misleading results.

Methods: We used ultrasound measures of biparietal diameter (BPD), head circumference, femur length, and abdominal circumference (AC), in addition to birth weight, from 9,446 pregnancies that were delivered at the Beth Israel Deaconess Medical Center from 2011-2016. Weekly prenatal pollutant exposures were estimated using satellite-based hybrid chemical-transport models, including nitrogen dioxide (NO_2), ozone(O_3), particulate matter ($PM_{2.5}$), and high-resolution data for temperature and relative humidity. We examined associations between weekly-averaged prenatal pollution mixture levels and outcomes using Bayesian Kernel Machine Regression-Distributed Lag Models (BKMR-DLMs) to identify susceptibility windows for each component and estimate a potentially complex mixture exposure-response relationship including nonlinear effects and interactions. We adjusted for sociodemographic and clinical characteristics, seasonal and long-term trends, and area-level factors.

Results: BKMR-DLMs identified the stronger effect for temperature at early gestation predicting lower BPD in mid-pregnancy (up to -0.10 z-score (95% CI -0.16 to -0.04) at 16 to 23 weeks). There was a negative association between birthweight z-scores and exposure to mixtures of air pollutants, where up to -0.18 (95% CI -0.23 to -0.13) or approximately 88 g decrease in birthweight, comparing the 75th percentile to the median level of exposure to the air pollutant mixture could occur. There was evidence for interactions between O_3, PM2 5, and temperature.

Conclusion: In this multi-pollutant model, we identified a strong association between exposure to higher temperature in early pregnancy and mid-pregnancy fetal brain measurements and a strong association between air pollutants and birthweight.
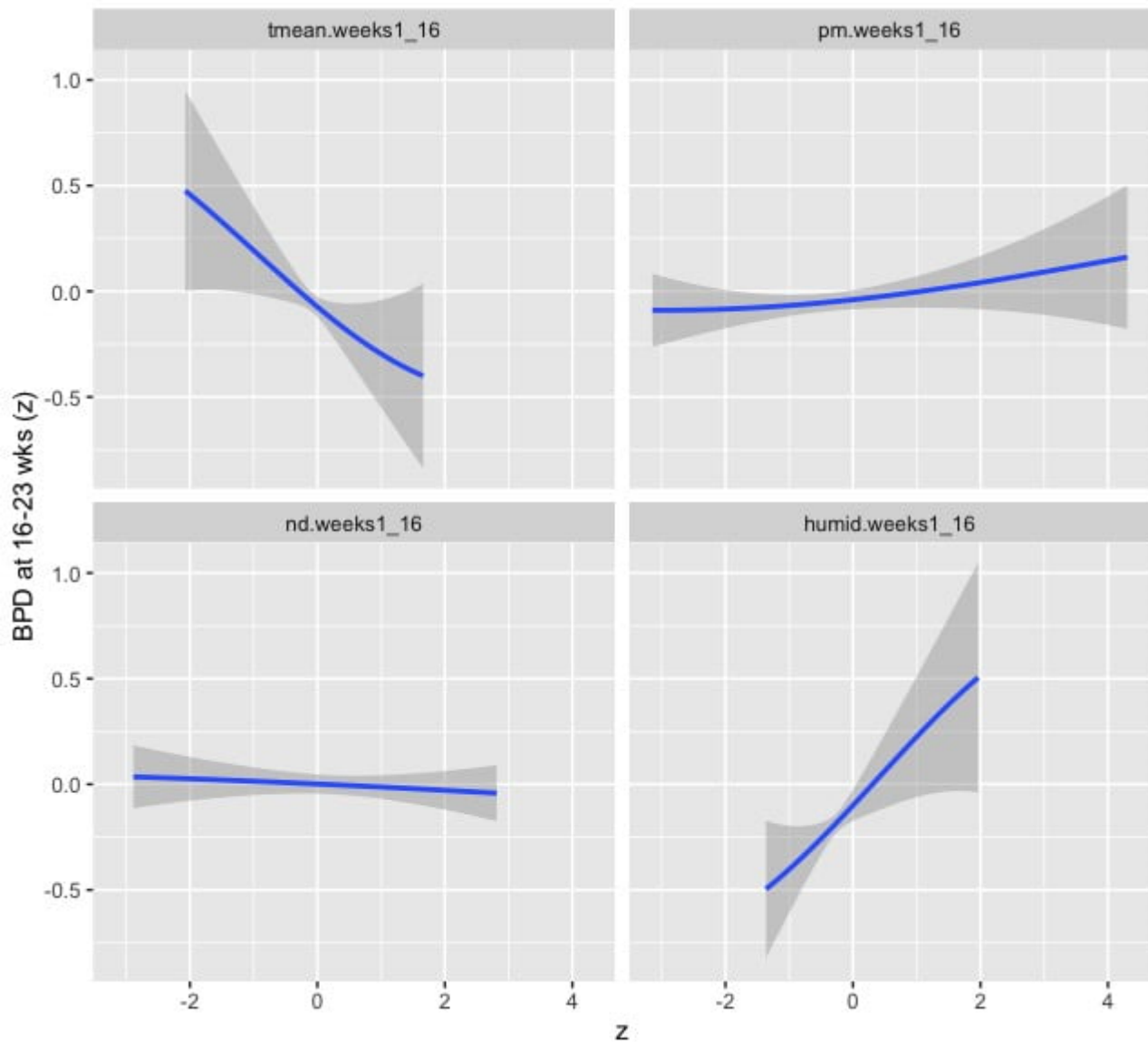
Extreme Heat Temperature and Hospital Admission among Older Adults in Greater Boston Metropolitan Areas. Youn Soo Jung* Youn Soo Jung Antonella Zanobetti Kari Nadeau Scott Delaney Daniel Mork Michelle Audirac Danielle Braun

Abstract

Importance Extreme heat (EH), a consequence of climate change, is a leading cause of weather-related fatalities in the United States. In Massachusetts, the average temperature has increased by nearly 3.5°F. Moreover, EH disproportionately affects different communities, which can exacerbate existing social inequities.

Objective: To identify the risk of heat-related hospitalizations due to EH events in each community of Greater Boston Metropolitan areas and how this differed by individual and neighborhood characteristics.

Design, Setting, and Population Using Medicare data (2000-2016), we constructed cohorts of individuals hospitalized with heat related illness during summer (May-September). EH day was defined as a day with a heat index over the 90th percentile, and Heatwave periods were defined as two or more consecutive days that had EH. We applied a case-crossover design to estimate city-specific associations between EH and heat-related hospitalizations by in the Greater Boston areas. Interaction terms between exposure and individual (>84 years, dual eligibility, sex, race (non-Hispanic white, non-Hispanic black, and others)) and residential ZIP-code (green space, percentage of population without high school degree, of below poverty line and of Black population) characteristics were included in the model for effect modification analyses. We pooled city-specific results using a random effects meta-analysis.

Results Heat-related admissions increased by 13.5% (95% confidence interval (CI) 7.8 – 19.5%) during the EH day and 16.9% (95% CI 11.4-22.7%) during the Heatwave. Associations were stronger in males, age group between 65-84 years and in zip codes with higher percentage of black population.

Conclusions Our data suggests that the risk of heat-related hospitalizations may be influenced by individual and neighborhood characteristics.

A Metaphor for Epidemiology: Return to the Sea of Person Time Douglas Weed* Douglas Weed

Metaphors are an essential if underappreciated part of epidemiology's conceptual foundation and everyday practice. The web of causation, weight of evidence, and gold standard are familiar examples. Less familiar but no less relevant is the metaphor of the sea of person time. Introduced to epidemiology in 1982 in a paper explaining the notion of incidence density, the sea of person time (or population time as it first appeared) illustrated how disease events in 2-dimensional space and time formed the numerator of the incidence measure. The y-axis represented the population; the x-axis was time. As a metaphor, the sea of person time expands to its full 3-dimensional significance. We epidemiologists are travelers on this "sea" in our method-laden boats as we seek explanations for the disease events that we "catch" in our fishing expeditions. At the same time, we exist as denizens of the population—we live in this "sea"—and we are at risk for the same diseases. The sea of person time represents this fundamental duality of our practice and our human existence. In this paper, a traveler on the sea of person time seeks to cross it and discover what lies on its distant shore. The form is an epic lyric poem with hand-drawn illustrations. The traveler has many adventures along the way. He witnesses storms on the turbulent sea, a loss of navigation, the death of his guide, and an appreciation of his own mortality.

Genetics

Relationship between Genetically Determined LDL-Cholesterol and Stroke: A Prospective Cohort Study Sun Ha Jee* Sun Ha Jee Sunmi lee

Background: Conventional epidemiologic studies have reported a significant association between low LDL cholesterol and the risk of hemorrhagic stroke. This association has even been incorporated into predictive models for hemorrhagic stroke. This study aims to analyze the relationship between genetically determined LDL-cholesterol and stroke through a prospective cohort.

Methods: Data from the Korean Cancer Prevention Study-II were used, with a total of 159,844 participants. These individuals underwent health check-ups at 18 screening centers in Korea from 2004 to 2013 and provided written consent for participation. The participants were linked to the National Health Insurance Service's hospitalization records to confirm stroke occurrences until 2021. Among them, 139,877 participants (86,874 males) underwent GSA and K-chip testing, and the data from both chips were combined and analyzed after imputation using 1000 Genomes and impute 5. Genetically determined LDL-c was created by extracting SNPs with a GWAS analysis of LDL and calculating a weighted genetic score. Cholesterol levels were divided into quintiles, and their association was analyzed using Cox proportional hazard ratios.

Results: The mean age of the participants was 41.0 years (41.7 years for males), and over a mean follow-up period of 13 years, 3,883 cases of ischemic heart disease (IHD) and 2,662 cases of stroke occurred. Ischemic stroke accounted for 1,213 cases, and hemorrhagic stroke for 525 cases. Overall, the risk of IHD was significantly increased in the highest LDL-c quintile (Q5) compared to the lowest quintile (Q1) in both conventional epidemiologic study (HR=1.58, 95%CI=1.42-1.77) and genetic epidemiologic study (HR=1.26, 95%CI=1.14-1.40). However, the risk of hemorrhagic stroke showed a different pattern. According to conventional epidemiology, the highest LDL-c quintile (Q5) was significantly associated with a lower risk of hemorrhagic stroke compared to other ranges (HR=0.74, 95%CI=0.57-0.96). However, the relationship between genetically determined LDL-cholesterol and stroke was not significant.

Conclusion: Low genetically determined LDL-cholesterol did not increase the risk of stroke. The previously reported association between low cholesterol and hemorrhagic stroke in conventional epidemiologic studies is considered biased due to confounding variables or reverse causation.

Genetics

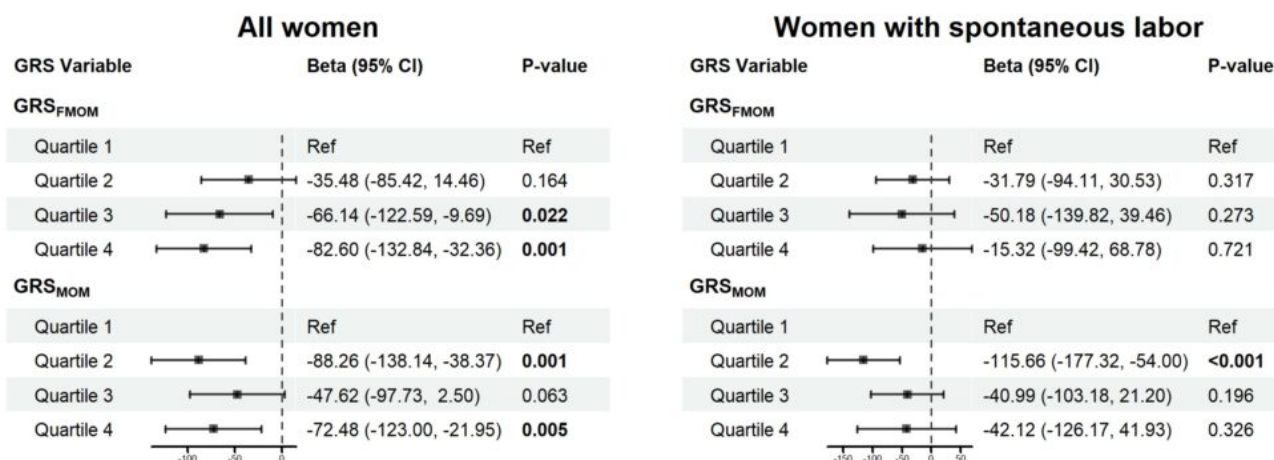**Polygenic effect of gestational duration reducing maternal variants on birth weight in an ancestrally diverse cohort** Tesfa Dejenie Habtewold* Tesfa Dejenie Habtewold Prabhavi Wijesiriwardhana Richard J. Biedrzycki Fasil Tekola-Ayele

Introduction: The maternal genome influences gestational duration and birth weight. However, whether genetic variants that control gestational duration influence birth weight is unclear. This study aimed to investigate the impact of gestational duration-reducing variants on birth weight in 2,056 ancestrally diverse pregnant women from the NICHD Fetal Growth Studies – Singletons cohort.

Methods: Genetic risk score (GRS) was calculated using 20 maternal variants associated with gestational duration irrespective of their effect through fetal genome (GRSFMOM) and a subset of 14 variants with maternal-only effect (GRSMOM) based on the latest genome-wide association study in Europeans. The association between GRSs and birth weight (in grams, g) was tested using linear regression analyses adjusted for fetal sex, gestational age, maternal sociodemographic factors, and the top five genomic principal components. Sensitivity analysis was performed in women with spontaneous onset of labor.

Results: The third and fourth GRSFMOM quartiles were significantly associated with 66.1 g (95% CI=-122.6, -9.7, p=0.022) and 82.6 g (95% CI=-132.8, -32.4, p=0.001) lower birth weight compared to the first quartile, respectively. The association was attenuated among women with spontaneous onset of labor. The second and fourth GRSMOM quartiles were significantly associated with 88.3 g (95% CI=-138.1, -38.4, p=0.001) and 72.5 g (95% CI=-123.0, -21.9, p=0.005) lower birth weight, respectively. Among women with spontaneous onset of labor, the second GRSMOM quartile was significantly associated with a 115.7 g (95% CI=-177.3, -54.0, p < 0.001) lower birth weight.

Conclusions: Among ancestrally diverse pregnant women, the polygenic effect of European-derived maternal genetic variants that shorten gestational duration also lowered birth weight. The findings do not support the hypothesis that fetuses with a maternal genetic predisposition to shorter gestation grow faster.

All women

GRS Variable	Beta (95% CI)	P-value
GRS_FMOM		
Quartile 1	Ref	Ref
Quartile 2	-35.48 (-85.42, 14.46)	0.164
Quartile 3	-66.14 (-122.59, -9.69)	**0.022**
Quartile 4	-82.60 (-132.84, -32.36)	**0.001**
GRS_MOM		
Quartile 1	Ref	Ref
Quartile 2	-88.26 (-138.14, -38.37)	**0.001**
Quartile 3	-47.62 (-97.73, 2.50)	0.063
Quartile 4	-72.48 (-123.00, -21.95)	**0.005**

Women with spontaneous labor

GRS Variable	Beta (95% CI)	P-value
GRS_FMOM		
Quartile 1	Ref	Ref
Quartile 2	-31.79 (-94.11, 30.53)	0.317
Quartile 3	-50.18 (-139.82, 39.46)	0.273
Quartile 4	-15.32 (-99.42, 68.78)	0.721
GRS_MOM		
Quartile 1	Ref	Ref
Quartile 2	-115.66 (-177.32, -54.00)	**<0.001**
Quartile 3	-40.99 (-103.18, 21.20)	0.196
Quartile 4	-42.12 (-126.17, 41.93)	0.326

Effects of small-quantity lipid-based nutrient supplements (SQ-LNSs) on early childhood growth trajectories compared to micronutrient powders (MNPs) Solis Winters* Solis Winters Lia Fernald

Background: Small-quantity lipid-based nutrient supplements (SQ-LNSs) show great potential to prevent stunting and wasting for children under two years old; however, large variability in study results suggests the need for a more nuanced understanding of when supplementation may be most impactful during infancy and childhood. The primary goal of this study is to evaluate the impact of SQ-LNSs compared to MNPs on characteristics of length and weight growth trajectories.

Methods: In 76 communities in Baja Verapaz, Guatemala, 1720 households with pregnant women or children under 4.5 months old were randomly assigned to usual care (micronutrient powders (MNPs); n=760), treatment 1 (SQ-LNSs plus nutrition education; n=546), or treatment 2 (MNPs plus a nutrition education intervention; n=414). Using a subset of longitudinal anthropometric data collected for children 6-36 months old in treatment households, we constructed SuperImposition by Translation and Rotation (SITAR) length and weight trajectory models, which estimate a child's deviation from the sample average growth curve across three dimensions – size, timing, and velocity. The intent-to-treat effects of SQ-LNSs vs MNPs on these trajectory characteristics were estimated for boys and girls separately.

Results: SITAR models, including 4737 measurements for 736 children (T1: n=420, T2: n=316), explained 90% and 88% of the variance in length of boys and girls, respectively, and 88% and 89% of the variance in weight. We found no evidence that there was a main effect of SQ-LNSs on any dimension of length or weight trajectories relative to MNPs. We are continuing to explore heterogeneity of effects by child age, sex, and baseline nutritional status, as well as by household size, income, and maternal education.

Conclusions: These findings suggest that supplementation with SQ-LNSs to children 6-24 months old in Guatemala provides no additional benefit on growth relative to MNPs, which is the current standard of care. While many existing studies compare SQ-LNSs to no supplementation, our study adds to the limited evidence comparing SQ-LNSs to MNPs. More research is needed to understand when and for which subpopulations SQ-LNSs are most cost-effective compared to MNPs.

Global Health

Seasonality of underweight among children 1-11 months old in Niger: a population-based analysis of repeated cross-sectional data from a cluster-randomized trial Brittany Peterson*

Brittany Peterson Ahmed M. Arzika, MPH Abdou Amza, MD Ramatou Maliki, MSc Bawa Aichatou, BSc Ismael Mamane Bello, MSc Diallo Beidi, BSc Nasser Galo, MD Elodie Lebas, RN Catherine E. Oldenburg, ScD, MPH Travis C. Porco, PhD Benjamin F. Arnold, PhD, MPH Thomas M. Lietman, MD Kieran S. O'Brien, PhD, MPH

Malnutrition in children is a risk factor for mortality, and around 45% of deaths of children under 5 globally are linked to malnutrition. Niger has strong seasonal patterns in rainfall, which influences infectious disease transmission and food security. Studies on the seasonal effects of weight show that nutritional status may fluctuate by season related to factors such as rainfall, food insecurity, and time of harvests. This analysis used data from the cluster-randomized AVENIR trial which compared the effect of biannual distribution of azithromycin versus placebo on mortality in children 1-59 months old. A subset of 133,781 children aged 1-11 months were included in the analysis, and weight-for-age z-score (WAZ) was assessed every 6 months over 2 years in a population-based census. We pooled time of measurement data to four seasons: dry, pre-rainy, rainy, and post-rainy, and used season and months since harvest as the exposures. Linear regression was used to estimate the cluster-level mean difference in WAZ by season using the dry season as a reference with mean difference, P-values, and 95% confidence interval reported. Linear regression was also used to determine the cluster-level mean change in WAZ by months since the last harvest. Compared to the dry season, the post-rainy season had the largest change in WAZ with a -0.11 reduction (95% CI -0.15 to -0.07, P-value <0.001). WAZ was also lower during the pre-rainy season, -0.07 (95% CI -0.11 to -0.03, P-value <0.001), and during the rainy season, -0.07 (95% CI -0.12 to -0.02, P-value 0.003). WAZ increased substantially 3 months after the harvest by +0.39 (95% CI 0.26 to 0.53, P-value <0.001). Given the mortality risk associated with low weight, the seasonality of WAZ young children in this setting may have implications for the timing of child survival and malnutrition programs and results of this study can be used to guide the timing of future programs.

Global Health
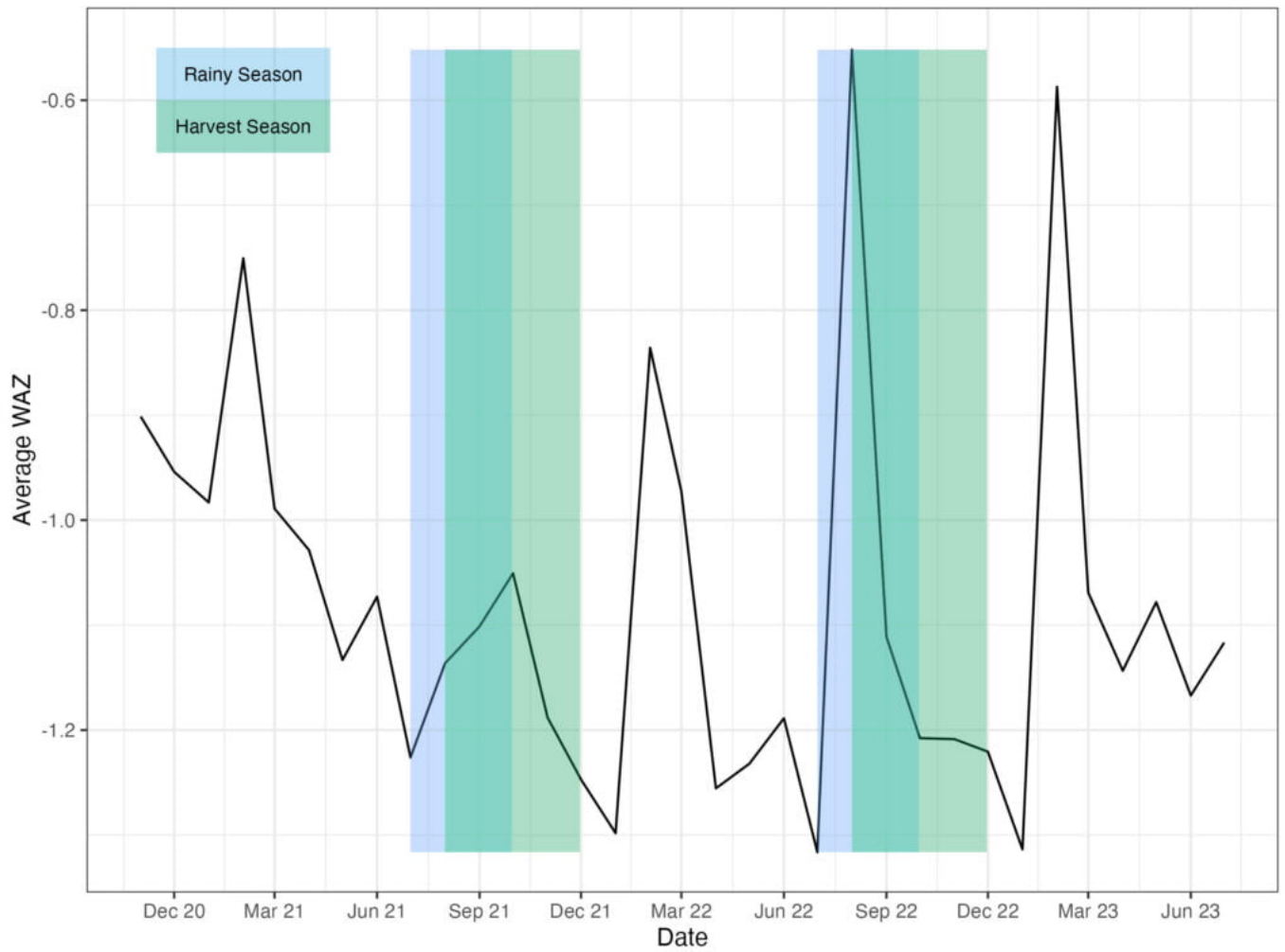
Estimating Mortality in Gallbladder and Biliary Diseases Using the CODEm Method: Insights from the Global Burden of Disease Study Mei Wang* Mei Wang Mae Dirac

GBD (Global Burden of Disease Study) is a global scientific effort to quantify the burden of over 360 diseases and injuries by age, sex, and location from 1990 to present. To estimate age, sex, year and location-specific death rates of gallbladder and biliary disease, we utilized Cause of Death (COD) data and applied Cause of Death Ensemble modeling (CODEm) tool. COD data for gallbladder and biliary disease was extracted from vital registration systems and verbal autopsies from 3701 sources covering 126 countries. Raw COD data were standardized to account for different coding practices and age-sex aggregations. Processed COD data were used as an input to CODEm—a highly systemized Bayesian, geo-temporal ensemble model—to analyze death rates of disease. CODEm tested a wide variety of submodels using different sets of predictive covariates and model types. Each submodel was weighted based on its out-of-sample predictively validity. The submodels with the highest predictive validity were combined to make the final ensemble model, ensuring accuracy and robustness in estimating cause-specific mortality rates across diverse populations and regions. Global deaths were estimated at 131,100 (113,600 to 161,800) in 2021. This was a 71.7% increase from 76,400 (60,900 to 85,300) deaths in 1990. The global age-standardized mortality rate was 1.62 (1.4 to 2) per 100,000 in 2021, which was a 28% decrease from 2.25 (1.83 to 2.51) per 100,000 in 1990. Although a significant global increase in gallbladder and biliary diseases death between 1990 and 2021 was noticed, there has been a notable decrease in the age-standardized mortality rate over the same period, suggesting potential advancements in healthcare and management strategies. The application of the CODEm method not only enhances the accuracy of mortality assessments but also facilitates informed decision-making and targeted strategies for addressing different challenges in different parts of the world.

Global Health

Use of unclean cooking fuel and late-life cognitive outcomes among older women in India

Adiba Hassan* Adiba Hassan Lara Cushing Jinkook Lee Emma Nichols Roch Nianogo Susan Cochran Elizabeth Rose Mayeda
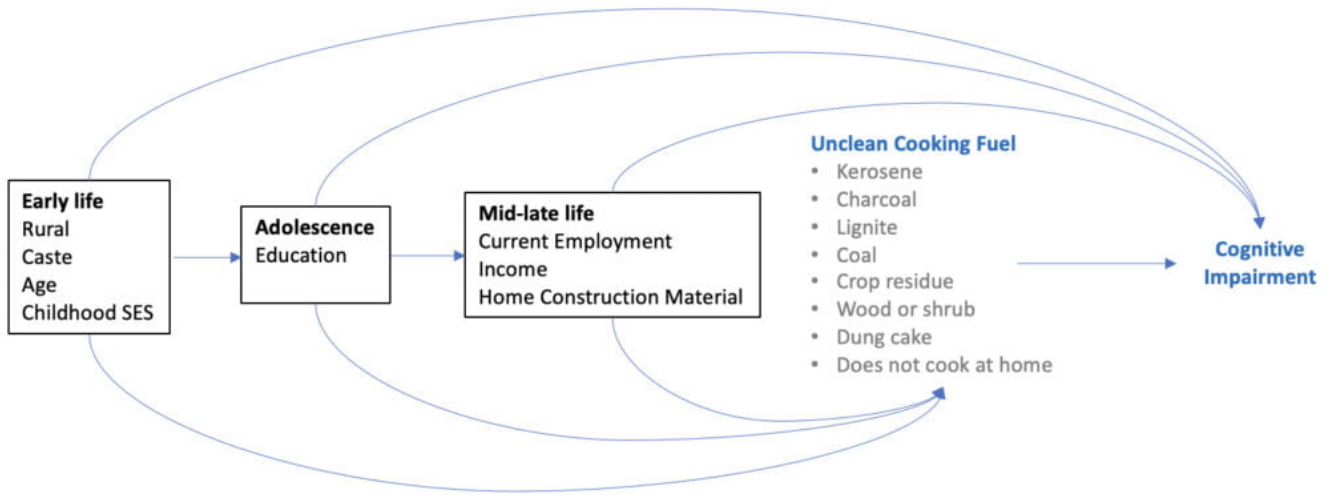
Introduction: Women in resource-limited settings are disproportionately at risk of dementia due to early-life disparities and prolonged exposure to indoor air pollution from cooking in enclosed space. In this study, we add to prior findings of the effect of unclean cooking fuel (kerosene, charcoal, lignite, coal, dung cake) on cognitive performance using culturally appropriate and harmonized measures of cognitive performance among older Indian women, and assess any role of home type in modifying this effect.

Methods: We used cross-sectional data from 2,152 women aged ≥60 years surveyed in the nationally representative Harmonized Diagnostic Assessment of Dementia for the Longitudinal Aging Study in India (LASI-DAD). Generalized linear models estimated the effect of using unclean cooking fuel on risk of cognitive impairment (defined by low cognitive and Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE) scores), and overall and domain-specific cognitive scores based on factor analysis structure of LASI-DAD cognitive battery, adjusted for potential confounders (Fig 1). As construction and material can influence home ventilation, filtration, and absorption capacity, we stratified on home type to evaluate effect measure modification.

Results: Compared with women using clean cooking fuel, women using unclean cooking fuel had 12% (95% CI 1.02, 1.23) higher risk of cognitive impairment, lower overall cognitive scores (-0.15, 95% CI -0.21, -0.09) and lower domain-specific cognitive scores. Home construction material modified this relationship: unclean cooking fuel was associated with 23% higher risk of cognitive impairment among women living in kutcha homes (grass, mud, polythene) (95% CI 1.06, 1.42), but not associated with cognitive impairment among women in pucca homes (cement, concrete, bricks), (RR=1.03, 95% CI 0.90, 1.18).

Conclusion: Upgrading kutcha homes and transitioning to clean fuel may reduce risk of cognitive impairment among Indian women.

Figure 1. Directed acyclic graph (DAG) illustrating the effect of unclean cooking fuel on late-life cognitive impairment among women 60≥ years in India from the LASI-DAD study.

Early life
Rural
Caste
Age
Childhood SES

Adolescence
Education

Mid-late life
Current Employment
Income
Home Construction Material

Unclean Cooking Fuel
- Kerosene
- Charcoal
- Lignite
- Coal
- Crop residue
- Wood or shrub
- Dung cake
- Does not cook at home

Cognitive Impairment

Health Disparities

Revealing Discrepancies: Exploring Racial Differential Item Functioning in Volunteering Activities and its Structural Underpinnings Yusuf Ransome* Ester Villalonga-Olives Abdolvahab Khademi Inez Adams Candace Hall

Introduction: In past quantitative studies, we identified racial Differential Item Functioning (DIF) in social capital items for Blacks and Whites, posing a challenge in examining racial disparities in social capital and its health-related implications. Few studies have qualitatively explored the roots of DIF in social capital questions. Our study aims to quantify DIF in questions assessing volunteering activities, a social capital indicator, and qualitatively investigate its underlying causes.

Methods: We conducted a mixed methods study to explore racial differences. We used longitudinal data (1995-2016) from the Midlife in the United States study (n= 6695). Volunteering activities, measured by monthly hours spent volunteering for organizations, were analyzed for DIF through Item Response Theory (IRT) and structural equation modeling. Additionally, we delved into the root causes of DIF through qualitative interviews (N=45).

Results: DIF was observed in IRT results for school volunteering items, with race affecting the conditional probability of volunteering. Black individuals consistently showed higher likelihood of choosing specific responses for volunteering in social organizations (P($\chi2,2$) = 0.00). Longitudinal DIF revealed a lack of metric and scalar invariance over time for White individuals. Qualitative findings suggested similar interpretations of volunteering questions and activities among Blacks and Whites, highlighting location distinctions, especially in urban versus suburban settings.

Conclusion: While the quantitative results indicated the presence of racial DIF, the qualitative study offered more insight into the underlying factors contributing to DIF. It proposed that the quantitative findings might be elucidated by the observation that Blacks are more commonly situated in urban settings, whereas Whites tend to be in suburban settings. Our study reveals the value of integrating qualitative insights to understand the nuanced factors contributing to DIF.

Health Disparities

Evaluation of participation in non-small cell lung cancer clinical trials in the US by race/ethnicity Meghann Wheeler* Meghann Wheeler Shama Karanth Hyung-Suk Yoon Joel Divaker Jae Jeong Yang Mindaugas Rackauskas Hiren J Mehta Dejana Braithwaite

Introduction: Despite efforts by organizations such as the NIH to increase diversity in clinical trial enrollment, significant racial/ethnic disparities remain. Given the significant disparities in NSCLC treatment and outcomes, improving diversity in lung cancer trials is of critical importance. Therefore, we sought to evaluate the distribution of racial/ethnic minority enrollment in NSCLC clinical trials using data from ClinicalTrials.gov.

Methods: We queried ClinicalTrials.gov for trials with the following restrictions: condition or disease: NSCLC; country: US; start date: on or after January 1, 2010 and before December 31, 2019; study type: interventional trials; study status: completed with results. We then extracted relevant trial characteristics and the number of participants by race and Hispanic origin from ClinicalTrials.gov or linked published results. Annual NSCLC incidence data was obtained from SEER*Stat 22 registries for each racial/ethnic group for the corresponding study years. A two-sample test for equality of proportions with continuity correction was applied to assess differences between incidence and trial participation. All data was analyzed in R.

Results: A total of 147 studies were included in the final analysis. Of the total 28,540 participants, 79.6% were White, 3.0% were Black, 10.4% were Asian or Pacific Islander, and 3.4% were Hispanic. Most participants were enrolled in trials that were phase 3 (63.8%), industry-sponsored (93.9%), and open-label (67.7%). When comparing trial participation to annual incidence data, we found overrepresentation among White participants (Difference: 5.8%) and underrepresentation among Black (Difference: -7.9%) and Hispanic participants (Difference: -3.2%).

Conclusion: There is persistent underrepresentation in NSCLC clinical trials among Black and Hispanic patients. Improving diversity in clinical trial accrual is critical to reducing health disparities and advancing the field of precision medicine.

Health Disparities

CAUSE-SPECIFIC MORTALITY IN PEOPLE WITH AUTISM SPECTRUM DISORDER, UNITED STATES, 1999-2021

STATES, 1999-2021 Guohua Li* Guohua Li Caleb H. Ing Zhixin Yang Ashley Blanchard Carolyn G. DiGuiseppi

Previous research suggests that people with autism spectrum disorder (ASD) are at a substantially increased risk of death compared to the general population. Little is known about the contributions of specific diseases to the excess mortality in people with ASD. This study aimed to assess major causes of death in people with ASD. We identified individuals with ASD (based on the International Classification of Diseases, 10th Revision, code F84.0) who died between 1999 and 2021 and were recorded in the multiple cause-of-death data files of the National Vital Statistics System. We calculated age-and sex-adjusted cause-specific proportionate mortality ratios (PMRs) and 95% confidence intervals (CIs) using 2010 mortality data for the US general population as the reference group. During the study period, 3554 deaths (2693 males and 861 females) in people with ASD were recorded in the United States. Annual numbers of decedents with ASD increased from 27 (accounting for 0.001% of total mortality) in 1999 to 514 (0.015% of total mortality) in 2021. Mean age at death for people with ASD was 39.9 years (SD 21.2 years; median 38.0 years) compared with 73.7 years (SD 19.2 years; median 78.0 years) for the general population. Of decedents with ASD, 693 (19.5%) were attributed to mental, behavioral, and neurodevelopmental disorders (PMR = 13.01; 95% CI = 12.06, 14.02), 435 (12.2%) to nervous system diseases (PMR = 3.58; 95% CI = 3.25, 3.93), 309 (8.7%) to respiratory system diseases (PMR = 1.82; 95% CI = 1.62, 2.03), 247 (6.9%) to endocrine, nutritional and metabolic diseases (PMR = 1.92 (1.69, 2.17), and 211 (5.9%) to digestive system diseases (PMR = 1.55; 95% CI =1.35, 1.78). These findings indicate a marked increase in the annual number of deaths among people with ASD and a 34-year gap in the mean age at death between those with ASD and the general population. Excess mortality in people with ASD is primarily due to mental, behavioral, and neurodevelopmental disorders and diseases of the nervous and respiratory systems.

Health Disparities

More Schooling is Associated with Lower Hemoglobin A1c (HbA1c) Overall and Especially for High HbA1c Values Among White and Latinx Older Adults, but Not Black Older Adults: A Conditional Quantile Regression Analysis Jillian Hebert* Jillian Hebert Amanda Irish Aayush Khadka Catherine Duarte Abigail Arons Anusha Vable

The relationship between education and hemoglobin A1c (HbA1c) varies by sociodemographic subgroup; however, most studies focus on mean HbA1c. Evaluating the relationship at different points of the HbA1c distribution is critical given links between higher HbA1c, diabetes, and cardiovascular disease mortality. Building on mean-based analyses, we test for race and gender heterogeneity in the relationship between education and HbA1c across the HbA1c distribution.

Data came from 7,327 Health and Retirement Study participants. Our exposure, educational attainment, was defined as number of years in school (5-17 years). Our outcome was first recorded HbA1c value (measured 2003-2016) from dried blood spots. We used conditional quantile regressions (CQR) to evaluate the relationship between educational attainment and HbA1c across the 1st-99th quantiles of the HbA1c distribution stratified by race and gender; all models were adjusted for participant demographics and parents' education.

The mean HbA1c level in the analytic sample was 5.9% (SD 1.2) with 15% of participants meeting the diagnostic threshold for diabetes (HbA1c > 6.5%). CQR results suggested a one-year increase in educational attainment was associated with lower HbA1c, especially at higher quantiles of the HbA1c distribution for White and Latinx men and women (e.g., White women 20th quantile (q20): b = -0.014, 95%CI(-0.031,0.002); q90: b = -0.069 (-0.116,-0.021)). However, results for Black respondents suggest that a one-year increase in educational attainment was either not associated with HbA1c (e.g., Black women q80: b = 0.002 (-0.074,0.078)), or potentially associated with higher HbA1c (e.g., Black men q80: b = 0.033 (-0.019,0.085)).

Education has a beneficial association on higher values of HbA1c for White and Latinx older adults, but not Black older adults. Further research is needed to understand why Black Americans do not seem to experience the same HbA1c benefits from education that other groups enjoy.
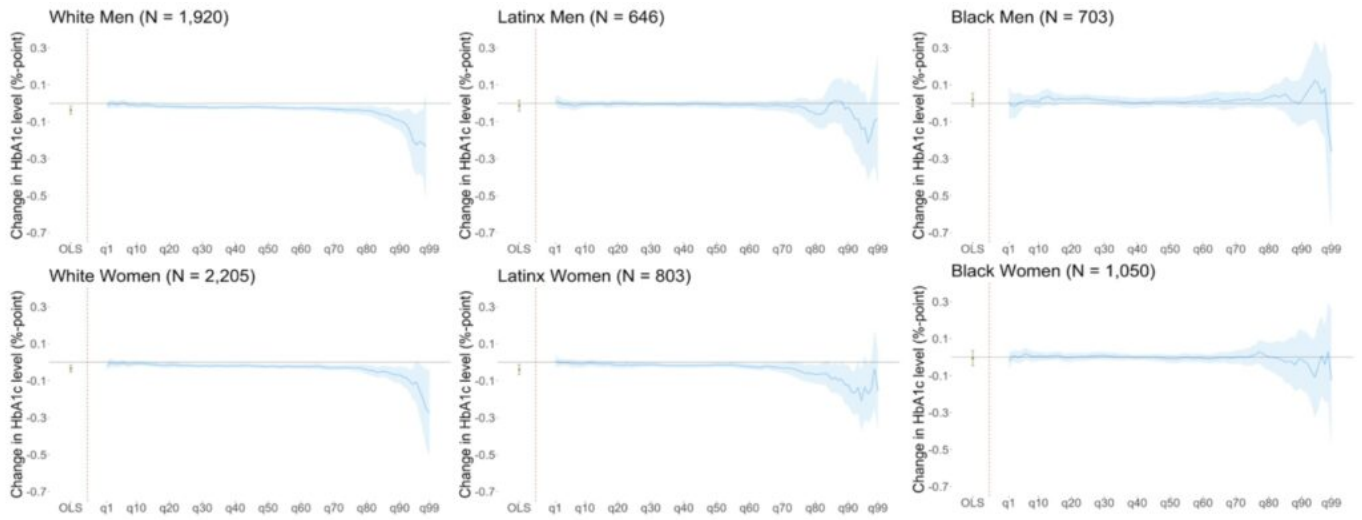
Figure. Ordinary least squares (OLS; left of the red dotted line) and conditional quantile regression (1st - 99th quantiles; right of the red dotted line) results with 95% confidence interval stratified by race/ethnicity and gender. Estimates were obtained using rotating reference groups to estimate subgroup effects. For x-axis labels, q10 represents the 10th quantile.

Health Disparities

Middle Eastern and North African Individuals in Kidney Transplantation Jesse Howell* Jesse Howell Alejandro Diez Oscar K. Serrano Anne Zehner

Purpose: Current federal standards for race/ethnicity data collection group Middle Eastern and North African (MENA) persons in the white racial/ethnic category. This has generated objections from MENA Americans who believe their experiences are not accurately reflected in this group. In 2023, the Office of Management and Budget proposed revising the standards. We reviewed Organ Procurement and Transplantation Network (OPTN) data to determine if there are disparities between MENA and non-MENA individuals in kidney transplantation.

Methods: We analyzed kidney (KI) registrations waiting on the OPTN waiting list (WL) and KI transplant (TX) recipients from 01/01/2018–12/31/2022. We filtered to those in the White, non-Hispanic race/ethnicity category (White alone) and U.S. residents, while excluding multiorgan listings and transplants. We grouped patients who reported Arab/Middle Eastern or North African race/ethnicity within the White alone category as MENA. All other White alone patients were grouped as non-MENA. We used Kaplan-Meier estimates for graft survival.

Results: In the White alone category, 1.9% (n=2411) of KI WL registrations and 1.7% (n=798) of KI TX recipients were MENA. MENA recipients were more likely to have delayed graft function (24.9%) compared to the non-MENA group (15.4%), though 6-month graft survival was similar. MENA registrations had higher median dialysis time at listing (134 days vs. 23 days). A higher proportion of non-MENA WL removals were for living donor TX (17.4% vs. 13.2%), and a higher proportion of MENA removals were for deceased donor TX (32.93% vs. 29.12%).

Conclusion: There were differences between the MENA and non-MENA groups, such as a higher chance of delayed graft function, but despite these differences, graft survival remained similar. The biggest barrier to transplantation is getting on the WL and disparities may be present prior to listing, as evidenced by the 111 added days in median dialysis time at listing for MENA candidates.

Decomposing Black/White inequities in hospitalization with Alzheimer's Disease and related dementias in Medicare Lauren Mock* Lauren Mock Michelle Audirac Daniel Mork Danielle Braun Antonella Zanobetti Scott Delaney

Background

Alzheimer's Disease and related dementias (ADRD) currently afflict more than six million Americans, with rates varying by location. Geographic variation in ADRD morbidity is caused by several factors, some of which are shared by Black and White Americans while others are not. Describing spatial variation that is shared across racial groups vs. race-specific is key to understanding effects of systemic racism, but prior studies mapping ADRD-related inequities often do not account for shared geographic variation.

Methods

Using 507,712,807 person-years of Medicare claims data from 60,879,784 non-Hispanic White and 6,497,198 non-Hispanic Black beneficiaries enrolled between 2000 and 2018, we fit a Bayesian shared component model to jointly estimate shared and race-specific variation in rates of hospital admissions with an ADRD diagnosis code. For each county, we obtained spatially smoothed relative risk estimates (based on observed vs. age- and sex-standardized expected rates) for both White and Black adults. We then calculated risk ratios (Black over White relative risk) to quantify the magnitude of racial inequities in each county after accounting for shared risk.

Results

Our data included 22,828,100 hospitalizations with an ADRD diagnosis code. Hospitalization risk varied substantially across space and race. Regarding relative risk, the median county-level estimate was 0.71 (range 0.25-2.05) for White adults vs. 0.99 (range 0.29-2.77) for Black adults. For Black/White risk ratios, the median ratio was 1.38 (range 0.72-2.93); 87% of counties had a risk ratio significantly greater than 1, indicating higher Black-specific risk, while white-specific risk was higher in 0.9% of counties. Inequities were greatest in the Midwest, Florida, Idaho, and parts of California.

Conclusion

ADRD racial inequities vary across the US. Estimating both shared and race-specific spatial risk can assist future efforts to disentangle contextual vs. sociodemographic risk factors.
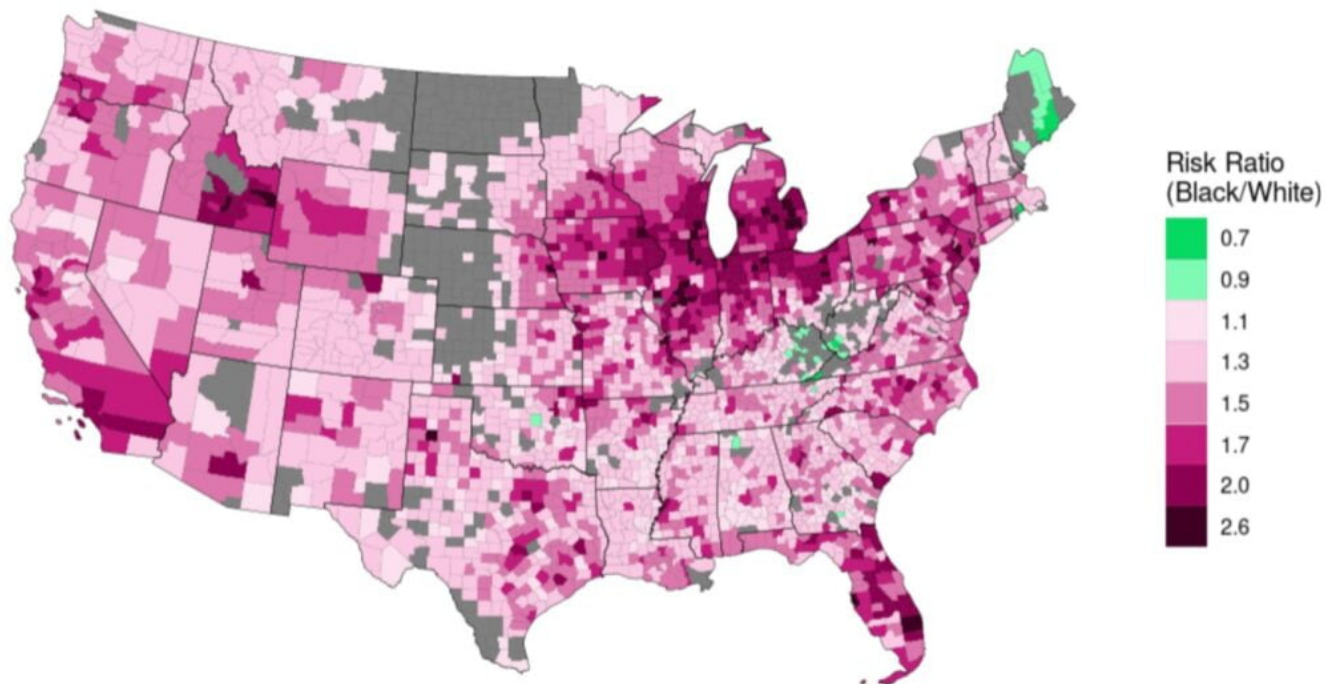
Figure 1. County-level risk ratios (Black relative risk/White relative risk) of hospital admission with an ADRD diagnosis code. Rates of hospitalization are standardized by sex and age. Counties with zero Black person-years and counties where the estimated risk ratio is not statistically significantly different from 1 are shown in gray, with significance defined as 80% of posterior risk ratio estimates above or below 1.
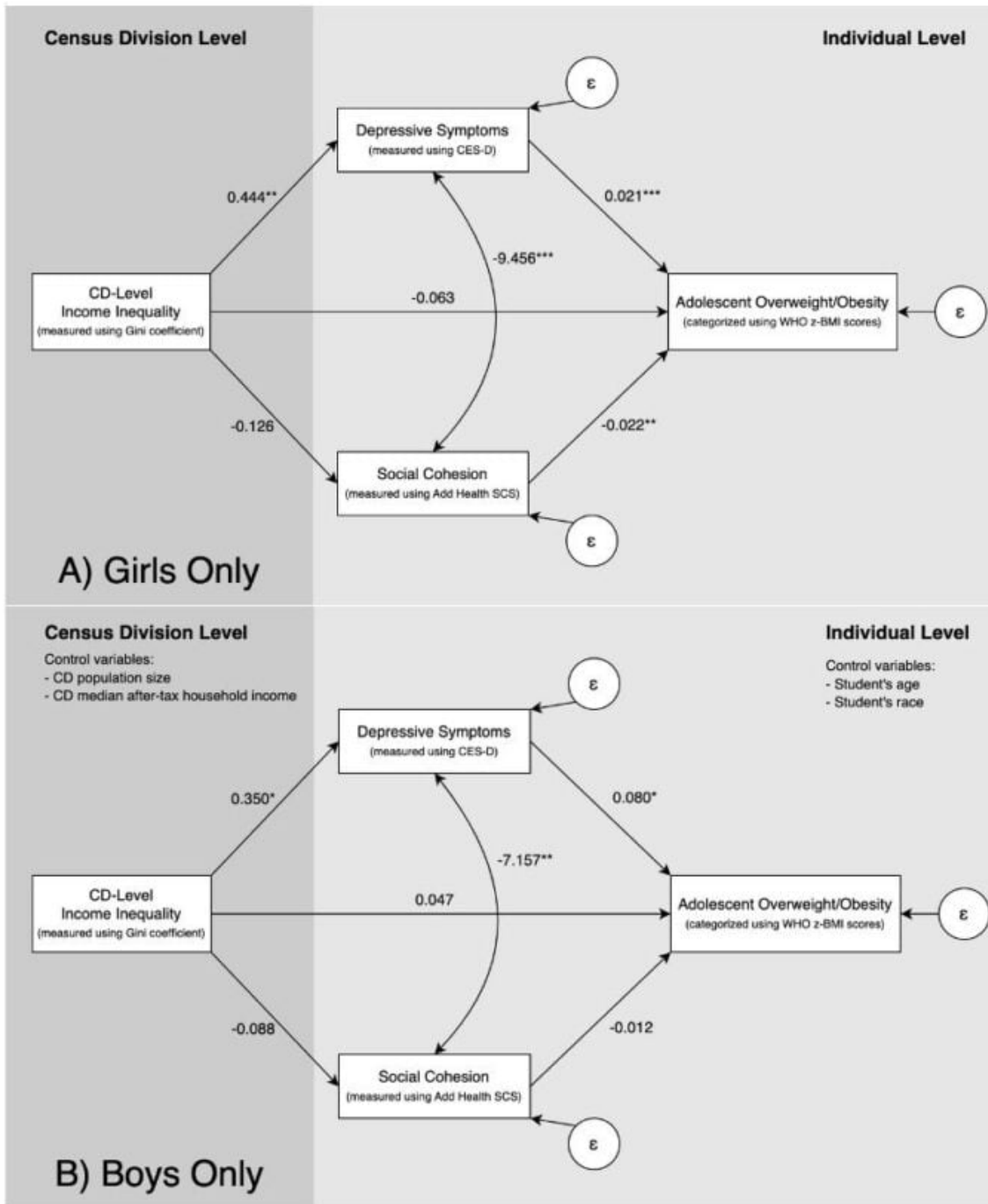
Do Depressive Symptoms and Social Cohesion Mediate the Association Between Income Inequality and Adolescent Overweight/Obesity? Luc Sauze* Luc Sauze Jason Were Karen Patte Valerie Carson Scott Leatherdale Roman Pabayo

Objectives Previous research has identified associations between income inequality and adolescent weight status, although the mediators in this association remain relatively unknown. This study explored mechanisms in the association between income inequality and overweight/obesity among Canadian secondary school students, with an added objective of identifying potential sex differences.

Methods Cross-sectional data from 47,370 students within 40 census divisions across Canada was obtained from the 2017-2018 wave of the Cannabis, Obesity, Mental health, Physical activity, Alcohol, Smoking, and Sedentary behaviour (COMPASS) study. Sex-stratified multilevel path analyses were conducted to determine if depressive symptoms and social cohesion mediated the association between census-division level income inequality and adolescent overweight/obesity (defined using WHO age- and sex-specific z-BMI scores).

Results Higher census-division level income inequality was associated with greater depressive symptoms for both sexes (Boys: ß = 0.350, 95% CI = 0.065 – 0.636; Girls: ß = 0.444, 95% CI = 0.157 – 0.731). Subsequently, higher depressive symptoms were associated with increased odds of overweight/obesity in boys (OR = 1.008, 95% CI = 1.000 – 1.015) and girls (OR = 1.021, 95% CI = 1.015 – 1.027). The indirect depression path was significant only for girls (OR = 1.009; 95% CI = 1.003 – 1.016). The social cohesion path revealed a significant association between higher social cohesion and reduced odds of overweight/obesity among girls (OR = 0.979, 95% CI = 0.967 – 0.990).

Conclusion The association between Census-division level income inequality and overweight/obesity appears to be mediated by depressive symptoms in adolescent girls, but not among adolescent boys. School-based interventions aimed at addressing depression and enhancing social cohesion could help alleviate the burden of overweight/obesity among Canadian adolescents.

A) Girls Only

Census Division Level

Individual Level

Depressive Symptoms
(measured using CES-D)

0.444**

0.021***

CD-Level
Income Inequality
(measured using Gini coefficient)

-9.456***

-0.063

Adolescent Overweight/Obesity
(categorized using WHO z-BMI scores)

-0.126

-0.022**

Social Cohesion
(measured using Add Health SCS)

B) Boys Only

Census Division Level

Control variables:
- CD population size
- CD median after-tax household income

Individual Level

Control variables:
- Student's age
- Student's race

Depressive Symptoms
(measured using CES-D)

0.350*

0.080*

CD-Level
Income Inequality
(measured using Gini coefficient)

-7.157**

0.047

Adolescent Overweight/Obesity
(categorized using WHO z-BMI scores)

-0.088

-0.012

Social Cohesion
(measured using Add Health SCS)

$* = p < 0.05, ** = p < 0.010, ***p < 0.001$

Figure Path diagrams and unstandardized coefficients of multilevel path analysis depicting the associations between CD-level income inequality and adolescent overweight/obesity, mediated by depressive symptoms and social cohesion, COMPASS (2017–2018). A) Girls Only Model and B) Boys Only Model

Health Disparities

Racial and Ethnic Inequalities in Zika Virus Infection and Congenital Zika Syndrome in Latin America: A Scoping Review. Céline Goulart* Céline Goulart Khardjatou Marianne Djigo Mabel Carabali Jay S. Kaufman

Zika (ZIKV), a virus primarily transmitted by mosquito bites can also be transmitted during pregnancy to the fetus, leading to several congenital malformations collectively known as congenital Zika syndrome (CZS). ZIKV was declared a public health emergency in 2016. Today, 89 countries and territories have reported transmission, while no vaccine to prevent ZIKV exists. ZIKV/CZS burden is not evenly distributed across populations, with higher burden among Black or non-white people. We conducted a scoping review to assess if and how ethnic/racial inequalities are measured in the context of ZIKV and CZS among pregnant individuals and their offspring in Latin America. Quantitative peer-reviewed literature was retrieved from 7 databases. Extracted data were analyzed descriptively to measure the frequency of: race/ethnicity variables (used as descriptors, confounders, or effect measure modifiers); study methods; ascertainment of ZIKV/CZS; study outcomes (disaggregated by race/ethnicity and measures of occurrence/association); and measures of inequalities (simple and complex). A bias assessment was conducted to determine the risk of selection, misclassification, or confounding bias, measures taken to address the bias, and whether race/ethnicity variables were used appropriately. From 518 articles identified, 13 papers were included, all from Brazil. Ten studies used race solely as a descriptive variable. Two studies considered race as a proxy for racism. One study used complex measures of inequality to examine race. Biases existed in all studies, with potential misclassification of ZIKV or CZS present in most studies, likely due to limited access to adequate testing. Few studies assessed the relationship between racial/ethnic inequalities and ZIKV, and those that exist rarely employ specific measures of inequality in their analyses. Our research highlights methodological gaps in the assessment of racial inequalities in the context of infectious diseases in Latin America.

Health Disparities

Adherence to the 9-5-2-1-0 Guidelines and Childhood Obesity in a Racially and Ethnically Diverse Sample of Children: An Ecological Momentary Assessment Study Junia de Brito*

Junia de Brito Yasemin Inceoglu Allan Tate Mark Pereira Jerica Berge

Background: In the United States, pediatric guidelines recommend daily adherence to 9 hours of sleep, 5 portions of fruits and vegetables, 2 hours or less of screen time, 1 hour of physical activity, and zero sugar-sweetened beverages (9-5-2-1-0 guidelines) to aid in the prevention of obesity and promote cardiometabolic health. This study aimed to 1) identify the sociodemographic characteristics of children who adhered to 9-5-2-1-0 guidelines and 2) examine the association between adherence to these guidelines and overweight/obesity in a socioeconomically and racially and ethnically diverse sample of children.

Methods: The analytic sample included baseline sociodemographic data from the Family Matters cohort of 1307 families with children (aged 7±1.5 yrs) from Minneapolis–St. Paul, MN. Pediatric 9-5-2-1-0 guidelines data were collected via a 7-day ecological momentary assessment for a subsample (n= 562; 3,596 observation days). BMI data were retrieved from electronic medical records. Descriptive statistics characterized children who adhered to the guidelines. Logistic regression models adjusted by sociodemographic factors examined the association between adherence to these guidelines and child weight status (overweight/obese vs. healthy weight).

Results: Ten, 7, 27, 23, 24, and 18% of the sample met none to 5 guidelines, respectively, across the observation period. Children who met all 5 guidelines were more likely to have a parent self-report White race, higher incomes, advanced education, and hold full-time employment. We did not find evidence that children meeting all 5 guidelines (vs. meeting 0-4) were more likely to have healthy weight status (OR 0.98, 95% CI 0.86-1.13).

Conclusions: There was no evidence indicating that meeting all guidelines was associated with lower weight status, highlighting complex relationships between adherence to recommended health behaviors, sociodemographic factors, and weight outcomes for children living in diverse households.

Experiences of in-group and out-group skin tone discrimination and their associations with incident cardiovascular disease among African American adults in the Jackson Heart Study

Sydney Barlow* Sydney Barlow Jessica R. Fernandez Juliana S. Sherchan Ellis P. Monk Jaime Slaughter-Acey Mario Sims

Background: African American adults face an elevated risk of cardiovascular disease (CVD) compared to other racial/ethnic groups in the United States. Although discrimination has been linked to this disparity, the relationship between skin tone discrimination and CVD incidence remains scarce. Therefore, this study investigated the associations of in-group skin tone discrimination (from African American individuals) and out-group skin tone discrimination (from White individuals) with incident CVD and whether these associations differed by sex and optimism.

Methods: We analyzed data from 3,519 African American adults (aged 21-95 years) in the Jackson Heart Study (JHS). Cox Proportional Hazards regression, including interaction terms, estimated HR and 95% CI to examine whether skin tone discrimination (in-group, out-group) was associated with incident CVD (stroke, coronary heart disease (CHD), congestive heart failure (HF)), adjusting for sociodemographic variables, health behaviors, and CVD risk factors.

Results: Over the 16-year follow-up period, 12.6% of JHS participants developed CVD, 3.9% developed stroke, 4.9% developed CHD, and 7.3% developed HF. In-group skin tone discrimination through better treatment (i.e., Black individuals treated participants better than other Black individuals due to their skin tone) was associated with a higher incidence of CVD. Out-group skin tone discrimination, whether better or worse treatment, was associated with a higher incidence of CHD (see figure 1). These associations did not vary by sex. Optimism moderated the association between out-group skin tone discrimination and HF, such that those who reported worse treatment and had the highest-level of optimism had the greatest risk of HF.

Conclusions: Findings suggest that in-group skin tone discrimination is associated with CVD for African American adults over time, presenting it as a possible risk factor for CVD for African American individuals.

Figure 1. Hazard Ratios for Associations between Skin Tone Discrimination and Cardiovascular Health Outcomes

Cardiovascular Disease includes Stroke, Coronary Heart Disease, and Heart Failure.

In-group Skin Tone Discrimination

Out-group Skin Tone Discrimination

- skin tone discrimination: better treatment versus no difference
- skin tone discrimination: worse treatment versus no difference
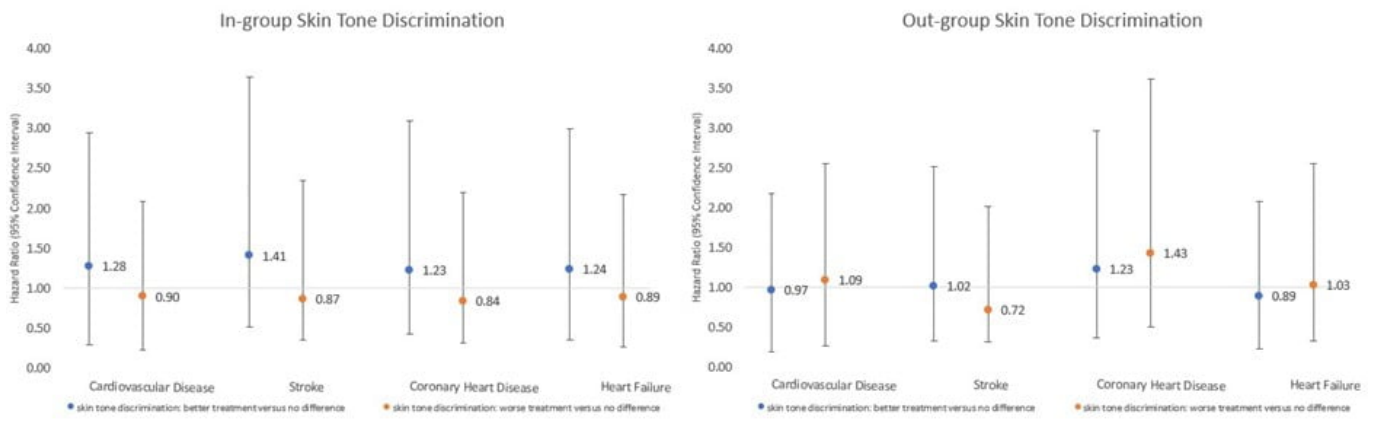
Healthcare Discrimination and Adherence to Preventive Services Guidelines in 2023 among a Nationally Representative, Diverse Sample of US Adults Paula Strassle* Paula Strassle Allana T. Forde

Preventive services, like cancer screenings and vaccinations, represent a critical avenue for reducing disease risk. It remains unclear how barriers, like experiencing healthcare discrimination, impact adherence to preventive services recommendations and potentially exacerbate health disparities. We used data from the Health Equity through Adherence to Preventive Services (HEAPS) study, a nationally representative, online survey of American Indian or Alaska Native (AIAN), Asian, Black/African American (Black/AA), Latino (English and Spanish speaking), Middle Eastern or North African, Native Hawaiian or Pacific Islander, White, and multiracial adults ≥35 years old from 6/2023-8/2023, N=4111. The validated Interpersonal Processes of Care (IPC-18) survey was used to measure discrimination due to race/ethnicity by medical providers. Adherence to preventive services guidelines was measured using a modified Medical Expenditure Panel Survey. Poisson regression with robust variance estimates, adjusting for sociodemographics and insurance status, were used to estimate the association between discrimination and preventive services. Analyses were weighted to be nationally representative within racial and ethnic groups. Overall, 20.0% of participants reported being discriminated by medical providers sometimes/always within the past year; Black/AA participants had the highest prevalence (28.9%), followed by Spanish-speaking Latino (27.4%), and AIAN (23.5%). Adherence to preventive care guidelines ranged from 51.0% to 85.5%. After adjustment, experiencing healthcare discrimination (sometimes/always vs. rarely/never) appeared to reduce breast, cervical, and colorectal cancer screening rates (IRRs 0.87-0.90) but confidence intervals were wide, Fig. Healthcare discrimination was associated with being less likely to have seen a doctor in the past year (IRR=0.89, 95% CI 0.81-0.98). Implementing antidiscrimination strategies could increase healthcare utilization and cancer screenings.
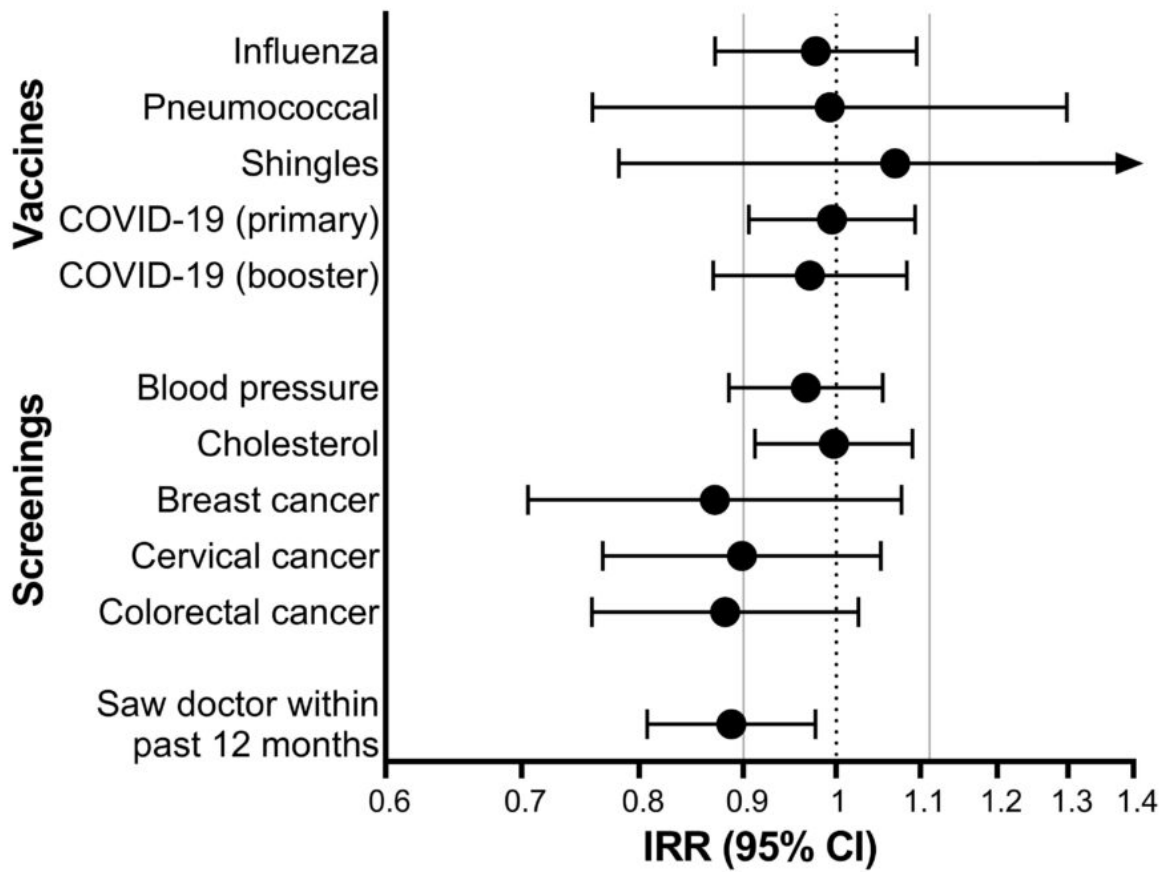
Measuring Health Trends of Transgender People Using Real World Data in The United States Theo Beltran* Theo Beltran Tonia Poteat Jennifer Lund Kathleen Thomas Shabbar Ranapurwala Brian Pence

Background

Due to the lack of standardized gender identity data in real-world data sources, researchers are unable to quantify mental health care trends among transgender people.

Objectives

We evaluate the performance of an existing computational phenotype (CP) in a claims database to identify transgender patients and assess the prevalence of mental health (depression and anxiety) and population trends over time.

Methods

We applied Jasuja et. al to establish a retrospective cohort of potential transgender patients from 2007 to 2021 using Merative MarketScan, a commercial insurance claims database. We measured trends over time for the total transgender population and sub-group with depression and anxiety using join-point regression.

Results

The Jasuja et. al CP identified 67,794 (0.2%) transgender patients from 2007 to 2021. The transgender population increased from 3 transgender patients per 100,000 enrollees in 2007 to 55 transgender patients per 100,000 enrollees in 2021. Gender identity related diagnoses increased from 45% in 2007 to 97% in 2021. Two join-points representing increases in TG patients in 2012 and 2017 with annual percentage changes (APC) of 44.6% (95% CI: 39.2, 55.9) and 22.5% (18.0, 26.3), respectively. 45.2%, 35.5%, and 55.7% of transgender patients were diagnosed with depression, anxiety, or both. One join-point in 2017 represented a 3.9% (-13.5, 2.1) APC declining trend among transgender patients diagnosed with psychiatric disorders.

Conclusion

The CP identified the largest transgender sample in commercial insurance claims data to date. Most TG patients were identified through gender identity related diagnoses which may be specific but not sensitive hence underestimating the true transgender population. Large increases in the total transgender patient population and among those with psychiatric disorders may represent an

increase in access to insurance covered gender affirming services and the continued need to reduce burdens of psychiatric disorders.

All: 2 Joinpoints

Legend:
- ■ Observed
- 2007-2012 APC = 7.38
- 2012-2017 APC = 44.57*
- 2017-2021 APC = 22.46*
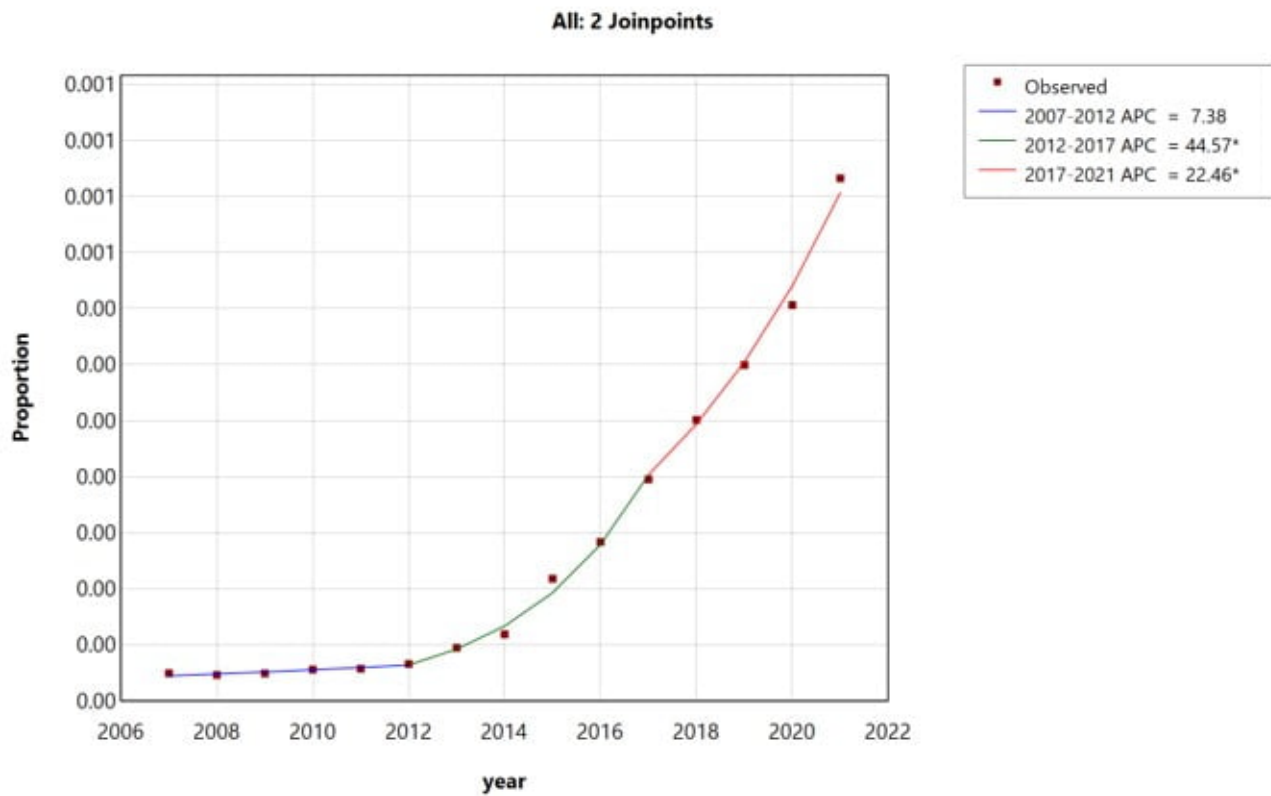
* Indicates that the Annual Percent Change (APC) is significantly different from zero at the alpha = 0.05 level.
-- Test Statistic and P-Value not available for the Empirical Quantile method.
Final Selected Model: 2 Joinpoints.

The Effect of Social Deprivation on Adverse Pregnancy Outcomes Akaninyene Noah*

Akaninyene Noah Brandie DePaoli Taylor Ashley Hill

Background

Socioeconomic factors have been linked to adverse pregnancy outcomes; however, there has been limited emphasis on the accumulative effect of multiple neighborhood-level risk factors on birth outcomes. The social deprivation index [SDI] is a commonly used measure of assessing area-level socioeconomic disadvantage. We hypothesize that women from locations with higher SDI scores have a higher risk of adverse pregnancy outcomes, specifically preeclampsia (PE), gestational diabetes [GDM], and preterm birth [PTB].

Methods

We conducted a retrospective cohort study of 41,834 singleton pregnancies between 2011 and 2024, using data from a perinatal database from Houston, TX. We linked patients' preconception zip codes with the SDI score associated with that zip code, using data from the American Community Survey. Pregnancies were categorized based on SDI score into 4 quartiles, where SDI Q1 were the least deprived and SDI Q4 was most deprived. Pregnancies from SDI Q1 were used as our reference group; our outcomes include PE, GDM and PTB. A modified Poisson regression model was used to calculate the relative risk and 95% confidence interval between SDI quartiles and our outcomes. Models were adjusted for age, education, payment method, chronic health issues, smoking, and gravidity.

Results

About 50% of our population was Hispanic and used Medicaid as their primary payment option. Adjusted models showed SDI Q2 (RR 1.09, 95% CI 1.00 – 1.21**)**, SDI Q3 (RR 1.11, 95% CI 1.02 – 1.21**)** and SDI Q4 (RR 1.12, 95%CI 1.02 – 1.23) were associated with an increased risk of PE. We observed the same patterns with GDM. However, there was no association among any SDI quartile – SDI Q2 (RR 1.02, 95% CI 0.94-1.10), SDI Q3(RR 0.94, 95%CI 0.86 – 1.02), SDI Q4 (RR 0.95, 95% CI 0.87-1.04) – with PTB.

Conclusion

We found evidence that social deprivation was associated with PE and GDM. Additional research is needed to further explore which social factors appear to be driving the association.

Association Between SDI Quartiles and Adverse Birth Outcomes
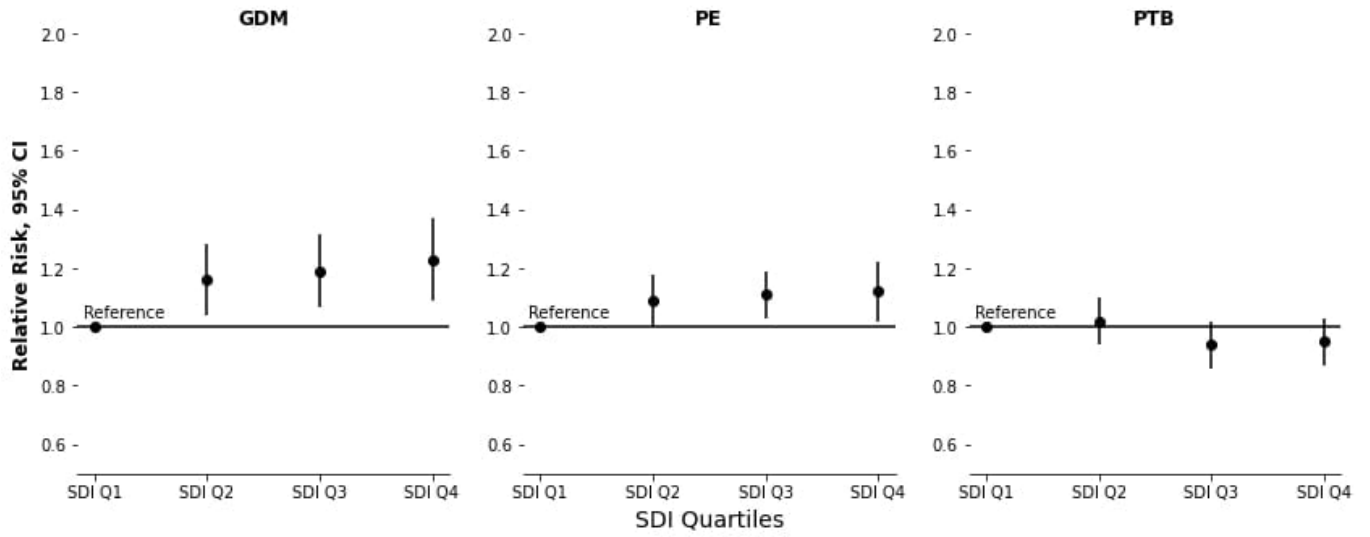
Discrimination and Impacts on Youth Sexual Behaviors Elizabeth Swart* Elizabeth Swart
Ashley Hill Phoebe Balascio

Introduction:

Promoting positive sexual health and well-being, including physical, emotional, mental and social well-being, are integral to advancing sexual and reproductive equity for young people. This includes an examination of social and structural factors, such as race-based discrimination. Several studies have examined community-level characteristics, such as neighborhood disadvantage, in youth and their impact on sexual risk behaviors, such as age at sexual debut and engaging in unprotected sex. However, few studies examine influences of interpersonal and individual racism and discrimination on sexual risk behavior. This study explored experiences of discrimination among Black youth aged 14-18 and influences of sexual/reproductive health behaviors (SRH).

Methods:

This study assessed adolescents' perceptions of racism (PRaCY), gender equitable attitudes (GEA), psychological distress, and teen dating/sexual violence victimization (TDV/SV) in adolescents living in lower-resource neighborhoods in Pittsburgh, PA. Participants were 14-18 years old and were recruited from community organizations. Data was collected from baseline surveys completed in-person at one of the study sites.

Multivariable logistic regression was used to examine associations between discrimination and SRH in youth. Sample characteristics included self-reported age, race/ethnicity, sexuality and gender. The study assessed three outcome variables: ever engaging in vaginal/anal sex, number of lifetime partners and age at sexual debut. Chi-square tests examined differences in distributions between girls and boys.

Results:

The study sample comprised of 244 adolescents with a mean age of 15. Approximately 75% of the sample identified as Black and the majority identified as straight. Girls reported higher mean PRaCY scores than boys (3.3 vs 2.4; p=0.02) and GEA significantly differed between genders (1.9 vs 2.3; <0.0001).

For the full sample, GEA, TDV, SV and experiencing any TDV or SV victimization were significantly associated with a higher likelihood of ever having had sex. The associations remained significant for all four variables after adjusting for age, race and sexuality. The magnitude of the associations increased after adjusting: GEA (OR: 2.02; p=0.03), TDV (OR: 3.5; p=0.02), SV (OR: 6.19; p=0.007), any TDV or SV victimization (OR: 3.83; p=0.02).

A higher PRaCY score was significantly associated with having more than one partner after adjusting for age, race and sexuality (OR 1.27; p=0.03). GEA (OR: 2.94; p=0.13), experiencing any TDV (OR 8.57; p=0.04), any SV (OR 5.37; p=0.008) were all significantly associated with early sexual encounters. Clinically significant distress also showed a marginally significant association (OR 4.14, p=0.07).

Pragmatic Recruitment Strategies for a mHealth Smoking Cessation Intervention for Sexual and Gender Minorities: SmokefreeSGM Feasibility Trial Samuel Tundealao* Samuel Tundealao Irene Tamí-Maury Rebecca Klaff Phoenix Matthews

Introduction: SmokefreeSGM, a text-based smoking cessation intervention, was developed to address the high prevalence of cigarette smoking among sexual and gender minorities (SGM). We implemented a pragmatic recruitment strategy for our feasibility trial to enroll a study sample representative of this hard-to-reach population. This manuscript outlines the strategies we employed to recruit SGM smokers for our study and provides a framework for researchers interested in working with this population.

Methods: We utilized field recruitment (flyer distribution and presentations), research panels, and advertising on social media and internet sites (Facebook, Instagram, Google, SGM dating apps) to enroll 79 SGM smokers in our study. Recruitment (proportion of individuals who were screened) and enrollment rates (proportion of screened individuals who were enrolled) were calculated. Chi-squared tests (or Fisher's exact, when appropriate) were used to compare socio-demographic and tobacco use characteristics by study arm. Intersectionality between the recruitment modalities and socio-demographic characteristics was also assessed.

Results: The recruitment rate for this feasibility trial was 20.5%, and the enrollment rate was 50.6%. Research panels yielded 53.2% of our sample, field recruitment yielded 21.5%, and advertisements on social media and internet sites yielded 25.3%.

Conclusions: Insights gained from this experience will play a pivotal role in our ability to successfully recruit participants in a future randomized controlled trial among a larger sample, inform the marketing of this program in a real-world setting, and work towards overcoming barriers to recruitment for SGM individuals in tobacco prevention and control research and public health at-large.

Social determinants of health are related with brain health over a 2 year of follow-up, beyond lifestyle behaviors: insights from the ABCD project Cristina Cadenas-Sanchez* Cristina Cadenas-Sanchez Harold W. Kohl Marcus V. Nascimento-Ferreira Augusto César F. De Moraes

BACKGROUND: Social determinants of health may influence children's health outcomes, including psychological and cognitive well-being. Nevertheless, previous studies have focused on cross-sectional associations rather than examining the potential effects of the social determinants of health on brain health.

PURPOSE: To examine the longitudinal association between social determinants of health and brain health over a 2-year follow-up period in children. Additionally, we aim to explore the role of lifestyle factors on this association.

METHODS: We included 4,948 participants (aged 8-10 years, 52.4% boys) from the Adolescent Brain Cognitive Development (ABCD) project. Social determinants of health were measured using children's opportunity index which comprises educational, health and environmental opportunities. Grey matter volume of the hippocampus was assessed through magnetic resonance imaging, and executive function (i.e., inhibition) was evaluated using the flanker test. Lifestyle behaviors (i.e., physical activity, screen time, and sleep) were self-reported through surveys. Participants were followed-up from study initiation (2016-2018) to the second-year follow-up. Multilevel mixed-effects were used to estimate beta coefficient and 95% confidence intervals (CIs). All the analyses were adjusted for age, sex, ethnicity, air pollution, population density and their baseline measures. In an additional model, we further adjusted for lifestyle behaviors.

RESULTS: Children categorized in the high and very high opportunity index presented significantly greater hippocampal volume compared to their peers with low or moderate opportunity levels (very high, beta coefficient=14.9, 95%CI=5.1-24.7 vs. low, beta coefficient 7.9, 95%CI=-3.8-19.5; P < 0.001). A similar pattern was observed for executive function, with children in the very high opportunity group demonstrating superior inhibitory control compared to those in the lower opportunity group (very high, beta coefficient=2.6, 95%CI=1.8-3.9 vs. low, beta coefficient 1.3, 95%CI=0.3-2.3; P < 0.001). Notably, after adjusting for lifestyle behaviors, the results remained consistent.

CONCLUSION: This study underscores the significant impact of childhood opportunities on both hippocampal volume and executive function in children. Those with high and very high opportunity indices exhibited notable advantages in brain health compared to their counterparts with lower opportunities. Importantly, these findings emphasize the enduring influence of social determinants on cognitive outcomes. Understanding these relationships contributes valuable insights for creating targeted interventions aimed at optimizing childhood brain development and well-being.

Health Disparities

Racial/Ethnic Disparities in Non-small Cell Lung Cancer Stage at Diagnosis: A Population-Based Study Qinran Liu* Qinran Liu Tulay Koru-Sengul Paulo S. Pinheiro

Background

The prognosis of lung cancer significantly relies on accurate and timely staging. However, notable disparities in staging and outcomes among different racial/ethnic groups exist. This population-based study aims to identify factors contributing to these disparities in the stage of non-small cell lung cancer (NSCLC) diagnoses, focusing on Hispanic ethnic subgroups.

Methods

Incident cases diagnosed from 2005–2018 were extracted from the Florida State Cancer Registry. Stage was categorized as resectable (Stage I-IIIA) or nonresectable (Stage IIIB/IIIC/IV). Multivariable logistic regression models were used to assess the association between race/ethnicity and stage at diagnosis, adjusted for socioeconomic, smoking status, and clinical factors. Regional stratification was further conducted (South Florida vs. Rest of Florida).

Results

Among 157,034 NSCLC patients, 81.0% were White, 8.3% Black, and 9.2% Hispanic; 43.2% were diagnosed at a resectable stage. Compared to White patients, Black patients had a 12% higher likelihood of non-resectable stage diagnosis (ORadj=1.12; 95% CI: 1.11-1.14). In age-adjusted models, all Hispanic patients and their subgroups demonstrated higher odds of non-resectable stage at diagnosis compared to White patients; however, in fully adjusted models, this association was significant only for Central Americans (ORadj=1.41; 95% CI: 1.35-1.47). Notably, regional differences were remarkable; Hispanic patients in South Florida showed better staging outcomes compared to those in the rest of Florida (South Florida: ORadj=0.95; 95% CI: 0.94-0.97 vs. Rest of Florida: ORadj=1.09; 95% CI: 1.07-1.10).

Conclusion

The study highlights significant disparities in NSCLC staging among Black and certain Hispanic groups. The marked regional differences between South Florida and the rest of the state underscore the importance of considering intra-state geographic and cultural factors in lung cancer prevention and control strategies, as well as in enhancing health access.

Health Disparities

Racial/ethnic and socioeconomic disparities in antibiotic prescription for lactation mastitis among commercially insured individuals Ashley Judge* Ashley Judge Christina Ludema

Lactation mastitis, an acute infection resulting in painful swelling of the breast, affects approximately 10% of breastfeeding people. The current US standard of treatment recommends the provision of antibiotic treatment 24-48 hours after the onset of symptoms. Few studies have examined demographic and socioeconomic characteristics associated with antibiotic prescription. Administrative datasets, like insurance claims, are an important data source for questions about provision of care, but use algorithms to generate demographic classifications. We examined the prevalence of antibiotic prescription after a lactation mastitis diagnosis by race/ethnicity and socioeconomic characteristics using Optum Clinformatics Data Mart healthcare claims dataset among individuals aged 15 to 49 diagnosed between January 1, 2007 to December 31, 2019. We used log-binomial regression to estimate risk ratios and 95% confidence intervals (CI) adjusted for age and stratified by race/ethnicity and socioeconomic characteristics. Seventy percent of race/ethnicity in Optum is imputed and prior research shows that Black individuals are especially likely to be misclassified using this algorithm. We perform a quantitative bias analysis using parameters from a prior validation study to estimate the impact of misclassification on our results comparing estimates of antibiotic prescription among Black and White participants. Among 9433 individuals diagnosed with mastitis, the median age was 31, 71.9% of individuals were White, 51.8% had some college education, 71.3% were a homeowner, 47.8% had an income over $100,000, 29.7% had a net worth over $500,000, and 57% were prescribed an antibiotic. Asian and Black individuals were 0.92 (53.1% vs 58.3%; [95% CI 0.86, 0.97]) and 0.89 (52.3% vs 58.3%; [0.82, 0.96]) less likely to have been prescribed an antibiotic than White individuals. Estimates further stratified by socioeconomic status revealed few statistically significant results. After accounting for misclassification, Black compared to White individuals were 0.82 less likely to have been prescribed an antibiotic.

Health Disparities

Association between a novel database of local policies and structural racism in Solano County, CA Tracy Lam-Hine* Tracy Lam-Hine Ángel Mendiola Ross Nafeesa Andrabi Tainayah Whitney Thomas Lesley Sept David Rehkopf

Intro: Legal epidemiology offers methods for identifying and coding policies as exposures in epidemiologic studies. Structural racism can operate through policy to affect racial health inequities, but to date, legal epidemiologists studying structural racism have mostly focused on the state level. However, localities implement state laws and also create policy. We aimed to create a local policy index and estimate associations with structural racism in Solano County, CA.

Methods: We reviewed administrative sources and consulted domain-specific experts to identify Solano County city policies adopted as of 2023, hypothesized to impact structural racism. We created a policy index by taking city-level differences in progressive and regressive policy counts. For structural racism, we averaged five tract-level measures: Black/White (B/W) rate ratios in college graduation, employment, and homeownership, B/W dissimilarity index; B/W index of concentration at the extremes with income. We regressed structural racism against the policy index in a crude hierarchical model to estimate cross-sectional mean differences.

Results: We identified 13 policies: 12 progressive and 1 regressive. Policy index scores ranged from 0 in unincorporated areas to 4 in Dixon and Vallejo. Tract-level structural racism ranged from -1.36 to 1.88; tract population-weighted city means were highest in Benicia (0.04) and lowest in Rio Vista (-0.05) (Fig 1). The association between the policy index and structural racism was null (mean difference: -0.003, 95% CI: -0.114, 0.107).

Discussion: Policies create an operating medium for structural racism. Our null findings may reflect the small number of locations in a single county and a lack of temporal data, as policies may take many years to influence measures of structural racism. Future research should extend this work to other localities and examine historical data to help fully characterize the place-based impact of (anti)racist policy exposures.
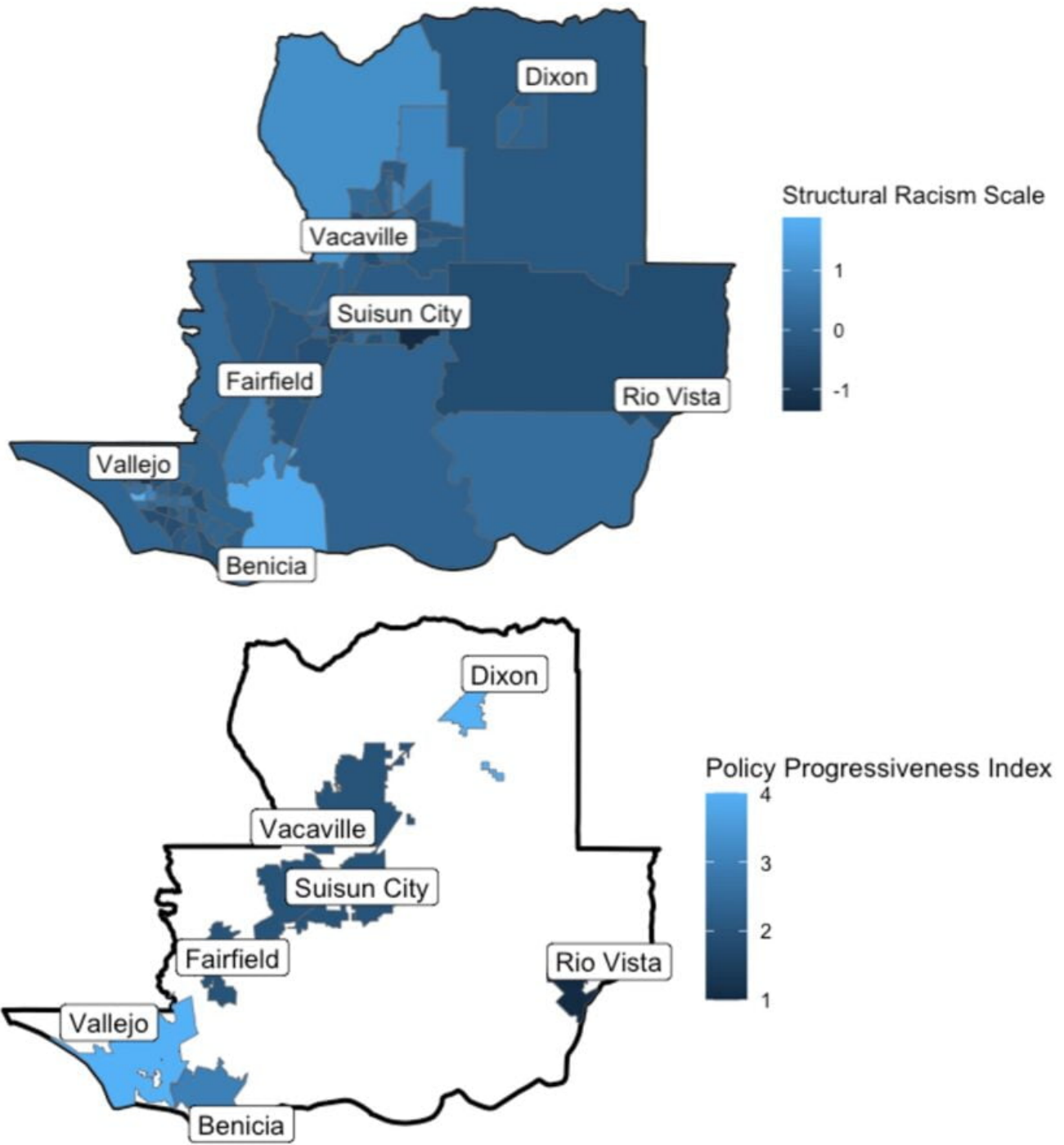
Figure 1: Maps of tract-level structural racism and city policy progressiveness index in Solano County, CA, 2022-2023

The changing prevalence and characteristics of total knee replacement recipients from 2003 to 2014 in Ontario, Canada

Tristan Watson* Tristan Watson Gillian Hawker Laura Rosella Peter Smith Arjumand Siddiqi

Background

Descriptive studies have shown increasing use of total knee replacements (TKRs) in North America, especially amongst younger patients (< 60 years old). Few studies have examined the prevalence and characteristics of people living with a TKR in Ontario. The current study sought to estimate the trends in the crude and age-standardized prevalence of primary TKR across age and sex in Ontario, Canada.

Methods

We conducted a population-based descriptive study of Ontario adult respondents (age 20-105) from the Canada Community Health Survey (CCHS) linked to health administrative data. The outcome was the prevalence of at least one primary TKR with a 10-year lookback from the survey date. We estimated the crude and standardized TKR prevalence across the six CCHS survey cycles (2003-2014) by age and sex. The 2014 Canadian population structure was used as the standard population.

Results

The estimated 2013 crude and standardized 10-year TKR prevalence in Ontario was 1.24% (95% CI: 1.10-1.38) and 1.30% (95% CI: 1.17-1.45), respectively. The crude and standardized 10-year prevalence increased between 2003 and 2012, with a significant increase in the prevalence in 2009. Across the age-specific 10-year TKR prevalence estimates, the largest relative increase from 2003 to 2014 was seen in the age group 60-69 (prevalence2013 = 4.81%; 92% increase) and 80-105 (prevalence2013 = 7.55%; 157% increase). The crude and standardized prevalence estimates were higher among females than males across all survey years.

Conclusion

We estimate that in 2013 about 125 000 adults in Ontario, Canada, were living with at least one primary TKR in the past 10 years. Given the increasing prevalence of younger patients, these findings highlight a growing group of individuals at risk for costly revision TKRs and may inform health services planning in healthcare provision.

Medicaid Expansion Among Non-Elderly Adults and Cardiovascular Outcomes: A Distributional Cost-Effectiveness Analysis Luke Barry* Luke Barry Roch Nianogo

Introduction

Evidence suggests Medicaid expansion has improved CVD outcomes, especially among lower SES groups. It remains unclear what the implications are of Medicaid expansion for cost-effectiveness and CVD disparities.

Methods

A Monte Carlo Markov-chain microsimulation model was developed to examine changes in CVD outcomes as a result of Medicaid expansion and the distributional cost and quality-of-life impacts.

Results

Medicaid expansion was associated with a reduction of 14 (SE: 3) myocardial infarctions, 12 (3 strokes, and 6 (2) CVD deaths per 100,000 person-years compared to no expansion with the largest reductions occurring for those with lower income and education, and those of Black and Hispanic race/ethnicity. Medicaid expansion was considered cost-effective from a healthcare perspective (Incremental Net Health Benefit [INHB] = 0.055 [SE = 0.0045]) but not cost-effective from a societal perspective (INHB = -0.004 [SE = 0.0035]); using a value of $100,000 per QALY. The most influential variables for cost-effectiveness were: the increase in total healthcare costs among those who received Medicaid; the cost of Medicaid administration per enrollee; the discount rate; and the change in systolic blood pressure from receiving Medicaid.. The targeting of Medicaid expansion to lower income groups helped reduce net health disparities according to family income and education.

Conclusion

Medicaid expansion reduced net health disparities across family income and education groups. It was cost-effective from a healthcare perspective, by improving health and reducing out-of-pocket costs for individuals, and reducing uncompensated care costs for hospitals, but not cost-effective from a societal perspective.

Figure: Incremental Net Health Benefit (WTP = $100,000) per-person for the base-case scenario across equity-relevant groups

Health Services/Policy
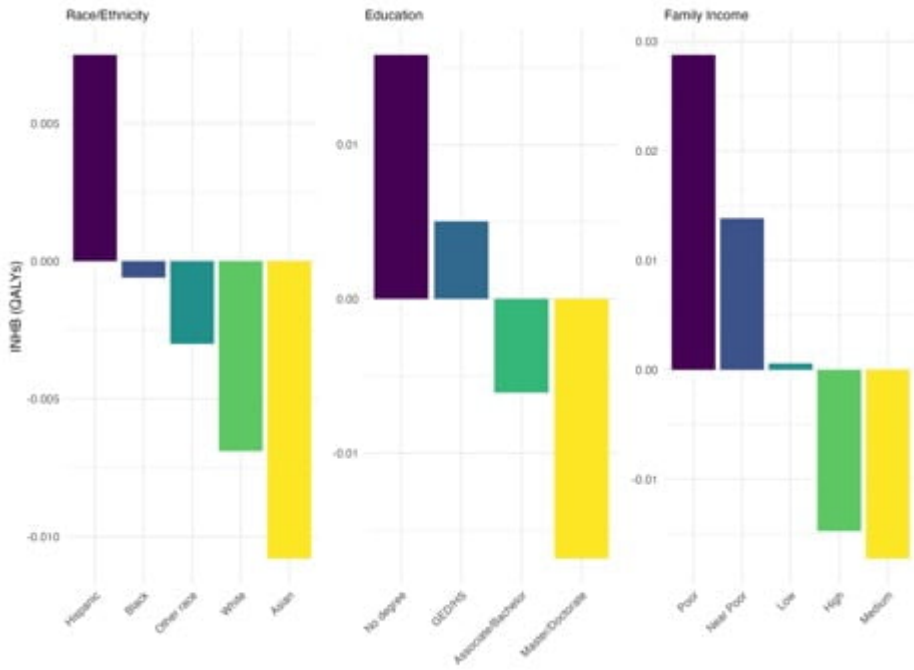
The cross-sectional association between state-level public health funding per capita and physical health among adults in the United States. Stephen Hunter* Stephen Hunter Sze Y Liu Daniel M Cook Kia Davis Brendan T Smith Roman Pabayo

Background: Funding is necessary for public health agencies to achieve their goals of providing essential public health services. To date, there is limited research on whether public health funding affects individuals' overall physical health.

Methods: Data from the 2018 Behavioral Risk Factor Surveillance System (BRFSS) was used. Participants reported the number of days they felt were physically unhealthy in the last 30 days. This was categorized into <14, ≥ 14 days of poor physical health. Individual-level confounders were self-reported in the BRFSS, while area-level confounders were from the 2018 American Community Survey. Since respondents were clustered within states, multilevel logistic regression was used to investigate the association between public health funding and poor physical health while adjusting for individual and area-level confounders. We also tested whether household income moderated any observed associations. Sampling weights were also applied to obtain estimates generalizable to the US population.

Results: State-level public health funding per capita did not have a main association with physical health (OR = 0.95, 95% CI: 0.89, 1.00). However, heterogeneity across household income was observed, where greater public health funding per capita was associated with lower odds of poor physical health (OR = 0.92, 95% CI: 0.86, 0.98) among respondents with low household incomes ($75,000 USD) household incomes.

Conclusion: State-level public health funding per capita was not associated with physical health at a population level. However, it may be protective against poor physical health in individuals with lower household incomes. Therefore, public health funding might help reduce physical health inequities. Future research is needed to determine whether this association is causal.

Predicted probabilities of ≥ 14 days of poor health by median household income and public health unit funding
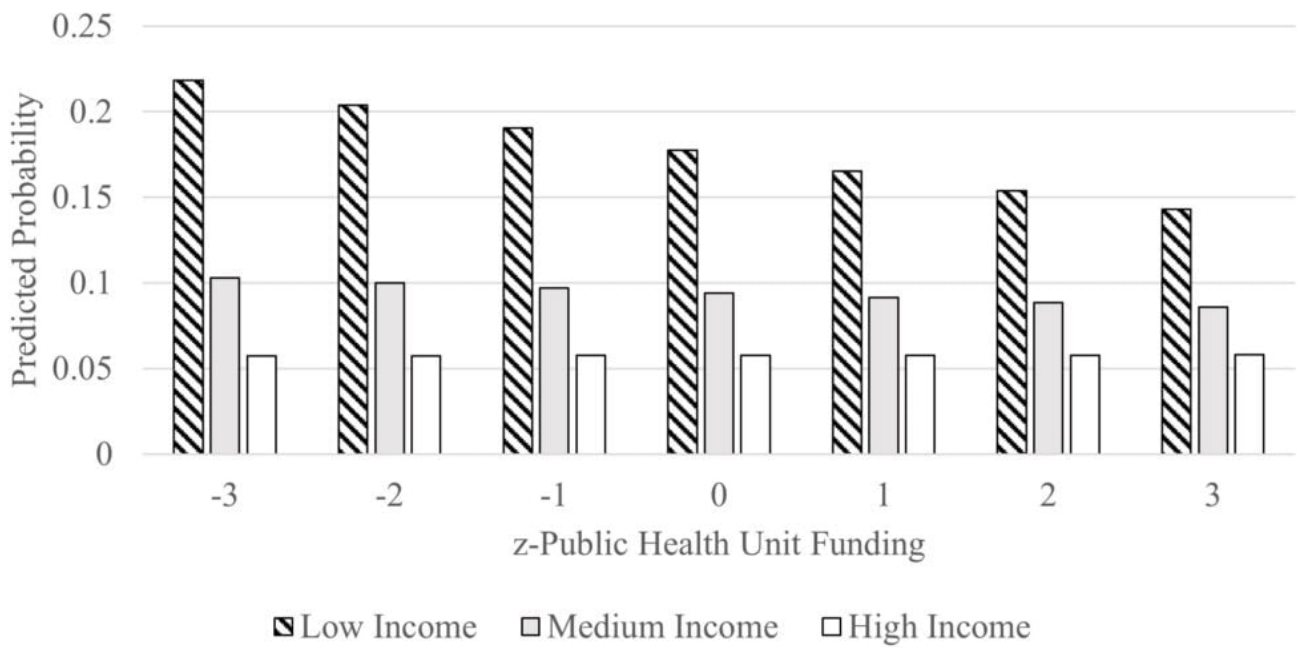
Evaluating Lack of Treatment Arm Exchangeability and Conditional Exchangeability in the End-Stage Renal Disease Treatment Choices (ETC) Medicare Payment Model Randomized Controlled Trial Ariana Mora* Ariana Mora Kelsey Drewry Daeho Kim Kalli Koukounas Amal Trivedi Adam Wilk Rachel Patzer

Objective: Evaluate lack of treatment arm exchangeability for Medicare's largest RCT, ESRD Treatment Choices (ETC), with particular focus on disparities and underlying ESRD trends by race/ethnicity prior to policy implementation.

Methods: Construction of a pre-policy cohort (2015-2019) using the United States Renal Data System national registry using ETC evaluation metrics (patients attributed to dialysis facilities as patient-months (p-m); ESRD outcomes: dialysis, waitlisting, and living donor kidney transplant). Conditional exchangeability assessed using multilevel fixed effects models.

Results: 25,797,647 p-m (n=784,777 patients) met inclusion for ETC pre-implementation analysis (ETC: 8,203,393 p-m; Control: 17,594,254 p-m). Patients treated at ETC and Control facilities had similar age, sex, BMI, pre-ESRD nephrology care, and dialysis modality, but otherwise were non-exchangeable. **(See figure)** Disproportionate ETC allocation within ESRD Networks occurred as a function of the randomization unit (ZIP Code clusters), leading to geospatial clustering and higher/lower than expected ethno-racial distribution by ETC assignment and ESRD Network. Adjusting for patient- and facility-level covariates and spatial-temporal fixed effects was unable to achieve conditional exchangeability by race/ethnicity for ESRD outcomes. Adjusted odds ETC:Control assignment differed by race/ethnicity: dialysis (ETC 5-8% higher), waitlisting (ETC 3-21% lower), and living donor transplant (ETC 4-33% lower).

Conclusions: There are underlying differences between ETC and Control groups prior to policy implementation, particularly with respect to race/ethnicity, that have resulted in non-exchangeability and confounding at baseline. Future evaluation of ETC Policy must account for cluster randomization failure and particular attention given to avoid exacerbating underlying ethno-racial disparities that exist between ETC and Control patient populations at baseline prior to policy implementation.

# Medicare RCT: End Stage Renal Disease (ESRD) Treatment Choices (ETC)

Policy RCT, randomization unit: Hospital Referral Regions (HRR) ZIP code clusters

ESRD Networks

Census Region: Northeast
- **1** (MA/CT/RI/VT/NH/ME)
- **2** (NY)
- **3** (NJ)
- **4** (PA)

Census Region: South
- **5** (VA/WV/MD)
- **6** (NC/SC/GA)
- **7** (FL)
- **8** (TN/AL/MS)
- **13** (AR/LA/OK)
- **14** (TX)

Census Region: Midwest
- **9** (OH/IN/KY)
- **10** (IL)
- **11** (MI/WI/MN/ND/SD)
- **12** (MO/IA/NE/KS)

Census Region: West
- **15** (CO/AZ/NM/UT/NV/WY)
- **16** (AK/WA/OR/ID/MT)
- **17** (HI/Northern CA)
- **18** (Southern CA)

Randomized HRR Policy Assignment

- Control
- ETC
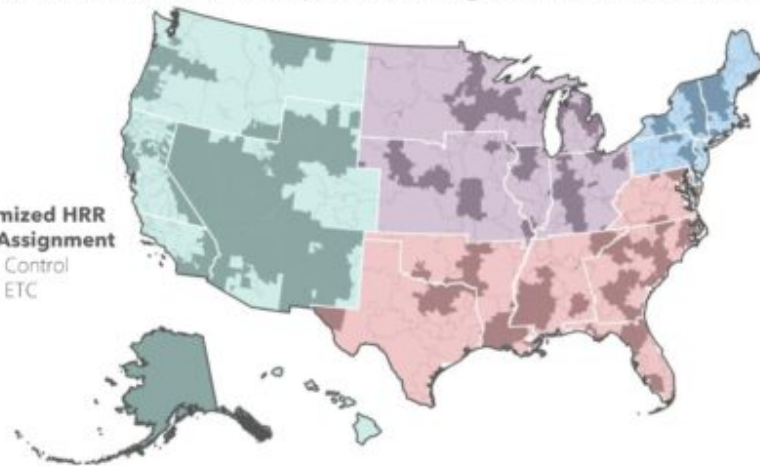
Proportion of Assignment by ESRD Network

Expectation 50/50, accounting for sampling characteristics

■ Northeast ■ South ■ Midwest ■ West

Overall

Control / ETC

ESRD Network 18

Expectation given randomization

Race/Ethnicity

- NH White
- NH Black
- Hispanic
- NH Other*

*Other: Asian/Middle Eastern/Native American/Pacific Islander/Multiracial, NH: Non-Hispanic
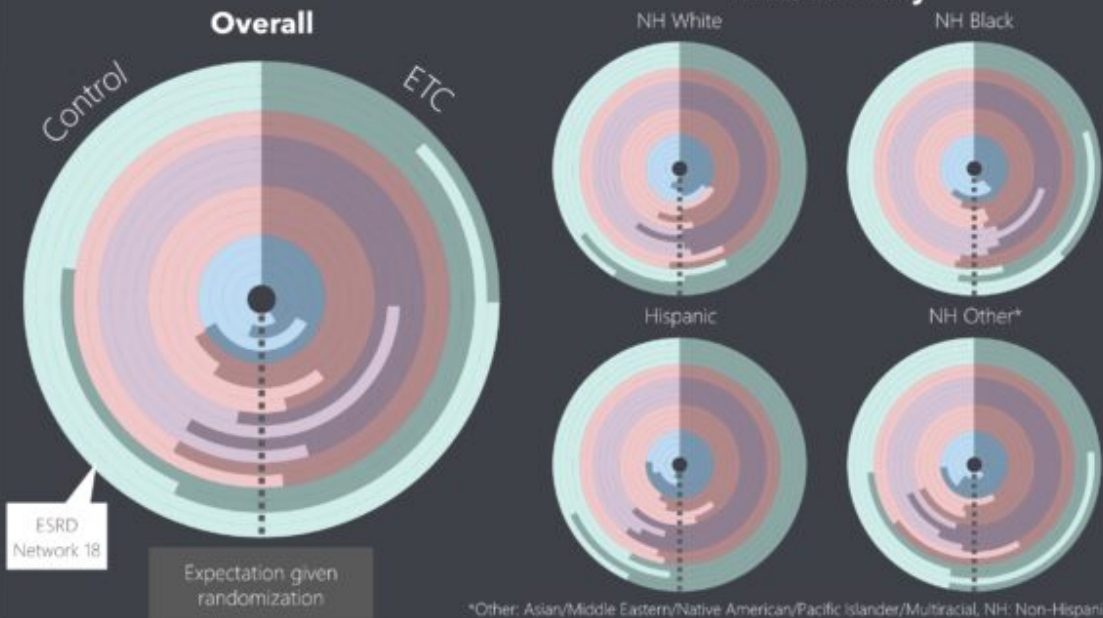
Adjusted ETC : Control Odds Ratio for Pre-Policy ESRD Outcomes

Conditional exchangeability expectation OR 1.0 (equal odds outcome prior to policy implementation)

Dialysis

Waitlisting

Living Donor Transplant

- 95% CI Upper
- 95% CI Lower
- ◆ Adjusted Odds Ratio
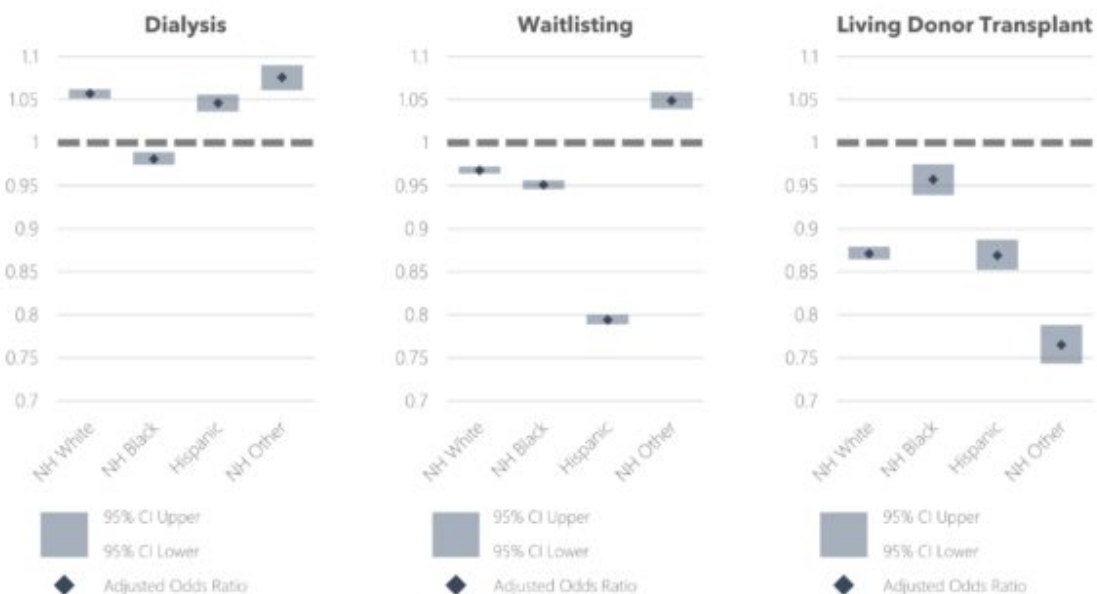
Covariates: patient-level (race/ethnicity, sex, insurance), facility-level (% Dual-Eligible Medicaid/Medicare patient case-mix, urban/rural location, median ZIP Code income, and state ACA-expansion status), and fixed-effects (ESRD Network and study year)

Depends on whom you ask: discrepancies in reporting spousal care between women and men across European welfare states Afshin Vafaei* Afshin Vafaei Ricardo Rodrigues Cassandra Simmons Eszter Zólyomi Johan Rehnberg Selma Kadi Marco Socci Stefan Fors Susan P. Phillips

Current research on determinants, prevalence and effects of informal care on health and other outcomes assumes that survey instruments are able to appropriately identify informal carers. We aim to investigate systematic differences across Europe in reporting spousal care between caregivers and cared-for persons and their possible effects for the analysis of care regimes and correlation of informal care with health. Using information on care provided/received from the Survey on Health, Ageing and Retirement in Europe (SHARE), we estimate prevalence rates of spousal care and discordance rate between caregivers and cared-for persons in the reporting of care among caregiving dyads. Multinomial regressions are used to estimate systematic differences in reporting spousal care. We then use multivariate logistic regressions to assess the effect of discordance in reporting informal care on the correlation of care with poor self-rated health and depression using the EURO-D scale. Results show that only 53.9% of dyads report care that is confirmed by both spouses. Multinomial regressions show that agreement on care being provided/received is more common when women are caregivers, while men are likely to underreport when providing or receiving personal care. Prevalence rates of spousal care across care regimes is sensitive to who reports care although their ranking remains unchanged. There is no effect on the association of care with SRH regardless of who is asked to identify the carer, while the magnitude and direction of the association between depression symptoms and care varies according to the choice of respondent. Possible explanations for the discordance found include social norms dictating gender roles and acceptability of men as carers. Relying on self-identification of carers as most surveys do or to access social benefits has the potential to underestimate their numbers.

Poor oral pre-exposure prophylaxis (PrEP) persistence in an integrated HIV PrEP program 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 T. Pedersen Edward Jere Mina C. Hosseinipour Zakaliah Mphande Irving F. Hoffman Sarah E. Rutstein

An estimated 860,000 people were infected with HIV in sub-Saharan Africa (SSA) in 2022, indicating the need for effective HIV prevention strategies. HIV pre-exposure prophylaxis (PrEP) may reduce new HIV infections, but its effectiveness has been hampered by poor persistence. Few studies have described PrEP persistence in integrated PrEP programs in SSA, and persistence definitions vary across studies, complicating comparisons.

We estimate oral PrEP persistence under Malawi's standard of care (SOC) PrEP services at a PrEP program integrated into an STI clinic in urban Malawi. The study population included 835 clients who newly initiated PrEP from March-December 2022. We define PrEP persistence as a combination of timely PrEP refills and self-reported adherence, and we assess these via routine clinical records data for visit dates, pill counts, and client-reported missed doses. We examine the sensitivity of persistence to different parameters: i.e., where the definition for persistent use allows no more than 7 days without PrEP coverage since PrEP initiation (strict), and where the definition allows up to 14 days without PrEP (flexible). We compute PrEP persistence among 662 clients who received the SOC and apply inverse probability weights to account for baseline differences in age, sex, and indication for PrEP between the SOC recipients and 173 clients who received additional services.

Median age at PrEP initiation was 28 (IQR: 24, 36), and 45% of clients were female. Under our strict definition of persistence, we estimated that had all 835 clients received the SOC, 17% (95% CI: 15%, 20%) and 4% (95% CI: 3%, 6%) would have persisted on PrEP at 1 and 6 months, respectively. Estimates were similar under our more flexible persistence definition. Under all definitions examined, persistence was incredibly low in this PrEP program in Malawi. Strategic evaluation is required to improve PrEP persistence among clients at risk of HIV acquisition in this and similar settings.

Depression and external-cause mortality among people engaged in HIV care in an urban clinic Tiffany Hsieh* Han-Chih (Tiffany) Hsieh Richard D. Moore Anthony T. Fojo Jeanne C. Keruly LaQuita N. Snow Catherine R. Lesko

Background: Depression is a major risk factor for poor HIV (human immunodeficiency virus) clinical outcomes and death among people with HIV (PWH). Although the effect of depression on the risk of external-cause mortality in the general population has been documented, the degree to which depression impacts external- versus natural-causes of death among PWH remains unclear.

Methods: We examined the association between recent (past 12-months) depression as measured by either self-reported depressive symptoms (PHQ-810) or clinical diagnoses of depression and the risk of mortality due to external and natural causes among PWH engaged in care in a single urban HIV clinic. We followed 3,724 adults with HIV who were engaged in HIV care in the Johns Hopkins HIV Clinical Cohort (JHHCC) from 2010 to 2019 until death, loss to follow-up, or administrative censoring. We compared the cumulative incidence functions, subdistribution hazards, and cause-specific hazards of deaths due to external and due to natural causes among PWH with versus without recent depression.

Results: The 3,724 patients in our analysis contributed 241,785 person-months (20,149 person-years) of follow-up. The majority of the study participants were male (65%), Black (76%), and non-Hispanic (98%). The crude subdistribution hazard ratio (sdHR) for external-cause mortality associated with depression was 2.31 (95% confidence interval (CI): 1.21, 4.42). After adjustment for age, sex, Black race, self-reported HIV acquisition risk factors, calendar time, and insurance status, the sdHR was 2.25 (95% CI: 1.16, 4.39). Depression was associated with over twice the hazard of death due to external causes among PWH.

Conclusion: Our results showed that depression was associated with increased risks of external death among PWH in a large urban cohort. This study motivates further analyses to understand the mechanisms that could describe the interplay between depression and other modifiable factors leading to mortality for HIV- infected population.

Social vulnerability increases age-adjusted years of potential life lost among people with HIV in Florida, 2020 Giselle A. Barreto* Giselle Barreto Tendai Gwanzura Tan Li Diana M. Sheehan Mary Jo Trepka

Community susceptibility to the adverse impacts of multiple physical, social, and systemic stressors, termed social vulnerability, reduces community resilience to epidemics and pandemics leading to higher rates of morbidity and mortality; this may be especially true for people with HIV (PWH), who may experience additional hardship accessing healthcare and support services. Therefore, this study aimed to measure the age-adjusted rate of years of potential life lost (aYPLL) and 95% gamma confidence intervals (95%CI) by ZIP Code level social vulnerability tertials (low, medium, high) among PWH during the first year of the COVID-19 pandemic (2020). Data utilized for this study included: (1) HIV surveillance data for the state of Florida, (2) ZIP Code level Social Vulnerability Index (SVI) calculated from American Community Survey data at the ZIP code level following Centers for Disease Control and Prevention methods, (3) US female and male life tables (2020), and (4) U.S. standard population (2000). PWH living in communities with high social vulnerability lost 6 and 5 more aYPLL per 100 persons due to all-cause mortality compared to those living in communities of medium or low social vulnerability, respectively, (H=32.2, 95%CI= 31.5-32.9; M= 27.2, 95%CI=26.5-28.0; L= 26.2, 95%CI=25.0-27.8). Additionally, as community vulnerability increased, aYPLL lost due to HIV/AIDS and COVID-19 specific mortality also increased (HIV/AIDS L= 6.4, 95%CI=5.8-7.2; M=9.4, 95%CI=8.9-10.0; H=12.5, 95%CI= 11.9-13.2; COVID-19 L= 1.0, 95%CI=0.7-1.7; M=1.4 95%CI=1.2-1.8; H=1.9, 95%CI= 1.9-2.1). In 2020, PWH living in communities with higher social vulnerability relative to those living in less vulnerable communities experienced greater aYPLL due to all-cause, HIV-, and COVID-19 specific mortality, underscoring the urgent need for improved public health resource allocation and policies to ensure continuity of healthcare and social services during disasters.

Table 2. Age-standardized[a] rates of YPLL per 100 persons among people in Florida with HIV by underlying cause of death and social vulnerability, 2020 (N=113757.

	Social Vulnerability Tertial aYPLL (95% Gamma Confidence Interval)		
	Low	Medium	High
Underlying cause of death category[b]	(n=11,220)	(n=25,178)	(n=77,359)
All causes	**26.2 (25.0-27.8)**	**27.2 (26.5-28.0)**	**32.2 (31.5-32.9)**
HIV/AIDS (ICD-10 B20-B24)	**6.4 (5.8-7.2)**	**9.4 (8.9-10.0)**	**12.5 (11.9-13.2)**
CVD[c]	3.9 (3.4-4.7)	3.6 (3.3-4.0)	4.1 (4.0-4.3)
Cancer[d]	4.6 (4.1-5.4)	3.3 (3.1-3.7)	2.7 (2.6-2.9)
Diabetes[e]	0.1 (0.1-0.9)	0.1 (0.1-0.5)	0.7 (0.6-0.8)
External[f]	**7.1 (6.5-8.1)**	**5.2 (4.9-5.6)**	**5.0 (4.8-5.2)**
Liver Disease[g]	-	0.4 (0.3-0.8)	0.4 (0.4-0.6)
Respiratory including COVID-19	1.9 (1.4-2.6)	2.1 (1.8-2.5)	2.7 (2.6-2.9)
Respiratory excluding COVID-19[h]	0.9 (0.6-1.6)	0.7 (0.6-1.0)	0.7 (0.7-0.9)
COVID-19 alone (ICD-10 U07-U12)	**1.0 (0.7-1.7)**	**1.4 (1.2-1.8)**	**1.9 (1.9-2.1)**
Other[i]	**1.7 (1.5-2.4)**	**2.8 (2.6-3.2)**	**3.2 (3.0-3.4)**
Unknown	0.2 (0.1-0.9)	0.0 (0.0-0.4)	0.3 (0.3-0.5)

[a]Age-standardized by the direct method using the 2000 U.S. standard population

[b]Underlying causes of death were coded with the International Classification of Diseases, Tenth Revision (ICD-10) codes. World Health Organization. International classification of diseases, tenth revision. 2019 [cited 2022 Nov 20]. Available from: URL: https://icd.who.int/browse10/2019/en

[c]CVD = Cardiovascular Disease (ICD-10 I00-I99)

[d]Cancer (ICD-10 C00-16, C18-C22, C25, C32-C34, C43, C46, C50, C53-C56, C61, C64-C67, C70-C72, C81-C96)

[e]Diabetes (ICD-10 E10-E14.9)

[f]External = Homicide (ICD-10 U01-U02, X85-Y09, Y87.1), suicide (ICD-10 U03, X60-X84, Y87.0), unintentional injuries (ICD-10 V01-X59, Y85-Y86), and other external causes (ICD-10 S09-S09.9, T01-T71)

[g]Liver Disease (ICD-10 K70-K77)

[h]Respiratory Excluding COVID-19 (ICD-10 J00-J47)

[i]Other (ICD-10 A00-B19, B25-B49, B58-B64, B99, D00-E09.9, E15-G99, J60-N16, N20-P08, Q00-R99)

HIV = human immunodeficiency virus (ICD-10 B20-B24)

AIDS = acquired immunodeficiency syndrome

ICD = International Classification of Diseases, Tenth Revision

Exposure to environmental metals and prevalence of human papillomavirus: data from NHANES 2003-2016 Brandie DePaoli Taylor* Brandie DePaoli Taylor Akaninyene Noah Victor Adekanmni Yuanyi Zhang Abbey Berenson

Objective: It is becoming increasingly important to understand the impact of environmental exposures on human health. Exposure to heavy metals can influence immune system function possibly altering susceptibility and progression of infections. Few studies have considered if exposure to environmental metals may also impact the risk of common sexually transmitted infections in the population.

Methods: We conducted a cross-sectional study using data from 4,363 non-pregnant adults ages 18 and older who participated in the National Health and Nutrition Examination Survey (NHANES). Human papillomavirus (HPV) high-risk genotypes were the outcome of interest. Nine metals measured in urine were included in the analysis. Using a modified Poisson model with robust error variance prevalence ratios and 95% confidence intervals were calculated. All models were adjusted for age, race/ethnicity, and the poverty index ratio.

Results: Urine barium (PR 1.17, 95% CI 1.06 -1.29), cadmium (PR 1.17, 95% CI 1.01-1.29), cesium (PR 1.28, 95% CI 1.06-1.55), mercury (PR 1.23, 95% CI 1.10-1.36), lead (PR 1.19, 95% CI 1.03-1.39), antimony (PR 1.27, 95% CI 1.11-1.46), tungsten (1.17, 95% CI 1.04-1.31), and uranium (PR 1.14, 95% CI 1.01-1.28) were associated with increased prevalence of HPV 16/18 genotypes. Interestingly, when stratified by males and females, these associations were only observed among female but not male participants (Figure 1).

Conclusions: We found that metal exposure is correlated with high-risk HPV genotypes, which are well known to cause cervical and other cancers. Future prospective studies and mechanistic studies should be conducted to better understand the impact of environmental pollutants on HPV.

Environmental Metal Exposure and High-Risk HPV: NHANES 2003-2016

Infectious Disease
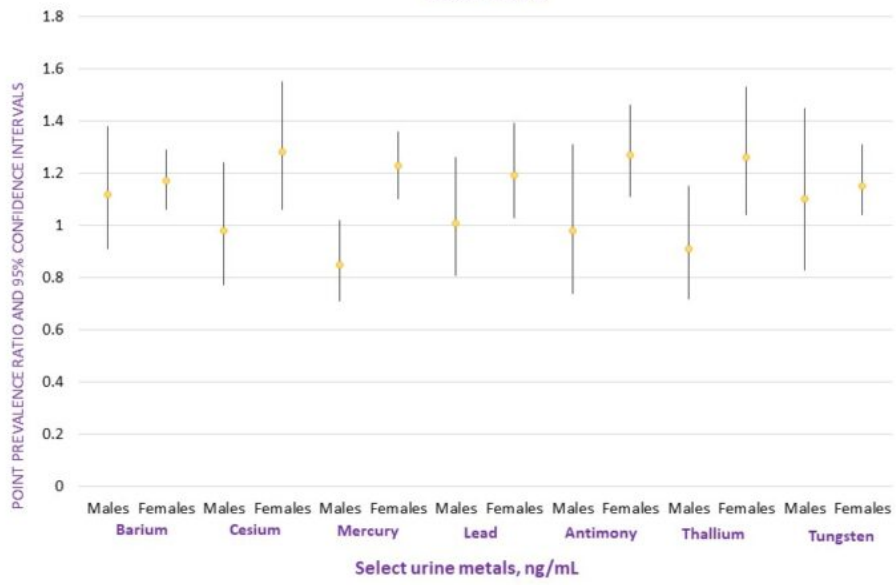
Post-COVID syndrome 24 months after a SARS-CoV-2 infection in adults of the general population: cohort study from South of Germany Dietrich Rothenbacher* Dietrich Rothenbacher Raphael S. Peter Alexandra Nieters Lisamaria Eble Hans-Georg Kräusslich Stefan O. Brockmann Siri Göpel Jürgen M. Steinacker Dietrich Rothenbacher Winfried V. Kern for the EPILOC Phase 3a Study Group

Besides morbidity and mortality in the acute phase of SARS-CoV-2 infection, considerable post-acute health problems are reported. This study aimed to describe post-acute sequelae up to two years after acute SARS-CoV-2 infection in a population-based sample of previously SARS-CoV-2 infected adults and to evaluate factors for persistence or improvement of the post-acute syndrome (PCS).

Analyses were done in a population-based, observational study including adults aged 18-65 years with positive SARS-CoV-2 polymerase chain reaction tested between October 2020 and April 2021 in defined geographic regions in the South of Germany and had to be notified to the regional public health authorities. Possible participants were contacted 6-12 months after the acute infection (baseline) and followed-up after two years (median 23.9 months) by a standardized questionnaire. PCS was defined as health or working capacity recovered ≤80% (compared to pre-infection) and any post-infection symptom with impairment moderate to strong. Prevalence of symptom clusters and results of adjusted logistic regression analyses for changes in PCS from baseline to follow-up were estimated.

Overall, n=6631 subjects (mean age 45.8 years, 60.9% females) were included in this analysis. Prevalence of symptom clusters at follow-up was 22.2% for fatigue, 17.6% for neurocognitive impairment, 17.2% for symptoms of anxiety or depression, 14.1% for musculoskeletal pain, and 13.8% for chest symptoms. Predictors of improvement of PCS-cases (n=514 improved, prevalence of PCS at baseline 29.9% and at follow-up 31.3%, respectively) were age (OR 0.79 per 10 years (95% CI 0.72; 0,87)), smoking at baseline (OR 0.60 (95% CI 0.40; 0.90)), treatment of acute infection (OR 0.73 (95% CI 0.58; 0.92)), and obesity (OR 0.71 (0.54; 0.92)) among others.

Even two years after acute infection, a considerable burden of PCS is present. An unhealthy lifestyle (smoking, obesity) is associated with persistence of PCS.

Reductions in recurrent otitis media and outpatient antibiotic use related to 13-valent pneumococcal conjugate vaccine Laura M King* Laura King Hilary L Colbeth Rouselinne Gómez Sara Y Tartof Joseph A Lewnard

Introduction: In the pre-pneumococcal conjugate vaccine (PCV) era, recurrent disease (4 episodes/year) accounted for a meaningful proportion of acute otitis media (AOM). Implementation of 13-valent PCV (PCV13) in routine infant immunization schedules in the US in 2010 is associated with reductions in both AOM incidence and antibiotic use; the extent to which these reductions are driven by decreases in recurrent AOM is unknown. We aimed to evaluate the effect of PCV13 on recurrent AOM and associated antibiotic use in a US pediatric cohort.

Methods: We measured AOM-associated outpatient visits and antibiotic prescriptions from the Optum Clinformatics™ DataMart for children aged 0–4 years in 2008–2018. We categorized children with 4 AOM visits in a year as having recurrent AOM and we categorized children born 2011 as post-PCV13 and children born 2011 as pre-PCV13. We estimated proportions of children with recurrent AOM and the average number of AOM episodes per child in pre- and post-PCV13 periods. Generalized estimating equations were used to evaluate associations of PCV13 and AOM visits and antibiotic prescriptions.

Results: In the pre-PCV13 period, 5.4% of children had recurrent AOM, compared with 4.6% in the post-PCV13 period (Figure). Across periods, children with recurrent AOM received approximately 3.6 antibiotics prescriptions per child-year compared with 0.4 prescriptions per child-year in those without recurrent AOM. Compared with the pre-PCV13 period, children in the post-PCV13 period had an 11% decrease in the odds of recurrent AOM (OR 0.89, 95% CI 0.85, 0.94), and an average of 0.06 (95% CI 0.04, 0.08) fewer AOM visits and 0.03 (95% CI 0.1, 0.5) fewer AOM antibiotic prescriptions per child-year.

Conclusions: In our study population, PCV13 was associated with notable decreases in recurrent AOM and associated antibiotic use. Our findings may inform AOM prevention and antibiotic stewardship as next-generation PCVs are implemented.

Figure. Children with recurrent AOM by PCV13 period

Infectious Disease
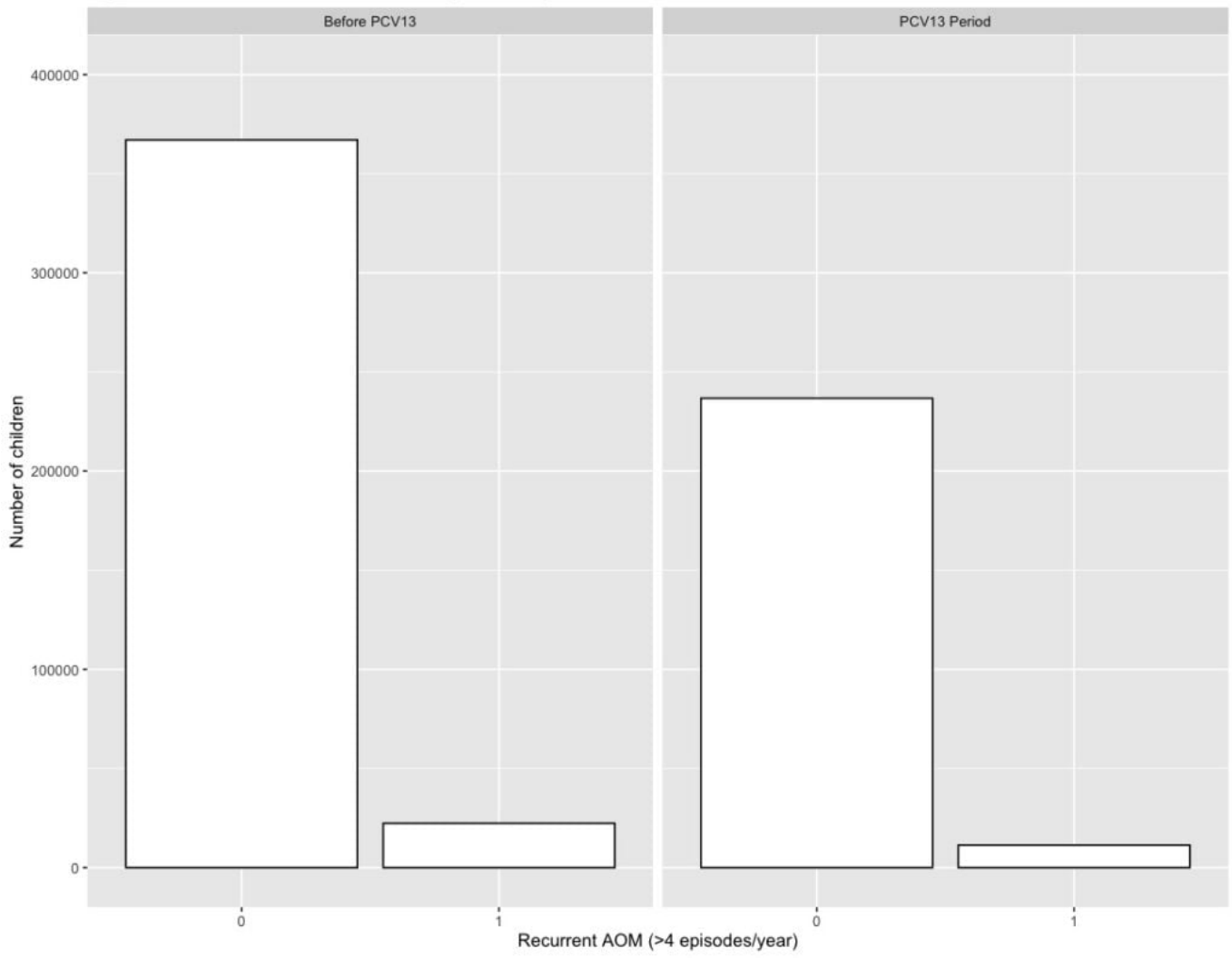
Getting to Full Disclosure: HCV testing and status disclosure behaviors among PWID and their injecting partners Maia Scarpetta* Maia Scarpetta Rachel Kanner Neia Prata Menezes Claire C. McDonell Julie Bruneau Kimberly Page Meghan D. Morris

Background: Hepatitis C virus (HCV) is primarily transmitted through injection drug use. While HCV testing access has improved for people who inject drugs (PWID), little is known about whether people share their results with people they inject with. Understanding the dynamics of HCV disclosure among primary injecting partners fosters informed public health decision-making and prevention strategies.

Methods: From 2017-2019, PWID and their primary injecting partners in Montreal, Canada, and San Francisco, USA (SF), underwent HCV screening and participated in a quantitative socio-behavioral survey. Using dyadic data, we estimated HCV-status disclosure prevalence, overall and by partnership HCV status. Statistical analyses included Kruskal-Wallis tests for nonparametric variables and Pearson chi-squared/Fisher exact tests for categorical variables.

Results: Overall, 91% received an HCV test, representing 162 individuals and 131 partnerships; most (57%) were positive for HCV infection (Montreal: 64%; SF: 43%). Most were male-male partnerships (Montreal: 63%, SF: 51%), and currently living together (Montreal: 57%, SF: 60%), but most Montreal partnerships were both over 30 (71%), while most SF partnerships were both were under 30 (71%). Overall, 90% (n=118) individuals disclosed their HCV result to their primary injecting partner; in 81% of partnerships results were mutually disclosed. Mutual disclosure was highest (41%) among seropositive (+/+) partnerships, less common (32%) in seronegative partnerships, and rarest (17%) in serodiscordant (+/-) partnerships. Neither member disclosed in 5% partnerships. None of the comparisons were significantly different (Figure 1).

Conclusions: Results highlight a high prevalence of HCV testing and disclosure within injecting partnerships. Encouraging result sharing, regardless of serostatus, and involving injecting partners in the HCV continuum can provide support for positive diagnoses and prevention strategies for negative diagnoses.

Figure 1: HCV Disclosure by Partnership Serostatus
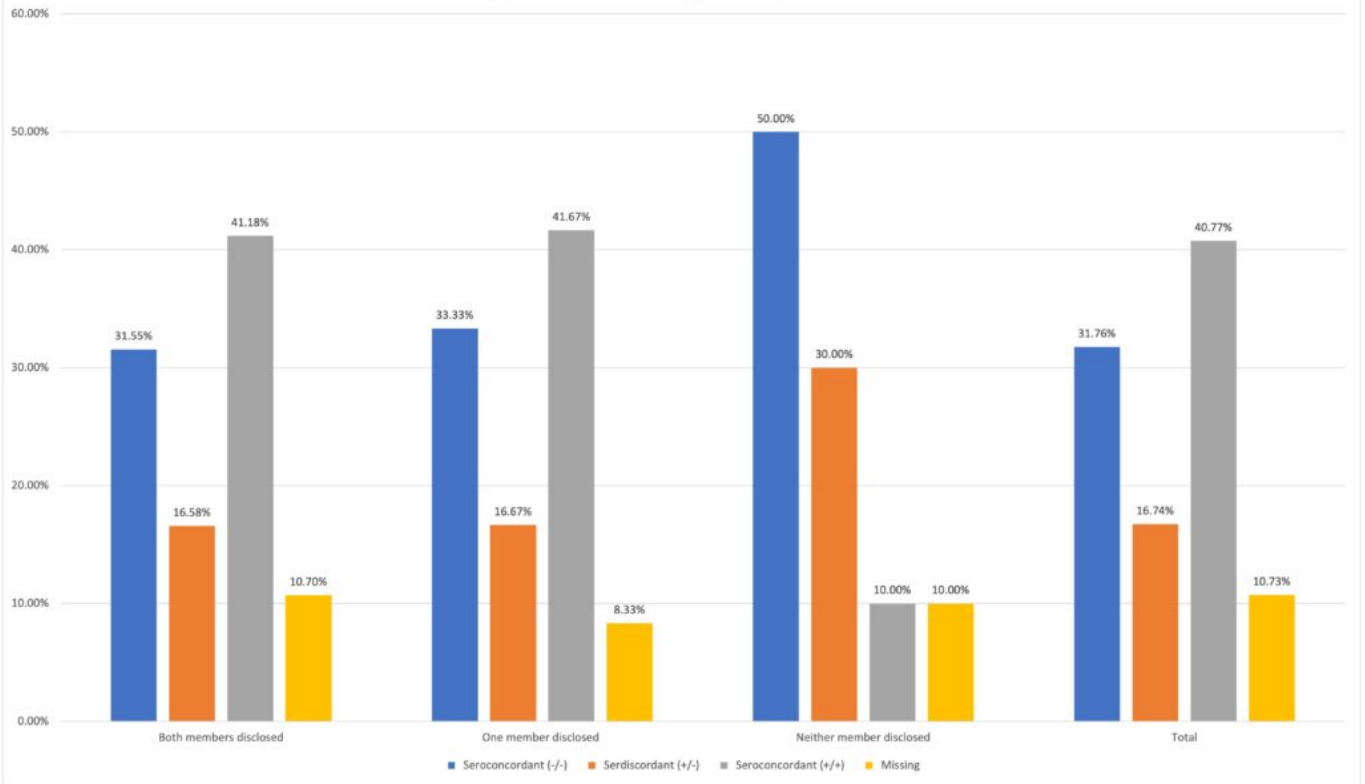
LATEBREAKER

Infectious Disease

Estimating real-time reproductive number and oral cholera vaccine effectiveness for outbreaks in Haiti and Cameroon, 2021-2023 Erin Hulland Frame* Erin Hulland Frame Marie-Laure Charpignon Ghinwa El Hayek Lihong Zhao Angel N Desai Maimuna S Majumder

Cholera sickens millions of people a year globally, mostly in low-income and conflict settings. Prior to improved water and sanitation systems cholera also routinely ravaged higher income countries. With crumbling infrastructure and climate change putting new locations at increased risk, the threat of cholera persists. Thus, understanding its transmission and prevention are critical.

Responding to a cholera outbreak is multi-pronged, with behavioral education and water treatment being among the most-used interventions. Oral cholera vaccination (OCV) is often used in complement, with a recent switch to single-dose implementation (OCV1) due to limited supply. Therefore, understanding where to best allocate OCV1—and doing so in a timely manner—is essential, especially in such settings where detailed data are often scarce.

In this pursuit, we leveraged EpiEstim—an open source modeling platform— to provide rapid estimates of time-varying disease transmission via the effective reproductive number (RE). An extension of this platform (VaxEstim) allows identification of gaps in vaccine coverage. We use VaxEstim to compare two recent cholera outbreaks in Cameroon and Haiti using aggregated publicly-available data; estimate the effectiveness of OCV1 campaigns; and identify climate and sociodemographic factors related to context-specific cholera transmission.

We observe high initial 4-day rolling average estimates of RE in both Haiti and Cameroon, with Haiti having larger initial values (2.1 [95% CI:2.0-2.3] vs. 1.8 [1.1-2.7]); both high transmission periods were followed by a longer period oscillating around 1. We observe higher OCV1 effectiveness in Haiti than Cameroon (75.3% [54.0-86.4] vs. 56.2% [18.9-84.9]), and note differences in improved water access, population density, and climate variables, likely contributing to this variability. This work demonstrates the utility of VaxEstim for quick and inexpensive estimation of vaccine effectiveness in data-poor outbreak settings.

Figure 1: (A) Effective Reproductive Number (R$_E$) and (B) Vaccine Effectiveness over time in Cameroon and Haiti
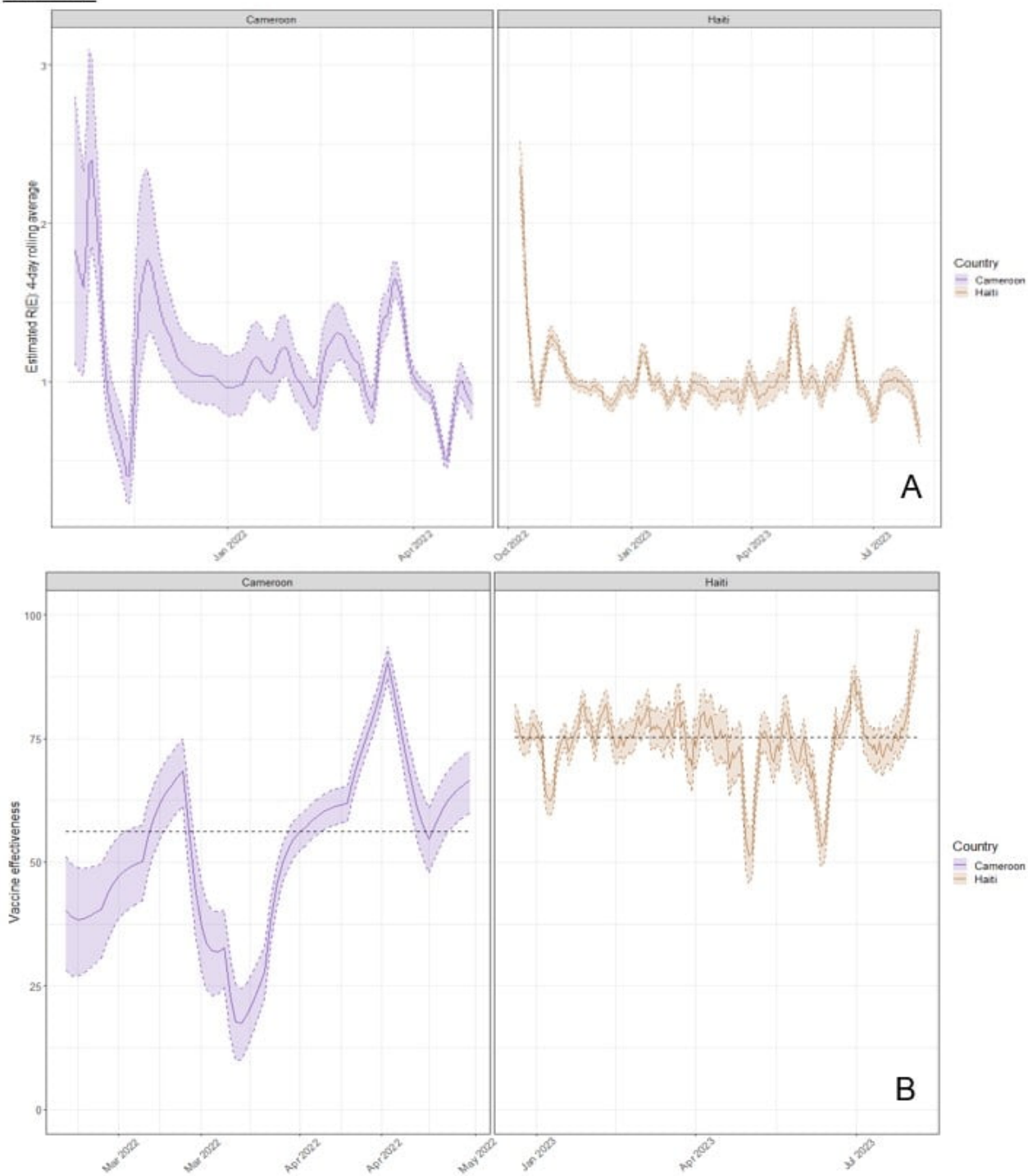
A rapid review contrasting the evidence on avian influenza A(H5Nx) clades 2.3.4.4b and 2.3.2.1c in humans Tricia Corrin* Tricia Corrin Kaitlin Young Mavra Qamar Kusala Pussegoda Austyn Baumeister Nicole Atchessi Erin Leonard Lisa

Background: Avian influenza viruses (AIV) circulate in wild and domestic bird populations posing an on-going risk for zoonotic transmission and virus adaptation to mammals and humans. The A(H5Nx) clades 2.3.2.1c and 2.3.4.4b currently circulating caused sporadic infections in humans including six cases of A(H5N1) 2.3.2.1c in Cambodia, 13 cases of A(H5N1) 2.3.4.4b across eight countries, and 31 cases of A(H5N6), assumed to be clade 2.3.4.4b, in China, since January 2022-December 2023. A rapid review (RR) was conducted to contrast the evidence on A(H5Nx) clade 2.3.2.1c and 2.3.4.4b infection in humans.

Methods: Adhering to PRISMA guidelines a protocol a was developed *a priori*. The search was conducted in December 2023 for English or French primary research articles pertaining to AIV clades 2.3.4.4.b or 2.3.2.1c in Scopus, PubMed and EuropePMC to capture both published and preprint articles. Search verification and a grey literature search was also conducted in January 2024. Full-text relevance screening was conducted independently by two reviewers. Data extraction and risk of bias (ROB) assessment was conducted by one reviewer and verified by a senior reviewer. ROB was assessed using Joanna Briggs Institute critical appraisal checklists and the Newcastle Ottawa Scale depending on the study design. Results were reported narratively.

Results: Forty articles were included in this RR and were published between 2014 and 2023. Studies found no discernible difference in the likely mode of exposure, transmission, or the potential of AIV infection in humans between A(H5Nx) clades 2.3.4.4b and 2.3.2.1c. Seropositivity, seroconversion, and hospitalization rates were also similar for the two clades, while intensive care unit admission and fatalities were higher for A(H5Nx) clade 2.3.2.1c. Several markers of mammalian adaptation and mutations associated with increased viral replication, polymerase activity, and virulence in mammals and/or mice were found in both clades. Most studies were considered to be at high ROB due to their study design and poor reporting, some well-designed cohort studies were at moderate ROB.

Conclusion: This summary can be used to inform what is known about A(H5Nx) in humans for the two clades and suggests that there is on-going adaptation pressure from circulating AIVs that should be closely monitored. Due to the scarcity of studies for each outcome and the low level of evidence based on the study designs, the conclusions from this RR could change with future research. It is important to continue surveillance in birds, mammals, and humans, conduct large epidemiological studies, and develop mitigation strategies from a one health perspective.

Infectious Disease

Hepatitis C RNA blood serum results at treatment completion predict sustained virologic response in a cohort of people who use drugs Claire C McDonell* Claire McDonell Meghan D Morris Jennifer C Price Ryan D Assaf Jeff McKinney

Sustained virologic response at 12-weeks post-treatment completion (SVR12) is considered the gold standard clinical efficacy endpoint for direct acting antiviral (DAA) hepatitis C (HCV) treatment. However, its origin dates back to interferon therapy which required close clinical observation and had cure rates closer to 60%, compared to DAA's 90-95%. While serology from the SVR12 timepoint consistently predicts cure in both cases, it also requires patients to return for bloodwork three months after they complete treatment. This may contribute to loss to follow up, especially for those who often face instability in their life, such as people who inject drugs. To explore shortening this gap, we assessed concordance between the presence of HCV RNA in serum samples at treatment completion, 4-weeks post-treatment (SVR4), and SVR12 "cure" by calculating positive predictive values (PPV) and negative predictive values (NPV). Clinical data was used from a single arm trial (NCT03987503) of participants who received a standard course of the DAA sofosbuvir/velpatasvir. Of the eighty-seven (N=87) participants who initiated treatment, 97% had an income below the national poverty line, 80% had recently injected drugs, and 43% were experiencing homelessness. Sixty-nine (79%) completed treatment and 58 (67%) attained SVR12. Six participants were lost to follow-up between treatment completion and SVR12. Both the PPV and NPV of SVR4 for SVR12 were 100%. The PPV and NPV of treatment completion for SVR12 was 100% and 97%, respectively. Those with discordance (n=2) had different genotypes pre- and post-treatment, likely indicating new (re)infection. Among this cohort, virologic response at treatment completion and SVR4 closely predicted SVR12. Additionally, fewer participants were lost to follow-up at these earlier timepoints. DAA clinical trial data should be analyzed to assess if earlier timepoints consistently predict HCV cure outside of this socially marginalized cohort.

A Prospective Study of Acute Gastroenteritis and Norovirus in the United States Emma Viscidi* Emma Viscidi Mark A Schmidt Holly C Groom Judy L Donald Matthew T Slaughter Sarah Vertrees

Background and Objectives: Norovirus is the leading cause of acute gastroenteritis (AGE) worldwide. Each year, an estimated 1.31 million deaths occur globally due to AGE, with ~200,000 related to norovirus infection. Noroviruses are among the top five leading causes of AGE hospitalizations and deaths in the US. Few laboratory-based data are available on the burden of noroviruses in sporadic cases of AGE in the US. The primary purpose of this study is to characterize the epidemiology and impact of medically attended AGE (MA-AGE).

Methods: The Study of Acute Gastroenteritis (SAGE) is an all-age, prospective surveillance study of Kaiser Permanente Northwest members living in Northwest Oregon and Southwest Washington. The study will assess the incidence and severity of MA-AGE, including healthcare utilization, and examine viral pathogens (including norovirus), determine norovirus genotypes, and describe serologic responses associated with norovirus. Approximately 2,000 individuals of any age will be enrolled during an 8-month surveillance period from November 15, 2023, through July 31, 2024. Symptomatic individuals will submit a stool specimen for testing and self-collect blood specimens, and complete a survey on signs and symptoms, vaccine attitudes and beliefs, exposure risk factors, and household transmission.

Results: As of December 11, 2023, we have recruited 1,848 individuals with MA-AGE, 92 (5.0%) of whom enrolled and were sent stool and blood sample collection kits. To date, 48 (52%) kits have been returned. Of those returned, testing has been completed on 24 (50%). Norovirus and sapovirus were detected in 2 (8%) samples each.

Conclusion: SAGE will provide critical information on the incidence and severity of MA-AGE in the community in a population-based sample of US participants. This study can increase our understanding of the burden and impact of AGE and norovirus infection, as well as serologic responses to infection.

Tdap and RSV Vaccine Recommendations and Practices for Pregnant Patients by Health Care Providers — Fall DocStyles Survey, United States, 2023 Ayeesha Sayyad* Ayeesha Sayyad Regina Simeone Beatriz Salvesen von Essen Jessica Meeker Sascha Ellington Rebecca Hall Carrie Shapiro-Mendoza Romeo Galang Grayson Waits Katherine Fleming-Dutra

Respiratory syncytial virus (RSV) and Tdap (Tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis) vaccination during pregnancy were recommended by the Centers for Disease Control and Prevention in 2023 and 2011, respectively, to reduce the risk of severe illness in infants. We used data from the 2023 DocStyles survey to describe provider practices for recommending and offering these vaccines to pregnant patients.

The Fall 2023 DocStyles survey, administered October 6 – 25, 2023, was a web-based nonprobability panel survey of U.S. Health Care Providers (HCPs). Our analysis included 1,371 respondents who reported caring for pregnant patients and were asked whether they recommended and offered Tdap and RSV vaccines to their pregnant patients. Adjusted prevalence ratios (aPR) and 95% confidence intervals (CI) estimated associations between provider type and affirmative responses to each question. Prevalence ratios were adjusted for provider age, gender, and years practicing medicine.

Providers had a median age of 47 years and 54.0% were male. Most respondents were Family Practitioners or Internists (65.6%), while 17.8% were Obstetrician-Gynecologists, and 16.6% were Nurse practitioners or Physician Assistants. Eighty percent of providers recommended the Tdap vaccine to their pregnant patients, and 73.7% offered the vaccination onsite. In contrast, 42.2% of providers offered the RSV vaccine to their pregnant patients, and only 23.1% offered onsite vaccination. Obstetrician-Gynecologists were more likely than Family Practitioners and Internists to recommend Tdap (aPR: 3.65, 95% CI: 2.09-6.35) and RSV (aPR: 3.24, 95% CI: 2.38-4.40) vaccines to pregnant people.

Public health messaging reinforcing recommended vaccinations during pregnancy is important for both HCPs and patients. HCPs caring for pregnant people play an important role in vaccine confidence and uptake, especially for newly approved vaccines, such as RSV.

An evaluation of evaluations: reflections on the COVID-19 emergency in New York City

Sharon K. Greene* Sharon Greene Shuo Feng Alyssa Bilinski

Background: Understanding the real-world impact of interventions to mitigate infectious disease is crucial for public health planning, policymaking, and building public trust. Observational methods for causal inference have become popular for assessing the effectiveness of policies instituted under non-emergency conditions. However, conducting evaluations during infectious disease emergencies presents unique challenges. We propose a framework for emergency policy evaluation, informed by past evaluations conducted during the COVID-19 emergency response in New York City (NYC).

Methods: We reviewed evaluations of policies involving the NYC Department of Health and Mental Hygiene related to COVID-19, documenting objectives, data sources, methods, and opportunities for expanding or improving future evaluations. We then characterized potential barriers to policy evaluation during future emergencies and outlined infrastructure and methodology to support real-time evaluation.

Results: We identified three key considerations for planning policy evaluations: 1) methods selection; 2) timely data on outcomes of interest, including for comparison groups unexposed to the policy; and 3) interpretation and implementation strategy (Table 1). During the COVID-19 public health emergency, mandatory individual-level reporting of immunizations for persons of all ages and of negative test results provided granular data that enabled rapid, high-quality evaluations. Future evaluations could be strengthened by applying recently developed methods that account for non-linearities in infectious disease transmission and by interrogating the sensitivity of results to different modeling choices.

Conclusion: Public health agencies should plan evaluations prospectively at the time of policy roll-out. Collecting data on comparison groups is critical for population-level evaluations, as is appropriately accounting for infection dynamics.

Table 1. Key considerations for evaluating policies implemented during infectious disease emergencies

	Selected prior COVID-19 policy evaluations involving the New York City Department of Health and Mental Hygiene	Prospective considerations

1) Methods
What is the untreated comparison group?
	• Difference-in-differences and controlled interrupted time series (DID/CITS) compare the outcome trajectories in treated and control groups pre- and post-intervention
	  ○ Policies evaluated: effects of return-to-office, public schools reopening, and vaccination mandates on cases (Greene et al., 2023)
	  ○ Policy evaluated: effects of vaccination requirement on vaccination rates (Rubenstein et. al., 2023)
	• Synthetic control methods (SCM) provide a data-driven strategy to use a weighted average comparison of units when donor pool is large but no single comparison group is well-matched
	  ○ Policies evaluated: effects of proof of vaccination, incentive payments, and employer-based mandates on vaccination rates (Cohn et al., 2022)
	• Regression discontinuity (RD) is useful when eligibility for treatment is based on continuous criteria such as age, allowing comparison between individuals just above and below the eligibility cutoff
	  ○ Policy evaluated: effect of vaccination program on hospitalization risk (Greene et al., 2022)
	• Methods with an identification strategy (experimental or quasi-experimental design) and untreated comparison group, like those above, yield more robust results than pre-/post-analyses (e.g., Lasry et al., 2020, Blaney et. al, 2022)
		Adopt recent best practices for:
		• DID/CITS: Account for staggered treatment timing and covariates
		• SCM: Consider new specifications/hybrids (e.g., intercepts, synthetic difference-in-differences, augmented synthetic controls)
		• RD: Compare parametric and non-parametric specifications
		• All methods:
		  ○ Adjust models to account for nonlinearities in infection transmission when incidence used as outcome
		  ○ Bound the potential impact of spillovers between treated and untreated units
		  ○ Conduct sensitivity analyses and placebo tests
		  ○ Assess how policy effects differ across subgroups, such as by race or ethnicity
		  ○ During periods of community-wide emergency, it can be difficult to identify truly untreated groups and to disentangle policies from social network effects
		Other approaches to consider:
		• Instrumental variables analysis estimates the effect of an intervention using an "instrument" that impacts the outcome only by shifting treatment uptake
		• Propensity score matching produces balanced samples between the treated and control groups among observables (e.g., Deming et al., 2018)

2) Data collection *How and when will data be collected?*	• Near real-time surveillance data on persons tested, persons immunized, reported cases, emergency department visits, and deaths • Demographic data, such as gender, age, race and ethnicity, area-based poverty level, and Index of Concentration at the Extremes • Community mobility, through mobile devices and surveys • Dates policies were implemented and modified • Outcome data for individuals exposed to the policy, unexposed comparators, and those potentially experiencing spillover effects	• In some contexts, it may be difficult to collect data on untreated groups • For new outbreaks, new data streams may need to be established
3) Interpretation and implementation *How will results be used and communicated?*	• Communicate benefits of vaccination to the public and health care providers • Understand effects of controversial policies, such as mandates • Disseminate findings rapidly by pre-print, followed by peer-reviewed journals	• When results are inconclusive, decision analytic methods that combine results with intervention costs and alternatives can be useful for decision-making

Infectious Disease

Demographic disparities in suboptimal uptake of human papillomavirus (HPV) vaccine among female schoolteachers in a middle eastern country: A generalized structural equation modeling approach Saeed Akhtar* Saeed Akhtar Juman Rezqalla Danah Omar Mariam Alshatti Houda Al-Failakawi Sarah AlGhurair Shamayel AlHaqqan Amna Ibraheem

Background: Suboptimal human papillomavirus (HPV) vaccine uptake among females is associated with several knowledge and behavioural factors. However, the complex mechanisms causing poor HPV vaccine uptake are not yet fully understood. Using generalized structural equation modeling (GSEM) with bootstrapping estimation, we sought to disentangle the direct, indirect, and total effects (DE, IDE, TE) of age, family history of cervical cancer and unawareness of HPV causal role in cervical cancer on the poor uptake of HPV vaccine among female schoolteachers in Kuwait.

Methods: A cross-sectional study was conducted among female schoolteachers employed in public and private-sector high schools in Hawalli governorate. Data were collected using a self-administered questionnaire during January 2018. Prevalence of HPV vaccine uptake was computed. The effects of age (years) ($\geq$ 30 vs. < 30), and family history of cervical cancer (yes/no), through mediator (i.e., unawareness of HPV causal role in cervical cancer) on to HPV vaccine uptake (no vs. yes) were examined in GSEM framework. The DE, IDE, TE were estimated as log odds and their SEs.

Results: Of 1341 participants, 60% were unaware of HPV causal role in cervical cancer. The prevalence of HPV vaccine uptake was 1.9%. There was evidence of a significant IDE of age on HPV vaccine uptake status through the mediator (mediated proportion 36%; IDE aOR: 0.54, $p = 0.004$; DE aOR: 1.96; $p = 0.108$; TE aOR: 1.07; $p < 0.001$). Moreover, a positive family history of cervical cancer mediated a significant protective effect through the mediator to the poor HPV vaccine uptake status (IDE aOR 0.42, $p = 0.006$; DE aOR = 0.21, $p < 0.001$; TE aOR 0.08, $p < 0.001$).

Conclusion: Health education intervention tailored to enhance the awareness about HPV causal role in cervical cancer, and benefits of HPV vaccine may augment the HPV vaccine uptake in this and other similar populations. If implemented future studies may look at the impact of such efforts.
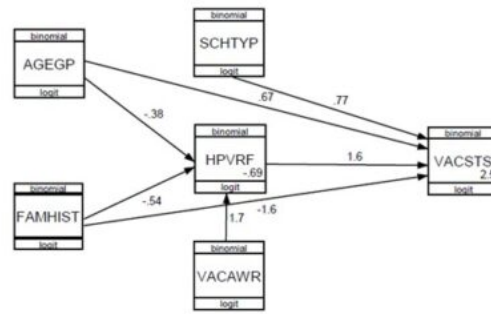
Figure 1. Generalized structural equation model of pathways for estimated direct and indirect effects of independent variables *i.e.*, AGEGP (age ≥ 30 vs. < 30 years), FAMHIST (family history of cervical cancer; yes vs. no) through the mediator HPVRF (unawareness of human papillomavirus (HPV) causal role in cervical cancer, yes vs.no) on to the outcome VACSTS (HPV vaccination status, no vs. yes) in a study of demographic disparities in suboptimal uptake of HPV vaccine uptake among female schoolteachers

Injuries/Violence

Evaluation of the Family Therapy Program: In This Together (ITT) for Survivors of Domestic Violence Michaela George* Michaela George Liliana Valle-Contreras Liliana Molina Cervantez Meghan Kehoe Patti Culross

Introduction:

Domestic violence affects one in every four women in the United States. Previous research shows the importance of group therapy for those who have experienced this trauma. The purpose of this study is to evaluate the "In This Together" (ITT) program that takes place in Marin County, CA, through the organization Center For Domestic Peace (C4DP).

Methods:

This quantitative analysis consisted of 10 cohorts, with a total of 65 participants. Eligibility criteria for survivors of domestic violence included being a parent and fluent in English or Spanish. Scaled questions were asked before and after the 10 week ITT therapy program. The questions were based on the *Regulating Emotions in Parenting Scale* (REPS), and *Hope for Parenting Scale* (HFPS) measurement tools. By asking participants before and after ITT, it allowed the researchers to measure the impacts of the program.

Results:

Based on preliminary results, show that on average, individuals who completed the ITT program were better communicators, strengthened their relationships with their children, and felt empowered against their abuser. Both the REPS and HFPS scales were statistically significantly improved after the 10 week therapy program ($p > 0.05$). Further analysis is underway to understand the components of these scales and how those were impacted by ITT.

Discussion:

ITT has shown to have impacted participants by improving their parent-child relationship after the trauma of domestic violence. Being more aware of feelings and finding empowerment gives survivors of domestic violence more tools to better their lives in many ways. Implementing ITT into different group therapy settings for other populations who have suffered traumatic experiences is crucial and encouraged.

Injuries/Violence

Suicidology across Transgender and Gender Expansive Populations: A Systematic Review
Shamsi Soltani* Shamsi Soltani Boglarka Huddleston Rebecca Bernert

Background: Lesbian, gay, bisexual (LGB), transgender and gender expansive communities– known as sexual and gender minority (SGM) populations– face elevated risk for suicide-related behaviors. Yet, most SGM suicide research is on sexual minorities (e.g. LGB groups), who may differ in risk from gender minority populations. Even gender-minority inclusive research often treats SGM people as at equivalent risk. To advance suicide prevention, it is critical to tailor knowledge to specific sub-populations. Thus, we conduct a systematic review of the English-language, peer-reviewed literature on transgender and gender expansive suicide risk. We evaluate whether risk factors are individual-, community-, or structural-level, and if intersectional social identities are assessed.

Methods: Search terms were selected with research librarian input (author BH) and validated using a selection of seed articles authors identified as relevant to the review. We queried PubMed, PsycINFO, Embase, and CINAHL databases for studies reporting suicide risk measures among transgender or gender expansive people for all dates through September 2023. We reviewed records in Covidence software (© Veritas Health Innovation Ltd). Two reviewers (SS and BH) conducted title and abstract review. Editorials, case reports, and reviews were excluded. All authors conducted full text review, with data abstracted in duplicate. Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines informed reporting of findings.

Data abstracted (or calculated) for relevant studies will include:

- Quality rating
- Sample size and sampling strategy
- Study design
- Suicide risk factor/outcome
- Age, gender, race/ethnicity
- Country/US region

Results and Conclusions: Our search identified 3028 unduplicated records. Title and abstract review eliminated 75% of records, with 765 remaining for full text review as of submission. Review and abstraction are currently underway, slated for completion by Spring 2024.

Suicidology across Transgender and Gender Expansive Populations: A Systematic Review
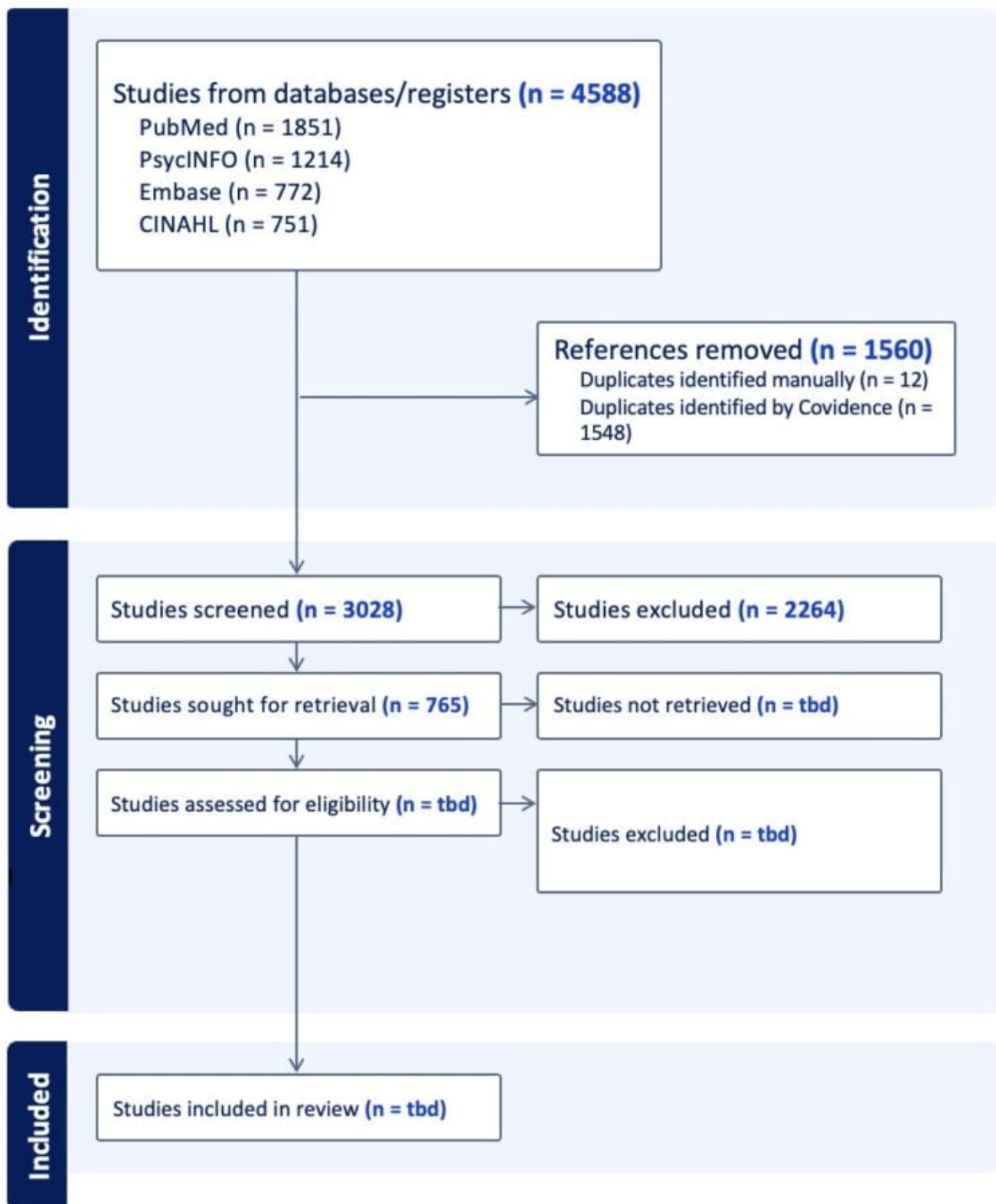
Spatiotemporal Analysis Exploring the Association Between Homeless Encampment Sweeps and Area Crime in Denver, Colorado, 2019-2023 Pranav Padmanabhan* Pranav Padmanabhan Samantha K Nall Cole Jurecka Joshua A Barocas

Crime and safety are top issues for U.S. voters and high priority for policymakers. Certain populations, including people experiencing homelessness (PEH), are viewed as criminogenic. Citing public safety concerns, policymakers in several U.S. cities have conducted involuntary displacement (i.e., "sweeps") of homeless encampments. Growing evidence suggests that sweeps are harmful to the health of PEH, but little is known about their effect on local crime. We aimed to evaluate the association between sweeps and area crime.

We performed a retrospective pre-post spatiotemporal analysis using data from Denver, CO from 11/1/2019 to 7/17/2023. Publicly available crime data contained the date and location of reported crimes. The date and location of every sweep was documented by the City of Denver. We assessed the relationship between sweeps and changes in total crime, crime by National Incident-Based Reporting System (NIBRS) category, and offense type using the Knox test statistic. We tested outcomes within 0.25-, 0.5-, and 0.75-mile radii of sweep locations and 7-, 14-, and 21-day periods before and after sweeps.

There were 303 sweeps during the study period. Within a 0.25-mile radius, there was a small but statistically significant decrease in total crime within 7, 14, and 21 days. For example, within 0.25-miles and 7 days, we expected to observe 0.07 more crimes post-sweep (95% CI: -0.54, 0.68), but found an average decrease of 1.31 crimes. Total crime did not change significantly at 0.5- or 0.75-mile radii, except within 0.5-miles and 7 days. Among NIBRS categories, crimes against property decreased significantly within all time periods at 0.25- and 0.5-miles. There were no consistent significant changes in crimes against persons or crimes against society. Changes in specific crimes are outlined in Table 1.

Involuntary displacement of PEH is not associated with a decrease in area crime and should not be considered an evidence-based solution to improving local safety.

Crime	Proportion of all crimes	Change in Crimes comparing the Pre- and Post-Sweep periods*
Total	100%	Decrease at 0.25 miles
Crimes against persons	10.1%	No change
Murder	0.1%	Increase at 0.75 miles
Aggravated assault	5%	No change
Other crimes against persons	5%	Increase at 0.25-0.5 miles
Crimes against property	58.4%	Decrease at 0.25, 0.5, and 0.75 miles
Robbery	1.7%	No change
Burglary	7%	No change
Larceny	14%	No change
Auto theft	16%	Decrease at 0.25, 0.5, and 0.75 miles
Theft from motor vehicle	18%	No change
Arson	0.2%	No change
White collar crimes	1.5%	No change
Crimes against society	30%	No change
Public disorder	15%	Decrease at 0.25 miles
Drug and alcohol crimes	4%	No change
All other crimes	11%	No change

*Result reported if statistically significant at 2/3 time periods within certain radius of sweeps

Table 1

Injuries/Violence

Determining the effect of changing training duration on injury risk in adolescent ice-hockey players: target trial emulation Chinchin Wang* Chinchin Wang Sabrina Yusuf Russell J. Steele Jay S. Kaufman Paul Eliason Jean-Michel Galarneau Carolyn A. Emery Ian Shrier

Objective: Few studies have estimated causal relationships between training load and injury risk**.** Here, we emulate a target trial to estimate the intent-to-treat effect of changing training duration on injury risk among adolescent ice-hockey players without recent injuries.

Methods: We performed a secondary analysis of data from a 5-year cohort study (2013-2018) in Alberta and British Columbia. We identified eligible player-weeks where players had been training and were not injured in the previous 4 weeks. The intervention was a change in training duration (practice and game minutes), defined as the ratio of the planned average daily training duration in the current week to the average daily training duration over the previous 4 weeks. The outcome was any medical-attention or time-loss injury occurring in the current week. We modelled the relationship between changes in training duration and injury using a generalized additive model with generalized estimating equations to account for repeated measures. We included age group and body-checking league (yes/no) as covariates. We estimated potential outcomes for each player-week under hypothetical interventions, and calculated injury risks and risk ratios relative to no change in training duration. We estimated 95% CIs with cluster bootstrapping.

Results: There were 3,226 eligible participants contributing 162,675 player-weeks and 837 injuries. Figure 1 shows the intent-to-treat effects of changing training duration. Injury risk is expected to be 2.5% for no change in training duration. The largest increases in injury risk occurred for changes in training duration up to 2-fold. Injury risk increased slightly for changes in training duration between 2- and 3-fold, and further for changes over 3-fold. Injury risk decreased with decreased training duration in the current week.

Conclusions: Injury risk increases slightly with increasing training duration among adolescent ice-hockey players without recent injuries.
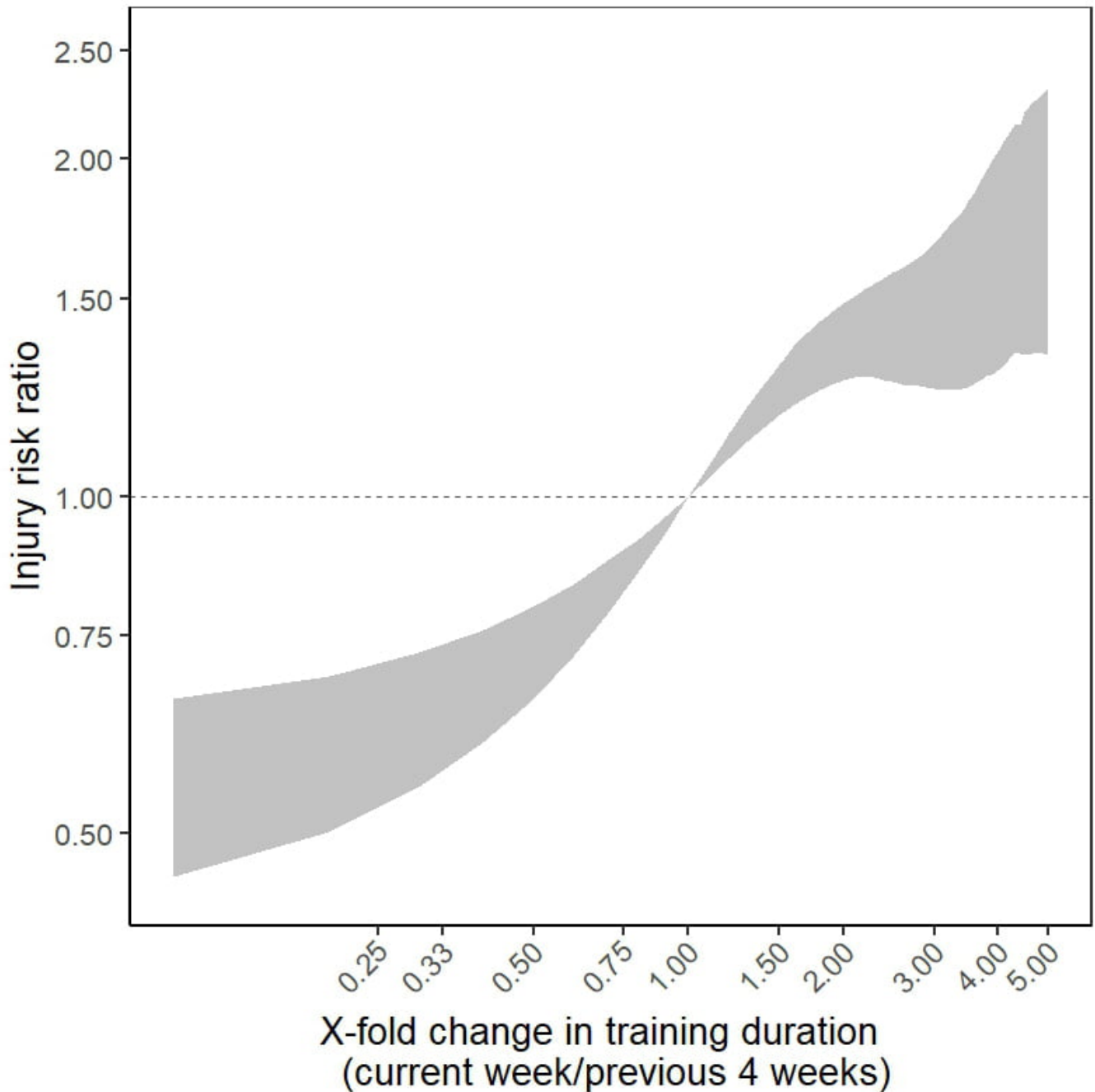
Figure 1. Intent-to-treat effect of changing training duration (practice and game minutes) on injury risk. Ftold changes are measured as the ratio of the planned average daily training duration in the current week to the average daily training duration over the past 4 weeks. Risk ratios are calculated relative to no (1-fold) change in training duration. Only the 95% cluster bootstrapped confidence interval (shaded area) is shown to highlight uncertainty.

Risk factors for the most common pediatric unintentional injury admissions in a rural district hospital- Botswana Keneilwe Motlhatlhedi* John Holmes Keneilwe Motlhatlhedi Billy Morara Tsima Dawei Xie Douglas Wiebe

Introduction. Unintentional child injuries are an important and preventable cause of child morbidity and mortality. We aimed to determine previously unknown risk factors for common unintentional injury admissions in a district hospital in Botswana in order to identify possible targets for future injury prevention strategies.

Methods. We conducted a cross-sectional study of children aged 6 months to 13 years admitted between 2018-2021 with an injury-related diagnosis. We characterized the injuries by frequency. The independent variables of interest were child gender, age, month of injury and maternal employment. Multivariate logistic regression was used to determine the adjusted odds of injury.

Results. Of the 637 children included in the study, 403 (63.27%) were male, the median age was 3.9 years (IQR 0.23-7.31). As shown in Figure 1, the most common injuries were poisoning 208(32.6%), falls 170 (26.8%), and burns 71 (11.2%). These three mechanisms were significantly more prevalent in males and in those younger than 5 years. The odds of having one of the three most common injuries was 40% lower with increasing age group while controlling for gender, month, mother's employment status, and primary caregiver, aOR 0.61 (95% CI 0.51-0.73).

Discussion. Younger age groups were significantly associated with higher incidence of poisoning, falls, and burns in this study population. The child's gender, mother's employment, and month of the year were not significantly associated with mechanism of injury.

Conclusion and recommendations. This is the first study of childhood injury frequency and risk in northwest Botswana. Several injury types predominated, all of which are potential candidates for preventive measures. Unintentional injury prevention efforts in this study population should target poisoning, falls, and burns in children younger than 5 years.

Distribution of Unintentional Childhood Injuries in Northwestern Botswana

Drowning(n=1, 0.2%)

Fall(n=170, 26.7%)

Poisoning(n=208, 32.7%)

MVC pedestrian(n=17, 2.7%)

MVC occupant(n=11, 1.7%)

Foreign body(n=44, 6.9%)

Other(n=48, 7.5%)

Domestic animal(n=25, 3.9%)

Wild animal(n=42, 6.6%)

Burn(n=71, 11.1%)

Injuries/Violence
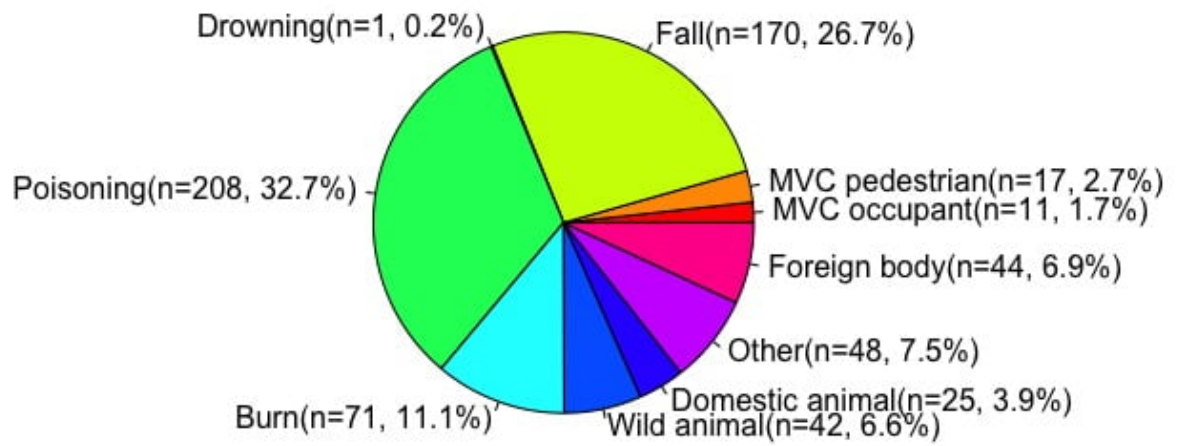
Assessing the concurrent validity of firearm-related mortality estimates from the Global Burden of Disease studies Sid Zadey* Sid Zadey Christopher N. Morrison

Background: Global Burden of Disease (GBD) studies are dominant in global public health and policymaking as they comprehensively model epidemiological parameters for 380+ conditions and injuries in 200+ countries over 30 years. GBD models have been criticized for being challenging to interpret, agnostic to theoretical nuances with limited work on the concurrent validity. We aimed to fill this gap using the firearm mortality outcomes for the United States (US), which are known to have accurate reporting at the state-level by the US Centers for Disease Control and Prevention (CDC).

Methods: We used US CDC WONDER and the GBD 2019 study as the sources for observed and estimated data. Data were extracted for mortality rates per 100000 people for all ages and both sexes for 50 US states and the District of Columbia from 2000-2019 for suicides, homicides, and unintentional injuries involving firearms. Outcome-wise validation was conducted using the Lin's concordance correlation coefficient (CCC). CCC >0.99 is considered 'almost perfect' agreement, 0.95-0.99 is considered substantial, 0.90-0.95 is moderate and <0.90 is poor. Analysis and visualization were conducted in R.

Results: Available data points across the three outcomes varied since the underlying count data for firearm-related mortality were suppressed or unreliable for certain states and years. Hence, our analytical dataset contained 2046 data points (67% of the total data). Lin's CCC revealed that agreements between the GBD estimates and CDC observations were substantial, moderate, and poor for homicide (n=830, CCC [95%CI]=0.971 [0.967, 0.975]), suicide (n=999, CCC=0.946 [0.939, 0.952]), and unintentional (n=217, CCC=0.851 [0.81, 0.884]) firearm-related mortality rates **(Figure 1A-C)**. For firearm-related suicide mortality rates, the deviation between sources was larger for higher values noting underestimation by GBD **(Figure 1B)**.

Conclusion: We chose firearm violence measures for validation due to their reliable reporting in a high-income country with relatively high mortality and public significance. For this, we found that concurrent validity of estimates from the GBD study may vary across outcomes, geographies and periods.

Significance: To our knowledge, this is the first such validation effort for any injury outcome from the GBD study. This cursory assessment should encourage more rigorous validation efforts to understand the appropriate use of and post hoc corrections to GBD estimates.
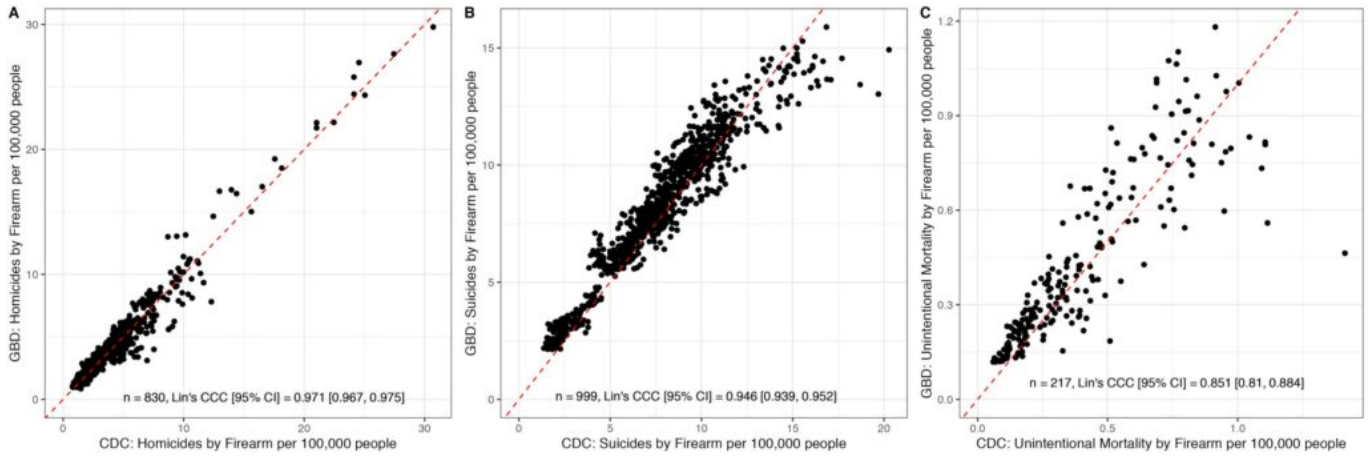
Agreement between GBD 2019 estimates and observed data from the US CDC for 51 states and territories across 2000-2019 for firearm-related mortality per 100,000 people due to A) homicides, B) suicides, and C) unintentional intent.

Area-Level Labour Force Participation and Mood & Anxiety Disorders in Ontario Maria Wong* Maria Wong Roman Pabayo

Background: Over 3.5 million (10%) of Canadians used health services for mood (depression, bipolar, mania, dysthymia) and anxiety (phobia, OCD, panic) disorders. Labour force participation (LFP) rates in regions may be an important socioeconomic determinant for health outcomes. However, the study of whether associations between LFP and health outcomes are heterogenous across socioeconomic groups, such as race or income, is rare. This study aims to address these gaps.

Objective: To examine the association between area-level LFP and mood or anxiety disorders among residents of Ontario aged 12+ years, and 2) to determine whether this association is heterogenous across gender, age, race, and income.

Methods: Data for this study was obtained from Ontario Marginalization Index (with exposure variable for LFP) and Canadian Community Health Survey 2017-2018 (with outcome variables for mood and anxiety disorders). The analytic sample comprised of 33,333 individuals (aged ≥ 12 years) from 34 health regions of Ontario. A weighted multilevel multivariable logistic regression was used. Stratified analyses by gender, race, income, and age were conducted to determine if associations were heterogenous across sociodemographic groups.

Results: There was no association between area-level LFP and mental health diagnoses in the fully adjusted model, nor in the gender-stratified analysis. In race-stratified analysis, a non-significant moderate association was observed between low LFP and mood or anxiety disorders among visible minorities (OR: 1.68, 0.92-3.04). Similarly, in income-stratified analysis, a non-significant moderate association was observed between LFP and mood/anxiety disorders among those with annual household incomes of $80,000+ (OR: 1.26, 0.99-1.61). In age-stratified analysis, there was a significant association between lower LFP and an increased odds for mood or anxiety disorders (OR=1.26, 95% CI:1.27,2.25) among adults aged 25-44.

Conclusion: This study observed the links between LFP and mood/anxiety disorders among those who are racialized, adults aged 25-44, or receive adequate household income.

Mental Health

The association between migraine and postpartum depression in Nurses' Health Study 3: a prospective cohort study Holly Crowe* Holly Crowe Kathryn Rexrode Hadine Joffe Brittany Charlton Janet Rich-Edwards

Migraine and depression are frequently comorbid, but rarely studied longitudinally. Individuals with pre-pregnancy migraine may be more hormonally sensitive than non-migraineurs and therefore at greater risk of postpartum depression (PPD). We examined the association between physician-diagnosed migraine and PPD among participants in the Nurses' Health Study 3 (NHS3, n=7,618 pregnancies among 5,387 individuals) between 2010 and 2023. At enrollment, NHS3 participants report if they have ever been diagnosed with migraine. Participants provide detailed pregnancy data including prospectively throughout follow-up. Participants who report a pregnancy on a biannual questionnaire receive an additional questionnaire at ~5 weeks postpartum. We ascertained PPD using the Edinburgh Postnatal Depression Scale (EPDS), a validated self-report screening tool. In separate models, we defined the outcome as an EPDS score of ≥11 (to maximize sensitivity), an EPDS score of ≥13 (to maximize specificity) and self-reported physician-diagnosis of PPD. We used log-binomial regression, accounting for non-independence of repeated pregnancies within individuals, to examine the association between migraine and PPD, adjusting for age and race/ethnicity. Overall, 26% of participants reported a history of migraine and 18% reported PPD using an EPSD cutoff of 11, while 8% reported PPD with a cutoff of 13.). Only 4% of participants reported a physician diagnosis of PPD. We found no appreciable association between pre-pregnancy migraine and PPD using an EPDS cutoff of 11 [risk ratio (RR)=1.02, 95% confidence interval (CI): 0.89–1.16) or 13 (RR=0.90, 95% CI: 0.74–1.08). Findings indicate that migraineurs may be slightly less likely to receive a PPD diagnosis (RR=0.79, 95% CI: 0.61–1.02). While depression symptom levels and antidepressant use before, after, and during pregnancy were similar among migraineurs and non-migraineurs, migraineurs were slightly less likely to report a PPD diagnosis.

Mental Health

Attention-Deficit/Hyperactivity Disorder and Relative Age in School Class: Evidence from the province of Quebec, Canada Geneviève Lefebvre* Geneviève Lefebvre Jesse Gervais Catherine Haeck Pierre Lefebvre Philip Merrigan

It is well known that the youngest children in a classroom have a greater chance of being diagnosed and medicated for attention-deficit/hyperactivity disorder (ADHD). This phenomenon has been observed over the years in many countries, including Canada. The aim of this study was to provide new Canadian evidence based on data from the province of Quebec, recognized as having among the highest rates of ADHD diagnoses and medication consumption in the world.

A cohort of children born between 1996 and 2005 was assembled from administrative data from the Régie de l'assurance maladie du Québec (n=748,075). Diagnostic codes (ICD-9 314.0) and ADHD-related medication purchases were identified for the elementary school period (kindergarten and grades 1 to 6). As the cut-off date for kindergarten entry is September 30 each year, the proportions of children born in September versus October with ADHD diagnoses and medications were compared using logistic regressions. Results stratified by sex and drug insurance type were also obtained.

We found that Quebec children born in September had an increased likelihood of being diagnosed with ADHD in elementary school compared with children born in October (marginal risk difference: 0.06, 95% CI: [0.05, 0.06]; odds ratio: 1.68, 95% CI [1.62, 1.74]). The relative age effect for ADHD medications was similar to the one found for diagnoses. We also observed a rising trend in the age relative effects among the birth year cohorts from 1996 to 2005. From an additive perspective, the relative age effect for boys was greater than the one for girls. Children covered by the type of drug insurance associated with the lowest socio-economic status were found more susceptible to be affected by this relative age effect phenomenon than children covered by other types of drug insurance.

The relative age effect for ADHD diagnostics and medications persists in Canada and is in fact more present than ever.

Mental Health

Characterizing stress variability typologies in a racially/ethnically diverse sample of adult participants Shiwani Sapkota* Shiwani Sapkota Allan D. Tate Emilie Ellis Andrea N. Trejo Anna Hochgraf Alicia Kunin-Batson Jerica Berge

Background: Stress is linked to biopsychosocial health outcomes, but the dynamic nature of adults' stress experiences is not well understood. This study used ecological momentary assessment (EMA) as a novel approach to examine adults' real-time stress experiences and links with individual and family wellbeing.

Methods: Self-report EMA data from the Family Matters study (n=631) were used to evaluate adults' stress levels and variability, including daily mean and diurnal slope of stress, average between-survey stress change, standard deviation of survey-stress change, and daily stress change variability (volatility; i.e., the stability of daily stress patterns within each day) over a one-week EMA period. Latent class analysis was used to categorize participants based on stress characteristics, and multinomial logistic regression was used to identify predictors of class membership and explore cross-sectional associations with self-reported wellbeing.

Results: A 3-class model (entropy=0.821) revealed distinct typologies of stress variability—low, medium, and high. Relative to adults in low stress variability class, adults in medium stress variability class had higher odds of elevated anxiety (OR=1.55), baseline stress (OR=1.25), and lower family functioning (OR=1.96), and adults in high stress variability class had higher odds of a high number of recent stressful events (OR=1.24) and both elevated anxiety (OR=2.34) and baseline stress (OR=1.35). Coping, self-esteem, and resilience were not linked with class membership. Stress typology was not substantively related to self-reported pain, energy, depression, or adverse childhood experiences based on small effect size r2 (range = 0.01-0.07).

Conclusion: High stress variability profiles were strongly linked with elevated anxiety and recent stressful events. Future research should investigate the long-term links between stress variability class membership and wellbeing, for developing the targeted interventions accordingly.

Mental Health

Differences in Prenatal Depression by Maternal Race and Ethnicity: A Retrospective Cohort Study Kendria Kelly-Taylor* Kendria Kelly-Taylor Sara Aghaee Joshua Nugent Ayesha Sujan Nina Oberman Ai Kubo Elaine Kurtovich Charles P. Quesenberry Jr Kathryn Ridout Mibhali Bhalala Lyndsay Avalos

Existing studies suggest that Black and Hispanic persons experience significantly higher rates of prenatal depression compared to White persons, yet little is known how these rates differ among subgroups of Hispanic (e.g., Mexican) and Asian (e.g., Korean) populations**.** The study examined racial and ethnic subgroup differences in prenatal depression diagnosis and severity among a large cohort of pregnant persons universally screened for depression. A retrospective cohort of pregnant persons receiving prenatal care at Kaiser Permanente Northern California from 2013 to 2019 (n=258,452) were analyzed. Twenty racial and ethnic groups were obtained from birth records, and depression diagnosis, severity (measured using the Patient Health Questionairre-9 [PHQ-9]), and covariates (maternal age, parity, education, neighborhood deprivation, delivery year) were captured via electronic health records. We calculated age-adjusted prevalence rates and used modified Poisson regression models to estimate adjusted relative risks. Puerto Rican persons had the highest prevalence of prenatal depression (25.3%), followed by Native American (23.5%) and Black (20.9%) persons, while Hmong persons had the lowest prevalence (4.3%). Severe depression (PHQ-9 15+) was highest among Black persons (7.5%) and lowest among Asian Indian (2.9%) persons. Puerto Rican, Black, and Native American persons had higher risks of prenatal depression compared to White persons in unadjusted models (RR:1.34, 95%CI: 1.22-1.48; RR:1.08, 95%CI: 1.04-1.11, RR:1.17, 95%CI: 0.98-1.40, respectively). In the adjusted models, the associations were attenuated (aRR:1.05, 95%CI: 1.03-1.07; aRR:1.00, 95%CI: 0.99-1.01; aRR:1.03, 95%CI: 1.00-1.06, respectively). Substantial variation in the prevalence and risk of depression diagnosis and severity were observed. The findings suggest differences in maternal characteristics and socioeconomic factors may partially explain racial and ethnic disparities in prenatal depression.

Loneliness in college students: prevalence and associations with substance use outcomes

Michelle Flesaker* Michelle Flesaker Christina E. Freibott Travis C. Evans Jaimie L. Gradus Sarah K. Lipson

Background: In 2023, the U.S. Surgeon General issued a report describing loneliness as a critical public health problem. While relationships between loneliness and mental health outcomes have been established, gender-specific associations between loneliness and substance use among young adults are unknown.

Objectives: This study quantified the prevalence of loneliness and associations between loneliness and substance use by gender in a sample of college students.

Methods: Participants were students enrolled in postsecondary institutions throughout the U.S. in the 2021-2022 wave of the Healthy Minds Study (n = 84,481). Data were self-reported. Gender was categorized as male, female, and transgender/nonbinary. Loneliness was measured with the UCLA 3-item loneliness scale and dichotomized as lonely and not lonely. Substance use included alcohol use in the past two weeks and marijuana, prescription stimulant, benzodiazepine, and opioid use in the past 30 days; use was dichotomized as any or no use. We used logistic regression and calculated 95% confidence intervals (CI) to estimate associations.

Results: Loneliness was prevalent overall, but highest among transgender/nonbinary students (79%) as compared to females (59%) and males (54%). Loneliness was associated with reduced odds of alcohol use (odds ratio [OR] = 0.91, CI = 0.87, 0.96) and increased odds of benzodiazepine use (OR = 1.87, CI = 1.29, 2.70) in all genders, and increased odds of marijuana, stimulant, and opioid use in females and males, but not transgender/nonbinary students.

Conclusions: Loneliness was prevalent in a large, national sample of college students, especially in transgender/nonbinary students, and was associated with increased odds of use of most substances examined. Results are limited by the cross-sectional design and use of self-reported measures. Future work should improve interventions to reduce loneliness in this population and integrate substance use prevention as part of these strategies.

Prevalence and predictors of non-presentation for mental health services among referred U.S. military personnel Andrew J. MacGregor* Andrew MacGregor James M. Zouris Amber L. Dougherty Sarah M. Jurick

Introduction: Mental health (MH) disorders pose a significant burden to the wellness of military personnel, and seeking care is an essential first step in the treatment pathway. To date, little information exists on non-presentation for MH services in the U.S. military.

Methods: The study sample included 14,289 U.S. service members who responded to an annual screening and were referred for MH services. Medical records were examined to identify those who did not present for MH services within 90 days of referral. Independent variables included demographics (age, rank, service branch, gender), behaviors (alcohol use, physical activity, tobacco use), perceived health (overall health, pain), and prior presenting behavior (contact with MH and primary care). Multivariable logistic regression was used to assess the association between independent variables and non-presentation for MH services. Among a subgroup of individuals with probable posttraumatic stress disorder (PTSD) and depression, adjusted means for severity scores were examined by non-presentation status.

Results: Overall, 34.0% of service members did not present for MH services after referral. ORs and 95% CIs for the independent variables are reported in the figure. Non-presenters were more likely to be men, in the Marines, and have lower prior presentation to MH and primary care, better perceived health, and healthier behaviors. Non-presenters also had significantly lower severity scores for PTSD and depression.

Conclusion: This study identified a key subgroup of military personnel who were less likely to present for MH services, with the strongest predictor being prior presenting behavior. Subsequent studies are needed to compare functional outcomes of those presenting versus not presenting for MH services. Future research could also develop clinical decision tools to identify personnel at risk of not presenting for MH services to allow for interventions that encourage follow-up care.

Figure: Odds ratios (with 95% confidence intervals) for independent variables and not presenting for MH services.
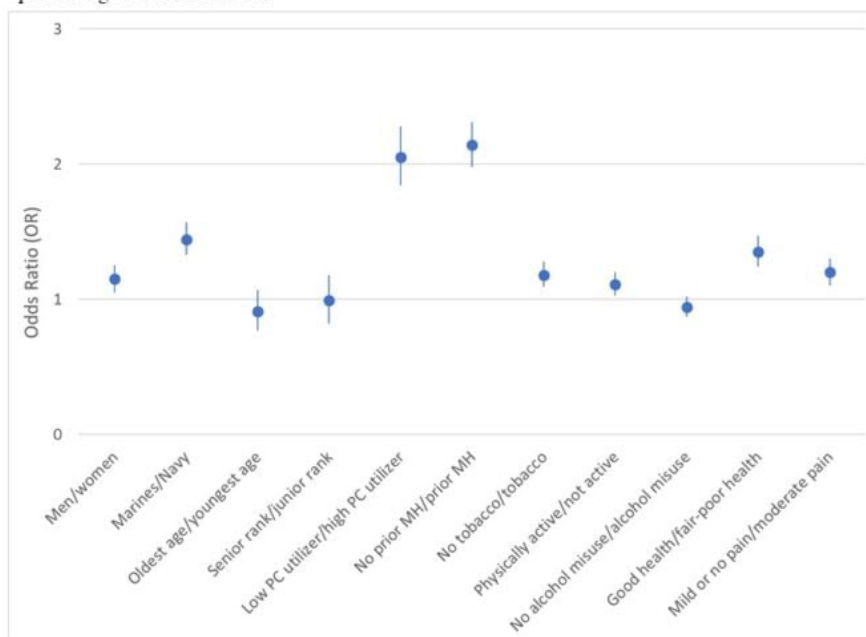
PC = primary care; MH = mental health

Mental Health

Association Between Depression Severity and Total Cost of Care: Findings From a Large, 2-year, Claims-Based, Retrospective Study in the USA Amber Shergill* Amber Shergill Tyson Barrett Andrey A. Popkov Michael Donohue Ryan Anderson Brad Karlin

Despite the substantial impact of depression on individuals and healthcare utilization, little is known about the specific relationship between depression severity and total cost of care (TCC). The current study aimed to evaluate the association between depression severity and TCC and how changes in depression severity affect changes in those costs.

Retrospective cohort analysis of insured individuals in the US was conducted using insurance claims data and data from electronic health records between January 1, 2019 and December 31, 2020. Information in the claims data were linked with the electronic medical records. Inclusion criteria comprised insured individuals with coverage during 2019 or 2020, aged one year or older, and stratified into either minimal, mild, moderate, or severe categories of depression in at least one year of the study. The main outcome was TCC per member per month (PMPM) evaluated across the two-year study period.

Across 2019 and 2020, 744,854 members met inclusion criteria. A total of 369,460 members were studied across both years. Greater depression severity was associated with higher TCC across both years (rho=0·156; 0·154, p<;0·001). Unchanged depression severity was associated with limited change (+$52-$79) in TCC from 2019 to 2020. Decrease in depression severity was associated with an average $41 reduction in PMPM spend (95% CI=[$5, $78], p=0·028), whereas increase in depression severity was associated with an average $608 increase in PMPM spend (95% CI=[$554, $661], p<;0·001).

Overall, greater depression severity was associated with higher total health care expenditures. Further, changes in depression severity over time were significantly associated with changes in TCC. Findings reveal significant financial opportunities associated with early identification and targeted, effective management of depression and changes in depression severity to reduce expenditures and inform allocation of resources.

Figure 1. Cross-tabulation of change in PMPM spend (2020 - 2019) by stratification for 2019 and 2020. Panel a) shows change in dollars, panel b) shows results as a percent change. Positive numbers indicate higher spending in 2020 than 2019. Numbers in brackets are the 95% confidence interval for each a) dollar change and b) percent change.
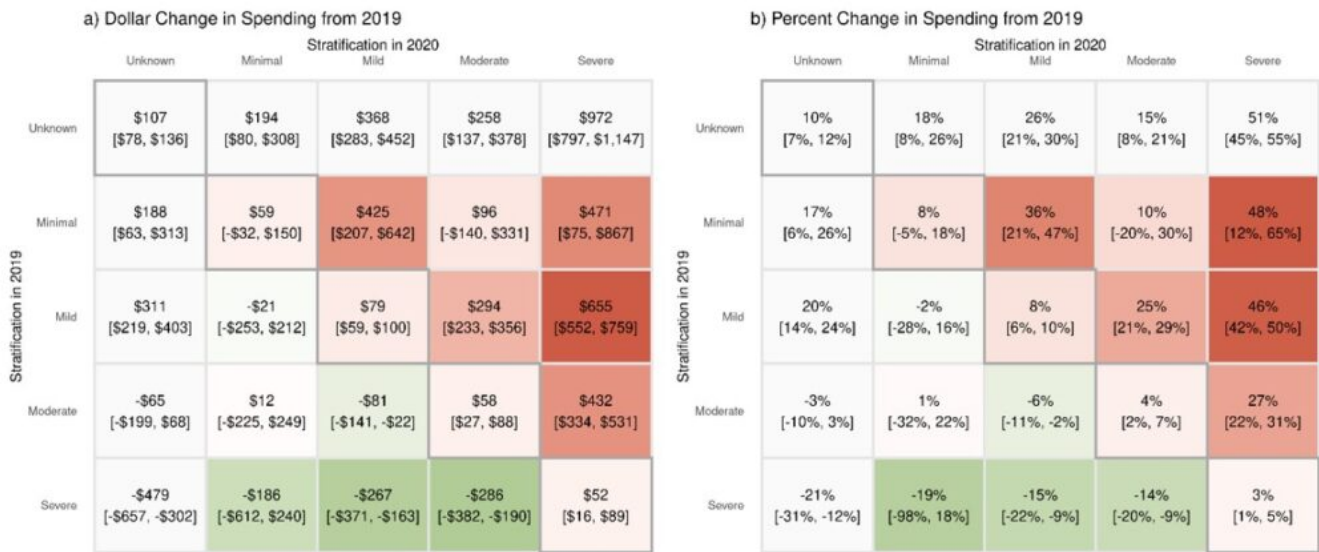
Macroeconomic antecedents of involuntary psychiatric commitments in Denmark Parvati Singh* Parvati Singh Marquianna Griffin Camilla Hvidtfeldt Lars H. Andersen

Economic downturns may precede reduced social tolerance towards the mentally ill that, in turn, may manifest as increased reporting of disordered individuals for involuntary psychiatric commitments (reduced tolerance hypothesis). In some instances, societies may also act out against vulnerable minority groups during economic downturns by way of increased scapegoating of such groups for involuntary psychiatric commitments (frustration-aggression-displacement hypothesis). We examine the relation between quarterly aggregated counts of unemployed persons (exposure) and involuntary psychiatric commitments (outcomes) in the 1) overall population (test of reduced tolerance), and 2) among non-western immigrants (test of frustration-aggression-displacement hypothesis) in Denmark, over 84 quarters, from 2001 to 2018 (72 quarters). We use AutoRegressive Integrated Moving Average (ARIMA) time-series analysis to examine the relation between the exposure (0, 1 quarterly lags) and outcomes, controlling for seasonality, trends, autocorrelation, and population denominators. Results from time-series analyses indicate 48 additional involuntary psychiatric commitments in the overall population, one quarter after increase in 100,000 additional unemployed persons (p-value < 0.01). Sub-group analyses show increased involuntary commitments among Danes (coefficient = 0.25, p < 0.01) as well as among non-western immigrants (coefficient= 0.12, p <0.01), one quarter following increase in the unemployed population. We do not observe an increase in overall as well as sub-group-level voluntary psychiatric admissions in relation to the exposure. Our findings support both reduced tolerance as well as frustration-aggression hypotheses, and highlight the relation between ambient macroeconomic conditions and adverse psychiatric outcomes in large populations.

Factors associated with poor mental health outcomes among New York City transit workers

Robyn Gershon* Daniel Hagen Michael Cziner Emily Goldmann David Vlahov Alexis Merdjanoff

Background: Transit workers were confronted with numerous stressors during the COVID-19 pandemic and continue to encounter heightened violence, yet little is known about the impact on mental health outcomes in this essential workforce.

Methods: Data were collected through a cross-sectional online survey from a convenience sample of N=1,381 bus and subway workers in New York City between December 2023 and January 2024. Socio-demographic characteristics, occupational exposure to violence, job satisfaction, self-rated health, COVID-19 experiences, and mental health outcomes (including the Patient Health Questionnaire [PHQ]-4 and a single-item measure to assess sleep problems) were ascertained. Correlates of probable depression (PHQ-2 score>2) and/or probable anxiety (Generalized Anxiety Disorder [GAD]-2 score>2), sleep problems, and self-reported worsened mental health compared to the start of the pandemic were examined using separate modified Poisson regression models.

Results: Approximately 34% of the sample met criteria for probable depression or anxiety; 11% reported trouble falling asleep, staying asleep, or sleeping too much more than half the days in the prior 2 weeks; and 16% reported worse mental health than at the start of the pandemic. Adjusted for socio-demographic factors, poor mental health outcomes were most associated with experience of verbal harassment and sexual assault at work. For example, respondents who had been verbally harassed at work (34% of the sample) had 2.09 times the prevalence of probable depression or anxiety (95%CI=1.53;2.87) than those who had not. Other significant correlates included COVID-19-related hospitalization (PR=1.61; 95%CI=1.15;2.26) and having known someone who died from COVID-19 (PR=1.86; 95%CI=1.36;2.56).

Conclusion: Poor mental health outcomes are highly prevalent in this sample and may be driven by occupational exposure to violence, suggesting that targeted interventions and measures to increase worker safety are warranted.

Mental Health

Status of resilience and the factors associated with it among secondary school level adolescents of Jaleshwar municipality, Nepal

Krishtee Napit* Krishtee Napit Pratap Shrestha Shinobu Watanabe-Galloway Arun R Napit Anil Kumar Singh

Background: Resilience is the ability of an individual to function competently in the face of adversity or stress. Resilient adolescents are likely to enter adulthood with a greater capacity to cope well under challenging circumstances and are less likely to engage in risky behaviors. Adolescent resilience is under-explored in Nepal. This study aimed to measure resilience and the factors associated with adolescents in Nepal.

Methods: Data was obtained from a self-administered questionnaire adapted from the Connor-Davidson Resilience Scale-10 for resilience. A total of 508 students of classes 9 to 12 within the Jaleshwar municipality were included. Resilience was divided into three categories: lowest (first quartile), intermediate (second and third quartiles), and highest (fourth quartile). We conducted a multinomial logistic regression analysis to determine factors associated with resilience.

Results: The mean resilience score was 28.27 (SD=6.92) out of 40. The categories of resilience were lowest (33). None of the demographic variables were found significant. The type of school- private compared to public (OR=2.27, 95% CI: 1.23-4.18), good academic performance (OR=3.93, 95% CI: 2.16-7.14), family support (OR=2.60, 95% CI:1.47-4.59), and good peer relation (OR=4.14, 95% CI: 2.25-7.61) were found significant for the highest resilience compared to the lowest resilience. Compared to the lowest resilience, good academic performance (OR=2.14, 95% CI: 1.34-3.41), family support (OR=1.71, 95% CI:1.05-2.79), and peer relation (OR=2.7, 95% CI: 1.68-4.33) were found to be significant for intermediate resilience.

Conclusion: Our study identified that family support, peer relations, types of school, and academic performance are associated with adolescent resilience and should be addressed to enhance resilience for a healthy transition to adulthood.

Association between skin tone and mental health status in the National Longitudinal Survey of Youth 1997 cohort Sarah Garcia* Sarah Garcia Patricia Louie Anjum Hajat

Background: While the relationship between race and mental health has been studied extensively, skin tone also contributes to social stratification and experiences of colorism can result in poor mental health. We evaluated the association between skin tone, a proxy for colorism, and mental health status, and if race and ethnicity modified the association.

Methods: We used data from the National Longitudinal Survey of Youth 1997 (N=3,089). Mental health was measured in the 2010 wave with the Mental Health Inventory (MHI-5) which asks about mental health factors in the past month. Scores ranged from 0-15 with higher scores indicating better mental health status. Interviewers identified skin tone in 2010 ranging from 0-10, with 0 as the lightest skin tone and 10 the darkest. Skin tone was combined into three groups: light (0-2), medium (3-4), dark (5-10). Poisson regression analysis was used to compute prevalence ratios (PR).

Results: Median MHI-5 score was 11 (IQR=9-13). The association between skin tone and mental health was null (medium vs light PR=1.00, 95%CI=0.98,1.02; dark vs light PR=1.01, 95%CI=0.99,1.03). However, race and ethnicity appeared to modify this association (Wald test p-value=0.04). Prevalence of a one-unit higher MHI-5 score was higher among White non-Hispanic individuals with medium skin tone (PR=1.03, 95%CI=1.00,1.05) than dark skin tone (PR=0.96, 95%CI=0.85,1.10) when groups were compared to light skin tone. Hispanic individuals of another race with medium skin tone (PR=0.95, 95%CI=0.91,1.00) had lower prevalence than dark skin tone (PR=1.01, 95%CI=0.93,1.09). Black non-Hispanic individuals with medium and dark skin tones had lower prevalence (PR=0.95, 95%CI=0.86,1.05; PR=0.98, 95%CI=0.89,1.07).

Conclusion: Although PR were approximately the same across skin tones, the association between skin tone and mental health is stronger for some groups. Specifically, Black non-Hispanic individuals with darker skin tones had poorer mental health status.

Methods/Statistics

Estimating absolute risks from case-cohort designs Caitlin A. Cassidy* Caitlin A. Cassidy Jessie K. Edwards

Case-cohort designs are useful in epidemiology when exposure or covariate measurement is resource intense, or an outcome of interest is rare. Here, we define a case-cohort design to include all cases from a cohort and a randomly selected sub-cohort from the entire risk set at baseline. Cox proportional hazard models are typically used to compute hazard ratios from this design. However, the absolute risks under each exposure are often also of interest. Here, we describe a nonparametric approach to estimate these risks and the risk difference (RD) directly from case-cohort data.

We propose a weighted Kaplan-Meier estimator to estimate risk and survival functions under each exposure of interest in a case-cohort design. We compare the proposed estimator to a weighted Kaplan-Meier estimator that includes only individuals from the random sub-cohort. The weights account for the probability of inclusion in the sub-cohort and confounding.

We simulate 2000 replicates of a cohort from which a sub-cohort is randomly selected. The time-to-event data are generated assuming an increasing hazard function with a Weibull distribution. We estimate the RD of a binary outcome $Y=1$ comparing levels of a binary exposure $A=1$ vs $A=0$. We vary the true RD, sub-cohort sampling methods, and sampling fractions. We consider censoring and confounding by a binary covariate X. We compare the bias and precision of these two estimators of the RD. We illustrate both estimators in an applied example using data from the Women's Interagency HIV Study.

In most scenarios, both estimators demonstrate low average bias (≤ 0.003). Bias decreases as sample sizes and sampling fractions increase. The inclusion of a confounding variable and censoring leads to marginal increases in bias in most scenarios (≤ 0.007). The proposed estimator utilizing the case-cohort design demonstrates average standard errors that are less than half of those from the estimator utilizing only individuals in the random sub-cohort.

Risk functions and risk differences can be directly estimated from a case-cohort design using a weighted Kaplan-Meier approach. A case-cohort design yields greater statistical efficiency compared to a design using a random sub-cohort and decreases the study resources required to estimate absolute risks and risk differences compared to a study of a full cohort.

Methods/Statistics

P-Hacking and Publication Bias in Epidemiology Research: Trends in Derived P-Values from the American Journal of Epidemiology from 2000-2022 Sarah Ackley* Sarah Ackley Ruijia Chen Jingxuan Wang Grisel Lopes Peter Buto Kendra D. Sims Isabel Elaine Allen Maria Glymour

Concerns about null-hypothesis testing and reporting of p-values have grown in the last two decades. However, it is unknown whether the movement to reduce reliance on p-values has resulted in changes in p-hacking or publication bias.

We obtained AJE abstracts from 2000-2022 with at least one CI. Two-sided p-values were calculated from scraped estimates and CIs. We contextualized findings using theoretical and simulated p-value distributions assuming all studies are equally powered and assuming a range of statistical power across studies. We evaluated linear trends and determined whether the empirical distribution of p-values changed over this time period. We also evaluated changes in the ratio of p-values just below and above 0.05. All reported odds ratios correspond to a one year difference.

A total of 3743 p-values were extracted from 1517 abstracts. From fits to theoretical p-value distributions, we find there is excess density between 0.01 and 0.05 and near 1, with a dearth of p-values <0.01 (see figure); this is the case for both early (2000-11) and later time periods (2012-22). Smaller p-values increased over time (p<0.05: OR=1.02, 95% CI: 1.01 to 1.03; p<0.01: OR=1.02, 95% CI: 1.01 to 1.03). Selecting only the smallest p-value for each abstract yielded similar results: (p<0.05: OR=1.02, 95% CI: 1.0 to 1.04; p<0.01: OR=1.01, 95% CI: 1.00 to 1.03). Statistically significant changes in the proportion of p-values just below versus just above 0.05 were not detected for the full sample (OR=1.01, 95% CI: 0.99 to 1.03) or just selecting the smallest p-value per abstract (OR=1.01, 95% CI: 0.98 to 1.04), although the point estimates indicate this ratio is increasing.

We find evidence of p-hacking but not publication bias in AJE. Decreasing p-values could reflect larger sample sizes, better-motivated hypotheses, or increased publication bias or p-hacking. We find no evidence that de-emphasizing p-values has reduced publication bias or p-hacking.

Methods/Statistics
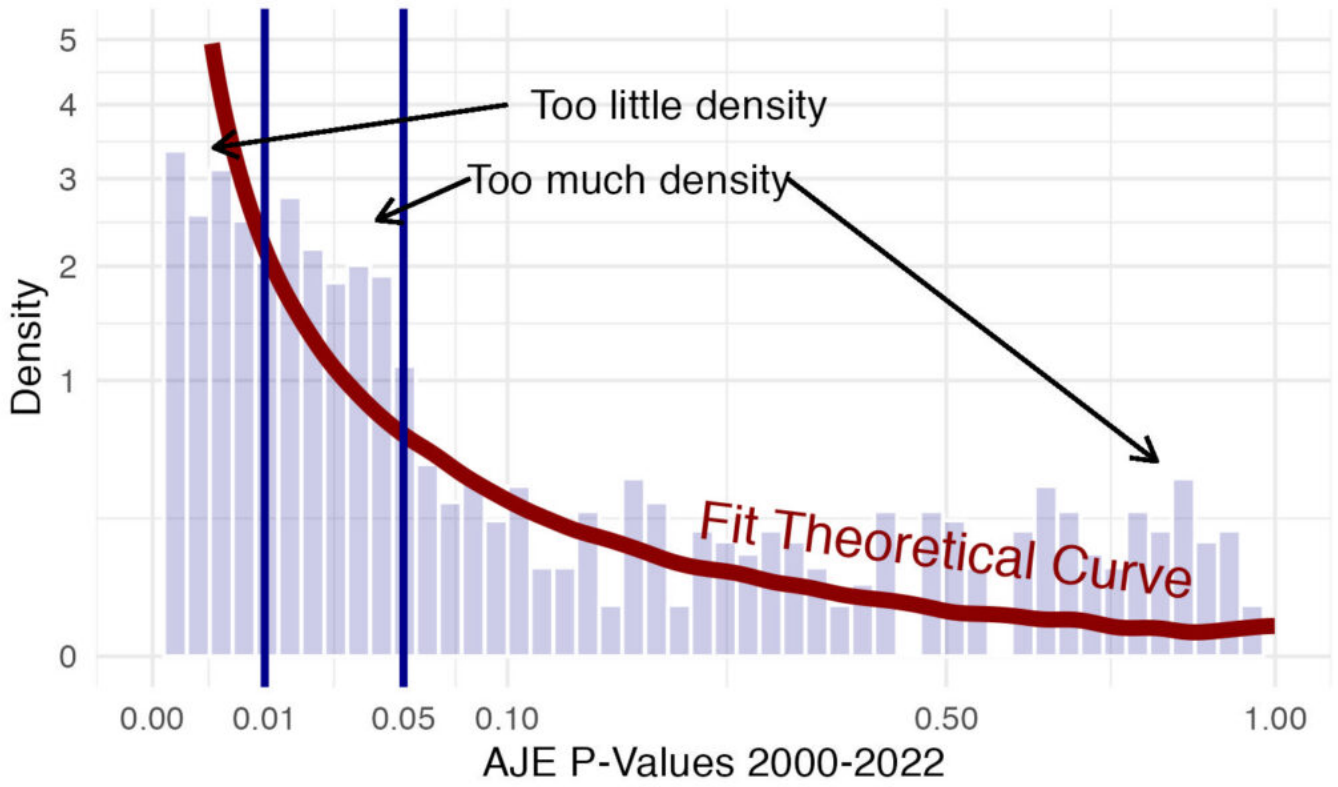
Reassessing positive results: Uncovering potential detection bias in epidemiologic studies of dementia using electronic health record data Jingxuan Wang* Jingxuan Wang Minhyuk Choi Scott C Zimmerman Ruijia Chen Catherine Schaefer Deborah Blacker M. Maria Glymour

Many epidemiologic studies of dementia use electronic health record (EHR) data, which are vulnerable to detection bias. Dementia is more likely to be detected when patients have more contact with the healthcare system, which can lead to a systematic difference in the ascertainment of outcomes across exposure groups. Using EHR data from the UK Biobank, we evaluated potential detection bias by estimating associations of two negative control exposures with dementia.

UK Biobank participants aged ≥ 55 without baseline dementia (N=141,060; mean age=62.5 years) were followed for a median of 13.7 years. We estimated associations of forearm fracture and urinary tract infection (UTI) with incident dementia. Diagnoses were from primary care, hospital inpatient, and death record data. We used Cox models to evaluate associations of binary exposure with all-cause dementia overall and in 4 time intervals after the exposure (0–1, >1–5, >5–10, and >10 years) compared to individuals with no prior exposure. All models adjusted for age, sex, race, education, assessment center, and healthcare utilization (number of clinic visits during the year before baseline).

Prior to baseline, 6,843 (4.9%) and 16,742 (11.9%) individuals had a forearm fracture and UTI diagnosis; 3,896 dementia cases accrued during follow-up. Forearm fracture (HR=1.19, 95%CI=1.06-1.33) and UTI (HR=1.83, 95%CI=1.70-1.96) were associated with dementia incidence, especially in the first year after exposure diagnosis (forearm fracture HR=1.93; UTI HR=6.53). The association attenuated in subsequent years (Figure).

The chance of receiving a dementia diagnosis increases sharply in the first year following a forearm fracture or UTI diagnosis, although the influence of either condition on dementia pathology is likely small. These short-term increases likely represent detection bias, i.e., they would not have received a dementia diagnosis at that time in the absence of the medical attention necessitated by forearm fracture or UTI.

Forearm fracture

UTI

Methods/Statistics
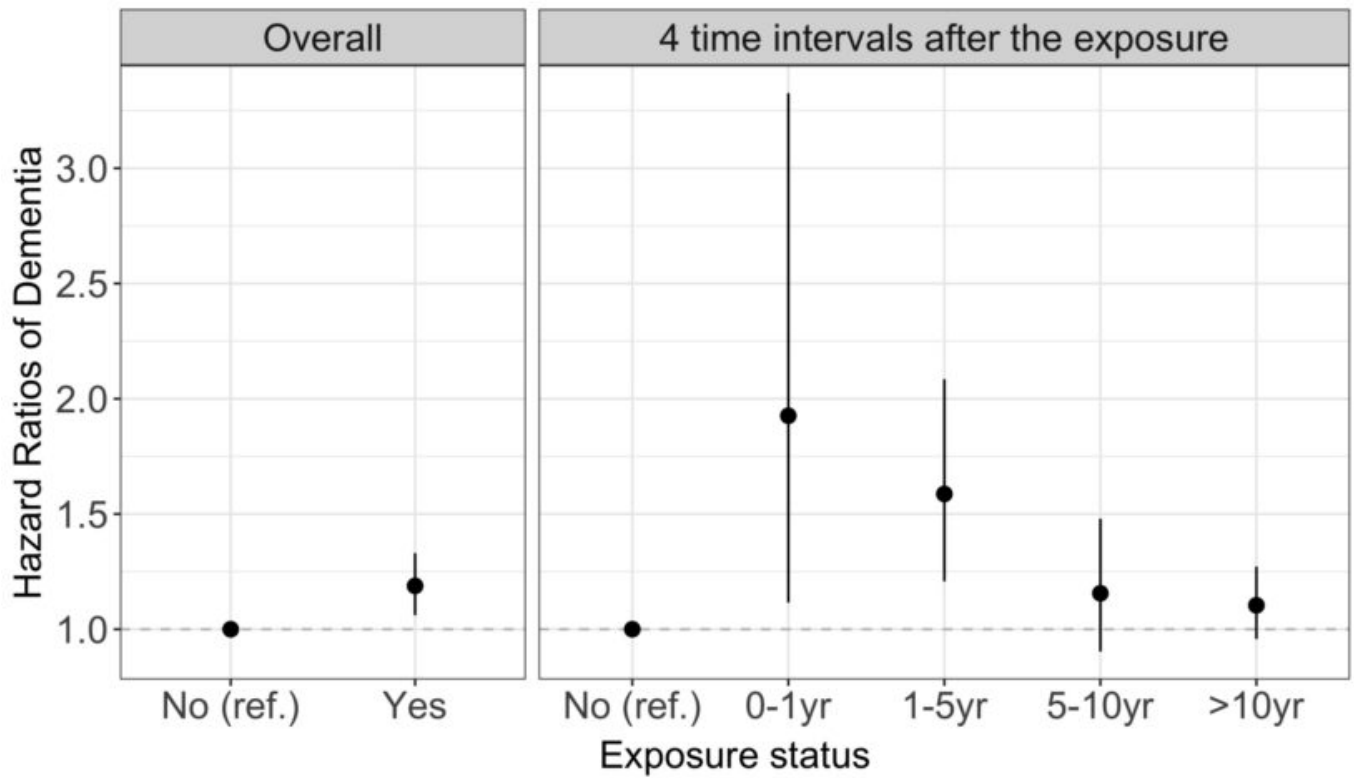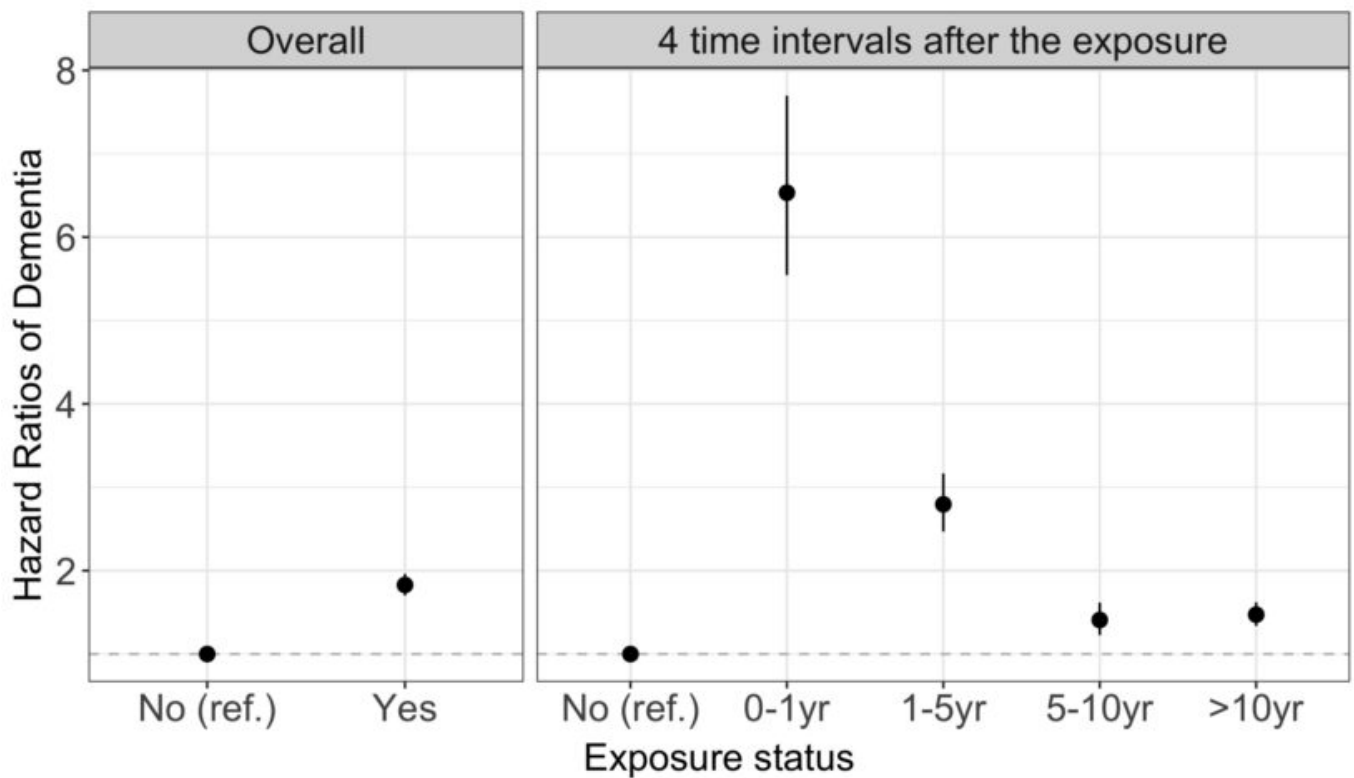
Assessing the Structural Determinants of HIV among Adolescent Girls and Young Women in Malawi: Application of the PC Causal Discovery Algorithm Domonique M. Reed* Domonique M. Reed Daniel Malinsky Jeanette A. Stingone Jessica Justman

Individual, interpersonal, community, and societal factors influence adolescent girls and young women's (AGYW; 15-24 years) HIV risk, yet their interconnectedness is understudied. The tiered PC (Peter-Clark) algorithm for causal discovery extends the constraint-based PC algorithm to accommodate temporal ordering between variables and uses patterns of conditional independence to determine causal structure. Using this algorithm, we characterized the multi-level paths leading to HIV among AGYW in Malawi.

We integrated data from the Population-based HIV Impact Assessment, Census, and UNAIDS Policy Indicators (2014- 2016). We applied the PC algorithm with a conditional Gaussian likelihood ratio test and test-wise deletion for missingness. We used an alpha level of 0.2 to obtain a graph with reasonable density and power.

We included data on 32 features from 2,644 AGYW in 2,485 households across 479 enumeration areas within 3 administrative regions of Malawi. Of 2,644 AGYW, 4.6% live with HIV. Most AGYW lived in a rural area, completed primary education, married, and lived in a middle wealth quintile household. Figure 1 displays a subset of 9 variables directly connected to HIV status. A region with lower average years of education for women and an average age of marriage <18 years have directed paths to community HIV prevalence and interpersonal relationship variables. HIV prevalence has a directed path to HIV status, as expected, but there are undirected paths between interpersonal relationship factors and HIV. While there is a directed path from transactional sex to HIV status, there are directed paths from HIV to sexual debut age and number of partners, often described as HIV predictors in the literature.

This application of the PC algorithm produced a graph that provides insight into the complex relationship shaping AGYW's HIV risk in Malawi. These findings are an example of causal discovery and contribute to our understanding of the underlying causal mechanisms of HIV.

Figure 1. Partial Causal Graph of Multi-level Factors of HIV among Adolescent Girls and Young Women in Malawi using the PC Algorithm

Methods/Statistics
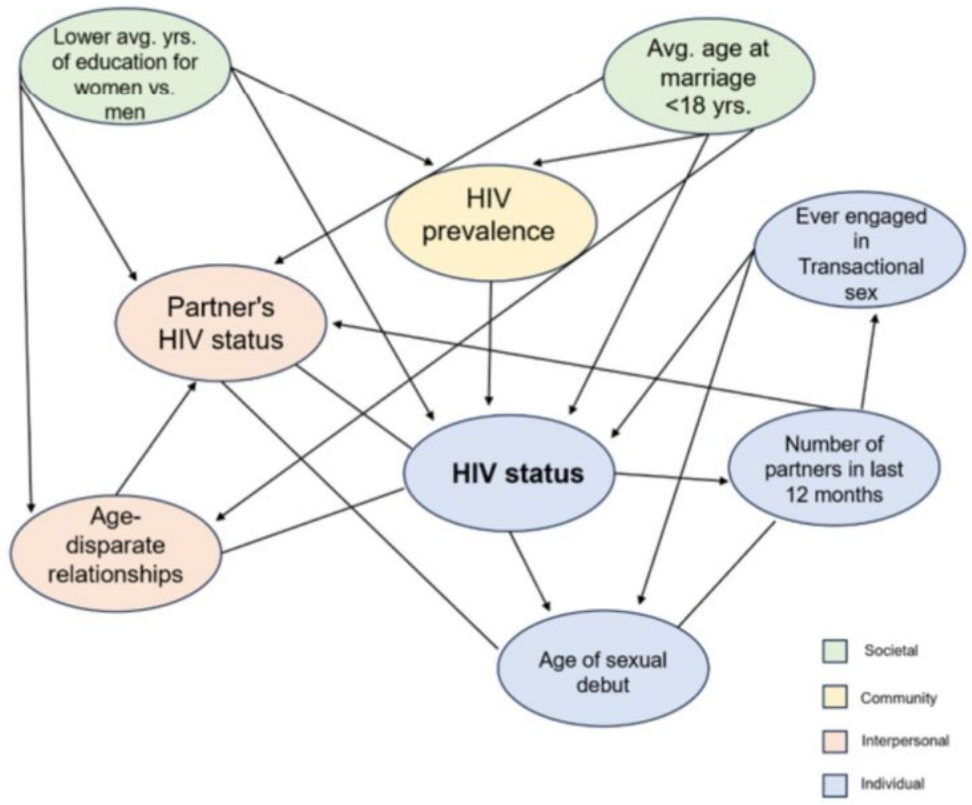
A measurement error analysis of prenatal phthalate effects on an infant outcome Jennifer Adibi* Jennifer Adibi Hai-Wei Liang Jiebaio Wang Nathaniel Snyder Donald DeFranco Janet Catov

Background: In epidemiology, confounding is rigorously addressed while measurement error is often overlooked. In the case of prenatal phthalate exposure, measurement error is likely when using a proxy (maternal urinary concentrations) instead of the gold standard (placental concentrations).

Objective: The aim was to evaluate measurement error in prenatal phthalate exposure when relying on maternal urinary concentrations, and to estimate the unbiased effects of prenatal phthalates on newborn anogenital distance (AGD).

Method: Sixty-eight pregnancies from the TIDES Study had data available on maternal urinary (3 trimesters) and placental tissue (3 tissue types villous (CF), chorion smooth (CS), basal plate (BP)) phthalate concentrations (at birth) from a full cohort (N=811). Intraclass correlation coefficients (ICC) were calculated to assess reproducibility. Linear associations between urinary and placental tissue concentrations were evaluated, with and without adjustment for confounding and heterogeneity by maternal characteristics. Measurement error correction in the effect of phthalates on infant AGD was evaluated and compared, using DAGs to identify sources of potential bias, and analytical approaches including regression calibration (RC), multiple imputation for measurement error (MIME) and machine learning.

Results: 12 phthalate metabolites were quantitated in over 70% of placental tissues and 100% of urine samples. Associations between urinary and placental phthalates were mostly negative or null. Reproducibility within maternal urine was low to moderate (ICC range 0.20-0.50, mean 0.27) and low within 3 placental tissue types (ICC range 0-0.11, mean 0.03). RC did not perform well due to lack of correlation between urinary and placental measures. The machine learning approach did not result in accurate prediction. Analysis is ongoing.

Conclusion: In the setting of weak correlation between the proxy and gold standard measures, standard approaches to measurement error correction do not perform well. In this scenario, we infer that urine and placental tissue phthalates are separate and distinct exposure constructs. Findings are presented, and generalizable recommendations are made on how to evaluate measurement error across tissue matrices as a crucial step in the application of biomarkers in epidemiology.

Using distributed lag models to account for nonlinearity of the lag-response association a study of air pollution and incident breast cancer Judy Ou* Judy Ou Jennifer Ish Alison Rector Alexandra White

Background: Understanding the lag-response association may be critical for outcomes with long latency periods. As common statistical models may assume a linear lag-response function, we used distributed lag models to determine if non-linear modeling of the lag-response function improved model fit in a study of air pollution and breast cancer.

Methods: Using data from the Sister Study, we included 34,616 women (ncases=2,704) with 15 years of continuous air pollution exposure history available before diagnosis or end of follow-up. Spatiotemporal models estimated fine particulate matter (PM2.5) and nitrogen dioxide (NO2) for participant residences from 1990 to 2017. The lag-response function was modeled linearly (standard Cox model), stratified every 3 years, and as a quadratic B-spline with a knot at 7.5 years. Using a linear exposure-response function, we developed Cox models with a cross-basis for the exposure-lag-response function to compute Akaike information criterion (AIC) for tumors occurring before and after menopause. We adjusted for race/ethnicity, education, household income, and census region.

Results: For PM2.5 and tumors occurring before menopause, AICS were lower for the B-spline (7578.7) and time-stratified lag-response functions (7582.9) than the linear function (7593.5). For tumors occurring after menopause, AICs for the time-stratified lag-response function (39773.9) were lower than the linear (39855.8) and B-spline functions (39794.0). For NO2 and tumors occurring before menopause, AICs were lowest for the linear lag-response function (6918.1) compared to the B-spline (6821.6) and time-stratified functions (6922.0). For tumors occurring after menopause, AIC for the linear lag-response function (38630.7) was comparable to the B-spline function (38632.3).

Conclusions. Future studies with historic air pollutant exposure estimates exploring the impact of PM2.5 exposure on cancer should account for nonlinearity of the lag-response function.

Examining the standard practice of race adjustment in prenatal screening biomarkers: a first step in a larger investigation Kharlya Carpio* Kharlya Carpio Demia Tyler Hannu Koistinen Janet Catov Jennifer J. Adibi

Background: Standardizing prenatal screening biomarkers involves adjusting for gestational age and other sources of variability, including race, to minimize nuisance parameters and enhance accurate risk prediction for adverse outcomes. This can be achieved without the inclusion of race, revising a practice that perpetuates the harmful idea that race differences are biologic. The first step is to establish a correctly specified model that is not conditional on race. Serum levels of the hCGa biomarker are lower in Black vs. white women and are associated with SDOH and psychosocial stress. **Methods:** hCGa was measured in maternal serum at the 1st, 2nd, and 3rd trimesters, labor and delivery, and two years postpartum, in pregnant people who delivered between 2020-2021 and enrolled in the Magee-Womens Hospital Biobank (N = 58). Overall distributions were examined as crude, logarithmic, and squared transformations. Log-linear and exponential equation models were used to examine the relationship between hCGa collected pre- and postpartum, in which covariate combinations of maternal age, pre-pregnancy weight, and gestational age at time of blood draw were included. We examined standard Akaike Information Criterion (AIC) and a bias detection tool to evaluate if model properties were considered "fair" across racial groups (fairmodels R package). **Results:** Multiple imputation was used to account for participants with missing serum levels in different trimesters. Log transformation reduced skewness but biased the gestational age association. Including all variables in an exponential model yielded the highest AIC, indicating the most accurate shape. None of the models satisfied the fairness criteria. **Conclusion:** Applying transformations for analyzing biomarkers in pregnancy is essential. More empirical and methodologic work is needed to reconsider the impact of race-based algorithms on accurate risk prediction to avoid potential harm. This work is a first step in that process.

Investigating Canada's Guidance on Alcohol and Health risk zones and major chronic disease in Canadian adults: A target trial emulation approach Claire Benny* Claire Benny Vanessa DeRubeis Erin Hobin Laura Anderson Brendan T. Smith

Introduction: Canada's updated Guidance on Alcohol and Health (the Guidance) warns that no amount of alcohol is healthy. Randomized studies on alcohol intake are largely unethical, so causal inference methods are necessary to estimate risk. This study aimed to assess if drinking in line with lower risk zones outlined in the Guidance was protective against major chronic disease in Canadian adults.

Methods: Data were from the Canadian Longitudinal Study on Aging from 2011 to 2021. This study employed a target trial emulation approach with marginal structural Cox proportional hazards modelling to assess the research aim. Participants (n=11,724) were categorized as corresponding to "low" (>0 to 2 standard drinks weekly), "moderate" (3-6 drinks weekly), or "increasingly high" (7+ drinks) risk based on the Guidance. Outcomes included a composite measure of major chronic disease and specific major chronic diseases (i.e., cancer, heart disease, stroke, type 2 diabetes, COPD).

Results: Low-risk drinking was protective against major chronic disease (HR: 0.91, 95% CI: 0.88-0.95) and moderate risk drinking was not protective against chronic disease compared to increasingly high risk drinking. Contrastingly, both low and moderate risk drinking were protective against cancer (HR: 0.93, 95% CI 0.90-0.95; HR: 0.96, 95% CI: 0.93-0.98, respectively), heart disease (HR: 0.93, 95% CI: 0.90-0.96; HR: 0.94, 95% CI: 0.92-0.97, respectively), stroke (HR: 0.94, 95% CI: 0.91-0.96; HR: 0.95, 95% CI: 0.92-0.97, respectively); type 2 diabetes (HR: 0.92, 95% CI: 0.89-0.95; HR: 0.93, 95% CI: 0.91-0.96, respectively); and COPD (HR: 0.93, 95% CI: 0.91-0.96; HR: 0.95, 95% CI: 0.93-0.98).

Conclusion: This study used novel causal inference methods to substantiate that drinking in low and moderate risk zones is protective against chronic disease compared to increasingly high risk drinking. The findings provide important implications for reducing alcohol intake for chronic disease prevention.

Comparing cohort and self-controlled designs for studying Extreme Risk Protection Orders

Nicole Asa* Nicole Asa Stephen Mooney Ali Rowhani-Rahbar

When studying treatments that apply to individuals for a fixed period of time, we learn differently from a cohort design and a self-controlled risk interval design. Whereas a cohort design compares treated and untreated individuals, the self-controlled risk interval design compares treated individuals during treated and untreated time. We compare these designs to study the impact of Extreme Risk Protection Orders (ERPOs) on arrests and convictions. ERPOs are a civil protection order which remove and restrict firearm access to individuals who demonstrate high-risk behavior until the order is expired, typically around one-year. A judge will either grant or deny ("non-granted") an ERPO to the individual demonstrating high-risk behavior (also known as the "respondent") based on the availability of evidence on whether the respondent poses substantial harm to themselves or others. In a traditional prospective cohort design, we can compare arrests and convictions among granted and non-granted ERPO respondents. Because the evidence used to inform the decision to grant an ERPO is linked to outcomes, we use propensity scores to increase conditional exchangeability. By contrast, in a self-controlled risk interval design, we compare arrests and convictions in the ERPO period ("control interval") with arrests and convictions after the ERPO has expired and firearm rights are restored ("risk interval"), among granted ERPO respondents. Whereas the self-controlled risk interval designs may better ensure exchangeability, it also limits sample size and is vulnerable to misclassification of "risk" and "control" time. Nonetheless, the self-controlled risk interval design may be used more broadly in epidemiology, particularly to analyze policies that affect people temporarily or to analyze individuals temporarily treated.
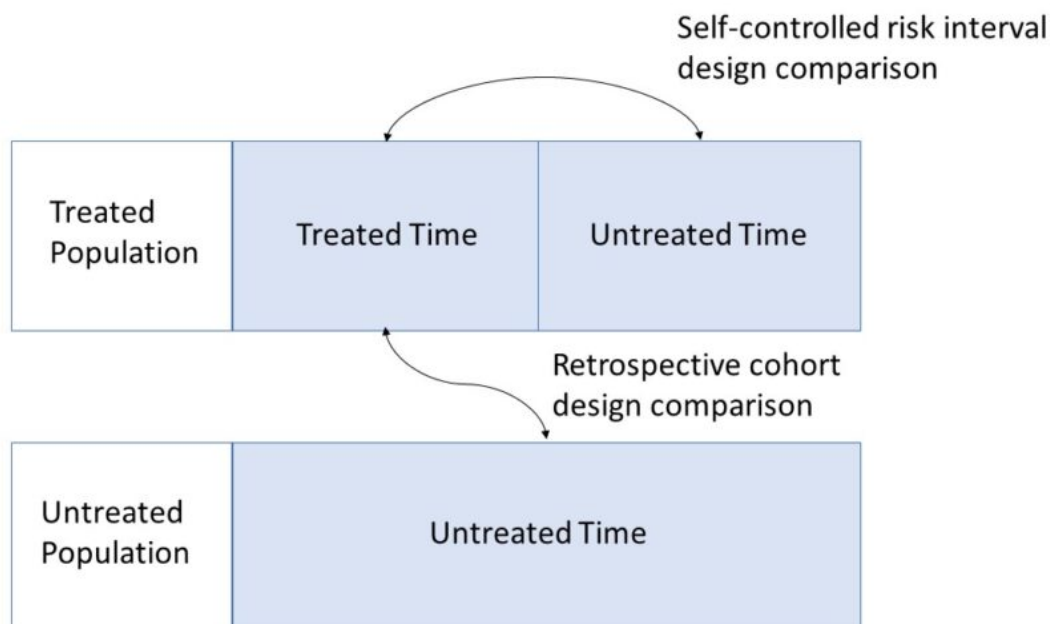
Induction dynamics of the Social R-naught on weight loss: RCT Evidence Daniel E. Zoughbie*
Daniel Zoughbie Dillon R. Huddleston Eric L. Ding

We present the first evidence from a randomized trial, demonstrating the epidemiological dynamics of the social-behavioral infectiousness of risk factors for obesity and diabetes, and the R0 of weight loss propagation. Via the trial design to infer causality, we calculated the Social R0 across multiple time points for weight change propagation (social-R0=1.2, $p<0.01$). We further show that health propagation of an intervention program can attain epidemic proportions; and that public health systems can intervene to modify the R0 value thereby potentially managing, preventing, or reversing social infections at epidemic scale (yielding population-averaged comparative R0 ratios, $7.77<Rc<15.58$, $p<0.01$, for weight loss propagation).

Difference-in-Differences with Unpoolable Data (UN-DiD) Nichole Austin* Nichole Austin Erin Strumpf Sunny Karim Matthew Webb

Background: Difference-in-differences (DiD) is an indispensable tool to estimate the effects of health policies and interventions. However, data sources are sometimes siloed by jurisdiction and are therefore considered unpoolable. This is a significant barrier to DiD estimation; no methods currently exist for conducting DiD analyses in these scenarios.

Methods: We propose an innovative approach to estimate DiD with unpoolable data. UN-DiD uses a weighted combination of siloed effect estimates and standard errors to recover pooled estimates. We begin with a simple two group two period case with no covariates, and then extend our analysis to include a single time-invariant covariate, and a single time varying covariate. We extend the UN-DiD model to more complex/realistic settings with multiple treated and control groups, multiple time periods, and various data generating processes. We use Monte Carlo simulations to compare UN-DID to conventional DiD before applying our estimator to an empirical example.

Results: Assuming a sufficiently large sample, we show the mathematical equivalence of our estimator with the conventional pooled estimator in varying data settings reflecting common real-world conditions. The UN-DiD estimate of the ATT is equivalent to the conventional estimate in the simple case, with no covariates and with time-invariant covariates. The estimates are no longer exactly equivalent in the presence of time varying covariates, but the estimates of the two methods (and the associated standard errors) converge as sample size increases.

Discussion: Our UN-DiD method can be used to estimate treatment effects when data are siloed by treatment and control units. This will facilitate policy evaluation when data cannot be combined across countries or other jurisdictional boundaries.

Accounting for heterogeneity in the effect of a mediator when estimating a controlled direct association: example of stem cell transplant as a mediator of racial disparities in death from adult acute myeloid leukemia Garth H Rauscher* Garth Rauscher Irum Khan Charles Poole

BACKGROUND: Mediation analyses often compare a total association (TA) with a controlled direct association (CDA) that estimates what the exposure, disease association might be if we intervened to equalize the mediator distribution. CDAs are exposure effects with mediator distributions held constant, and these methods do not typically account for heterogeneity in the mediator's effect on the outcome. METHODS: We compared different formulations of CDA to address different hypothetical interventions on the receipt or non-receipt a stem cell transplant as a mediator of racial disparities in death from adult acute myeloid leukemia (AML). All CDA were estimated from a single logistic regression of AML death against race, transplant status, and their product term. When estimating CDAs, in addition to equalizing the mediator distributions by race, we further accounted for differential effects of the mediator on the outcome during marginal standardization, forcing the effect of transplant on death to be homogenous by race and equal to that among non-Hispanic White (NHW) patients. RESULTS: Overall, the AML death disparity was 14 percentage points (TA RD=0.14, 95% CI: 0.04, 0.25). Fixing everyone to have a transplant doubled the death disparity (CDA RD=0.29, 106% increase) but reduced the risk of death in both race groups. Universal absence of transplant eliminated the death disparity (CDA RD=0.02, 89% decrease) but increased the risk of death in both race groups. Equalizing the distribution of transplant by race slightly reduced the death disparity (CDA RD=0.13, 7% reduction). Additionally forcing the preventive effect of transplant on death to be homogenous by race and equal to the better effect for NHW patients eliminated the death disparity (CDA RD=0.01, 92% reduction) and reduced risk of death in both race groups. CONCLUSION: Controlled direct associations might miss important mediation if they do not account for heterogeneity in the mediator's effect on the outcome.

Table. Impact of hypothetical interventions on stem cell transplant on the racial disparity of AML death.					
	NHB	NHW	RD	95% CI	PR[1]
Racial disparity in AML death					
Total Association	0.52	0.37	0.14	(0.04, 0.25)	Referent
Transplant - Controlled Direct Associations					
If we eliminated transplant for all paitents	0.55	0.54	0.02	(-0.07, 0.10)	89%
Equal transplant prevalence by race[2]	0.52	0.39	0.13	(0.00, 0.27)	7%
If every patient received a transplant	0.47	0.18	0.29	(0.03, 0.55)	-106%
Equal prevalence and effect = to that for NHW[3]	0.40	0.39	0.01	(-0.06, 0.09)	90%
Transplant = Yes and effect=that for NHW[4]	0.20	0.18	0.01	(-0.05, 0.07)	92%

NHW, non-Hispanic White; NHB, non-Hispanic Black; PR, proportionate reduction; RD, risk difference.

All logistic models adjusted for age, gender and diagnosing hospital, followed by marginal standardization.

[1]Proportionate reduction in the AML death disparity associated with each hypothetical intervention.

[2]If we equalized prevalence of transplant by race to be that of the total sample prevalence.

[3]If we equalized prevalence of transplant by race, and set the effect of transplant on death for NHB to be that for NHW.

[4]If we intervened so that all patients received a transplant, and set the effect of transplant for NHB to be that for NHW.

Marginal standardization of logistic regression results to obtain risk differences

Methods/Statistics

Statistical Methods to Address Sparse Data at Low PM2.5 Concentrations Alesia Jung* Alesia Jung Ethan Roubenoff Abeer Hasan Megan Leonhard Jessica Lin Tiffani Fordyce

Background: Several epidemiologic studies have reported an association between mortality and exposure to fine particulate matter ($PM_{2.5}$) at concentrations below the EPA's standard of 12 µg/m^3. A literature review was conducted to examine study specific factors that may explain the inconsistent findings about the concentration response function (CRF) at low $PM_{2.5}$ and statistical methods for sparse data that could improve the accuracy of modeling the CRF at low exposure levels.

Methods: PubMed was searched for original human epidemiologic studies published in the past ten years that evaluated the relationship between long-term $PM_{2.5}$ exposure and individual-level, all-cause or non-accidental mortality and the CRF or dose-response function.

Results: Of 5,512 articles, 353 were identified as potentially relevant. Full text review resulted in 42 included articles many of which did not have sufficient data at concentrations below 12 µg/m^3. Studies that focused on modeling CRF curves for low exposure reported conflicting results regarding the shape of the curve and linear versus non-linear relationship. We identified strengths and limitations of each study and potential sources of bias.

Conclusions: Variations in methods made it difficult to compare and generalize findings. Statistically, there are significant limitations when using a model built for high levels of exposure to study the relationship between mortality and exposure at levels outside the data range; data sparsity may explain the steeper CRF slope reported at lower exposure levels. More research is needed to understand the impact of models used to quantify exposure and the optimal way to impute missing exposure data.

Concordance of LexisNexis Accurint address information with address at diagnosis recorded in a population-based registry Rebecca Nash* Rebecca Nash Lauren E. McCullough Deirdre Cronin-Fenton Joellen Schildkraut Kevin C. Ward Timothy L. Lash

Background: The LexisNexis Accurint database is a commercially available source of residential data that has been used to obtain follow-up information, including emigration status, for disease registries and cohort studies. However, accuracy of Accurint address information has not been examined among adults in a population-based registry.

Methods: We assessed concordance between address at diagnosis recorded in the Georgia Cancer Registry (GCR) and an address identified in Accurint to cover a period that included diagnosis date among a cohort of breast cancer survivors (N=25,730). Concordance was assessed by text string matching of city and state, allowing for up to two-character differences in city name. To account for Accurint providing addresses with overlapping coverage periods, we assessed concordance by selecting a single address using different selection criteria: (1) longest duration, (2) most recent end date, and (3) prioritizing better matches. Concordance was quantified overall and by race and ethnicity.

Results: LexisNexis provided a total of 51,447 address records that covered a period including the diagnosis date among 25,323 (98%) breast cancer patients. Two-thirds of these records (66%) matched the city and state of the address recorded in the GCR, 22% matched the state only and 11% were non-matches. Most patients (95%) had at least one record that matched both the city and state; 30% had at least one address that matched on state only and 16% had an address that did not match the GCR-recorded address. Concordance on city and state ranged from 75% (longest duration) to 95% (prioritizing better matches). American Indian and non-Hispanic White patients had the highest and Asian and Pacific Islander patients had the lowest concordance for all three methods.

Conclusion: Concordance between addresses recorded in GCR and Accurint was moderate among a cohort of breast cancer survivors. There were differences by selection criteria and race and ethnicity.

Partial Effects in Environmental Mixtures – Guidance on Methods and Implications Alex Keil* Maria Kamenetsky Barrett M. Welch Paige A. Bommarito Jessie P. Buckley Katie M. O'Brien Alexandra J. White Thomas F. McElrath David E. Cantonwine Kelly K. Ferguson Alexander P. Keil

Exposure mixtures such as water contamination are pervasive in the environment. Mixtures methods, such as quantile g-computation (QGC) and weighted quantile sums (WQS) regression, focus on the joint effects of increasing all components of the mixture simultaneously. There is also an interest in refining those estimands to target negative and positive "partial effects", which estimate impacts of increasing only a subset of the mixture. While the performance of QGC and WQS regression have been evaluated for how well they estimate joint effects, their performance for estimating partial effects is unknown. We study the performance of QGC and WQS and their data-adaptive extensions (sample-splitting, model-averaging, penalized regression, no sample-splitting) in estimating partial effects. We contrast these methods with an approach based on a priori knowledge (QGCAP), that determines the partition of negative and positive exposures using subject-matter expertise. In simulations, we compare performance across methods and assess the impact of four study characteristics on performance: 1) exposure correlation, 2) sample size, 3) spread of partial effect across more exposures, and 4) imbalance in negative and positive effects. Only accurate a priori knowledge of exposures guaranteed precise estimation by QGC, measured by mean squared error (MSE). Other methods demonstrated some bias in nearly every setting (Figure 1). Error and bias increased as exposure correlation increased, sample sizes shrunk, as the partial effect was spread across more exposures, and as imbalance between negative and positive effects increased. QGC-based methods yielded more predictable bias and were the only approximately unbiased methods at large sample sizes. Outside of QGCAP, no method for estimating partial effects was best in all scenarios. We provide guidance for practitioners on the use and limitations of statistical approaches for disentangling harmful and helpful components of a mixture.

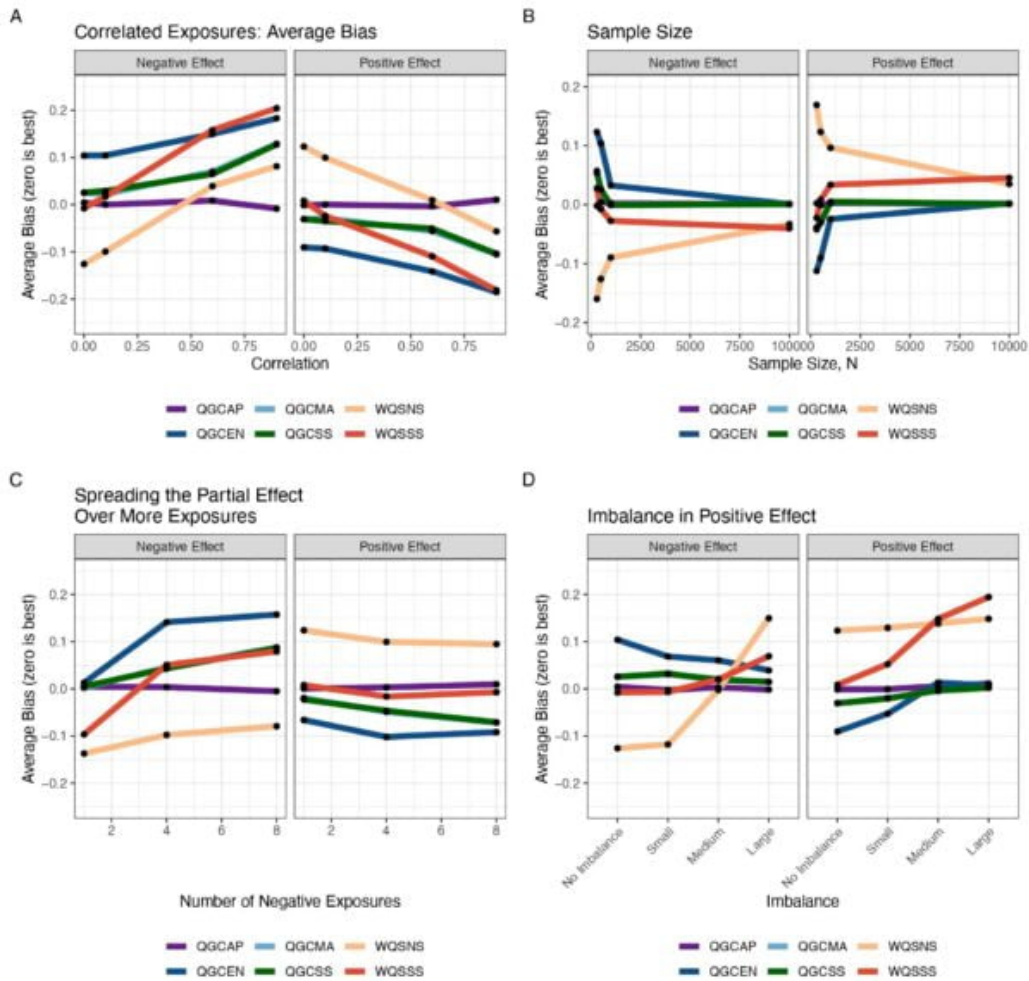Comparison of Average Bias Across Methods Estimating Partial Effects

Figure 1: Average bias over 200 realizations across four simulation settings using a generalized linear model with identity link (A: correlated exposures; B: sample size; C: spread in effect; D: imbalance in positive effect). Each figure compares QGC with *a priori* knowledge about exposures (QGCAP), QGC with sample-splitting (QGCSS), model-averaging (QGCMA), and penalized regression (QGCEN) as well as weighted quantile sums regression with no sample-splitting (WQSNS) and with sample-splitting (WQSSS) for estimating partial effects. Except in panels where each feature is varied, exposures are uncorrelated, sample size is 500, each partial effect is spread over 2 exposures, and there is no imbalance in the magnitude of the partial effects.

A State-Wide Assessment of Dynamic Prediction Modeling Strategies for 30-day Postoperative Mortality in Transcatheter Aortic Valve Replacement (TAVR) Jackie Pollack*

Jackie Pollack Wei Yang George Arnaoutakis Michael Kallan Stephen Kimmel

Background: With the increasing use of TAVR for severe aortic stenosis, robust mortality prediction models in this population are crucial. Early reliance on surgical aortic valve replacement (SAVR) models may inadequately capture evolving TAVR patient risks and differences in patient selection for the procedure. Deriving optimal TAVR-specific models initially faced challenges due to small sample sizes and the rapidly evolving nature of TAVR patients. One innovative strategy involves dynamically updating existing SAVR models for TAVR patients.

Methods: A baseline model, using all 14,070 surgical procedures (557 deaths) in Pennsylvania from 1999-2006, was developed to predict 30-day postoperative mortality in SAVR patients. In the subsequent test data (2012-2018, n=21,083 SAVRs, 514 deaths, and n=13,247 TAVRs, 348 deaths), we evaluated three distinct modeling strategies: 1) a static, non-updating approach, 2) updating the model in a combined SAVR+TAVR population, and 3) only updating the model in TAVR patients. Calibration regression (CR), which annually recalibrates the model intercept and slope, was applied to scenarios 2 and 3. Model performance was assessed in TAVR-only patients through measures of calibration and discrimination.

Results: TAVR mortality significantly decreased (from 4.9%-1.7%, p=0.016), while SAVR mortality remained stable (from 2.7%-2.0%, p=0.55). The static model consistently overpredicted the risk of TAVR mortality, with low discrimination (c-statistic (c-stat)=0.629). In contrast, both CR scenarios exhibited improvements in calibration (see figure) and modest discrimination improvement (combined population c-stat=0.651 and TAVR only 0.649, respectively) in TAVR patients.

Discussion: While waiting for ample TAVR data to facilitate the development of robust prediction models, the interim use of dynamic model updating is preferable over static methods. Yet, there is a need to develop and update new TAVR-specific models.
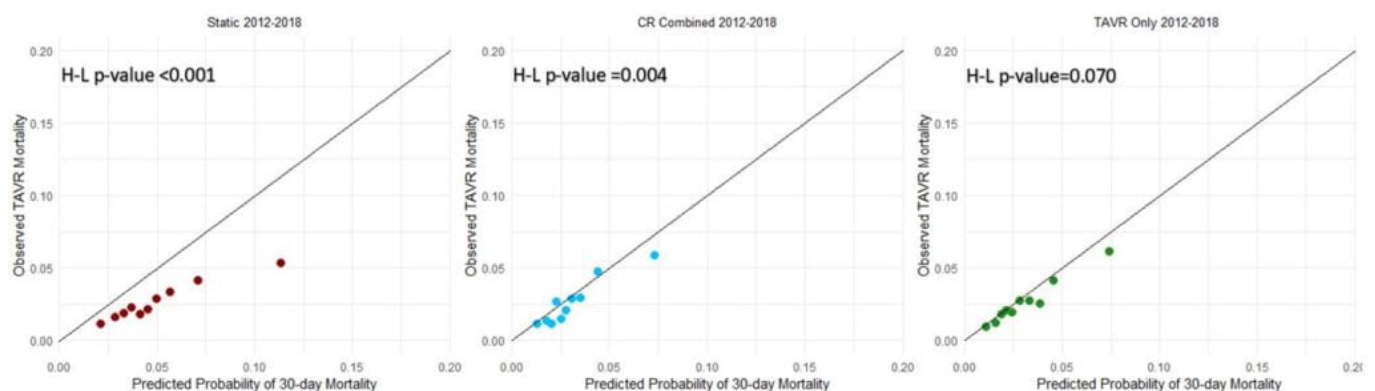
Static-Yearly application of the baseline model without dynamic updates. CR: Calibration Regression Combined - Baseline model collectively updated on the combined SAVR + TAVR population (2012-2018), with performance metrics measured in the TAVR subset. TAVR Only: The baseline model was first updated in 2012 in the TAVR population exclusively, continuing to 2018 with yearly recalibration in the TAVR-only subgroup.
SAVR-Surgical Aortic Valve Replacement
TAVR-Transcatheter Aortic Valve Replacement.
H-L-Hosmer-Lemeshow Chi-Square Statistic.

Methods/Statistics

Revisiting Representativeness Haidong Lu* Haidong Lu

The concept of representativeness has long been a key concept in epidemiology and other social sciences. Nonetheless, the interpretations of what constitutes representativeness and non-representativeness can differ among researchers. Some associate non-representativeness with a lack of generalizability, while others tend to conflate it with collider bias. In this paper, I aim to provide a comprehensive understanding of the underlying mechanisms of representativeness. Specifically, I will introduce and delineate two fundamental concepts: sample representativeness and estimate representativeness. Through the use of two distinct simulation studies involving causal diagrams, I will elucidate the reasons behind the occurrence of estimate non-representativeness when there is sample non-representativeness. Furthermore, I will discuss the settings in which estimate representativeness can be maintained even in the presence of sample non-representativeness.

The metabolic vulnerability index in subclinical hypothyroidism: a cross-sectional analysis from ELSA-Brasil Vandrize Meneghini* Vandrize Meneghini Carolina Castro Porto Silva Janovsky William R. Tebar José Augusto Sgarbi Patrícia de Fatima dos Santos Teixeira Steven R. Jones Michael J. Blaha Peter P. Toth Paulo A. Lotufo Isabela M. Benseñor

Introduction: The metabolic vulnerability index (MVX) is a novel biomarker of cardiovascular mortality risk derived from inflammation (IVX) and malnutrition (MMX) markers. Elevated MVX scores correlate with increased cardiovascular mortality. These indices have not been studied in thyroid disorders.

Objective: To explore the association of subclinical hypothyroidism with IVX, MMX, and MVX scores.

Methods: This is a cross-sectional analysis using baseline data from the São Paulo Research Center of the ELSA-Brasil study. Individuals with normal thyroid function (n=3722, mean age 51±9) and subclinical hypothyroidism (n=395, mean age 52±9) were included. Thyroid function was classified according to thyrotropin and free thyroxine levels and thyroid replacement therapy. Individuals taking medication that interferes with thyroid function were excluded. The components of IVX (GlycA, small high-density lipoprotein particles) and MMX (valine, leucine, isoleucine and citrate) were measured by nuclear magnetic resonance spectroscopy (LipoProfile® 4 test spectra, LabCorp). Sex-specific MMX and IVX scores were calculated and combined as MVX scores. We performed generalized linear regression analysis and included sociodemographic and lifestyle factors, chronic diseases, cardiovascular history, and glomerular filtration rate as confounder variables.

Results: Subclinical hypothyroidism was associated with higher MMX (β=1.16, 95% CI=1.05-1.28) and MVX (β=1.13, 95% CI=1.02-1.25) scores. After full adjustment, subclinical hypothyroidism was positively associated with MVX scores (β=1.12, 95% CI=1.02-1.23) compared with normal thyroid function. Participants with subclinical hypothyroidism showed positive, but not significant, association with MMX (β=1.09, 95% CI=0.99-1.20) and IVX (β=1.09, 95% CI=0.99-1.20) scores.

Conclusion: The association of subclinical hypothyroidism with these novel indices indicates that this disorder is a potential risk factor for cardiovascular mortality.

Neurology

Paraquat and Parkinson's Disease: A Systematic Assessment of Recent Epidemiologic Evidence Douglas Weed* Douglas Weed

A systematic assessment of recent evidence of the possible relationship between exposure to paraquat and Parkinson's disease was undertaken. A literature search was performed to identify all recently published relevant papers investigating, reviewing, or commenting upon the potential relationship between exposure to paraquat and Parkinson's Disease. MEDLINE (via PubMed) and EMBASE library databases were searched from 2019 to 2023 using search terms "paraquat" and "Parkinson." PRISMA guidelines for reporting systematic reviews were consulted and applied along with the AMSTAR2 evaluation tool used to assess the quality of reviews. A total of 517 publications were identified in the first search and 923 publications in the broader search. After removal of duplicates, 21 publications were determined to be potentially relevant. Identified cohort studies were published between 2019 and 2021 and represented analyses using data from the Agricultural Health Study (AHS) a study designed and funded by the U.S. National Institutes of Health. These studies revealed no association between paraquat exposure and Parkinson's disease. With the results of the most recent analyses, there is no compelling scientific argument for claiming causality. These studies examined not only general population groups but especially occupationally exposed populations and found no statistically significant increased risk and no evidence of an exposure-response relationship. In the absence of these key causal considerations, the fact that these studies contribute to the inconsistency of the entire epidemiologic database, nonexistent risk increases and dose-response relationships, a lack of experimental evidence, and the absence of a similar—analogous—example in the practice of causal inference, there is no scientific justification for a causal claim. Organizational conclusions are consistent.

LATEBREAKER

Neurology

Impact of Preoperative Frailty and/or Sarcopenia on Postoperative Outcomes in Adults with Degenerative Cervical Myelopathy. Hussein Samhat* Hussein Samhat Karlo M. Pedro Genevieve Gore Kristian B. Filion Raphaële Charest-Morin Oliver Lasry

Introduction: Degenerative Cervical Myelopathy (DCM) is the leading cause of non-traumatic spinal cord dysfunction in adults worldwide, causing spinal cord compression with symptoms ranging from neck stiffness to severe neurological deficits. Surgical intervention to decompress and stabilize the cervical spine is the mainstay treatment. However, surgery has inherent risks and results in heterogeneous outcomes. This highlights the need for effective risk stratification. Frailty (diminished physiological reserve) and sarcopenia (loss of muscle mass and function) are emerging risk-stratification tools, yet their roles in DCM outcomes remain unclear. This systematic review investigates the association between frailty/sarcopenia and post-operative outcomes in adult patients undergoing surgery for DCM.

Methods: We conducted a systematic search across eight databases (Figure 1), adhering to our comprehensive criteria (Table 1) outlined in the PROSPERO protocol (CRD42024477896). Screening, data extraction, and risk of bias via RoBANS-2, were performed by two independent reviewers.

Results: After screening 3,937 manuscripts, 14 met the inclusion criteria — nine addressing frailty and five focusing on sarcopenia. Preliminary findings show higher frailty levels consistently associated with increased post-operative complications, extended hospital stays, frequent non-routine discharges, and increased healthcare costs. Similarly, sarcopenia was associated with poorer spinal alignment, reduced functional outcomes, and lower patient satisfaction after surgery. These relationships held true across diverse patient demographics and hospital settings.

Conclusion: This review establishes the importance of frailty and sarcopenia assessments in preoperative evaluation for DCM, offering critical insights for surgical risk prediction. Integrating these assessments into clinical decision-making can inform personalized care and potentially optimize post-surgical recovery in DCM.
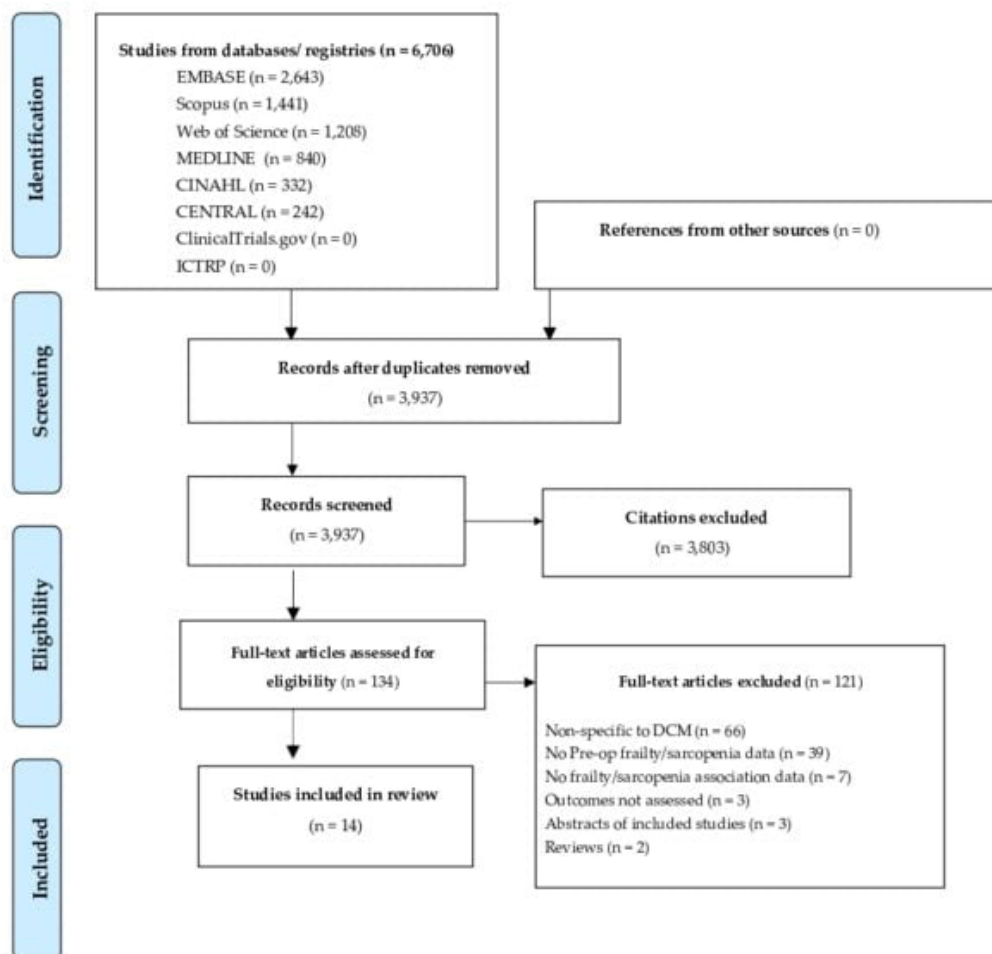
Impact of Preoperative Frailty and/or Sarcopenia on Postoperative Outcomes in Adults with Degenerative Cervical Myelopathy.

Figure 1. PRISMA Flow Diagram illustrating selection process for included studies.

Table 1. Summary of inclusion criteria

Criteria	Description
Population	Adults (≥18 years) undergoing surgery for degenerative cervical myelopathy (DCM).
Exposure/Characteristic	Presence of preoperative frailty or sarcopenia.
Comparison	No or low preoperative frailty or sarcopenia.
Outcome	Post-surgical outcomes including adverse events, complications, readmission rates, reoperation rates, discharge disposition, length of stay, and patient-reported outcome measures (PROMs).
Timing	Preoperative assessment and postoperative follow-up within one year of surgery.
Setting	Hospital and relevant post-discharge settings, with no geographical limitations.
Study Design	Clinical trials and observational studies.
Language	Any; no restrictions
Publication Date	Since inception of database/registry; no restrictions

Nutrition/Obesity

Longitudinal associations of maternal pre-pregnancy income variability with childhood overweight and obesity Mehrnaz Siavoshi* Mehrnaz Siavoshi

Childhood obesity is growing in the United States and has been linked to significant negative health outcomes, including youth-onset Type 2 Diabetes, hypertension, negative mental health outcomes, and other comorbidities. Therefore, there is a growing interest in understanding factors that contribute to childhood obesity. Previous research has demonstrated that mothers in poverty have children with increased odds of overweight and obesity. However, there is limited understanding of how stability or variability in maternal pre-pregnancy income and poverty status impact these odds. The National Longitudinal Surveys of Youth from 1979 and the associated child dataset was used to explore pre-pregnancy income variability and child overweight outcomes. Six years of pre-pregnancy maternal income data and poverty status was analyzed for a cohort of 6,404 children born between 1988 and 2016. Sustained maternal poverty in the six years before a child's birth was associated with increased incidence of childhood overweight and obesity (OR = 2.49, 95% CI [1.50, 4.16]). Moving from poverty status out of poverty, or moving into poverty when previously not in poverty status did not result in significantly different rates of childhood overweight or obesity as compared to those who were sustained in the out of poverty category. Race did not play a significant role in the relationship between poverty status variability and childhood obesity. The results from this study suggest that even short-term poverty reduction programs may have a sustained positive impact on reducing the prevalence of childhood overweight and obesity among the vulnerable low income population.
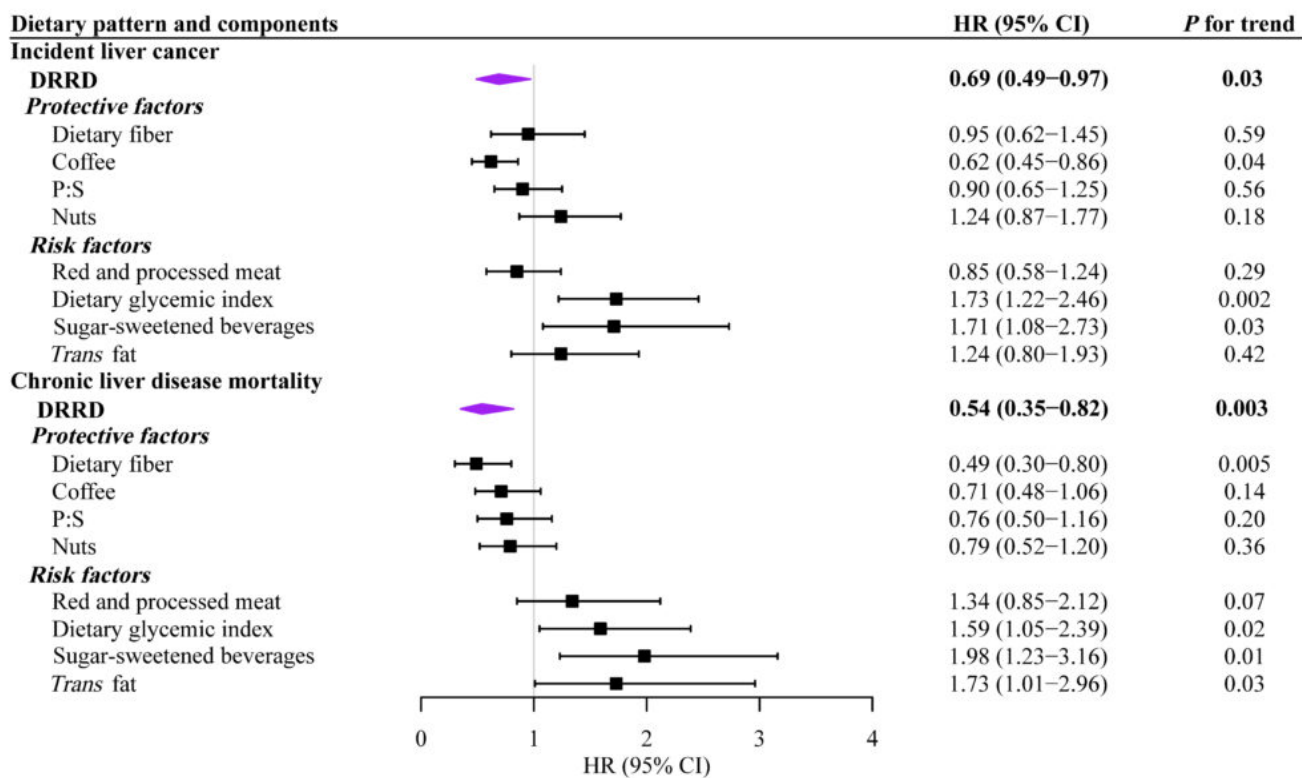
Nutrition/Obesity

Diabetes risk reduction diet and risk of liver cancer and chronic liver disease mortality: a prospective cohort study Yun Chen* Yun Chen Longgang Zhao Su Yon Jung Margaret S. Pichardo Melissa Lopez-Pentecost Thomas E. Rohan Nazmus Saquib Yangbo Sun Fred K. Tabung Tongzhang Zheng Jean Wactawski-Wende JoAnn E. Manson Marian L Neuhouser Xuehong Zhang

Background: Global incidence of type 2 diabetes mellitus (T2DM) continues to increase rapidly and is an important risk factor for end-stage liver diseases. Better understanding of the role of lifestyle factors for T2DM could help prevent the development of liver diseases. We evaluated the association between adherence to a diabetes risk reduction diet (DRRD) and the risk of liver cancer development and chronic liver disease mortality in postmenopausal women.

Methods: We included 98,786 postmenopausal women from the Women's Health Initiative Observational Study and the usual diet arm of the Diet Modification trial. The DRRD score was estimated based on responses to a food-frequency questionnaire administered at baseline (1993-1998). Adherence to the DRRD is characterized by high intakes of dietary fiber, coffee, nuts, and polyunsaturated fatty acids, and low intakes of red and processed meat, foods with high glycemic index, sugar-sweetened beverages (SSBs), and trans fat. Multivariable HRs and 95% CIs for liver cancer incidence and chronic liver disease mortality were estimated using Cox proportional hazards regressions adjusted for liver disease risk factors.

Results: After a median follow-up of 22.0 years, 216 incident liver cancer cases and 153 chronic liver disease deaths were identified. A higher DRRD score was significantly associated with a reduced risk of developing liver cancer (HRTertile 3 vs. Tertile 1 = 0.69; 95% CI: 0.49-0.97; Ptrend = 0.03) and chronic liver disease mortality (HRT3 vs. T1 = 0.54; 95% CI: 0.35-0.82; Ptrend = 0.003). We further found that high dietary fiber and coffee intake showed inverse associations, while dietary glycemic index, SSBs, and trans fat showed positive associations.

Conclusions: Adherence to a DRRD was associated with reduced risk of developing liver cancer and chronic liver disease mortality among postmenopausal women. Further studies are needed to validate our findings and elucidate the underlying biological mechanisms.

Dietary pattern and components	HR (95% CI)	*P* for trend
Incident liver cancer		
DRRD	**0.69 (0.49−0.97)**	**0.03**
Protective factors		
Dietary fiber	0.95 (0.62−1.45)	0.59
Coffee	0.62 (0.45−0.86)	0.04
P:S	0.90 (0.65−1.25)	0.56
Nuts	1.24 (0.87−1.77)	0.18
Risk factors		
Red and processed meat	0.85 (0.58−1.24)	0.29
Dietary glycemic index	1.73 (1.22−2.46)	0.002
Sugar-sweetened beverages	1.71 (1.08−2.73)	0.03
Trans fat	1.24 (0.80−1.93)	0.42
Chronic liver disease mortality		
DRRD	**0.54 (0.35−0.82)**	**0.003**
Protective factors		
Dietary fiber	0.49 (0.30−0.80)	0.005
Coffee	0.71 (0.48−1.06)	0.14
P:S	0.76 (0.50−1.16)	0.20
Nuts	0.79 (0.52−1.20)	0.36
Risk factors		
Red and processed meat	1.34 (0.85−2.12)	0.07
Dietary glycemic index	1.59 (1.05−2.39)	0.02
Sugar-sweetened beverages	1.98 (1.23−3.16)	0.01
Trans fat	1.73 (1.01−2.96)	0.03

HR (95% CI)

Association between lifecourse employment instability and midlife word recall S. Amina Gaye* S. Amina Gaye Lucia Pacca Anusha M. Vable

There is a relationship between longest held or last occupation and dementia risk through mechanisms such as income and job demands. However, little work has evaluated the effect of employment on cognition over the lifecourse. Using the National Longitudinal Survey of Youth 1979 (NLSY79), we assessed whether employment instability is associated with midlife word recall.

We used weekly employment status of NLSY79 participants (N = 4424) from ages 22-48. Each week was classified as employed, unemployed, out of the labor force, or unreported. Due to marked heterogeneity in employment patterns by gender, we stratified analyses by men and women. Cognitive measure was immediate word recall evaluated at age 48. We used sequence analysis to quantify differences between employment trajectories and cluster analysis to group similar trajectories. We used linear regressions to estimate the association between employment instability and midlife word recall adjusted for race, education, parental education, and birthplace.

Five employment trajectories were identified for men (predominantly employed, seldom unemployed/out of the labor force, predominantly employed after 35, precariously employed, and out of the labor force), and six for women (predominantly employed, precariously employed until 35, precariously employed then out of labor force at 35, precariously employed, out of the labor force then precariously employed, out of the labor force). Compared to men who were predominantly employed, those who were out of the labor force (β:-0.92, 95% CI:-1.3,-0.58) had the lowest immediate word recall scores. Compared to women who were predominantly employed, those who were out of the labor force and then precariously employed had the lowest immediate word recall scores (β:-0.4, 95% CI:-0.71,-0.11).

In both men and women, cognitive performance was worse among those who were predominantly out of the labor force or precariously employed compared to those with more consistent employment.
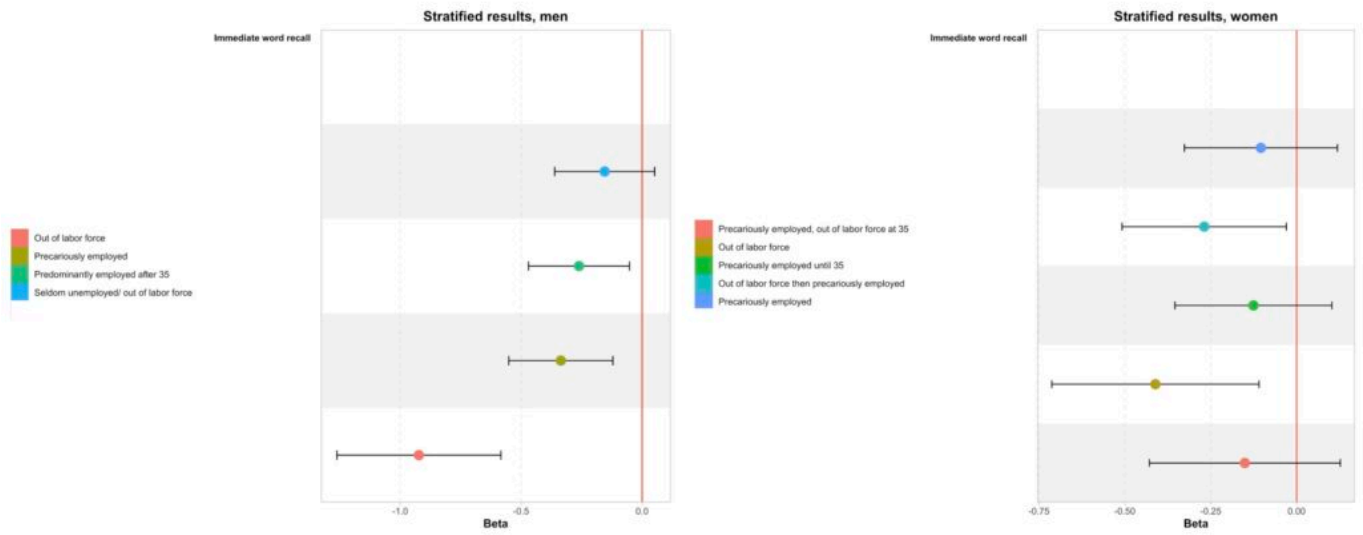
Figure Linear regression estimates on the association between weekly employment trajectories from age 18-48 and cognitive performance in immediate word recall evaluated at age 48. Results are stratified by gender with the predominantly employed trajectory serving as the reference group in both men (N = 2190) and women (N = 2234). Negative estimates are indicative of poor cognitive performance.

Working time variability, flexibility, and advance notice of work schedules among U.S. workers: Data from the 2021 National Health Interview Survey Toni Alterman* Toni Alterman P. Timothy Bushnell Jia Li Abay Asfaw

Unpredictable work schedules are associated with poor health including depressive symptoms, psychological distress, poor sleep quality, and poor fatigue recovery. Unpredictable schedules are common among low wage workers, service workers, food workers and hourly retail workers when management tries to closely align staffing with demand. Many workers receive little advance notice of their work schedules, and their scheduled work hours and workdays may change substantially week to week. In 2021, questions about the predictability and flexibility of work schedules were added to the National Health Interview Survey, a nationally representative survey on the health of non-institutionalized persons residing in the U.S. Among the 16,452 workers interviewed, 20% (95% CI 19.2, 20.8) reported that their work schedule was variable and 21.5% (95% CI 20.7, 22.3) said that it was difficult to change their work schedule. Of those whose work schedule was variable, close to half also received short notice (≤4 days) of their work schedule. Weighted national prevalences of schedule unpredictability and inflexibility will be presented by demographic characteristics, including occupation, and industry. Occupations with difficult-to-change work schedules included Education/Training and Library, Production, and Healthcare Practitioners and Technical occupations. The prevalence of jobs with a short notice of changes in work schedule differed significantly (p<0.05) by sex, race, education, and disability. Workers in Construction and Extraction (18.7%, 95% CI 15.4, 22.4), Personal Care and Services (18.6%, 95% CI 13.8, 24.1) and Transportation and Material Moving occupations (14.8%, 95% CI 12.5, 27.4) have among the highest rates of inflexible and less predictable work schedules. Understanding work schedule precarity is important as lawmakers have begun to introduce fair schedule legislation to provide workers with more predictable and flexible work schedules.

Occupational

Occupational Exposure to Ultraviolet radiation and Cataract Risk in Denmark Chisom N. Iwundu* Chisom Iwundu Johnni Hansen Anne L. Coleman Julia E. Heck

Introduction: Ultraviolet (UV) radiation has been implicated as a contributing factor to lens opacities, with occupational exposure to UV radiation raising concerns for individuals across various industries. Despite this, the relationship between workplace UV radiation exposure and the risk of cataract development remains understudied. Our goal is to investigate the association between occupational UV radiation exposure and the risk of cataract development, using a large-scale population-based study.

Methods: In this cohort study, validated datasets nationally representative of the Danish population were linked based on a unique ID, applied to all residents. Employment history was identified through the Supplementary Pension Fund register, which keeps historical records on each job held, including dates and type of industry for all employees since 1964. UV radiation was assessed using a Danish job-exposure matrix which was applied to the individual employment history. Demographic information, covariates, such as sex, birth year, and region of birth were derived from the Central Population Registry. Cataract diagnosis was retrieved from the National Patient Register (International Classification of Diseases (ICD-8 & 10). Cox regression models were used to estimate the risk of cataract among workers exposed to UV radiation.

Results: Using the linked databases (N=4,142,173 employees), cataract diagnosis was reported in 2.7% of the population. Preliminary results suggest increased risk of cataract among workers exposed to UV radiation (Hazard Ratio: 1.53; 95% Confidence Interval: 1.47-1.56), after adjustment for diabetes and birth year.

Conclusion: Cataract, a leading cause of visual impairment worldwide, poses a significant public health concern in UV-exposed workers. The findings raise additional concerns for worker protection in such jobs.

Association between acculturation and dental caries among Asian children aged 1-17 living in the United States. Rohit Baal Balasundaram* Rohit Baal Balasundaram Rohit Baal Balasundaram Nihmath Nasia Maliq Sarah Al Khatib

Background: Asians living in the US have reported poor oral health and less frequent utilization of dental services than non-Hispanic Whites. Studying the factors affecting the oral health of the increasing Asian population in the US is crucial to addressing these disparities. **Objective:** This study aimed to examine the association between household acculturation and pediatric oral health in the Asian population using a nationally representative sample of children. **Methods:** Data from the 2021-2022 National Survey for Children's Health, acculturation levels were determined using primary household language and parental nativity. Low acculturation group consisted of a household where the primary language was not English and at least one parent was foreign-born. The high acculturation group consisted of a household where the primary language was English, and both parents were US-born; those not in these groups were considered moderate. Children's oral health was evaluated as presence or absence of dental cavities based on parental/guardian report. Logistic regression was used to estimate OR and 95% CI between acculturation and dental caries adjusting for age, sex, federal poverty level, dental visit, household structure, education, special health care needs, no. of children, and insurance. Covariates were determined based on previous literature related to pediatric oral health. The analyses accounted for complex survey design. **Results:** Analysis included 10369 Asian children. In total, 11.7% experienced dental caries (95% CI:11.2 – 12.1%). Having low acculturation was associated with 2 times the odds of having dental caries compared with high acculturation [aOR 2.1, 95% CI 1.5 – 3.0] **Conclusion:** Children residing in low acculturated households were at greater risk for caries. Linguistically and culturally appropriate public health intervention is needed for better oral health in Asian children in the US.

Changes in gestational diabetes subtypes following a screening change in British Columbia, Canada: an interrupted time series analysis Elizabeth Nethery* Elizabeth Nethery Jennifer Hutcheon Julie Lee Patricia Janssen Laura Schummers

Background: In October 2010, regional guidelines for gestational diabetes mellitus (GDM) screening changed to use a lower diagnostic threshold for GDM. The new approach diagnosed GDM in pregnant individuals at lower hyperglycemia levels, which nearly doubled the incidence of GDM. It is unknown, however, whether the additional diagnoses were less severe GDM cases ("diet-controlled GDM", treated through lifestyle changes) or more severe cases ("medication-dependent GDM"). We examined the effect of a screening guideline change on GDM subtypes.

Methods: We used a population-based linked cohort of all singleton pregnancies >28 weeks gestational age in 2008-2019, with GDM screening records. We identified GDM cases based on international classification of diseases coding on the delivery admission record and medication-dependent GDM based on one or more outpatient prescription records for glucose control medications during pregnancy. We used an interrupted time series design using linear regression to estimate changes in GDM types (medication-dependent and diet-controlled) following the policy change. We estimated risk ratios comparing the observed incidence of each GDM type with the expected incidence of each type in the post-policy period, controlling for underlying time trends.

Results: Among 472,595 singleton pregnancies, 7.9% were diagnosed with GDM during the pre-2010 period and 12.1% in the 2011-2019 period. The incidence of diet-controlled GDM increased from 6.2% pre-2010 to 8.9% post-change. From our interrupted time series models (Fig 1), we found a 1.33 (95% CI: 1.26, 1.41) relative risk increase (level change) in diet-controlled GDM. We found no change in the level or trend for medication-dependent GDM (level change: RR 0.94 [95% CI: 0.84 to 1.05]).

Conclusion: A change in GDM screening policy resulted in a 33% increase in the incidence of less severe diet-controlled GDM, but had no impact on incidence of more severe, medication-dependent GDM.
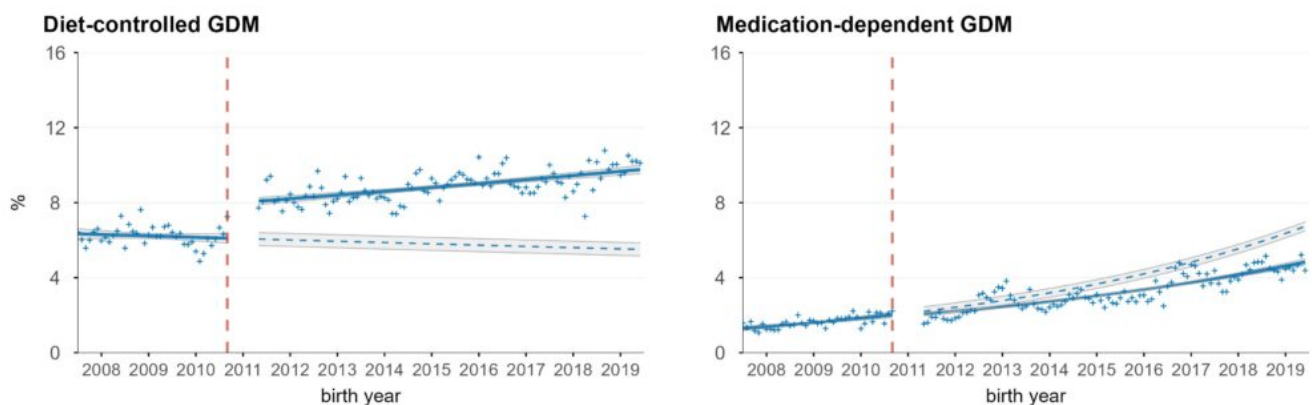
Recent reductions in gastroschisis prevalence in the United States and Puerto Rico largely explained by population-level decline in younger maternal age at live birth Julie M. Petersen*
Julie Petersen Jeremy Schraw Mahsa Yazdy Martha Werler

Background: Gastroschisis is an abdominal wall congenital anomaly. The strongest risk factor is young maternal age. Over several decades, gastroschisis had been increasing, but North American data suggest a recent decrease. We estimated population-based time trends in gastroschisis prevalence in the United States (US) and Puerto Rico 2000–2020 and indirectly examined whether the recent shift may be attributed to population-level declines in younger maternal age.

Methods: We pooled US state/territory summary-level data from 17 active surveillance systems and 29 passive (or combination) systems or birth certificates, the latest of which became public in 2024. We estimated crude prevalence per 10,000 live births and 95% confidence intervals (CI) within 5-year periods with moving averages every 2 years. We estimated the expected prevalence of gastroschisis based on the distribution of maternal age among US live births (<20, 20–24, ≥25 years) and previously published maternal age-based prevalence estimates.

Results: Gastroschisis prevalence increased since 2000, peaked in 2008–2012, and then declined, with an average reduction of ~4.8% every 2 years. The same trends occurred when restricted to active systems but absolute prevalence estimates were higher (2008–2012: 5.44, 95% CI 5.23, 5.65; 2016–2020: 4.47, 95% CI 4.27, 4.67, among systems with all years available). The proportion of all US births among individuals <20 years decreased (2000: 11.8%, 2020: 4.4%). Applying prior prevalence estimates based on maternal age yielded near identical expected gastroschisis prevalence as observed. If these trends continue, we project gastroschisis prevalence will be the same as 2000–2004 by 2026.

Conclusions: These data confirm that gastroschisis prevalence decreased in recent years and provide indirect support that the reduction largely reflects the decline in US births among younger maternal ages, rather than a substantial change in gastroschisis risk among younger individuals.
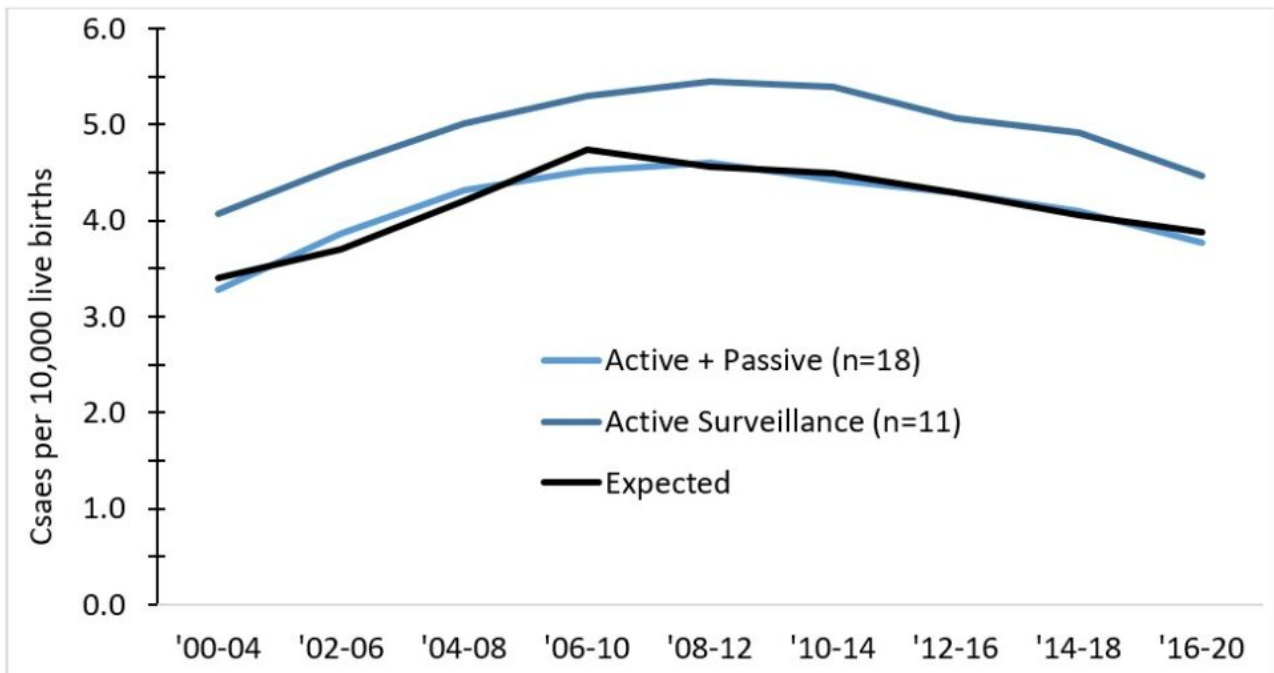
FIGURE. Trends in gastroschisis prevalence in the United States and Puerto Rico, observed by surveillance system type versus expected (2000–2020). Figure restricted to programs with data for all years. Active surveillance systems included: Arizona, Arkansas, California, Georgia, Iowa, Massachusetts, North Carolina, Oklahoma, Puerto Rico, Texas, and Utah. Passive surveillance systems included: Colorado, Illinois, Indiana, New Jersey, New York, Rhode Island, and Tennessee. The expected number of gastroschisis cases within maternal age-based subgroups (<20, 20–24, ≥25 years) were derived by applying previously published maternal age-based gastroschisis prevalence estimates (Jones 2016, Short 2019) to the number of all US births with each age-based subgroup. We summed the number of expected cases and divided by the total number of US births to determine overall expected prevalence.

Fetal Growth Associated with Maternal Rheumatoid Arthritis and Juvenile Idiopathic Arthritis. Eugenia Chock* Eugenia Chock Zeyan Liew Lars Henning Pedersen Mette Oestergaard Thunbo

Introduction: Maternal chronic inflammatory arthritis, including rheumatoid arthritis (RA) and juvenile idiopathic arthritis (JIA), is associated with a higher risk of preterm delivery and infants with low birth weights, but the timing and trajectory of fetal growth during pregnancy associated with these maternal conditions have not been well studied.

Methods: We conducted a population-based cohort study in Denmark from 2008-2018 which included 503,491 singleton pregnancies. Among them, 2,206 mothers have received an RA or JIA diagnosis (RA/JIA) before or during pregnancy. We analyzed 2nd trimester fetal ultrasound measurements (at 18-22 weeks' gestation) extracted from the Danish Fetal Medicine Database. We first examined the estimated fetal weight (EFW) at the 2nd trimester and the recorded birth weight separately. Then, we calculated the fetal growth gradient by computing the mean difference between the fetal weight and the birth weight Z-scores. We conducted linear regression analyses for these outcomes comparing pregnancies with or without RA/JIA adjusting for confounding factors. We further stratified the maternal RA/JIA groups by the antirheumatic therapies received during pregnancy.

Results: Maternal RA/JIA was not associated with a reduction of EFW in mid-pregnancy, but a lower birth weight (Z- scores mean difference: -0.08; 95%CI -0.13, -0.04). Maternal RA and JIA was associated with fetal growth gradient reduction computed using the 2nd trimester EFW and birth weight measures (Z-score mean difference: -0.14; 95%CI -0.08, -0.19), with the largest growth reduction observed among mothers with RA/JIA who used corticosteroids (-0.26; 95%CI -0.11, -0.41) and sulfasalazine (-0.61; 95%CI -0.45, -0.77) during pregnancy.

Conclusion: Offspring born to individuals with RA/JIA had lower birth weight; with the greatest gradient of fetal growth reduction noted during the late pregnancy period, and among corticosteroid and sulfasalazine users.

Association between Hypertensive Disorders of Pregnancy and Child Developmental Pattern: TMM BirThree Cohort Study in Japan Geng Chen* Geng Chen Mami Ishikuro Hisashi Ohseto Aoi Noda Genki Shinoda Masatsugu Orui Taku Obara Shinichi Kuriyama

BACKGROUND

Hypertensive disorders of pregnancy (HDP), particularly preeclampsia (PE), is associated with increased risk of developmental delay in different ages of children. Child development problems at an early age could persist into later years. Identifying child development pattern which contributes to early intervention might help them catch up.

OBJECTIVES

To investigate child development pattern in 5 developmental domains. To reveal the association between fetus exposure to HDP or PE and child development pattern.

METHODS

The study included 11748 mother-child pairs from TMM BirThree Cohort Study, a prospective cohort study in Japan. HDP and PE prevalence were identified by antenatal records. The Ages and Stages Questionnaires, 3rd edition (ASQ-3) were collected at 6, 12, 24, 42, 48 months of age to measure child development in communication, gross motor, fine motor, problem solving and personal/social. Latent class trajectory model was applied to z-score-scaled ASQ-3 scores, fitting with 3 polynomial functions (linear, quadratic, cubic), refining class numbers from 2 to 7. After assessments, models with lowest Bayesian information criterion value were recognized best-fitting. Poisson regression analysis was conducted between HDP or PE and development patterns to calculate risk ratios (RRs), adjusted for maternal age at pregnancy, family annual income, maternal educational attainments, maternal pre-pregnancy BMI, parity, gestational diabetes mellitus prevalence, maternal tobacco use in pregnancy, maternal alcohol use in pregnancy, maternal folic acid intake in pregnancy and child sex.

RESULTS

The 3-class linear model fits the data best. Child development patterns could be described as normal, delay and catch-up. HDP prevalence is associated with delay pattern in gross motor (RR 1.28, 95% CI 1.06-1.53). PE prevalence is associated with delay pattern in communication (RR 1.42, 95% CI 1.00-1.96), gross motor (RR 1.51, 95% CI 1.07-2.07), and problem solving (RR 1.74, 95% CI 1.02-2.75).

CONCLUSION

In 5 domains, child development could be characterized into 3 patterns: normal, delay, and catch-up. Fetal exposure to HDP, particularly PE, is associated with a delay pattern in child development. We suggest screening from multiple domains in children exposed to PE during fetal stage to catch up.

Maternal Characteristics by Manual versus Automated Occupation Coding Among Infants with Cleft Lip and Palate Jenil Patel* Jenil Patel Omobola O. Oluwafemi A.J. Agopian Renata H. Benjamin David Gimeno Ruiz de Porras Charles Shumate

In association analyses of large datasets, it may be tempting to restrict to subjects for whom occupation may be coded using automated software without requiring more burdensome manual coding, but there are hypothetical concerns for selection bias. Thus, we aimed to compared maternal characteristics by manual versus automated occupation coding status. Utilizing data from the Texas Birth Defects Registry, we focused on infants with cleft lip and/or palate (1999-2009). The NIOSH Industry and Occupation Computerized Coding System (NIOCCS) was employed for automated coding, with manual coding for unclassified cases. Maternal characteristics were analyzed by manual vs. automatic occupation coding status. Logistic regression was used to explore associations between major occupation groups and the occurrence of orofacial clefts.

Automatic coding could be conducted on over 90% of all mothers. After excluding nonworking mothers, there were a total of 3,865 subjects analyzed (1,063 infants with CLP, 511 infants with CP, and 2,291 controls without birth defects). There was a significant demographic difference between automatically and manually coded control mothers by race/ethnicity (p=0.001), marital status (p=0.006), and diabetes status (p=0.009), but differences were not observed by maternal age at delivery, maternal BMI, maternal education, parity, and smoking. Specific occupation groups were associated with clefts, such as building, grounds cleaning, and maintenance occupations adjusted Odds Ratio (aOR): 2.21, 95% CI: 1.30, 3.76), as well as office and administrative support occupations (aOR: 0.77, 95% CI: 0.63, 0.93), after adjustment for maternal age at delivery, education, race/ethnicity, parity, any diabetes, and smoking during pregnancy. Notably, these associations persisted even after excluding manually coded occupations.

Association analyses were consistent before and after the exclusion of manually coded data, suggesting that machine learning, specifically the NIOCCS system, can play a valuable role in facilitating occupation-related birth defects research. The findings emphasize the reliability and efficiency of automated coding systems in large-scale epidemiological studies, providing insights into potential occupational factors contributing to cleft lip and palate.

Assessing the Impact of Environmental Factors on the Prevalence and Safety of Children's Active School Transportation Juan Garcia* Juan Garcia Zoabe Hafeez Christopher Kulesza Augusto César F. De Moraes

Background: In the U.S., childhood obesity is notably prevalent in lower-income Black and Hispanic families, linked to lifestyle and environmental factors. This study examines how active commutes to school, like walking or biking, impact children's BMI and weight management. We hypothesize that these active commutes can significantly reduce obesity in these demographics in Houston school-children.

Methods: The Houston Independent School District Child Health Study was a multi-site volunteer-administered survey by the Baker Institute of Public Policy at Rice University encompassing students from 14 high schools from September 2018 through April 2019. The survey contained 48 questions, including form of transportation to school, neighborhood characteristics, health information, age grade, sex, race, and language spoken at home. We tested the association by chi-squared test performed for all analyses with an $\alpha = 5\%$ to determine a significant association.

Results: A total of 8868 responses were analyzed. 76% identified as Hispanic, 49% were female, 29% were in 9th grade, and 61% of households spoke Spanish primarily. 11% of respondents reported using ATS as their primary form of commute with 74% reporting a non-active form of transport. Males, African Americans, and Caucasian children were statistically more likely to commute to school actively when compared to their counterparts. These students who biked or walked to school were also more likely to state that their neighborhood (15%) and commute (16%) were unsafe ($\alpha < 5\%$). Regarding health conditions (diabetes, weight problems, high blood pressure), no statistically significant difference was found between students who used ATS and those who didn't.

Conclusion: In examining the health impacts of active school transportation (ATS), such as biking or walking, our study found no significant health differences between ATS users and non-users. Notably, a significant number of ATS users expressed safety concerns regarding their neighborhoods and commute routes.

Associations Between Maternal Hypertensive Disorders of Pregnancy and Vascular Birthmark Development in Infants Jessica J. Wong* Jessica Wong Yajnaseni Chakraborti Ellen C. Caniglia David Margolis Enrique Schisterman Sunni L. Mumford Stefanie N. Hinkle

Background: Investigating the developmental origins of vascular birthmarks, such as port-wine stains (PWS) and hemangiomas, in the context of hypertensive disorders of pregnancy (HDP), offers a unique lens to explore the relationship between maternal health and infant dermatological outcomes. While often considered cosmetic, these birthmarks can signify serious conditions like Sturge-Weber Syndrome in facial PWS cases or vision impairment from hemangiomas near the eyes. Recognizing the shared developmental pathways between hemangiomas and preeclampsia (PE), this study examined the association between HDP and vascular birthmarks.

Methods: The Collaborative Perinatal Project (1959-1966) was a prospective study at 12 US clinical centers. Contemporary clinical guidelines defined HDP as chronic hypertension (HT), gestational HT, PE/eclampsia, and superimposed PE. Vascular birthmarks were diagnosed in infants at one year by general practitioners. Adjusted log-binomial regression models with multiple imputations for missing data estimated the association between HDP and infantile birthmarks, adjusting for confounders.

Results: Of 55,676 maternal-infant pairs, 50,487 were normotensive, 2,087 had chronic HT, 943 had gestational HT, 519 had PE, and 1,011 had superimposed PE. At one year, 1.3% of infants had hemangiomas, and 0.5% had PWS. For PWS, the RRs (95% CI) were 1.12 (0.48-1.76) for chronic HT, 1.01 (0.22-1.8) for gestational HT, 1.34 (0.35-2.34) for PE, and 2.25 (1.56-2.94) for superimposed PE. For hemangiomas, the RRs were 1.38 (0.98-1.78) for chronic HT, 1.01 (0.52-1.51) for gestational HT, 1.75 (1.2-2.3) for PE, and 0.95 (0.31-1.58) for superimposed PE.

Conclusion: This study suggests that superimposed PE could be associated with an increased risk of developing PWS, while PE might be linked to an increased risk of hemangiomas. These observations highlight the need for further exploration into the role of HT in the development of vascular birthmarks in infants.

Cumulative Incidence of Medical Complexity through Early Childhood and Associations with Birth Outcomes in a U.S. Military Birth Cohort Jackielyn Lanning* Jackielyn Lanning Clinton Hall Celeste J. Romano Anna T. Bukowinski Gia R. Gumbs Jordan A. Taylor Sarah Craig Monica A. Lutgendorf A. James O'Malley Elizabeth M. Perkins David C. Goodman Ava Marie S. Conlin JoAnna K. Leyenaar

Background: Children with medical complexity (CMC) have one or more chronic medical conditions that impact daily living. While CMC represent a small proportion of the pediatric population, they experience a disproportionate fraction of medical care and costs. This study estimated the cumulative incidence of CMC by age 60 months in a cohort of live births among United States military families and measured associations between CMC and birth outcomes.

Methods: Department of Defense Birth and Infant Health Research program data captured births among military families, 2005-2015. Healthcare claims through 60 months of age identified CMC using two validated algorithms: the Pediatric Medical Complexity Algorithm and the Complex Chronic Condition Classification System. Birth characteristics were compared by CMC status. Accounting for death as a competing event and loss to follow-up, the cumulative incidence of CMC by age 60 months was estimated and Fine-Gray regression models calculated adjusted hazard ratios (aHR) and 95% confidence intervals (CI) for associations of CMC with birth outcomes.

Results: Overall, 980,246 live births were identified and the estimated cumulative incidence of CMC by age 60 months (n=104,077) was 11.3% (95% CI=11.3-11.4). CMC were more likely to be delivered by cesarean section (36.9 vs 27.4%) and have intensive neonatal care (23.0 vs 3.6%) than children without medical complexity. Hazard of CMC was highest for children born with vs without congenital anomalies (aHR=26.4; 95% CI=25.6-27.2), very preterm (<32 weeks' gestation) vs term (aHR=2.5; 95% CI=2.4-2.5), and very low birthweight (<1500 grams) vs normal birthweight (aHR=14.4; 95% CI=13.9-14.8).

Conclusions: Approximately 1 in 10 military children developed medical complexity by age 5; understanding the burden of CMC in this population can guide future research and planning of services. Adverse birth outcomes were highly associated with risk of medical complexity through early childhood.

Three-dimensional fetal body composition and organ volume growth patterns across pregnancy-associated hypertensive disorders Kathryn Wagner* Kathryn Wagner Jessica Gleason Zhen Chen Stefanie Hinkle William Grobman Roger Newman Wesley Lee John Owen Daniel He Seth Sherman Robert Gore-Langton Luis Goncalves Daniel Skupski Edward Chien Ronald Wapner Sabrina Craigo Magdalena Sanz Cortes Angela Ranzini Anthony Sciscione Lauren Mack Jimmy Espinoza Mary D'Alton Michael Nageotte Cuilin Zhang Jagteshwar Grewal Katherine Grantz

Hypertensive disorders of pregnancy (HDP), which complicate 5-8% of pregnancies, are associated with lower birthweight and fetal growth restriction. Differential accumulation of fetal lean and fat tissue, and organ volume growth, may better define normal versus abnormal fetal growth. No studies have evaluated the association between HDP and three-dimensional (3D) measures of fetal body composition or organ volumes across pregnancy.

In the NICHD Fetal 3D Study (n=2425 pregnancies), fetal body composition and organ volumes were measured at up to five 3D ultrasound scans between 15 to 40 weeks. Women were identified as having severe preeclampsia (PE) (n=32, 1.3%), mild PE (n=51, 2.1%), gestational hypertension (GH) (n=84, 3.5%), or no hypertension (referent group; n=2258, 93.1%). Trajectories of 3D fetal measures were modeled using linear mixed effect models. Overall and weekly differences in trajectories, by HDP status, were tested, adjusting for covariates and multiple comparisons using Tukey's method.

Compared to fetuses of normotensive women, fetuses of women with severe PE had smaller fractional lean arm volume at 15-17 weeks gestation and at 28-34 weeks (0.5-1.3 cm3). Fetuses of women who developed mild PE had larger maximum abdominal and thigh subcutaneous tissue thickness (SCTT) starting, on average, at 24 weeks and continuing through gestation, and larger cerebellar volume from 19-34 weeks gestation (0.3-4.5 cm3). Lastly, fetuses of women who developed GH had smaller fractional arm and thigh volumes (overall and lean) and abdominal area starting in the 2nd half of pregnancy, larger maximum abdominal SCTT starting at 29 weeks (0.3-0.6 mm), and larger cerebellar volume at 17-23 weeks.

Patterns of lean and fat tissue growth and cerebellar volume varied across HDP categories, often prior to clinical diagnosis. Future investigation is needed to determine whether these findings have clinically important implications for offspring cardiometabolic function and health.

DNA methylation of the Lamin A/C gene is associated with congenital heart disease Nandini Mukherjee* Nandini Mukherjee Elijah H. Bolin Amna H. Qasim Mohammed S. Orloff Philip J. Lupo Wendy N. Nembhard

Background: Prior studies report maternal serum Lamin A, encoded by the LMNA gene, to be linked to fetal congenital heart disease (CHD). It is unknown whether DNA methylation (DNAm) of cytosine-phosphate-guanine (CpG) sites in LMNA impacts CHDs. We investigated the associations of LMNA DNAm with CHDs in a cross-sectional study.

Methods: We used publicly available data of CHD cases (n= 197) and controls (n= 134) from the Gene Expression Omnibus repository with accession numbers GSE159930 and GSE36054, respectively. Peripheral blood DNAm was measured using Illumina Infinium Methylation 850K BeadChip for cases and 450K BeadChip for controls. We tested 31 LMNA CpGs to identify differences in DNAm between cases and controls using linear regression correcting for multiple testing with false discovery rate (FDR). In a case-only analysis, we tested the variations in LMNA DNAm between CHD subtypes. To identify consistency across tissue types we compared peripheral blood (n= 197) and heart tissue DNAm (n= 20) in CHD cases.

Results: We detected significant differences in 17 among the 31 LMNA CpGs between CHD cases and controls adjusting for sex, age, and cell types at FDR p-value <=0.05. DNAm of cg09820673 located at 3'UTR exhibited lower methylation for Hypoplastic Left Heart Syndrome compared to other Left-sided lesions, Lateralities, and Conotruncal defects. DNAm of three CpGs was consistent between peripheral blood and heart tissue in CHD cases.

Conclusion: We demonstrate that LMNA DNAm may influence CHD susceptibility. The findings inform future studies to explore associations of maternal LMNA DNAm with CHDs to develop preventive interventions.
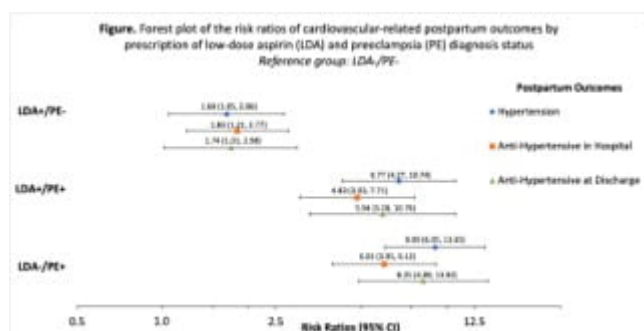
Low-dose aspirin prophylaxis for preeclampsia and the risk of postpartum cardiovascular outcomes: a propensity score analysis Ema Mujic* Ema Mujic Sojourna Ferguson Christina D. Yarrington Nyia Noel Samantha E. Parker

Background: The U.S Preventative Service Task Force recommends initiating low-dose aspirin (LDA) before 16 weeks of pregnancy to prevent developing preeclampsia among people with certain risk factors. While there are robust data supporting the effectiveness of LDA for the prevention of preeclampsia, limited data exist regarding its impact on postpartum outcomes.

Methods: We abstracted electronic medical record data on pregnant people who had a live birth from 2018-2019 and met criteria for LDA prophylaxis (n=1,862) at single safety-net hospital. We created propensity scores using major and moderate risk factors and prenatal care site and used 1:1 matching to identify unexposed (LDA-) matches for the 376 patients that received a prescription for LDA at ≤ 16 weeks of gestation (LDA+). Postpartum outcomes included anti-hypertensive use, postpartum hypertension and readmission. We calculated risk ratios (RR) and 95% confidence intervals (CI) for LDA and postpartum outcomes using log-binomial models. We also assessed the joint effect of LDA and preeclampsia on postpartum outcomes by calculating RRs for combinations of LDA and preeclampsia using those without either as the reference.

Results: After propensity score matching, our sample included 318 LDA+ and 318 LDA- patients with a similar distribution of preeclampsia risk factors. LDA+ was not associated with the postpartum outcomes examined in the overall cohort. However, in the presence of preeclampsia, LDA- patients had the highest risk of postpartum outcomes (e.g. hypertension; RR: 9.09; CI: 6.05, 13.65), while LDA+ patients saw an attenuation in risk (e.g. hypertension; RR: 6.77; CI:4.27, 10.74). (Figure)

Conclusion: Our findings suggest that LDA prescription does not decrease the risk of postpartum cardiovascular-related postpartum outcomes in diverse population of those at risk of preeclampsia. However, among those affected by preeclampsia, antepartum exposure to LDA may attenuate the risk of these outcomes.

Figure. Forest plot of the risk ratios of cardiovascular-related postpartum outcomes by prescription of low-dose aspirin (LDA) and preeclampsia (PE) diagnosis status

Grandmaternal breastfeeding and neurodevelopmental disorders in third-generation children of the Nurses' Health Study II Jingyuan Xiao* Jingyuan Xiao Gyeyoon Yim Tormod Rogne Andrew Thomas DeWan Jorge E. Chavarro Marc G. Weisskopf Zeyan Liew

The interest in studying multigenerational effects on neurodevelopment is growing, yet the influence of grandmaternal breastfeeding remains unexplored. We evaluated whether grandmaternal breastfeeding during the mothers' infancy was associated with grandchildren's autism spectrum disorder (ASD) and attention-deficit/hyperactivity disorder (ADHD) risk.

We analyzed 25,901 grandmother-nurse (mother)-child triads who participated in the Nurses' Health Study II since 1989 and the Nurses' Mothers' Cohort Study in 2001. We estimated OR and 95% CI for grandchildren's ASD (reported in 2005 and 2009 by the nurses) and ADHD (reported in 2005 and 2013) based on grandmaternal breastfeeding status, duration, and introduction of supplemental feeding (reported by the grandmothers), adjusting for grandmaternal socioeconomic (e.g., education, occupation, race), health-related, and life-style factors (e.g., age at delivery, smoking), as well as nurses' parity and grandchild's birth year. We examined potential effect modifications by the nurses' breastfeeding and grandchild's sex. Sensitivity analyses were conducted, such as restricting to grandchildren born 1989–1999 to consider potential insufficient follow-up for later diagnoses.

In this cohort, 56.6% of the grandmothers breastfed their daughter; grandchildren's ASD (OR = 0.92, 95% CI = 0.69, 1.21) and ADHD (OR = 1.06, 95% CI = 0.95, 1.19) were not associated with grandmaternal breastfeeding. The associations remained null when evaluating breastfeeding duration and whether breastfeeding was supplemented with formula. There was no evidence of effect modification by the nurses' breastfeeding or the grandchild's sex. Results did not change in sensitivity analyses.

Grandmaternal breastfeeding during the mother's infancy was not associated with ASD or ADHD risk in grandchildren. Our study did not support a protective effect of breastfeeding on neurodevelopmental disorders in the subsequent generation, but further replication is warranted.

Nationwide Regional Trends in Proportion of Adolescent Suicides During the COVID-19 Pandemic Marie-Laure Charpignon* Marie-Laure Charpignon Johnattan Ontiveros Oliver Nizet Kenneth Mandl Maimuna Majumder

In October 2021, the American Academy of Pediatrics declared a state of emergency regarding child and adolescent mental health. We investigate the relative proportion of adolescent suicides across geographic regions of the United States (US). Using the CDC WONDER platform, we analyzed yearly mortality (2010-2021) among 528,805 all-age US decedents with suicide as the underlying cause of death. We compared pre-pandemic (2010-2019) and pandemic-period (2020-2021) suicides for adolescents aged 10–19 inclusive and the overall population. To examine how suicides shifted among age groups, we computed the yearly proportion of overall suicides among adolescents.

Since adolescent suicide is a rare event, we selected LOESS (locally estimated scatterplot smoothing), a flexible nonparametric approach, to model our primary outcome. Data were disaggregated by the ten Health and Human Services regions. Baseline models were fitted using historical data over ten-year windows (2010–2019 for 2020 and 2011–2020 for 2021 projections, respectively).

Relative to 2010-2019, the proportion of nationwide suicides among adolescents increased in 2020 (6.1% observed versus 5.2% [95% CI: 4.5–5.9%] projected), i.e., 401 [77–724] excess deaths. This shift was not geographically uniform. From 2020-2021, the nationwide adolescent suicide proportion remained stable at 6.1%; however, the reported suicide count in 2021 (2941) exceeded the expected value (2484 [2046–2922]).

Such trends may owe in part to pandemic-period caregiver loss, among many stressors affecting adolescent psychosocial outcomes. Alone, the three regions most affected by changes in the age distribution of suicides in 2020 account for 40% of US adolescents; the two regions newly affected in 2021 raise the total percentage to 53%. Further examination of regional trends in the burden of adolescent suicide and its multiple drivers, including racial-ethnic disparities, is imperative to address this ongoing public health crisis.
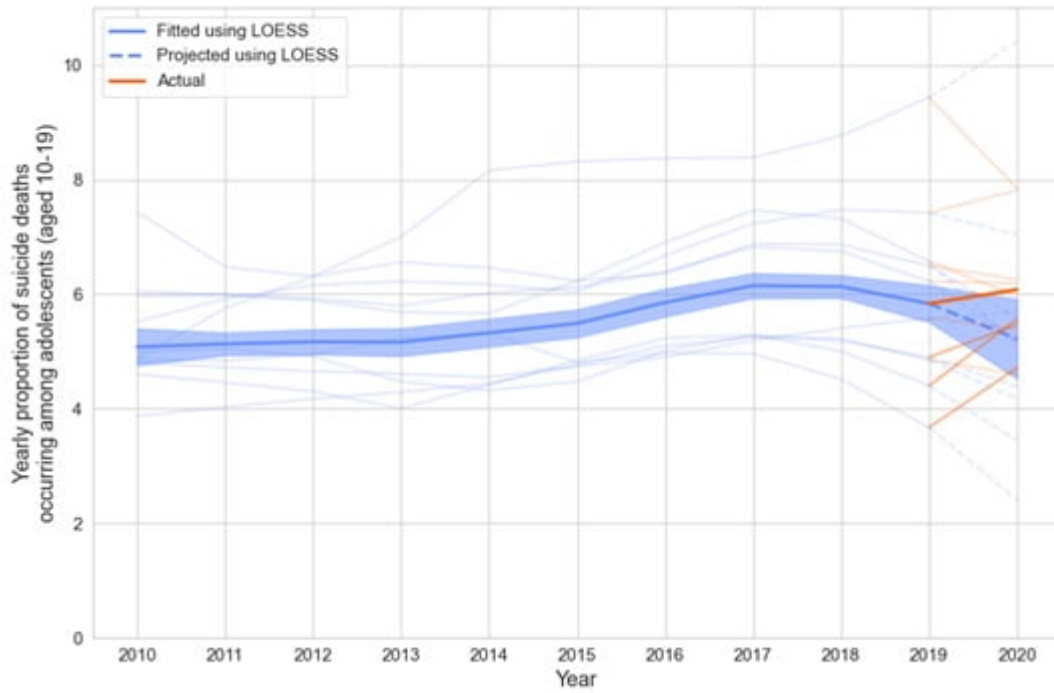
Paternal and Maternal Prenatal Exposures to Per- And Polyfluoroalkyl Substances (PFAS) and Child Behavioral Difficulties at Ages 5 to 9 Years

Pengfei Guo* Pengfei Guo Jiajun Luo Onyebuchi A Arah Gunnar Toft Zeyan Liew

Background Per- and polyfluoroalkyl substances (PFAS) are widespread environmental pollutants with potential developmental neurotoxicity. Prior research of prenatal PFAS exposure and offspring neurodevelopment have focused on maternal exposure with no study considering paternal PFAS exposure. Studying PFAS exposures in both parents may offer insights into the intrauterine effect from maternal exposure and the influence from unmeasured confounding. We evaluated the parent-specific associations of prenatal PFAS exposures and offspring behavioral difficulties in mid-childhood.

Methods We studied 334 father-mother-singleton triads from the INUENDO birth cohort in Greenland, Poland, and Ukraine. We measured five PFAS in matched parental serum samples collected during pregnancy (median weeks of gestation: 31). We assessed child behavioral difficulties at ages 5-9 years using the parent-rated Strength and Difficulties Questionnaire (SDQ). We conducted logistic regression analyses to estimate the parent-specific associations between log2-PFAS (ng/ml) and offspring SDQ outcomes defined using country- and sex-specific cut-offs (≥90th percentile), adjusting for spousal PFAS exposure and other confounders. We used quantile g-computation model to estimate mixture effects per quartile increase in all paternal and/or maternal PFAS.

Results Multiple maternal PFAS were associated with the total (mixture OR=2.58, 95% CI: 1.29, 5.16) and externalizing behavioral difficulties (mixture OR=2.57, 95% CI: 1.30, 5.07) in male children. Some associations between maternal individual PFAS and internalizing behaviors in female children were also noted (OR=2.18, 95% CI: 1.04, 4.58 for perfluorononanoic acid (PFNA)). In contrast, paternal exposure to each PFAS or PFAS mixture was not associated with the SDQ behavioral outcome measures in male and female children.

Discussion Prenatal exposure to maternal PFAS, but not paternal PFAS, was associated with offspring childhood behavioral difficulties in a sex-specific manner. Paternal PFAS exposure may act as a negative control indicating unmeasured confounding shared between parents is unlikely to explain the findings concerning maternal and intrauterine programming effect of PFAS exposure on offspring neurodevelopment.

Associations of glyphosate and aminomethylphosphonic acid (AMPA) with length of gestation and birth size
Kelsi Morris* Kelsi Morris Brad Ryva Maria Cinzori Khyatiben Pathak Patrick Pirrotte Brooke Lovell Susan Schantz Rita Strakovsky

Background: Pregnant women are exposed to the herbicide glyphosate and its major metabolite aminomethylphosphonic acid (AMPA), but their associations with birth outcomes are unclear. We evaluated associations of glyphosate and AMPA with birth outcomes and considered differences by fetal sex and pre-pregnancy BMI (ppBMI).

Methods: Illinois pregnant women (n=300) provided urine samples at median 13 weeks gestation for glyphosate and AMPA assessment. We calculated gestational age at birth using ultrasound-confirmed due date and birth date. We measured body length and head circumference within 24 hours of birth and calculated sex-specific birthweight (BW)-for-gestational-age z-scores (BWz). In primary analyses, we used multivariable linear regression to evaluate associations of specific gravity-adjusted glyphosate or AMPA with birth outcomes. We conducted secondary analyses stratified by fetal sex in which we added a multiplicative interaction term to consider differences by ppBMI.

Results: The median (25th, 75th percentile) birthweight was 3515.3 g (3231.9, 3838.5) and gestational age at birth was 39.4 weeks (38.6, 40.3). Glyphosate levels were lower than in other U.S. women. Overall, each 2-fold increase in glyphosate was associated with -21.4g lower BW (95% confidence interval (CI): -48.7, 5.9) and -0.05 lower BWz (95%CI: -0.11, 0.01). These associations were due to women carrying males (BW: β = -31.2, 95%CI: -63.1, 0.7; BWz: β = -0.06, 95%CI: -0.1, 0.0). Further, in women with overweight or obesity carrying males, each 2-fold increase in glyphosate was associated with -40.7g lower BW (95%CI: -80.8, -0.6) and -0.08 lower BWz (95%CI: -0.2, 0.00). Glyphosate was not associated with other birth outcomes. AMPA was not associated with any birth outcomes.

Conclusion: This pilot study points to differences in associations of glyphosate with fetal growth by fetal sex and maternal ppBMI. Future studies may need to consider underlying mechanisms and implications of our findings.

Twin-singleton infant growth differences exist independent of gestational age at birth Anna Booman* Anna Booman Alex Foster Miguel Marino Teresa Schmidt Jonathan M. Snowden Janne Boone-Heinonen

Background: Infant weight trajectory is routinely screened in clinical settings, with infants compared to a normative reference and interventions recommended. A common reference uses data from a population of singletons. Twins typically have lighter birth weight than singletons, in part due to earlier gestational age at birth (GA), so comparing them to this external reference may result in recommendations to increase feedings, with unknown appropriateness. Here, we compare growth trajectories of twins versus singletons, independent of GA, to inform twin-specific recommendations.

Methods: We used data from the PROMISE study, an electronic health record-based study derived from a network of community-based health care organizations. We included infants with a recorded GA and at least two weight measures before two years of age. We matched each of 320 twin males and 332 twin females to ten singletons on sex and GA (totaling 3,200 singleton males and 3,320 singleton females). Growth trajectories were fit using the Jenss mixed-effects model: parameters reflect (a) starting weight, (c) rate of growth in early infancy, (d) decreasing rate of growth in mid-infancy, and (b) rate of growth in late infancy.

Results: Twin males had the fastest weight gain in early infancy (c=1.70, 95% confidence interval [CI] 1.65, 1.75), catching up to and surpassing singleton males (c=1.59, 95% CI 1.58, 1.61) in weight by 8.5 months of life. Twin females had a similar rate of growth as singleton females throughout follow-up (e.g., c=1.52 for both), but given their lighter starting weight, caught up to, but did not surpass, singleton females by two years.

Discussion: Differences in growth between twins and singletons exist independent of GA and differ by infant sex. There may be unique factors related to twin gestation that affect infant growth beyond GA. Further research is needed to identify optimal growth and construct weight references for twins.

Growth trajectory for 320 twin males, 332 twin females, 3,200 singleton males, and 3,320 singleton females fit using the Jenss model in the PROMISE study, 0-2 years
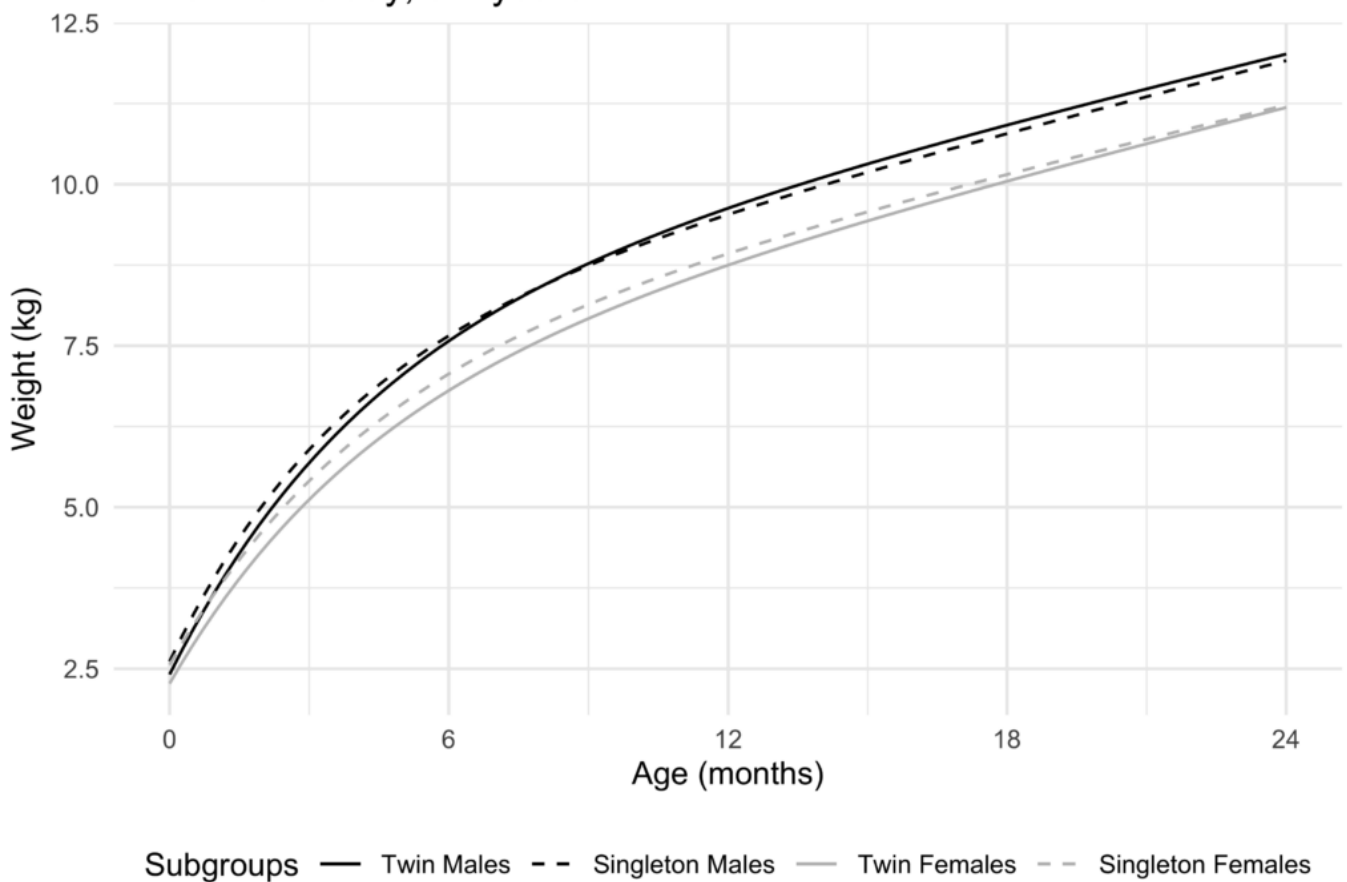
Racial and ethnic differences in COVID-19 infection and the pandemic period on perinatal health in California Emily Liu* Emily Liu Shelley Jung Kara Rudolph Jennifer Ahern

Few studies have examined differences in the effects of COVID-19 infection and the pandemic period on perinatal outcomes by race and ethnicity. Race and ethnicity are social constructs, shaped by structural forces, that have relevance for health through the embodiment of social experiences. We linked individual hospital and birth records in California from 2019 and 2020 to examine preterm birth, pregnancy-associated hypertension, severe maternal morbidity, and gestational diabetes by race and ethnicity. Our analysis estimated (1) the effect of COVID-19 infection alone by comparing infected births to uninfected births in 2020 and (2) the effect of the pandemic period alone by comparing uninfected births in 2020 to births in 2019. We used targeted maximum likelihood estimation to estimate "average effect of treatment on the treated" risk differences (RD) adjusted for community- and individual-level confounders. When examining COVID-19 infection, we observed differences in risk of all outcomes by racial and ethnic group (Figure 1A). For example, COVID-19 infection was associated with excess burden of preterm birth for Asian (RD [95% Confidence Interval (CI)] = 4.4% [0.9, 7.8]), Hispanic (RD [95% CI] = 4.0% [1.6, 6.3]), and White (RD [95% CI] = 2.5% [1.6, 3.4]) pregnancies, but no differences were observed among Black pregnancies. Generally, for all racial and ethnic groups, the pandemic period had a very small protective effect on preterm birth, but increased risk of the other outcomes examined, except for severe maternal morbidity among White pregnancies (Figure 1B). Next steps include examining differences in pre-pregnancy health, characteristics of those infected, and mechanisms of effect that may explain the findings.
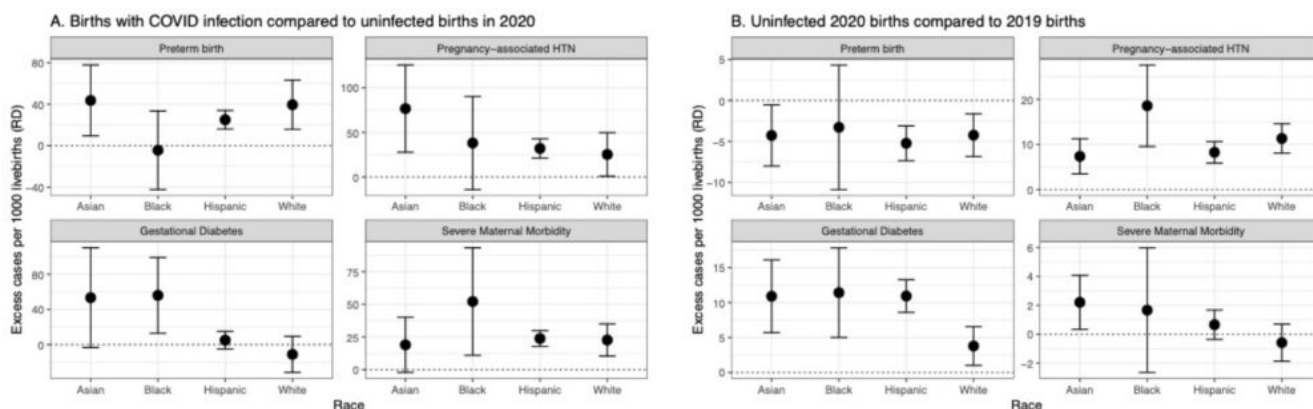
Associations of early-to-mid-pregnancy per- and polyfluoroalkyl substances with maternal gestational weight gain Maria Cinzori* Maria Cinzori Diana Pacyga Libeth Rosas Sabrina Smith June-Soo Park Joseph Gardiner Joseph Braun Susan Schantz Rita Strakovsky

Background: Per- and polyfluoroalkyl substances (PFAS) are metabolic disruptors, but their impact on gestational weight gain (GWG) is unknown. Thus, we evaluated overall and pre-pregnancy body mass index (ppBMI)-specific associations of PFAS with GWG.

Methods: Pregnant Illinois women (n=486) reported weights pre-pregnancy and at their last obstetric appointment before delivery, which we used to calculate gestational age- and ppBMI-specific GWG z-scores (GWGz) using an international reference. We quantified serum perfluorononanoic acid (PFNA), perfluorooctane sulfonic acid (PFOS), perfluorooctanoic acid (PFOA), perfluorohexane sulfonic acid (PFHxS) and perfluorodecanoic acid (PFDeA) levels. We calculated ppBMI and categorized women as having under/normal weight (BMI<25 kg/m2), overweight (BMI 25–29.9 kg/m2), or obesity (BMI≥30 kg/m2). Using linear regression adjusting for potential confounders (e.g. age, race, employment, income, parity, smoking, alcohol use, stress), we evaluated associations of ln-transformed maternal PFAS levels with GWGz. We also explored differences by ppBMI using a multiplicative interaction term.

Results: In a sample of healthy women with low PFAS levels, the median (25th, 75th percentiles) GWGz was 0.4 (-0.3, 1.1). Overall, only PFNA and PFOS were associated with lower GWGz, but associations differed by ppBMI. In under/normal weight women, each 10% increase in PFNA (β: -0.8, 95% confidence interval (CI): -1.4, -0.2), PFOA (β: -0.3, 95%CI: -0.6, 0.0), PFOS (β: -0.3, 95%CI: -0.5, -0.1), and PFHxS (β: -0.2, 95%CI: -0.5, 0.0) was associated with lower GWGz. However, in women with obesity, each 10% increase in PFNA (β: 1.0, 95%CI: -0.1, 2.0), PFOA (β: 0.5, 95%CI: -0.1, 1.0), and PFDeA (β: 3.2, 95%CI: 0.4, 5.9) was associated with higher GWGz. We observed no associations in women with overweight.

Conclusions: Associations of PFAS with GWG may differ by ppBMI. Studies could consider implications of these findings for maternal and fetal health.

Longitudinal twin growth trajectories, are twins destined to be smaller or do they catch up? Jessica L Gleason* Jessica Gleason Rajeshwari Sundaram Kathryn A. Wagner Katherine L. Grantz

Background: Twins are smaller than singletons at birth. Mounting evidence suggests that intrauterine growth in twins is adaptively different from that of singletons to maximize survival in an intrauterine setting of shared resources. At question is whether twins catch up in growth to that of singletons and at what age. Few studies have evaluated twin growth longitudinally, and none have evaluated twin growth trajectories relative to singletons from birth through adulthood.

Methods: Using data from the National Longitudinal Survey of Youth – 1979 and Child and Young Adult, we compared growth trajectories of twins (n=254) and singletons (n=11,291) from birth through age 20 years. Height and weight were collected every two years from birth through the latest age at interview in 2020. We calculated and compared predicted means for each year of age using linear mixed effects models with quadratic and cubic terms for child age in months, cubic splines for age, and a random intercept and slope, including a nested intercept by family to account for clustering between twins and other siblings. Models were adjusted for child sex and birth year.

Results: Twins were smaller in height, weight, and BMI at birth, appearing to "catch up" at various ages. Differences in height ranged from 3.1 cm (95% CI 2.2, 4.0) at birth to 0.86 cm (0.1, 1.7) at age 8, with the difference becoming 0 by age 12 (β=0.03, -0.98, 1.04). For weight, twins remained from 1.1 kg (0.2, 1.9) smaller at age 5 to 2.0 kg (0.2, 3.9) smaller at age 13, with a 0.6 kg (-2.7, 3.8) difference persisting to age 20. Twin BMI remained smaller through age 16 (β=0.8, 0.1, 1.5), with a small difference remaining at age 20 (β=0.3, -0.8, 1.4).

Conclusions: Although twins caught up to singletons in height by age 12, they remained slightly smaller in weight and subsequent BMI through adolescence. Persistent differences in weight may reflect differential accumulation of fat tissue, which may begin early in utero.

ASSOCIATION BETWEEN SEVERE MATERNAL MORBIDITY AND EPILEPSY IN CHILDREN: A POPULATION BASED BIRTH COHORT STUDY.

Bénédicte Driollet* Bénédicte Driollet Emmalin Buajitti Asma Ahmed Jennifer Hutcheon Laura Rosella Seungmi Yang

Introduction. Severe maternal morbidity (SMM) has shown to be associated with adverse perinatal outcomes. However, its association with the emergence of pediatric neurodevelopmental disorders is scarce, particularly with epilepsy, whose etiology is poorly understood. Thus, this study aims to investigate the effect of severe maternal morbidity on the risk of epilepsy in offspring.

Methods. We included all children born in hospitals between 2002 and 2018 in Ontario, Canada, with a follow-up until March 2020. Epilepsy diagnosed before 18 years and SMM were defined using administrative health datasets. We estimated the crude and the adjusted risk of epilepsy associated with SMM, using a Cox model, and examined the robustness of results using quantitative bias analyses.

Results. Of the 2 060 317 children (mean gestational age 38.9 weeks (SD 1.7)), 17 853 were diagnosed with epilepsy within a median follow-up time of 10 years, and 40 830 were exposed to SMM. In a model adjusted for maternal, birth, and area-level characteristics, children exposed to SMM had, at any time after birth, a 48% increase in risk of diagnosis of epilepsy compared to those unexposed (aHR:1.48, 95%CI 1.35-1.62). The risk of epilepsy increased to 70% in children whose mothers were exposed to severe pre-eclampsia, HELLP (Hemolysis, Elevated Liver enzymes, and Low Platelets) syndrome, and eclampsia (aHR:1.70, 95%CI 1.36-2.13), 3 most frequent and preventable subtypes of SMM.

Conclusion. In this population-based birth cohort study, our findings suggest that SMM is associated with an increased risk of epilepsy in children. These results open new perspectives in understanding neurodevelopmental diseases in children and underline the importance of ensuring a healthy pregnancy. Monitoring and evaluation of the development of children exposed to SMM may be deemed necessary.

Fetal body composition and organ growth patterns in pregnancies complicated by first-trimester vaginal bleeding: NICHD Fetal 3D Study Alexandra Jean-Louis* Alexandra Jean-Louis Jessica L. Gleason Kathryn A. Wagner Zhen Chen Daniel He Roger B. Newman William A. Grobman Robert E Gore-Langton Seth Sherman Magdalena Sanz Cortes Edward K. Chien Luis F. Goncalves Katherine L. Grantz

Background: In the NICHD Fetal Growth Study, women who self-reported more than one day of vaginal bleeding in the first trimester had lower estimated fetal weight (EFW) by 2-dimensional ultrasound at 35 to 39 weeks, and lower birthweight compared to women without bleeding. We followed up these findings to explore associations between bleeding and fetal body composition and organ volumes by 3-dimensional (3D) ultrasound.

Methods: The NICHD Fetal 3D Study (2009-2013) included singleton pregnancies at low risk for fetal growth abnormalities (n=2634). Fetal fat and lean measures of arm, abdomen, and thigh, and organ volumes, including cerebellum, lung, kidney, and liver volumes were measured up to five times between 15-40 weeks using 3D ultrasound. Women were grouped by cumulative days of first trimester bleeding: 0 (reference), 1, or >1 day. Linear mixed models, with quadratic and cubic terms for gestational age, including global tests for overall differences in trajectories and weekly pairwise comparisons, were fit to compare bleeding groups for each 3D volume, adjusted for maternal age, race/ethnicity, and pre-pregnancy BMI.

Results: Most women had 0 days of bleeding (n=2144, 81.4%), while 211 (8.0%) bled for 1 day and 279 (10.6%) bled for >1 day. Compared to those with no bleeding (Figure), fetuses of women with >1 day of bleeding had smaller abdominal area (-78.4 mm2 to -293.8 mm2) between 29-40 weeks, and smaller fractional thigh volume (-2.2 cm3 to -4.1 cm3) between 36-40 weeks. Fetuses of women with 1 day of bleeding also had smaller liver volume compared to no bleeding (-3.8 cm3 to -6.1 cm3) between 29-33 weeks, though results were attenuated when adjusting for estimated fetal weight.

Conclusion: First-trimester bleeding was associated with smaller fetal abdominal area, thigh, and liver growth. Fetal 3D measures may provide additional insight into how early pregnancy bleeding may potentially impact fetal growth and subsequent postnatal health outcomes.
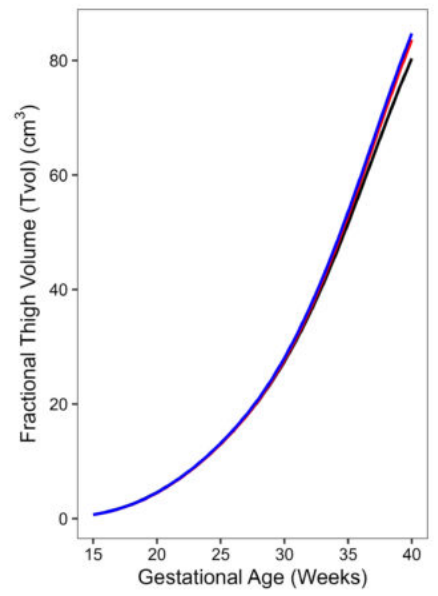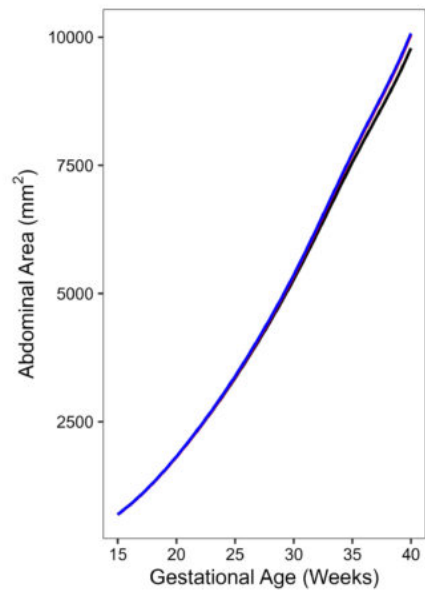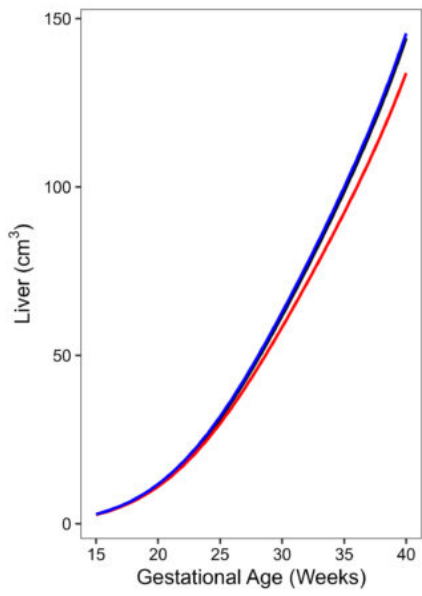
COVID-19 Infection and Hypertensive Disorders of Pregnancy, 2020-2022 Angela Malek*
Angela Malek Chun-Che Wen Kalyan Chundru Julio Mateus Hermes Florez Brian Neelon Jeffrey
Korte Dulaney Wilson John Pearce Sarah Simpson Kelly Hunt

Introduction: COVID-19 infection increases the risk of pregnancy complications; however, its
association with hypertensive disorders of pregnancy (HDP) and its subtypes, preeclampsia and
eclampsia (PE and E), remains unclear. We aimed to investigate the association between COVID-19
infection pre- and during pregnancy with these hypertensive conditions in South Carolina (SC).

Methods: We evaluated SC livebirth data (2020-2022) from 145,033 deliveries among pregnant
people aged 12-52 years: 80,927 non-Hispanic White (NHW); 43,797 non-Hispanic Black (NHB);
13,150 Hispanic; and 7,157 of other race/ethnic groups. Linked birth certificate and
hospitalization/emergency department (ED) visit data was used to define HDP, and
hospitalization/ED visit data defined HDP subtypes (PE and E). Logistic regression models with
matched pairs and covariate adjustment were conducted.

Results: The overall rate of HDP was 18.5% (22.7% in those with COVID-19 pre-pregnancy, 20.3%
with 1st/2nd trimester infection, 19.6% with 3rd trimester infection, and 18.0% without COVID-19).
On the other hand, 9.2% experienced PE or E (11.5% with COVID-19 pre-pregnancy, 10.7% with
1st/2nd trimester infection, 10.0% with 3rd trimester infection, and 8.8% without COVID-19). The
odds of HDP increased by 9% (95% CI: 1.02-1.16) in those with COVID-19 pre-pregnancy compared
to those without COVID-19, after adjusting for demographic, lifestyle and clinical factors (Table).
Similarly, PE and E increased in those who had COVID-19 pre-pregnancy (OR=1.12, 95% CI:
1.03-1.21). COVID-19 infection during pregnancy was not associated with HDP or PE/E.

Discussion: Our data demonstrated pre-pregnancy COVID-19 infection is a significant independent
risk factor of hypertensive disease during pregnancy even after accounting for the contribution of
traditional risk factors, highlighting the importance of preventive measures including vaccination for
people of reproductive age.

Table. Adjusted Odds of Hypertensive Disorders of Pregnancy (HDP) and Preeclampsia and Eclampsia in South Carolina among Pregnant People with and without COVID-19 Infection[a, b]

Predictor	HDP OR (95% CI)	Preeclampsia and Eclampsia OR (95% CI)
COVID-19		
No history of COVID-19	referent	referent
Prior to pregnancy	**1.09 (1.02-1.16)**	**1.12 (1.03-1.21)**
First and/or second trimester	0.96 (0.90-1.03)	1.06 (0.97-1.15)
Third trimester	0.94 (0.87-1.02)	1.02 (0.91-1.13)
Age	**1.01 (1.01-1.02)**	**1.02 (1.01-1.03)**
Education level		
< High school	1.07 (0.98-1.18)	**1.21 (1.07-1.36)**
High school graduate	1.01 (0.94-1.08)	1.08 (0.98-1.18)
Some college	1.07 (1.00-1.14)	**1.11 (1.02-1.22)**
≥College graduate	referent	referent
Rural residence (vs. urban)	**0.91 (0.87-0.96)**	0.95 (0.89-1.01)
WIC participation during pregnancy	0.96 (0.91-1.02)	0.94 (0.88-1.01)
Calendar time	1.00 (0.99-1.01)	0.99 (0.98-1.00)
Race/ethnic group		
Non-Hispanic White	referent	referent
Non-Hispanic Black	0.98 (0.93-1.04)	**1.09 (1.02-1.18)**
Hispanic	**0.75 (0.68-0.83)**	**0.82 (0.71-0.95)**
Other	**0.85 (0.74-0.96)**	0.94 (0.78-1.11)
Medicaid	1.01 (0.95-1.08)	**1.17 (1.08-1.27)**
Tobacco use during or pre-pregnancy	1.06 (0.97-1.16)	1.04 (0.92-1.17)
Firstborn	**1.79 (1.69-1.89)**	**2.00 (1.86-2.15)**
Previous preterm delivery	**1.52 (1.39-1.67)**	**1.69 (1.51-1.89)**
Pre-pregnancy hypertension	**2.59 (2.43-2.75)**	**3.74 (3.48-4.02)**
Pre-pregnancy diabetes	**1.38 (1.23-1.55)**	**1.73 (1.51-1.97)**
Pre-pregnancy BMI		
Underweight	**1.38 (1.23-1.55)**	0.91 (0.71-1.14)
Normal	referent	referent
Overweight	**1.51 (1.41-1.61)**	**1.41 (1.29-1.55)**
Obese	**2.17 (2.05-2.31)**	**1.73 (1.60-1.88)**

BMI, body mass index; COVID-19, coronavirus disease 2019; OR, odds ratio; WIC, Women, Infants, and Children.
[a] Matched Analysis (1:1 matching): The exposure group (COVID-19 never/prior to pregnancy/first or second trimester/third trimester) was aligned with the control group based on both (1) exact match for delivery quarter time, race/ethnic group, Medicaid, and (2) the nearest neighbor method for maternal age, with an age difference between the two groups ranging from −3 to 4.
[b] Adjusted for demographic (maternal education, rural residence, Women, Infants & Children), lifestyle and clinical factors (tobacco use during and pre-pregnancy, firstborn, previous preterm birth, pre-pregnancy hypertension, pre-pregnancy diabetes, maternal pre-pregnancy BMI category).

Prescribing preferences for Antidiabetic Medications among older Type 2 Diabetes (T2D) patients with Alzheimer's Disease (ADRD) and multimorbidity, 2013-2019 Julia Liaw* Julia Liaw Chintan Dave

Older adults with T2D face high levels of multimorbidity burden and are more likely to be diagnosed with ADRD. In recent years, >20 new medications have been approved for managing T2D making significant strides on morbidity and mortality outcomes; however, there is paucity of data evaluating the trends in their uptake by multimorbidity levels and ADRD status.

We used Medicare fee-for-service (2013-2019) data to identify a cohort of older T2D patients newly initiating the following second-line antidiabetic medications: glucagon-like peptide-1 receptor agonist (GLP-1RA), sodium-glucose cotransporter-2 inhibitor (SGLT2i), dipeptidyl peptidase-4 inhibitor (DPP4i), sulfonylurea (SU), thiazolidinedione. Initiation trends were analyzed based on ADRD presence and by severity of multimorbidity.

Among 1,788,762 T2D patients, SU initiations declined significantly by 24.4% from 50.3% in 2013 to 25.8% in 2019, replaced largely with SGLT2i initiations which increased by 20.8% (1.3% to 22.0%); these trends were less pronounced among patients with ADRD (n=180,512) versus those without (n=1,549,100). By 2019, individuals with ADRD favored DPP4i as the most initiated medication, with a 13.3% higher initiation rate compared to those without ADRD (34.3% vs. 21.0%). Consequently, they were less likely to initiate SGLT2i and GLP-1RA by 8.0% (14.4% vs. 22.4%) and 5.9% (17.1% vs. 23.0%), respectively. Higher multimorbidity correlated with increased DPP4 inhibitor utilization and decreased SGLT2 inhibitor utilization.

Initiation of newer T2D agents increased regardless of ADRD presence, but with diminished likelihood in severe multimorbidity. This reduced adoption may stem from unique clinical challenges (e.g., distinctive adverse reactions) and high cost in a medically complex population, and limited evidence in older, multimorbid patients due to trial exclusion or underrepresentation, warranting further investigation in multimorbidity and its impact on prescribing.

Degarelix and the Risk of Severe Urinary Tract Infections Among Patients Diagnosed with Prostate Cancer: A Population-Based Cohort Study Farzin Khosrow-Khavar* Farzin Khosrow-Khavar Elisa Bandera Chintan Dave

Background: Gonadotropin-releasing hormone (GnRH) antagonist (degarelix) and agonists (leuprolide, goserelin, histrelin, triptorelin) are mainstay prostate cancer treatments. Results from RCTs have indicated a potential differential effect of these drugs on risk of urinary tract infections (UTI). We examined this safety concern in detail in this study.

Methods: Using Medicare (2008-2020), we conducted a retrospective cohort study among male patients with prostate cancer initiating either degarelix or GnRH agonists. The primary outcome corresponded to severe UTI events, defined as a hospitalization for primary UTI, urosepsis, or pyelonephritis. Secondary outcome corresponded to outpatient treated UTI. Patients were followed from date of treatment initiation until the earliest of the study outcome, treatment switch or discontinuation, disenrollment, or end of the study period. Cox proportional hazards models incorporating inverse probability of treatment (IPT) weights were used to estimate weighted HRs and 95 CIs accounting for 65 a priori defined baseline confounders.

Results: The study included 18,875 patients initiating on degarelix and 141,764 on GnRH agonists with mean (std) age corresponding to 76.1 (7.5) and 75.7 (7.5), respectively. Patients' characteristics between exposure groups were balanced after IPT weighing (standardized differences <0.05). Patients receiving degarelix had 134 severe UTI events (incidence rate [IR]/1,000 person-years [95% CI]: 19.8 [16.7-23.4]) compared to 1,939 events in the GnRH agonists group (IR [95% CI]: 13.0[12.5-13.6]), with a weighted HR of 1.17 (95% CI: 1.08-1.27). Degarelix was also associated with an increased risk of outpatient treated UTI (weighted HR: 1.16, 95% CI: 1.13-1.19). Consistent results were observed across range of sensitivity analyses.

Conclusion: In this population-based study, degarelix in comparison with GnRH agonists, was associated with an increased risk of severe and non-severe UTI.

Clinical comorbidities among users of glucagon-like peptide 1 (GLP-1) agonists without type II diabetes, a real-world data study Djeneba Audrey Djibo* Djeneba Audrey Djibo Jonathan DeShazo Smita Bhatia Cheryl N McMahill-Walraven

Background. Recently, glucagon-like peptide 1 (GLP-1) agonists originally developed for T2D management, were approved for obesity/weight loss applications among those without T2D. These novel applications of GLP-1 agonists could significantly change the clinical profiles of patients on these drugs.

Objective. We sought to examine the yearly prevalence of clinical conditions among persons using GLP-1 agonists without T2D.

Methods. We conducted a retrospective analysis of health insurance and pharmacy claims from 01 January 2019 to 31 October 2023 among eligible enrollees aged 12 years and above without T2D. Filled prescriptions of all GLP-1 agonists were identified using national drug codes (NDCs). Prevalent clinical conditions included HT, type 1 diabetes, stroke, CHD, gout, NAFLD, and all cancers and were identified using the International Classification of Disease (ICD-10-CM) diagnosis codes. Yearly prevalence per 1,000 enrollees were examined and compared a test for trend with statistical significance of $p < 0.05$.

Results. For every 100,000 enrollees aged >12 years without T2D, 493 persons used GLP-1 agonists in 2019, 697 in 2020, 838 in 2021, 774 in 2022, and 973 persons in 2023, respectively. The proportion of GLP-1 agonists users with at least 1 comorbidity of interest increased per year ($p < 0.0001$). Specifically, there were 13.0‰ users with prevalent hypertension in 2019 compared to 20.1‰ in 2023. Additionally, there were 0.4‰ users of GLP-1 agonists with prevalent stroke diagnoses in 2019 compared to 1.9‰ in 2023. Concerning obesity, 10.5‰ users of GLP-1 agonists were found in 2019 compared to 50.1‰ in 2023.

Conclusion. We observed increasing trends of GLP-1 agonists users with chronic clinical conditions as the uptake and applications are widening. Future directions may include investigations of pharmacovigilance using clinical and real-world evidence.

Pharmacoepidemiology

Gabapentin Use During Pregnancy and Adverse Neonatal Birth Outcomes: A Canadian multisite Population-Based Cohort Study Alekhya Lavu* Alekhya Lavu Payam Peymani Silvia Alessi-Severini Chelsea Ruth Jamison Falk Karina Kowalec Christine Leong Shelley Derksen Roxana Dragan Marcus C. Ng Brandace Winquist Joseph Delaney Sherif Eltonsy

Introduction

Gabapentin is a new-generation antiseizure medication approved for epilepsy. Due to gabapentin's perceived safety in pregnancy and efficacy in reducing pain, there has been an increase in the off-label use of gabapentin. We aim to study the association between gabapentin treatment during pregnancy and adverse neonatal outcomes in two Canadian provinces.

Methods

We conducted a multi-site population-based retrospective cohort study of pregnant people in Manitoba from 1998 to 2021 and Saskatchewan from 1995-2023. We examined the association between gabapentin and the risk of small for gestational age (SGA), low birth weight (LBW), preterm birth, NICU admissions, infants' length of hospital stays (LOS) (> 3 days), infant mortality (≤27), neonatal mortality (≤365 days), neonatal respiratory distress syndrome (NRDS), severe neonatal morbidity (SNM) and neonatal readmissions among all pregnant people. Multivariate regression models were adjusted for clinical covariates and confounders. We meta-analyzed aggregated data from both sites using random effects model.

Results

We included a total of 545,121 pregnancies in our analysis including 1663 pregnant people exposed to gabapentin. We observed a significant increase in the risk of SGA (adjusted odds ratio [aOR] 1.19,95%CI 1.06-1.33), preterm birth (aOR 1.62,95%CI 1.37-1.91), LOS infant (aOR 1.82,95%CI 1.40-2.36), infant mortality (aOR 1.48,95%CI 1.04-2.11), neonatal mortality (aOR 1.56,95%CI 1.04-2.34), neonatal readmissions (aOR 1.29,95%CI 1.02-1.64), SNM(aOR 1.22,95%CI 1.08-1.38) and a non-significant increased risk of LBW (aOR 1.19,95%CI 0.45-3.12), NICU admissions (aOR 1.57,95%CI 0.97-2.60), and NRDS (aOR 1.85,95%CI 0.72-7.78) when compared with unexposed pregnant people.

Conclusion

Gabapentin exposure in pregnant people was associated with a significantly increased risk of several adverse birth outcomes in infants. Future studies must focus on gabapentin safety among epilepsy and non-epilepsy conditions.

LATEBREAKER

Reproductive

Impact of Gestational Age Measurement Technique on Estimated Associations of Maternal Age and Body Mass Index (BMI) with Birth Outcomes Ginna Doss* Ginna Doss Julie Daniels Sunni Mumford Charles Poole Anne Steiner Anne Marie Jukic

Background

Measurement error of gestational age (GA) at birth may influence the detection of factors which are associated with preterm birth. Our objective was to show how exposure-outcome associations are impacted by GA measurement technique.

Methods

We included 387 participants who delivered a live birth in the Effects of Aspirin in Gestation and Reproduction (EAGeR) trial. We calculated prevalence odds ratios (PORs) for the associations of dichotomized maternal age and body mass index (BMI) with preterm birth when GA at birth was measured three ways: prospectively recorded last menstrual period (LMP), ovulation tracking by fertility monitor, and early first trimester ultrasound crown-rump length. Based on both clinical guidelines and Akaike's information criterion, age was dichotomized as <35 and ≥35 years and BMI was dichotomized as <25 and ≥25 kg/m2.

Results

GAs were shorter when measured by ultrasound (10.2% of births preterm) and longer when measured by LMP (6.6% of births preterm). Ovulation classified 8.4% of births preterm. The association between BMI and preterm birth was strongest when GA was measured by ovulation with higher BMI associated with 3.38 times the odds of preterm birth (95% Confidence Interval (CI)): (1.59, 7.19) and weakest when assessed by LMP (POR 2.60 CI: 1.15, 5.89). The association between maternal age and preterm birth was strongest when GA was measured by ultrasound (POR 2.06 CI: 0.66, 6.43) and weakest when measured by LMP (POR 1.44 CI: 0.32, 6.54). Precision of estimates varied by method with ultrasound assessment of preterm birth providing the smallest confidence limit ratios.

Conclusion

Although the direction of the associations between maternal age and BMI with preterm birth was consistent for all three measurement techniques, the strength of the associations and confidence interval widths differed. Preterm birth measurement technique warrants consideration for its potential to alter both the strength and precision of findings.

PORs for Maternal Age and BMI in Relation to Preterm Birth Measured Three Ways

Reproductive
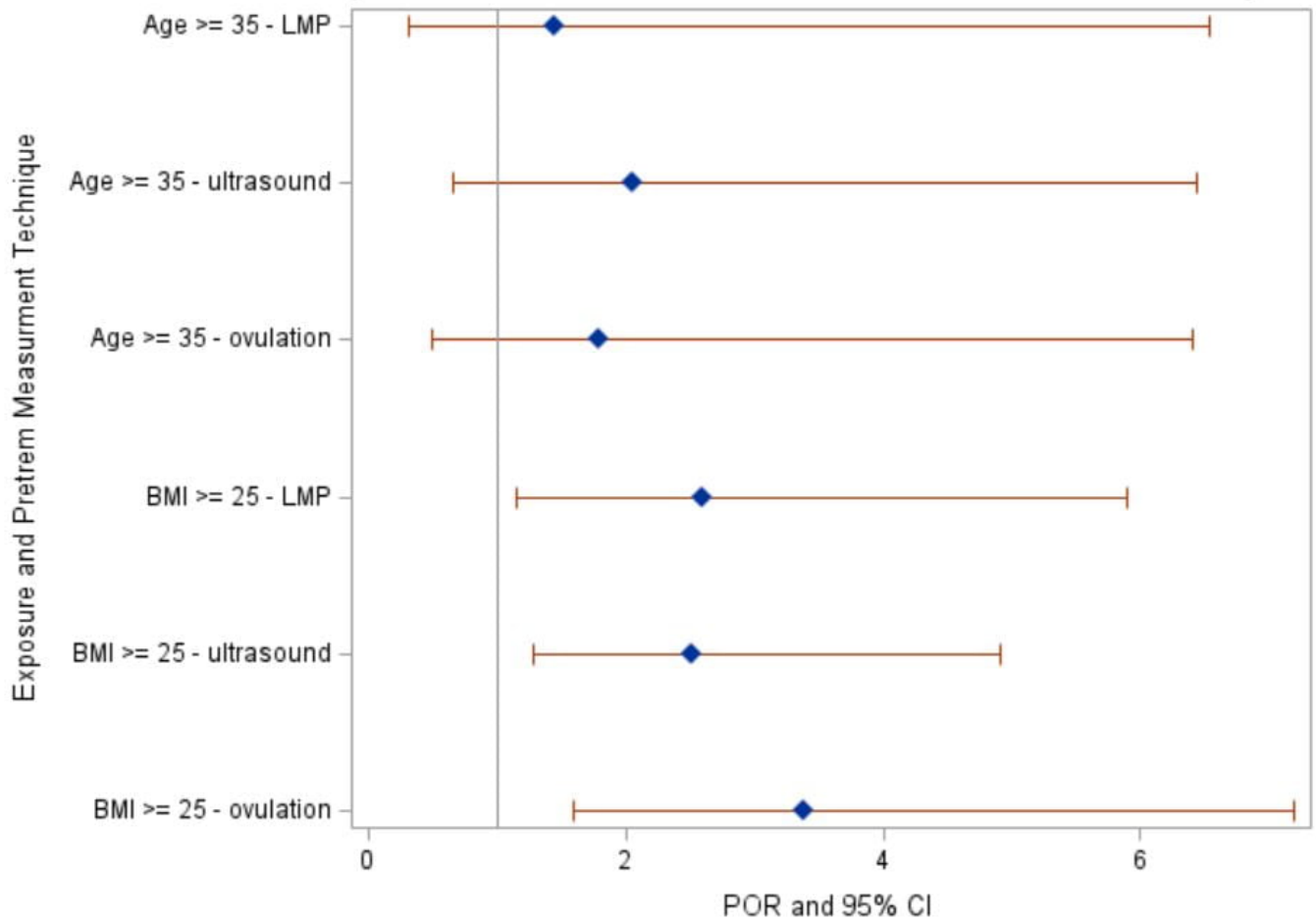
Women's pregnancy history and partners' cardiovascular mortality Liv Grimstvedt Kvalvik*
Liv Grimstvedt Kvalvik Rolv Skjærven Gerhard Sulo Aditi Singh Quaker Harmon Allen Wilcox

Background: A woman's full pregnancy history is associated with her risk of dying from atherosclerotic cardiovascular disease (CVD). We assessed whether a woman's total pregnancy history is associated with her spouse's risk of dying from CVD.

Methods: In this population-based, prospective study we used data from Norwegian registries including The Medical Birth Registry of Norway, in the period 1967-2020. We identified 566 187 men born after 1944 and registered as partner to women with a pregnancy in 1967 or later, and surviving to age 40. The main outcome is premature CVD mortality (up to age 69) across their partners reproductive history by categories of combined parity (1, 2, 3, or 4 recorded pregnancies) and number of complicated pregnancies (preterm delivery <35 gestational weeks, preeclampsia, placental abruption, perinatal death (stillbirth or death within first 7 days) and term or near-term birth weight <2700grams). Men whose partners had three pregnancies and no complications had lowest CVD risk and served as the reference group. Estimates were adjusted for women's birth year.

Results: For fathers contributing with up to two pregnancies, the risk of premature CVD increased with increasing number of complicated pregnancies. For men contributing to 3-4 pregnancies, the shape of the association was less clear, peaking at two complications [HR=1.8; 95% confidence interval 1.2-2.8).

Conclusions: While the number of pregnancy complications seem to increase CVD mortality for women in a linear pattern, this seem not to be the case for their partners. Pregnancy history seems to be less useful in prediction of men's risk of dying from CVD. CVD risk factors are known to increase risk of pregnancy complications. However, the correlations between partners of diet, SES, and other CVD risk factors is apparently not strong enough to produce a strong pregnancy-related CVD risk in male partners.

Reproductive

Neighborhood socioeconomic position and use of preconception folic acid-containing supplements in the National Birth Defects Prevention Study, 1997-2011 Anne Marie Darling*

Anne Marie Darling Eirini Nestoridi Rashida Smith-Webb Wendy Nembhard Jenil Patel Bailey Wallace Shannon Evans Suzan Carmichael Gary Shaw Mahsa Yazdy

Background: Neighborhood socioeconomic position has been associated with the occurrence of neural tube defects (NTDs). Our objective was to determine any differences in folic acid-containing supplement use, which reduces the risk of NTDs, by neighborhood. **Methods:** This study included 10,504 control participants from the National Birth Defects Prevention Study who gave birth to liveborn infants between 1997-2011. The neighborhood-level socioeconomic position indicator (nSEPI) was derived through a principal components analysis that incorporated 17 census socioeconomic indicators pertaining to the census tract in which participants lived longest during the 3 months prior to conception. The nSEPI was categorized into tertiles, with the highest tertile representing the lowest socioeconomic position. Folic acid-containing supplement use was defined as any use of folic acid or multivitamins containing folic acid during the 3 months prior to conception. Generalized estimating equations accounting for census-tract clustering and adjusted for individual-level socioeconomic and demographic factors were used to estimate the association between nSEPI tertiles and preconception folic acid-containing supplement use. Associations with individual components of the nSEPI were also examined. **Results:** Participants residing in low socioeconomic neighborhoods (nSEPI tertile 3) were less likely to report preconception folic acid-containing supplement use (Odds Ratio [OR] 0.66, 95% Confidence Interval [CI] 0.56, 0.77). Individual components of the nSEPI were consistently associated with supplement use, including census tracts with high unemployment ratio (T3 vs. T1: OR 0.61, 95% CI 0.52, 0.72), and high ratio of female headed households with dependents (T3 vs. T1: OR 0.61, 95% CI 0.52, 0.71). **Conclusions:** Neighborhood socioeconomic inequalities in preconception folic acid-containing supplement use are present and highlight potential opportunities for policy and community level interventions to address these inequalities.

Reproductive

The Association Between Infertility Causes and Live Birth Outcomes in Assisted Reproductive Technologies Post Preimplantation Genetic Testing for Aneuploidy (PGT-A): A Comparative Analysis of 2017-2018 the UK-HFEA Data Chidinma Oli* Chidinma Oli Amadou Barrow Anamege Adaeze Kelly Gurka

Background: Assisted reproductive technologies (ART) are commonly used to treat infertility. Since the success of ARTs in achieving live births is significantly impacted by aneuploidy, Preimplantation Genetic Testing for Aneuploidy (PGT-A) is utilized to improve the likelihood of live births by identifying embryos without aneuploidy, consequently maximizing their potential for successful pregnancies. However, it is still unclear whether the success of PGT-A in ART treatments is influenced by the specific underlying cause of infertility. This analysis aimed to examine the association between infertility causes and live birth occurrence post PGT-A testing among infertile women.

Methods: We used the 2017-2018 United Kingdom Human Fertilisation and Embryology Authority (UK HFEA) data, one of the largest global databases of fertility treatment. We used multivariable logistic regression models to estimate the aORs and 95% CI adjusting for age, ethnicity, and specific type of ART treatment.

Results: Overall, our results show a significant association between infertility causes and live birth outcomes post PGT-A treatment ($X2 = 18.07$, $P = 0.0012$). The predominant causes of infertility were male factor (35.2%) and unexplained (34.5%) infertility. Compared to male factor infertility, women with unexplained infertility had increased odds of live birth post-PGT-A (aOR 1.18; 95% CI, 1.06–1.31). Conversely, women with infertility due to ovulatory disorder presented lower odds of live births (aOR 0.82; 95% CI, 0.71–0.95). Infertility caused by Endometriosis showed a non-significant trend towards increased odds of live birth occurrence (aOR 1.14; 95% CI, 0.87–1.51) post PGT-A. tubal disease infertility had comparable odds of live birth (aOR 1.02; 95% CI, 0.86–1.22) relative to male factor infertility.

Conclusions: The occurrence of live birth post PGT-A testing varied with the different causes of infertility and emphasize the importance of personalized treatment plans in ART.

A prospective study of objective preconception sleep health and fecundability Chad M. Coleman* Chad M. Coleman Amelia K. Wesselink Traci N. Bethea Andrea S. Kuriyama Tanran R. Wang Margaret Seo Jacob Pothen Joe Kossowsky Suzanne M. Bertisch Lauren A. Wise

Introduction: Fragmented sleep may inhibit routine hormonal fluctuations, which can impact ovulation and pregnancy initiation. There is epidemiologic evidence of an association between sleep and fertility; however, most studies have relied on self-reported sleep assessments, which may introduce bias.

Methods: We estimated prospectively the association between objective sleep health and fecundability, the per-cycle probability of conception, among 432 female-identified participants at risk of pregnancy in Pregnancy Study Online, a web-based preconception cohort study (2021-2023). Participants wore a study-issued Fitbit for 24 hours/day for up to two months during preconception to measure sleep characteristics, including duration (hours/day), efficiency (total sleep time divided by total time in bed), and wake after sleep onset (WASO; minutes awake after initial sleep onset). We averaged sleep measures across the first seven days of participation. Participants reported pregnancy status on bimonthly follow-up questionnaires. We used proportional probabilities regression models to estimate fecundability ratios (FRs) and 95% CIs, adjusting for socio-demographic, behavioral, and reproductive factors.

Results: Using life-table methods, 75% of participants conceived during 12 months of follow-up. The medians (interquartile ranges) for sleep duration, efficiency, and WASO were 7.2 (6.7-7.7 hours/day), 88.4% (87.1%-89.7%), and 56 (48-66 minutes), respectively. Compared with ≥7 hours/day (clinically recommended duration), FR (95% CI) for <7 hours/day was 1.08 (0.83, 1.42). The lowest quartile of sleep efficiency (≤87.0% vs. >89.0%) and highest quartile of WASO (>66.3 vs. ≤48.8 minutes) were associated with reduced fecundability (FR for sleep efficiency 0.82, 95% CI 0.55, 1.21; FR for WASO 0.73, 95% CI 0.50, 1.07). Results were consistent when exposures were modeled as continuous.

Conclusions: Reduced sleep efficiency and increased WASO may be risk factors for delayed conception.

Reproductive

Sexual Orientation Disparities in Pregnancy Loss: A Meta-Analysis of Three Longitudinal Cohorts Colleen A Reynolds* Colleen Reynolds Payal Chakraborty Tabor Hoatson Jarvis T. Chen Lori Chibnik Janet-Rich-Edwards Brittany M. Charlton

Background: Emerging research suggests sexual minority women may be at an increased risk of pregnancy loss, but these studies have adjusted for potential mediators and have not included certain subgroups (i.e., "mostly heterosexual" women).

Methods: We used data from three longitudinal cohorts: the Nurses' Health Study 2 and 3 and Growing Up Today Study (N=235,150 pregnancies from 85,547 participants). In each cohort, participants reported lifetime pregnancies and whether each pregnancy ended in an induced abortion, loss (miscarriage <20 weeks, stillbirth ≥20 weeks), ectopic/tubal, or livebirth, as well as their sexual orientation. We used log-binomial generalized estimate equation models to compare the risk of pregnancy loss among pregnancies to completely heterosexual participants (reference) to those among heterosexual participants with same-sex attractions/partnerships, mostly heterosexual, bisexual, and lesbian participants. To address confounding, selection, and multiple pregnancies per participant, models were weighted by the product of inverse probability of treatment, inverse probability of censoring, and inverse cluster size weights. Cohort-specific results were combined using fixed-effects meta-analysis.

Results: Pregnancies among heterosexual participants with same-sex attractions/partnerships (RR:1.07; 95%CI:1.02–1.13) as well as those among mostly heterosexual (1.27; 1.20–1.35), bisexual (1.50; 1.29–1.75), and lesbian (1.70; 1.45-1.99) participants were more likely to end in a loss than those to completely heterosexuals. Notably, risk of stillbirth was elevated among pregnancies to lesbian (3.48; 2.05–5.90) participants compared to those among completely heterosexuals; stillbirth risk was not elevated among other sexual minority subgroups.

Conclusion: Future research must examine mechanisms of sexual orientation-related inequities in pregnancy loss (e.g., heterosexism, maternal age, use of medically assisted reproduction, preconception health).

Risk of Loss by Sexual Orientation Across Cohorts

Respiratory
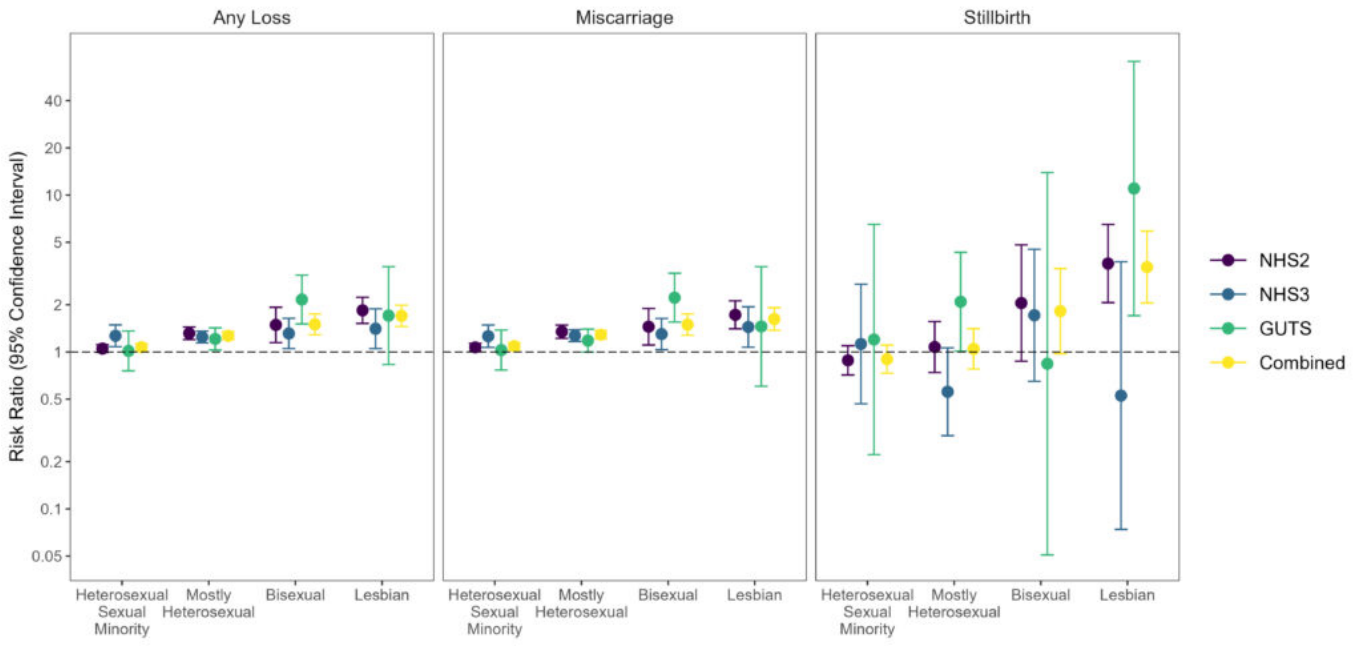
A synthetic control analysis examining associations between smoke-free public housing policies and pediatric asthma emergency department visits in New York City Andrea R. Titus* Andrea Titus Elle Anastasiou Donna Shelley Brian Elbel Katarzyna Wyka Lorna E. Thorpe

Introduction: Secondhand smoke (SHS) remains a leading cause of morbidity in the US. To address high SHS exposure rates in multi-unit housing, the U.S. Department of Housing and Urban Development (HUD) required public housing authorities to implement smoke-free housing (SFH) policies by July 2018. We examined associations between HUD-mandated SFH policies in New York City Housing Authority (NYCHA) developments and pediatric asthma ED visits.

Methods: Children living in NYC census block groups (CBGs) comprised solely of NYCHA buildings were considered policy-exposed, while children in CBGs without NYCHA buildings were considered unexposed. We combined geocoded all-payer claims and census data to calculate quarterly, CBG-level asthma ED visit rates among children aged 0-17 from November 2015-December 2022. We used synthetic control matching to compare rates among exposed and unexposed CBGs before and after the policy, incorporating pre-policy outcome rates and CBG-level confounders, including housing age and size and sociodemographic characteristics. We estimated models for the full post-policy period, and for pre-COVID-19 and COVID-19 pandemic periods. We examined associations in the year prior to policy introduction as a negative control.

Results: We observed slightly higher asthma visit rates in policy-exposed versus unexposed CBGs (rate difference = 22.9%, 95% CI = 8.6%, 39%). Rate differences were apparent only in the pandemic period. Negative control analyses did not suggest strong residual confounding (rate difference in year prior to policy = 6.5%, 95% CI = -15.5%, 34.2%).

Conclusions: The NYCHA SFH policy was not associated with reduced pediatric asthma ED visits. Slightly elevated rates among NYCHA CBGs may represent random variation, potential behavior changes during the pandemic (e.g., displacement of smoking indoors), or differential impacts of the pandemic on health care use. Further research into the implementation and impacts of SFH policies is needed.

Quarterly pediatric asthma ED visit rates among block groups exposed to the SFH policy ("Treatment") and matched synthetic control block groups. Dashed red line indicates policy introduction. The onset of the COVID-19 pandemic occurred in Quarter 18.
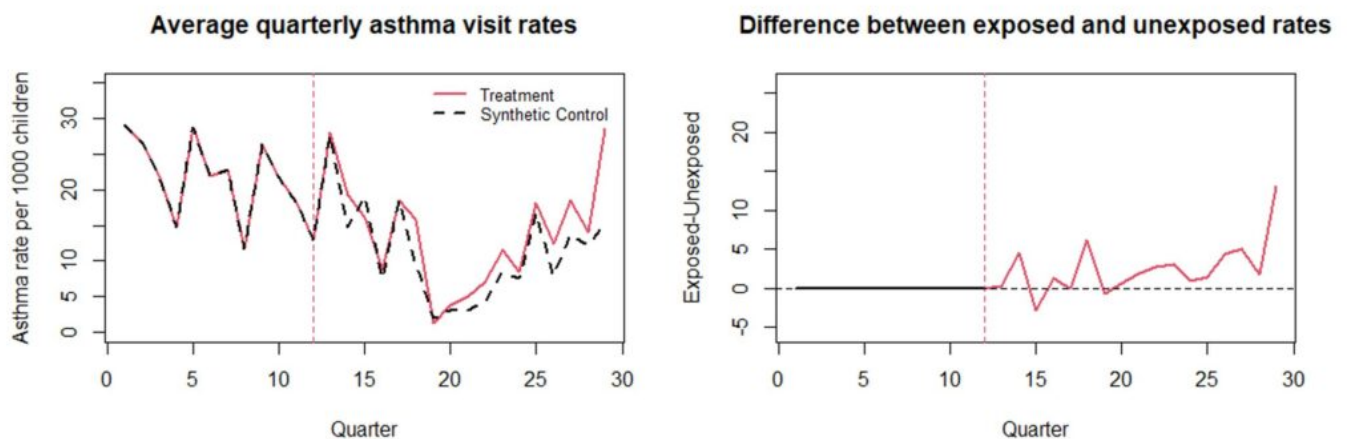
Preprinting of clinical studies subsequently published in high-impact journals and associations with Altmetric score and citation Seth Zissette* Seth Zissette Anant Gautam Joseph S. Ross Joshua D. Wallach

The use of preprints – preliminary research reports that have not yet undergone peer review – in clinical and health science research has increased in recent years. Although high-impact factor journals have largely adopted policies that are supportive of preprints, concerns remain that preprinting a manuscript prior to submission to a peer-reviewed journal may jeopardize consideration or preclude publication. Currently, little is known about how frequently research articles published in the highest-impact factor clinical journals are preprinted and associations between preprinting and the attention and citations that published articles receive. We identified all original research articles published in the 25 highest-impact factor clinical journals (7 general medicine and 18 internal medicine subspeciality journals) in 2022 (after the COVID pandemic had largely subsided). We used the bioRxiv/medRxiv API to identify any preprints with linked peer-reviewed publications in our sample. We then conducted Google searches to identify preprints for all remaining articles on other preprint servers (e.g., The Social Science Research Network). We identified the Altmetric Attention Score and number of citations for each article and used Wilcoxon tests to compare the distributions of these metrics among articles with and without a corresponding preprint. Among the 5,739 research articles published in 25 journals in 2022, 317 (5.5%) had a corresponding preprint. The median Altmetric Attention Score among articles with and without a corresponding preprint was 88.7 (IQR: 23.5-465.9) and 38.3 (IQR: 11.1-183.5), respectively ($p<0.001$). The median citation count among articles with and without a corresponding preprint was 24 (IQR: 11-60) and 11 (IQR: 5-25), respectively ($p<0.001$). We found that although relatively few research articles published in the highest-impact factor clinical journals in 2022 had a corresponding preprint, those that did received greater attention and citations.

Historic redlining and epigenetic depression risk in the Future of Families and Child Wellbeing Study Isabella Palomba* Helen Meier Isabella Palomba

Introduction: Historic structural racism has disproportionately burdened low-income and predominantly minority neighborhoods, and studies have shown associations with present day neighborhood health outcomes. Less well understood is whether historic structural racism is associated with individual-level outcomes including depression.

Methods: Data come from wave 6 (age 15) of the Future Families and Child Wellbeing Study (FFCWS), a cohort study representative of urban births from large US cities. Historic redlining scores, one indicator of historic structural racism, were calculated from the Home Owners' Loan Corporation (HOLC) residential rankings contained within the 2010 US Census Tract boundaries. A polyepigenetic score for Major Depressive Disorder (MDD) risk was estimated from participant salivary methylation data. This score was generated based on a meta-analysis that identified variably-methylated CpG sites in individuals with MDD to characterize risk of MDD. Linear regression controlling for assay type, maternal education, birth city, maternal smoking and cell proportions of the sample, estimated the association between historic redlining and epigenetic MDD risk (N=2084).

Results: Approximately 31.3% of participants lived in formerly redlined areas. We did not observe a statistically significant association between living in historic redlined neighborhoods at age 15 and epigenetic markers of MDD (β=0.017, 95% CI [-355.842, 864.804]).

Conclusions: Epigenetic signatures of MDD may not explain the increased prevalence of depression in individuals living in historically redlined neighborhoods during adolescence.

Associations between social needs and healthcare access: Findings from the 2022 BRFSS social determinants and health equity module J'Neka Claxton* J'Neka Claxton Guixiang Zhao Machell Town

Background: Access to health services is important to promoting health through the prevention and management of diseases. We aim to understand the associations between the burden of unmet social needs and healthcare access among US adults.

Methods: We used the 2022 Behavioral Risk Factor Surveillance System–Social Determinants and Health Equity module data, which were collected by 39 states, DC, and 2 US territories. A social needs summary measure was created by summing unmet social needs including questions that assessed life satisfaction, social and emotional support, social isolation, employment stability, food security, housing security, transportation access, and stress. Measures of healthcare access included no health insurance, no personal healthcare provider, inability to afford a doctor when needed, and a routine checkup 2 or more years ago. Cox regression with a robust variance estimator was used to estimate prevalence ratios, adjusting for sociodemographic variables.

Results: 257,758 respondents were eligible for inclusion. 43% of adults had zero unmet social needs. In adjusted analyses, an increase in the number of unmet social needs was associated with increased prevalence of no health insurance, no personal healthcare provider, inability to afford a doctor when needed, and a routine checkup 2 or more years ago. The largest magnitude in estimates of unmet social needs compared to zero unmet social needs occurred for the inability to afford a doctor when needed. Adults who reported 1, 2, 3, 4, and 5+ unmet social needs had 1.94, 3.18, 4.71, 6.46, 9.11 increased prevalence when compared to those who reported 0 unmet social needs. The adjusted estimates for the other outcomes were smaller in magnitude, but still statistically significant (Table).

Discussion: Incremental increases in the number of unmet social needs were independently associated with increased prevalence rates for each measure of healthcare access.

Table. Prevalence[a] and Adjusted Prevalence Ratios[b] for Four Measures of Healthcare Access by Number of Unmet Social Needs, BRFSS, 2022

Number of Unmet Social Needs	No health insurance		No personal healthcare provider		Inability to afford a doctor when needed		Routine checkup ≥ 2 years	
	% (95% CI)	APR (95% CI)	% (95% CI)	APR (95% CI)	% (95% CI)	APR (95% CI)	% (95% CI)	APR (95% CI)
0	3.8(3.6-4.1)	Ref.	10.5(10.1-10.9)	Ref.	2.8(2.6-3)	Ref.	9.4(9-9.8)	Ref.
1	7.1(6.6-7.6)	1.20(1.09-1.32)	15.2(14.5-15.9)	1.08(1.03-1.14)	6.5(6.1-7)	1.94(1.75-2.16)	11.6(11-12.2)	1.05(0.99-1.12)
2	10.4(9.6-11.3)	1.34(1.21-1.48)	19.6(18.5-20.6)	1.19(1.12-1.27)	12.3(11.5-13.2)	3.18(2.86-3.53)	14.4(13.5-15.3)	1.18(1.10-1.27)
3	12.1(11-13.2)	1.34(1.20-1.50)	21.9(20.5-23.3)	1.19(1.11-1.28)	19.6(18.4-20.8)	4.71(4.24-5.24)	17.2(15.9-18.5)	1.32(1.22-1.43)
4	14.6(13-16.2)	1.38(1.22-1.57)	23.7(21.9-25.5)	1.20(1.11-1.30)	28.5(26.7-30.3)	6.46(5.80-7.19)	18.1(16.4-19.7)	1.33(1.20-1.47)
5+	18.7(17.3-20.1)	1.51(1.35-1.70)	27(25.5-28.5)	1.23(1.14-1.31)	43.9(42.2-45.6)	9.11(8.24-10.07)	20.7(19.2-22.1)	1.47(1.36-1.60)

[a] Values are weighted prevalence.
[b] Adjusted prevalence ratios (APRs) are adjusted for race/ethnicity, age, sex, educational attainment, marital status, and income.

A Not-Too-Distant Future: Engaging with Stakeholders to Develop a Vision for Public Health Surveillance in Canada by 2030 Elissa Giang* Elissa Giang Dhilal Alhaboob Claire Betker Margaret Haworth-Brockman Chia-Yu Lin Faith Layden Sally Park Jean-Paul R. Soucy Chi-Hang Jonathan Sinn Lynda Tjaden Louis Wong Sarry Zheng David L. Buckeridge

Background: A clear vision for public health surveillance is critical for navigating complex health landscapes and allocating limited resources effectively. To develop this vision, the Public Health Agency of Canada (PHAC) is actively engaging stakeholders to ensure diverse perspectives are considered, with the goal of enhancing and ensuring collaboration in addressing future public health challenges.

Objectives: The objectives of the resulting vision are two-fold: 1) to describe the future characteristics, values, and guiding principles essential to a high-functioning system of surveillance systems in Canada, and 2) to identify strategic opportunities to accelerate movement towards the vision.

Methods: Our engagement approach is designed to reflect a broad range of perspectives from public health personnel and allied stakeholders. To this end, we determined to meet with practitioners, academics, and equity-deserving groups including First Nations, Inuit, and Métis public health staff and organizations, as well as the public. We conducted in-person and virtual workshops and administered an online questionnaire to ensure there were a number of ways people could contribute. Transcript data and notes were analyzed qualitatively using a reflexive thematic approach.

Results: Between September 12, 2023, and March 1, 2024, we held 29 facilitated workshops with 816 participants across all Canadian provinces and territories. The online questionnaire received 925 unique responses from across the country. Our analysis identified 6 themes describing current gaps in surveillance; five areas for opportunity; and 44 proposed objectives to strengthen public health surveillance Canada.

Next steps: The identified themes and proposed objectives are undergoing validation by consulting experts outside of and within PHAC, who will refine the values, future characteristics and guiding principles of a high-functioning surveillance ecosystem in Canada. Results from this work will contribute to the development of a framework guiding stakeholders toward a desired vision for strengthened surveillance systems throughout Canada.

Social

Prospective associations between the quality and quantity of social relations and self-rated health in the National Social Life, Health, and Aging Project (NSHAP) Taymara Abreu*

Taymara Abreu Joreintje Mackenbach Joline Beulens Ilonca Vaartjes Ichiro Kawachi

Background: Little is known about the joint effects of quality and quantity of social relations on health and few studies differentiate between positive and negative social support.

Aim: We prospectively examined the association between quality and quantity of social relations and self-rated health (SRH).

Methods: Community-residing older U.S. adults aged 57–85 years at baseline were prospectively followed over 10 years in the population-based National Social Life, Health, and Aging Project (NSHAP). Social relation measures were obtained through the baseline survey and reported about friends, family and partner. Large social network, high positive social support and high negative social support were defined as their highest quartile. These three binary measures were combined into a multicategorical exposure variable generating eight distinct categories. SRH was measured on a 5-point Likert scale and dichotomised. Odds ratios (OR) for poor SRH (lower than "fair") were estimated with covariate-adjusted logistic regression.

Results: In total, 1,592 participants were included. Based on the combined multicategorical exposure variable as well as independent exposure variables, only higher levels of negative social support were prospectively associated with increased likelihood of poor SRH (aOR=0.65; 95%CI 0.44-0.98). From the different social ties, only family-related negative social support was associated with SRH (aOR=0.59; 95%CI 0.39-0.90). This association was similar between genders, but only statistically significant among women. Sensitivity analysis with depressive symptoms as outcome (aOR=0.65; 95%CI 0.48-0.90) supported the hypothesis that the findings for SRH may be partially driven by mental health.

Conclusion: Negative social support particularly from family is prospectively associated with poor SRH. Our findings may offer insights for possible public policies, such as policies to alleviate the burden of informal care on families.

Social

Cumulative neighborhood poverty and biological aging Alena Sorensen D'Alessio* Alena Sorensen D'Alessio Kathleen Mullan Harris Allison E. Aiello Brandt Levitt Lauren Gaydosh Chantel L. Martin

Background: Neighborhood socioeconomic disadvantage has been linked to proxies of accelerated biological aging using DNA methylation; however, limited knowledge exists of the relationship between cumulative exposure to neighborhood poverty and biological aging measured with epigenetic clocks.

Methods: Using data from 3,426 participants followed for 25 years in the National Longitudinal Study of Adolescent to Adult Health, we examined the association between number of time periods residing in neighborhood poverty from Waves I (1994-95) to V (2016-18), operationalized as census tracts below the federal poverty level, and biological aging, calculated from five epigenetic clocks (DunedinPACE, GrimAge, Horvath, PhenoAge, Zhang2017). Survey linear regression models were adjusted for gender, college degree attainment, employment, and self-rated health. Models were stratified by race and ethnicity (Non-Hispanic Asian/Pacific Islanders, Non-Hispanic Black, Non-Hispanic White, Hispanic).

Results: Most participants had at least one time period in neighborhood poverty (1 period: 26.5%, 2 periods: 12.8%, 3+ periods: 14.5%). Each additional period was associated with faster biological aging for all race and ethnicity groups using DunedinPACE (βAsian/Pacific Islanders=0.23 (0.001, 0.45); βBlack=0.15 (0.03, 0.26); βWhite=0.08 (0.03, 0.13); βHispanic=0.14 (0.03, 0.24)), Blacks and Whites using GrimAge (βBlack=0.77 (0.36, 1.18); βWhite=0.64 (0.38, 0.90)), Asian/Pacific Islanders and Whites using PhenoAge (βAsian/Pacific Islanders=1.38 (0.45, 2.32); βWhite=0.29 (0.01, 0.58)), and Whites using Zhang2017 (βWhite=0.06 (0.005, 0.12)). Associations were not observed for Horvath.

Conclusion: Our results suggest a relationship between cumulative exposure to neighborhood poverty and accelerated biological aging across key epigenetic clocks. Future analyses will investigate possible effect modification by social integration or support and explore timing of neighborhood poverty exposure.

Social

The association between life-course SEP trajectories and cardiometabolic diseases in older adults: a retrospective cohort study in Brazil Taymara Abreu* Taymara Abreu Margot Bonsing Fabiola Bof de Andrade Joline Beulens Joreintje Mackenbach

Background: The burden of cardiometabolic diseases (CMD) has increased in low- and middle-income countries (LMIC), where substantial socioeconomic inequality exist. Socioeconomic position (SEP) can exert influence from early life onwards, implicating childhood and adulthood SEP as determinants of health in later life. However, research in LMIC is scarce and inconsistent.

Aim: To investigate the association between life-course SEP trajectories and CMD outcomes among Brazilians aged 50 years or older.

Methods: We used data from N=8,238 participants of the retrospective cohort study ELSI-Brazil. SEP was measured with a single-variable approach at three time points: subjective SEP (childhood), own education (early adulthood) and subjective SEP (older adulthood). CMD diagnosis and date of onset were self-reported. A robustness check with different SEP indicators was conducted. Latent Class Growth Analysis was used to identify life-course SEP trajectories. Logistic regression with sampling and attrition weights assessed the association between life-course SEP trajectories and CMD. Sensitivity analysis excluded participants diagnosed with CMD more than five years prior to baseline (N=5,743) and explored effect modification by sex.

Results: The main and sensitivity analysis identified two SEP trajectories: upward-stable and upward-downward. In the robustness check we found two upward-downward trajectories. The odds of developing CMD in older adulthood for those in the upward-downward trajectory compared to those in the upward-stable trajectory was 1.08 (95%C 0.95-1.22). We observed similar findings in the robustness check and sensitivity analysis. Stratification by sex did not reveal any differences.

Conclusions: No association between life-course SEP trajectories and CMD in older adulthood was observed in this Brazilian cohort. Due to the scarcity and inconsistency of research, more studies with a longer follow-up and different approaches are needed in LMIC.

Vacant Property Conversions in Baltimore: Effects on Mental Health Dustin Fry* Dustin Fry
Michelle C. Kondo Kristin Mmari

Visible signs of neighborhood disinvestment, including unmaintained vacant properties, have been shown to negatively affect mental health, with Black residents of economically-deprived neighborhoods being among the most affected. However, vacant properties also present an opportunity to create publicly-accessible pocket parks, community gardens, and playgrounds in neighborhoods that lack access to greenspace. In Baltimore City, there are over 25,000 vacant lots and an additional 17,000 abandoned buildings. As city agencies and community-based organizations have restored some of these spaces, Project VITAL (Vacant Lots to Transform Adolescent Lives) has been implemented to study the impacts of greening vacant lots on the health of adolescents. Although positively identifying vacant lots from observations or secondary data can be unreliable, the City of Baltimore maintains databases of recent building demolitions, so outcomes from newly-created vacant lots can be assessed over time. This analysis uses mapped records of 1,143 building demolitions in Baltimore, Maryland conducted between 2009 and 2017 to quantify the effect of vacant property conversions on adolescent mental health. We are conducting longitudinal virtual audits of Google Street View imagery at demolition sites to categorize the outcomes of building demolitions over time (e.g., the creation of an unmaintained vacant lot, a greened vacant lot, or the replacement of a demolished building with a new building), and to assess the content and quality of sites before and after building demolitions. Audits will conclude in March 2024. Changes to lots will be used to predict changes in adolescent mental health outcomes in subsequent years. Pilot audits of 50 vacant lots found a median of six images per site, with imagery dates ranging from November 2007 to May 2022. Six sites experienced significant improvements in rater-assessed overall quality over time, with changes such as the installation of garden plots and playground equipment. Two sites experienced significant declines in quality, with changes including previously-maintained vegetation becoming overgrown. Maintaining vacant lots after building demolitions may provide an opportunity to improve access to health-promoting greenspace in disadvantaged urban neighborhoods.

Disparities in mortality by sexual orientation in a large, prospective cohort of female nurses Brittany Charlton* Sarah McKetta Tabor Hoatson Landon Hughes Bethany Everett Sebastien Haneuse S. Bryn Austin Brittany Charlton

Background: Extensive evidence documents health disparities for sexual minority women, including worse physical, mental, and behavioral health than their heterosexual peers. These factors have been linked to premature mortality, yet few studies have investigated premature mortality disparities among sexual minority women and whether these disparities differ by identity (e.g., lesbian or bisexual). Our objective was to examine differences in premature mortality by sexual orientation.

Methods: This prospective cohort study included female nurses born 1945-1964, recruited in 1989 and followed through April 2022. Sexual orientation (lesbian, bisexual, heterosexual identity) was assessed in 1995. We examined differences in time to all-cause mortality from assessment of exposure, analyzed using accelerated failure time models, adjusting for birth cohort.

Results: Among 90,833 participants, 89,821 (98.9%) identified as heterosexual, 318 (0.3%) as bisexual, and 694 (0.8%) as lesbian. Compared to heterosexual participants, and adjusting for birth cohort, sexual minority participants evidenced earlier mortality (acceleration factor [AF]: 0.74, 95% CI: 0.65–0.84). Examining subgroups, these differences were highest in magnitude among bisexual participants (AF: 0.63, [0.51–0.78]; for lesbian participants AF: 0.80 [0.68–0.95]).

Conclusion: Participants who identified as lesbian and bisexual had markedly earlier mortality over the study period relative to those who identified as heterosexual. These dramatic differences in the timing of mortality, in an otherwise largely homogenous sample of female nurses, highlight the urgency of addressing modifiable risks and upstream social forces that propagate and perpetuate disparities.

Social

Healthcare avoidance and sexual orientation identity among college students in China: a cross-sectional survey Stephen W. Pan* Stephen Pan Cheng Yu Katelyn Sileo Sudais Imtiaz Etienne Jaime

Background: Due partly to stigma (anticipated, internalized, enacted, structural), healthcare avoidance behaviors may be more prevalent among sexual minorities. However, research on sexual orientation and healthcare avoidance in China remains limited. In response, we examined the extent to which sexual orientation identity is associated with healthcare avoidance among college students in mainland China.

Methods: In 2020, 806 first-year college students >18 years old in East China completed a baseline online survey. Sexual orientation identity was self-reported as heterosexual, gay, bisexual, and other/unsure. Non-heterosexual categories were coded as "sexual minority." Healthcare avoidance was defined as refraining from seeing a doctor in the past 12 months, despite an illness or injury. Multiple logistic regression was used to assess associations between sexual orientation identity and healthcare avoidance. Males and females were analyzed separately. Standardized predicted probabilities were calculated controlling for socio-demographics, health insurance, and medical history.

Results: Prevalence of healthcare avoidance among males was 22.5% and 29.6% among females. Prevalence of sexual minority identity was 10.8% among males and 20.05% among females. The odds of reporting healthcare avoidance were 2.17 times significantly greater for sexual minority males than heterosexual males (95% CI: 1.10 – 4.27). Among females, no significant association was observed between healthcare avoidance and sexual orientation identity.

Conclusion: Uptake of healthcare services may be suboptimal for sexual minority male college students in China. Further studies are needed to elucidate generalizability of these findings, mechanisms of association, and explore potential interventions to mitigate healthcare avoidance among sexual minority male college students in China.

Figure: Adjusted predicted probability of college students in China who have avoided seeing a doctor in the past 2 years despite being ill or injured (84% confidence intervals)
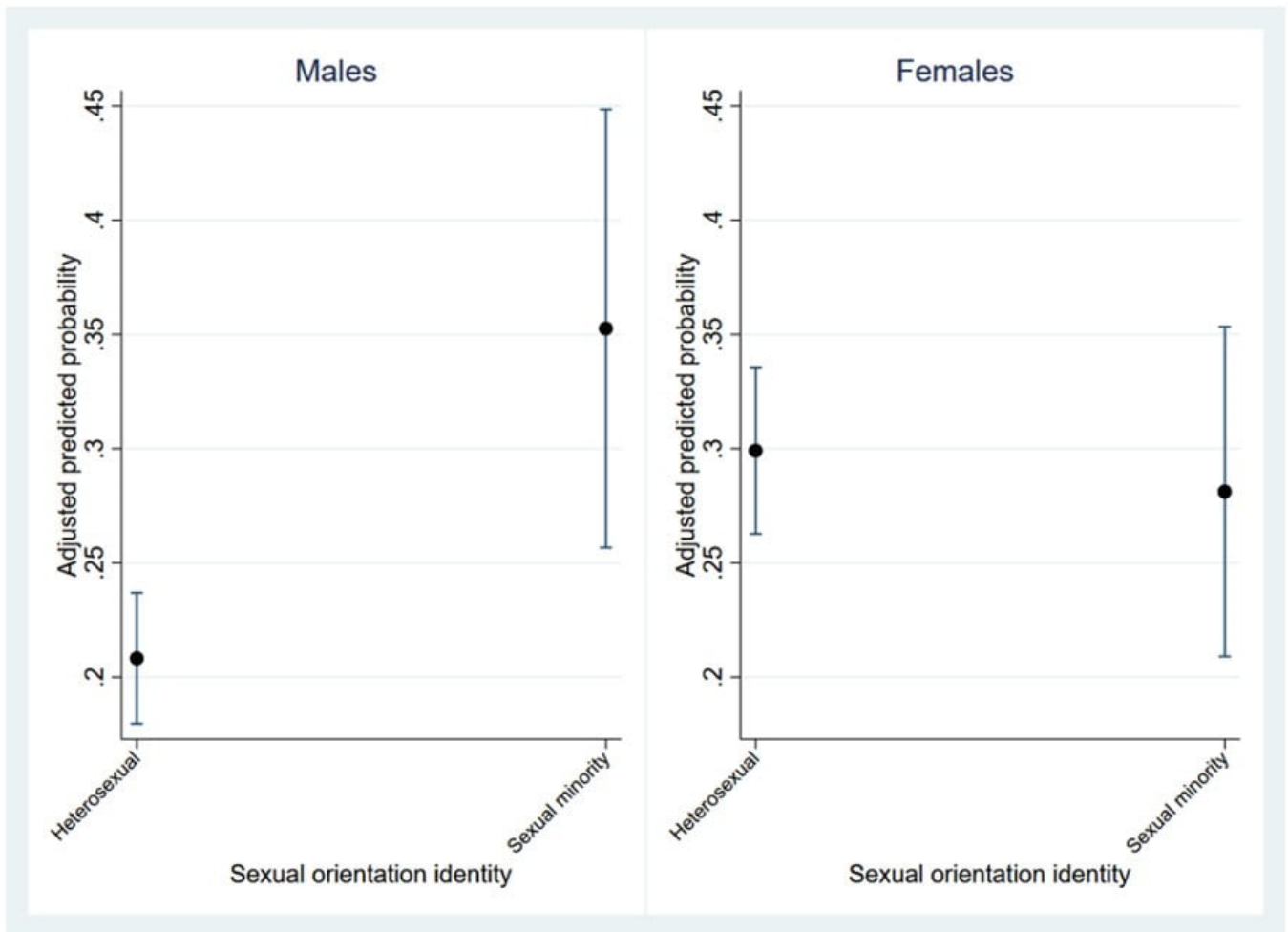
Volunteering and psychological distress among college students in China: a longitudinal study Alex Torres* Alex Torres Sudais Imtiaz Stephen W. Pan

Background: In China, research suggests that volunteering activities protect against psychological distress. However, such research has primarily relied on cross-sectional study designs susceptible to reverse causality. In response, we used a longitudinal study design to examine potential associations between volunteering and psychological distress among college students in East China.

Methods: In 2020, 806 first-year college students over 18 years old in East China completed a baseline survey [t0] and were enrolled into the study. Follow-up surveys occurred 4 [t1], 8 [t2], and 12 months later [t3]. Generalized Estimating Equations were used to assess associations between volunteering [t1 & t2] and psychological distress 4 months later [t2 & t3, respectively]. Control variables included baseline psychological distress [t0], volunteering [t0], loneliness [t0], and sociodemographics [t0]. Analysis was conducted with multiple imputation and 100 imputed datasets. Volunteering was measured as self-reported number of hours the student engaged in unpaid work (excluding work for family members) each month. Psychological distress was measured by depressive and anxiety symptom severity using the PHQ-4 (range for each: 0-6).

Results: Compared to those who did not volunteer, odds of psychological distress were significantly greater among those who volunteered 3-7 hours (AOR: 3.14, 95 % CI: 1.47 – 6.77) and >8 hours (OR: 3.03, 95% CI: 1.12 – 8.16). Volunteering < 3 hours was not associated with depressive symptomology. Anxiety symptomology was not associated with any level of volunteering.

Conclusion: To the best of our knowledge, this is the first longitudinal study of volunteering and psychological distress among college students in China. Contrary to previous cross-sectional studies, results indicate that volunteering may be undermining mental health. Longitudinal and qualitative studies are needed to confirm these findings and elucidate possible mechanisms of association.

Social

Paternal Involvement and Child Development among Low Birthweight Children in Japan

Kota Nakayama* Kota Nakayama Naomi Matsumoto Etsuji Suzuki Ichiro Kawachi

Background: Previous studies have shown that paternal involvement is associated with positive development outcomes among normal birthweight children, but no studies have examined the association among LBW children. Accordingly, we aim to assess the association among LBW children in a population-based study.

Methods: By using the data from the nationwide Japanese Longitudinal Survey of Babies in the 21st Century 2010 Cohort, we analyzed 1674 male and 1968 female LBW children, born from May 10th to 24th, 2010. Paternal involvement was assessed at the age of 18 months and dichotomized (low vs. high) based on the median hours of childcare per week, both on weekdays and weekends. We assessed motor and language development, which were evaluated at 30 months of age, and cognitive development, which was evaluated at 66 months of age. We estimated ORs for adverse development outcomes adjusting for potential confounders such as child sex, parental education, maternal involvement, paternal workhours, parental smoking status, residence with grandparents, and use of childcare services.

Results: Regarding the paternal involvement on weekdays, we found no clear association; the adjusted ORs (95% CIs) for adverse motor, language, and cognitive development were 1.30 (0.86, 1.97), 1.06 (0.81, 1.39), and 1.17 (0.71, 1.95), respectively, among children with high paternal involvement. Though not significant, the patterns were reversed on weekends, and the corresponding ORs (95% CIs) were 0.95 (0.61, 1.48), 0.88 (0.66, 1.17), and 0.63 (0.36, 1.08), respectively.

Conclusion: Our study indicates that longer paternal involvement on weekends may have a positive influence on language and cognitive development among LBW children. However, we found no clear association for paternal involvement on weekdays, and further studies are warranted to examine longer term effects of paternal involvement from a perspective of both quantity and quality.

Social

Differences in the Relationship Between Voter Registration and Birth Outcomes by Race in South Carolina

Michael P. Huynh* Michael Huynh Woo Jung (Amy) Lee Nancy L. Fleischer Abigail Kappelman Yanmei Xie Annie Ro

Background. Political factors are an untapped social determinant of health, and little is known about their influence on birth outcomes, including differences by race. Greater levels of voter registration may be indicative of more agency and health equity. We examined the link between voter registration and birth outcomes, with effect modification by race. **Methods**. We linked South Carolina (SC) State Election Commission data to SC singleton birth certificate data from 2004-2020 (n=871,709). Our exposure was a non-White to White (NW-W) ratio of county-level voter registration. We divided counts of registered voters by those eligible to vote at the county level. Outcomes were low birthweight (LBW, <2,500g) and preterm birth (PTB, <37 weeks). We used multilevel logistic regression models to examine the county-level relationship between voter registration and birth outcomes, adjusting for infant sex, maternal age, parity, maternal education, Medicaid insurance, presidential term years, polling sites, and urbanicity. We ran effect modification, then stratified analysis by race. **Results**. Our sample included 57.5% White, 32.9% Black, and 9.6% Hispanic moms. LBW prevalence was 7.9%, and PTB prevalence was 9.6%. On average, more White voters were registered than non-White voters (NW-W ratio=0.93). A higher NW-W ratio (i.e, a larger share of non-White voter registration) was associated with higher odds of LBW for Hispanic moms (OR=1.83, 1.11-3.03), with no association for White and Black moms. A higher NW-W ratio was associated with lower odds of PTB for White moms (OR=0.78, 0.61-0.99) and Black moms (OR=0.75, 0.59-0.96), with no association for Hispanic moms. **Conclusion**. Racial differences in voter registration had mixed associations with adverse birth outcomes in SC. Policy-level programs targeted at improving civic engagement may help improve agency and birth outcomes, but these mechanisms need closer investigation into what factors explain the possible racial differences.

Social

Relative age for grade is associated with differences in late -life memory: findings from the Health and Retirement Study Life History Mail Survey Chloe Eng* Chloe Eng Anusha M. Vable Whitney Wells Benjamin Domingue David H. Rehkopf

Introduction: Education consistently predicts late-life cognition, but degree attainment is influenced by preceding factors such as school enrollment age and age relative to peers. Birth seasonality impacts when and in what grade one enrolls, and school-year cutoffs create up to a year difference across students entering at the same age; evidence on long-term cognitive effects of school entry is sparse.

Methods: Relative age for grade was characterized as the interaction of enrollment age in calendar years, birth (old: September-December; average: January-April; young: May-August), and entry grade (Kindergarten; 1st) for Health and Retirement Study participants over age 50 entering school between 4 and 7 years of age (Life History subsample n=6,915). Linear mixed models examined associations between relative age for grade and late-life episodic memory for all available biennial visits from 1998-2020, adjusted for linear/quadratic age, gender, race/ethnicity, birthplace region, parental education, memory practice effect, and preschool attendance.

Results: Late-life memory differed across strata of enrollment age, birth trimester, and entry grade (interaction p=0.01). Earlier enrollment age benefitted memory in old-for-grade Kindergarteners compared to those with similar birthdays enrolling at later ages (age 5 vs. age 6 β: 0.05; 95% CI: 0.01, 0.09), but not for average- or young-for-grade kindergarteners. Earlier enrollment age was also beneficial for memory in young-for-grade 1st graders compared to enrollment at later ages (age 5 vs. age 6 β: 0.05; 95% CI: 0.02, 0.08), but not for average- or old-for-grade 1st graders.

Conclusion: Earlier enrollment age was associated with late-life memory for Kindergarteners turning a calendar year older soonest after the start of school year and 1st graders most recently advancing in age by the start of the school year, suggesting benefits for those most susceptible to variability in grade placement decisions.

Figure: Associations between relative age for grade (age at school entry, birth trimester, and entry grade) with late-life memory among Health and Retirement Study participants (Life History Mail Survey subsample n=6,915)
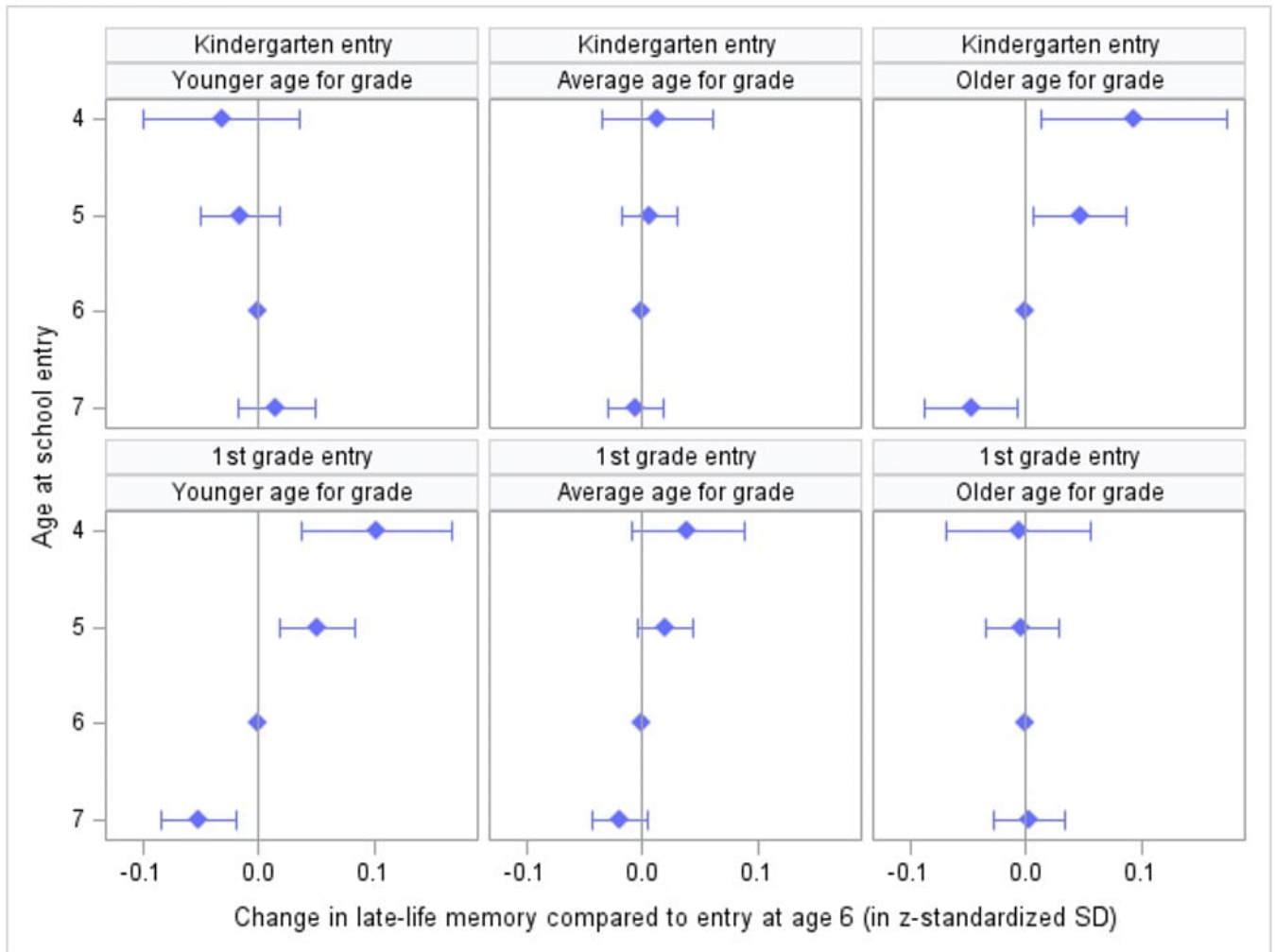
Structural determinants of diabetes technology use: a descriptive analysis Chloe Bennett*
Chloe Bennett Rob Cavanaugh Louisa Smith

Continuous glucose monitors (CGM) have been shown to significantly improve diabetes control, yet CGM use differs by race/ethnicity. Evidence suggests systemic barriers affect CGM use.

This study assessed the relationship between two structural determinants and CGM use among a cohort of people with self-reported type 2 diabetes (T2D) enrolled in the NIH All of Us Research Program. CGM use was determined via procedural codes in electronic health records. Participants were surveyed on healthcare provider bias, rating how often healthcare providers treat them with less respect than others. Logistic regressions estimated associations between state-level acceptance of Medicaid expansion, defined as implementation prior to 2023, and participant-reported healthcare provider bias and CGM use. We also assessed effect modification by race/ethnicity.

Among the participants with self-reported T2D (N=17,507), 56% had hemoglobin A1c data. Of these, 4.5% (N=438) had any procedural codes relating to CGMs. 5.1% of White and 3.6% of Black participants had evidence of CGM use. CGM users were similar in age to non-users (mean years 65.4 and 64.8, respectively). 70% of CGM users lived in Medicaid expansion states vs. 64% of non-users. After adjusting for race/ethnicity, gender, and mean A1c, living in a state that adopted Medicaid expansion was associated with increased odds of CGM use (OR: 1.31; 95% CI 1.04, 1.67). Interaction analyses revealed that the association was strongest among Black participants (6.03; 2.93,12.42). Healthcare provider bias was not associated with CGM use (1.02; 0.79, 1.29) overall. However, both Black (0.68; 0.33, 1.39) and Hispanic (0.78; 0.32, 1.89) people who reported not always feeling respected by a healthcare provider were less likely to ever use CGMs.

These findings highlight the importance of considering the effect of federal and state-level policy changes on reducing racial disparities in diabetes technology access and use.

Study Design

Exploring the Application of Target Trial Emulation in Vaccine Evaluation: Scoping Review
Kayoko Shioda* Kayoko Shioda Kayoko Shioda Toshiaki Komura

Background: Target Trial Emulation has gained popularity in evaluating treatments and health interventions. However, its application to infectious disease outcomes requires careful consideration, as infectious diseases violate the assumption of no interference. We conducted a scoping review to understand how target trial emulation approaches have been applied for vaccine evaluation and how the indirect effects (or spillover effects) of the vaccines have been assessed in the target trial emulation framework.

Methods: We conducted a systematic search of literature published in PubMed and Embase between January 2012 and October 2023, using keywords related to target trial emulation, infectious diseases, and vaccines. Two independent reviewers screened titles and abstracts for relevance. Full-text articles meeting inclusion criteria were further assessed for eligibility.

Results: Our search identified 117 studies. Of these, 25 original research studies employed target trial emulation approaches to estimate the effect of vaccines, predominantly published in 2022 and 2023. Most studies evaluated the effect of COVID-19 vaccines, except for one that evaluated rotavirus vaccines. The majority used Kaplan-Meier estimator and/or Cox proportional hazards model, while two applied the cumulative incidence function and Fine-Gray model to adjust for competing risks. Most studies did not define the type of vaccine effect they evaluated (e.g., direct, indirect, total, or overall effect). None of the studies addressed interference or estimated the indirect effect of vaccines.

Discussion: Our review highlights the increasing popularity of target trial emulation in vaccine evaluation, but indirect effects have been overlooked. Agent-based modeling is a potential solution, as demonstrated in studies evaluating pre-exposure prophylaxis for HIV prevention.

Study Design

Use of ZIP Codes and ZIP Code Tabulation Areas: Bias Analysis and Research Implications

Futu Chen* Futu Chen Beau MacDonald Yan Xu Wilma Franco Alberto Campos Lawrence Palinkas Jill Johnston Sandrah P. Eckel Erika Garcia

The U.S. census' American Community Survey (ACS) offers a geography called ZIP Code Tabulation Areas (ZCTA) which is similar to but different from US Postal Service ZIP Codes (ZIPs). Best practice for combining ZIPs and ZCTA datasets is largely undiscussed in the epidemiology literature. Without a "crosswalk" linkage, if ZCTAs containing ≥1 ZIP without the same 5-digit identifier, then the non-matching ZIPs are dropped. We compared standard crosswalk and non-crosswalk linkage results nationally and in a case study of California zero-emission vehicles (ZEV) adoption.

We obtained crosswalk files from the Uniform Data System Mapper. ZCTAs containing ≥1 ZIP without the same 5-digit identifier are dropped in non-crosswalk linkage. Nationally, we related an indicator for a ZCTA containing non-matching ZIPs to 2019 ACS ZCTA population characteristics using logistic regression, adjusted for state. In California, we used linear regression to relate ZIP-level 2019 ZEV adoption per 1,000 population (California Energy Commission) to ZCTA neighborhood socioeconomic status (SES) index quintiles (California Neighborhoods Data System), using crosswalk and non-crosswalk linkages.

Nationally, 15% of ZCTAs (range 3%-100%, median=14%) contained non-matching ZIPs. ZCTA with higher % population below poverty level or with higher % renters had a higher odds of non-matching ZIPs (OR=2.0 [95% CI: 1.5,2.7]; OR=26.0 [22.9,31.8], respectively). For California ZEV data, 31.7% of 2,580 ZIPs were excluded without crosswalk linkage. The difference in ZEV adoption rate comparing low SES (Q1-2) to high SES (Q5) ZCTAs was -25.7 [-28.5,-22.8] without cross-walk versus -26.0 [-28.8,-23.1] with cross-walk, an underestimate of 1.15%.

Non-crosswalk linkage may cause bias by differentially excluding ZIPs for disadvantaged populations. Crosswalk linkage is recommended with ZCTA as the final unit of analysis. Results are relevant to a wide range of ZIP data (e.g., business, health outcomes, transportation).

Figure 1. Distribution of 2019 ZCTA SES (% Non-Hispanic White, % income below poverty level in the past 12 months, and % renters) across the number of ZIPs crosswalked to ZCTA in the United States. Higher number implies more ZIPs without the same 5-digit identifier are dropped in non-crosswalk linkage. AS, GU, MP, PW, and VI were excluded due to small sample sizes.

Study Design
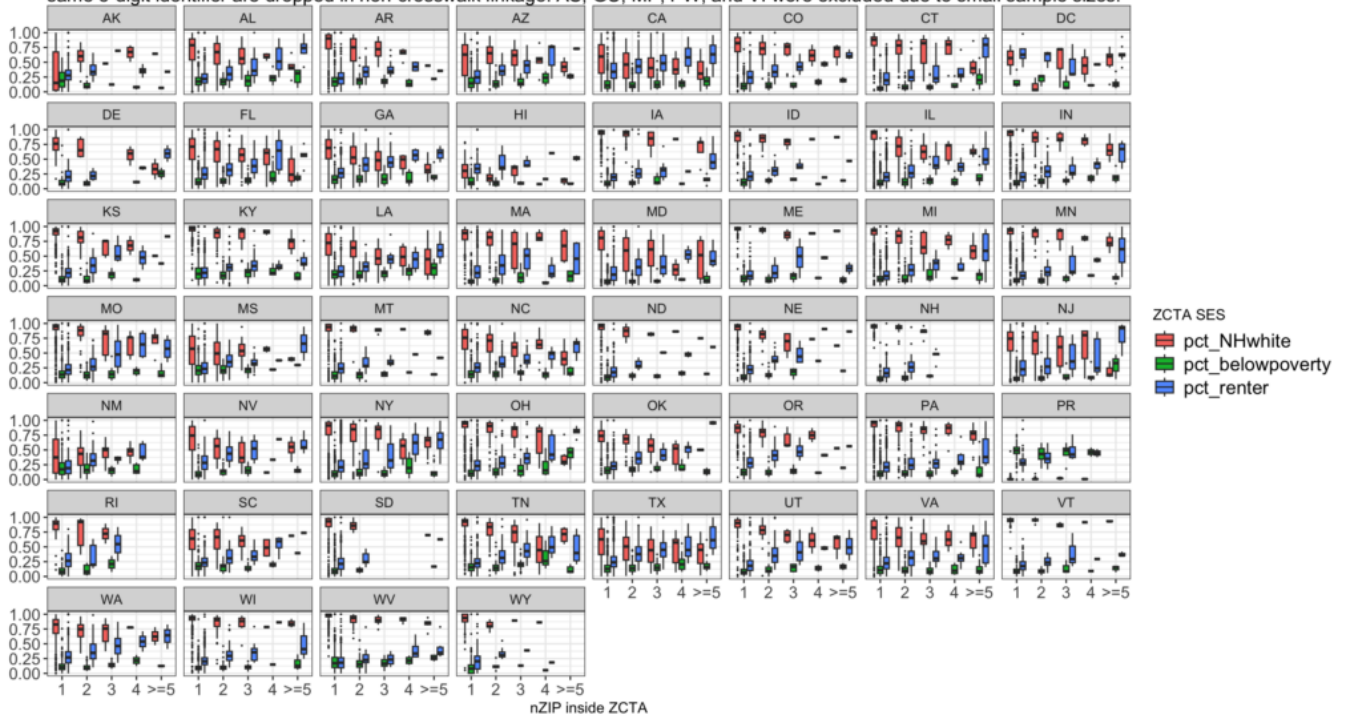
Lessons learned from implementing respondent driven sampling to recruit people experiencing homelessness in California: The California Statewide Study of People Experiencing Homelessness
Paul Wesson* Ryan D. Assaf Paul Wesson Angelica DeGaetano Meghan D. Morris Margot Kushel

Over 181,400 people experience homelessness (PEH) in California (Ca), accounting for 28% of the US PEH population and half of its unsheltered population. Probability sampling methods, e.g. venue-based sampling (VBS), have advantages over convenience or single-site sampling, but miss "hidden" subgroups. In a statewide representative study of PEH, we conducted multi-stage VBS across 8 CA counties complemented by respondent driven sampling (RDS) to sample "hidden" subgroups of PEH through their social networks: transitional aged youth (TAY), individuals who experienced domestic violence (DV), LGBTQ+ individuals, and day laborers. We adapted RDS to overcome recruitment challenges with options for digital coupons, phone surveys, and mailed or emailed incentives. To assess the approach we describe VBS and RDS participants, recruitment chains, and population homophily estimates (where a value greater than 1 indicates preferential, not random, recruitment). Pre-specified subgroups were more represented in the RDS arm (n=158) than the VBS arm (n=3041) (**Table**). Recruitment chains were longest for the largest county and for those who opted for a phone interview. We note high levels of homophily for each of the subgroups: TAY= 3.27; LGBTQ+= 1.48; DV= 9.03; day laborers= 1.51. Despite our adaptations, RDS sample size and recruitment chains were smaller than expected. Still, homophily and comparison of sample proportions support RDS for targeted recruitment of hidden subgroups. We offer several recommendations to strengthen RDS for PEH: 1) partner with community liaisons who can champion in the field; 2) conduct interviews at dedicated physical study sites as well as via phone over longer recruitment periods; 3) dedicate trained personnel and resources for the RDS arm. Given our experience and the everyday challenges in the lives of PEH, RDS added value to our overall sampling design by representing voices of those who would have otherwise been missed.

Table 1- Respondent-drive sample and venue-based sample demographics and characteristics of people experiencing homelessness in California, 2022

	Respondent-driven sample	Venue-base sample
	n (%)	n (%)
Total	158 (100.0)	3041 (100.0)
Demographics		
Age, years		
Median (interquartile range)	23 (20 - 32)	48 (37 - 57)
Family type		
Adult in family	20 (12.7)	175 (5.8)
Single adult	47 (29.8)	2764 (90.9)
Transitional age youth	91 (57.6)	103 (3.4)
Gender identity		
Cisgender women	57 (36.5)	1091 (36.2)
Cisgender men	76 (48.7)	1889 (62.7)
Transgender and gender non-conforming	23 (14.7)	34 (1.1)
Sexual orientation		
Heterosexual/straight	102 (66.2)	2704 (90.4)
Gay	11 (7.1)	94 (3.1)
Bisexual/pansexual	33 (21.4)	160 (5.4)
Other	8 (5.2)	33 (1.1)

Substance Use

Transaminases'' characteristics among consumers of indigenous alcohol "Lutuku" and no consumers in Lubumbashi Laetitia Ngongo Mwavua* Chadrack KABEYA DIYOKA Criss KOBA MJUMBE

Contexte : Le manque de connaissances sur les processus biochimiques dans le processus de traitement du Lutuku constitue un réel problème. L'étude compare l'activité enzymatique des transaminases chez les consommateurs d'alcool Lutuku natif et les non-consommateurs.

Méthodes : Il s'agit d'une étude cas-témoins portant sur 40 sujets sains et consommant du Lutuku. Les activités enzymatiques de la glutamo-oxaloacétique transaminase (SGOT) et de la glutamo-pyruvique transaminase (SGPT) ont été réalisées à l'aide de méthodes chimiques cliniques standard développées par BIOLAB.

Résultats : Au total 80 participants ont été recrutés, dont 40 consommateurs du Lutuku et 40 témoins. L'âge moyen dans le groupe des consommateurs de Lutuku était de 36.11 ± 8.61 ans (20-57 ans) ; une répartition inégale entre les groupes des filles (controls=19 et consumers Lutuku=11) et des garçons (controls=21 et consumers Lutuku=29) dans les 2 groupes ($\chi2$=3.413, p= 0,065). En nous référant aux valeurs de référence, le niveau sanguin de la SGOT et TGP étaient statistiquement plus élevés chez les alcooliques (test t de Student, p<0,0001), et une différence de risque statistiquement significative de présenter des taux sériques de SGOT (p=0.000), et SGPT (0.000) en comparaisons au témoins. Chez les consommateurs du Lutuku le SGOT au SGTPT [positivement (r=0.417 ; p < 0.01)] et l'index de De Ritis [positivement (r=0.524 ; p < 0.01)] et le SGPT à l'index De Ritis (-0.490 : négativement). Dans le groupe témoin, nous avons identifié des valeurs de SGOT et du SGPT significativement corrélés à l'index de De Ritis (p < 0.01), respectivement r=0.818 (positivement) et -0.553 (négativement).

Conclusion : La consommation de Lutuku induit quatre à cinq fois plus d'activités transaminases (SGOT et SGPT) par rapport à celles observées chez les sains.

Substance Use

Systematic Review and Meta-Analysis: Hepatitis C Treatment Outcomes by Housing Status Among People Who Inject Drugs Sarah Kimball* Sarah Kimball Marley Reynoso Courtney McKnight Don Des Jarlais

Background

The prevalence of hepatitis C virus (HCV) among people who inject drugs (PWID) is between 50-70%. Prior systematic reviews demonstrated that PWID have similar direct-acting antiviral treatment outcomes compared to non-PWID; however, reviews have not examined treatment outcomes by housing status. Given the links between housing and health, identifying gaps in HCV treatment can guide future interventions.

Methods

We conducted a systematic review using Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. We searched six databases for articles from 2014 onward. Two reviewers conducted title/abstract screenings, full-text review, and data extraction. We extracted effect measures for treatment initiation, adherence, completion, success/cure, and reinfection by housing status. Studies underwent quality and certainty assessments, and we performed meta-analyses as appropriate.

Results

Our search yielded 473 studies, eight met inclusion criteria. Only initiation had sufficient measures for meta-analysis. Using a random-effects model, we found those with unstable housing had 0.40 (0.26, 0.62) times the odds of initiating treatment compared to those with stable housing. Other outcomes were not amenable for meta-analysis due to a limited number of studies or differing outcome definitions.

Conclusions

Among PWID, unstable housing appears to be a barrier to HCV treatment initiation; however, the existing data is limited for initiation and the other outcomes examined. There is a need for more informative studies to better understand HCV treatment among those with unstable housing. In particular, future studies should better define housing status beyond a binary, static measure to capture the nuances and complexity of housing and its subsequent impact on HCV treatment. Additionally, researchers should meaningfully consider how they define outcomes and if they truly measure the outcome of interest for someone experiencing unstable housing.

Substance Use

Causal decomposition to explore disparities in cannabis-Impaired Driving: A Sociodemographic and Behavioural Analysis Based on the Canadian Automobile Association (CAA) Surveys in Ontario, 2021-2023 Renzo Calderon Anyosa* Renzo Calderon Anyosa Robert Colonna Christine M. Wickens Michael Stewart Brice Batomen

Objective: To assess the influence of behavioral and sociodemographic characteristics on the prevalence of driving under the influence of cannabis (DUIC) in Ontario, identifying modifiable factors that account for prevalence disparities across demographic characteristics such as age, gender, and education.

Methods: Utilizing 'Drug Impaired Driving' survey data from 2021-2023, provided by the Canadian Automobile Association, we targeted English-speaking Ontario residents, aged 19-75, who consume cannabis and hold a valid driver's license. The main outcome was DUIC prevalence by demographic and behavioral characteristics. Causal decomposition analysis was applied to further our understanding of why certain demographic groups, demonstrate higher levels of DUIC prevalence, focusing on behavioral mediators including perceptions of impaired driving, concerns regarding cannabis edibles, general cannabis concerns, and concerns related to alcohol consumption.

Results: The Lifetime DUIC prevalence of 27.3%, with annual rates of 13.1% in 2021, 12.6% in 2022, and 18.0% in 2023 among the 1,897 participants. Higher DUIC prevalences were elevated among men, individuals under 35, those with secondary education or less, widowed persons, those with an income under $49,999, and daily cannabis users. Those less concerned about the impact of cannabis-impaired driving on their own safety and that of their loved ones had a higher past 12-month DUIC prevalence. Individuals believing that cannabis-impaired driving had no worse effect or was better than non-impaired driving had a higher DUIC prevalence. These patterns persisted over the survey years.

The causal decomposition identified the perception of cannabis-impaired driving as safer or benign as the primary factor in the DUIC prevalence disparity by gender, education, and age, accounting for 40%-60% of the existing prevalence differences.

Conclusion: The study identifies key demographics with higher DUIC prevalence, suggesting the need for focused intervention and policy reform. Although sociodemographic aspects are relevant, the perceptions of cannabis's effects on driving emerge as the main driver of existing disparities. Comprehensive strategies, including tailored interventions to impaired driving perceptions, are recommended to address DUIC.

Causal Decomposition of past 12-months DUIC Prevalence by Demographic Characteristics and Mediators
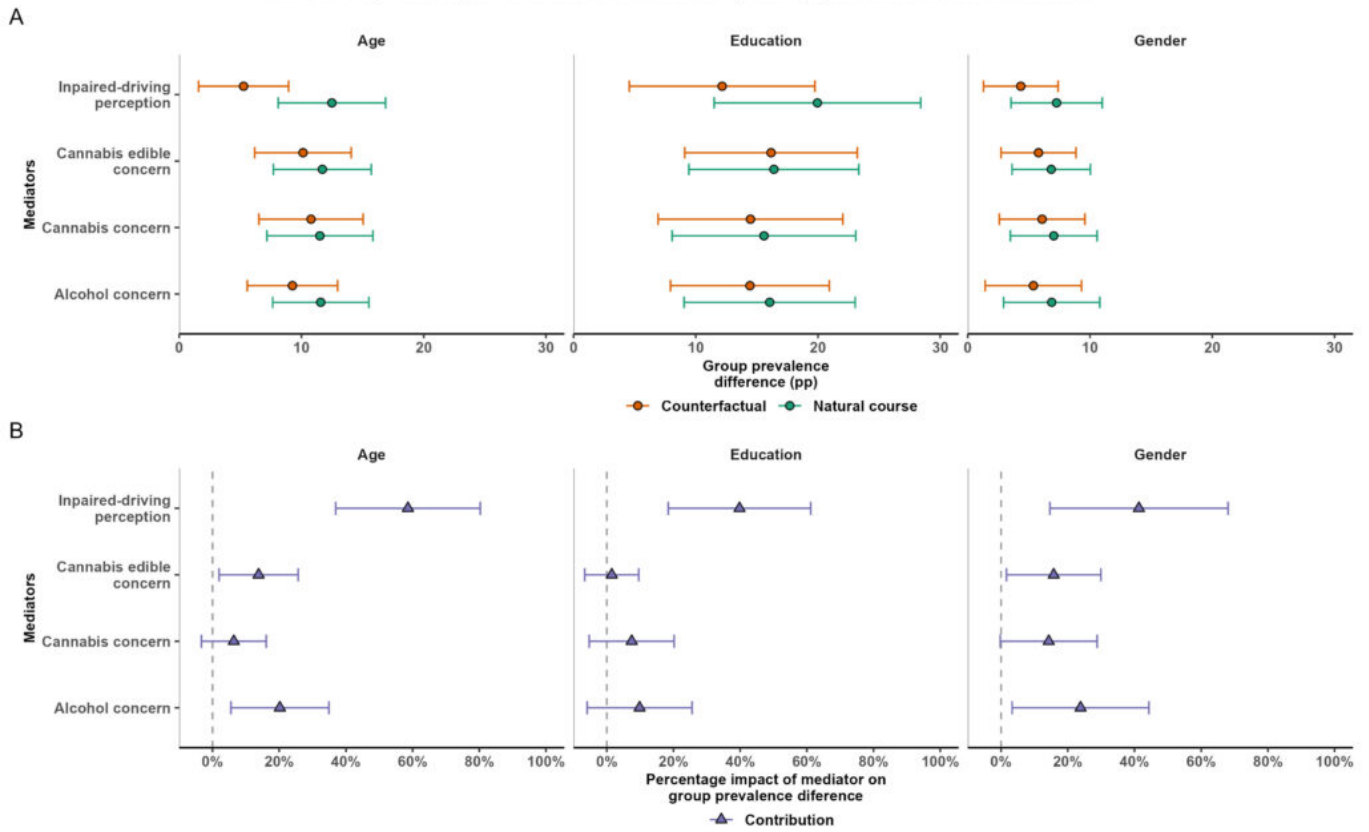
Note: The graph represents a causal decomposition analysis of DUIC prevalence over the past 12 months. Prevalence differences are presented by groups: age (<34 years, vs. 35+ years), education (secondary or less vs. higher) and gender (male vs. female). The top panel A illustrates the marginal prevalence differences among the groups. The 'Natural Course' represents the difference in prevalence with the existing levels of mediators, while the 'Counterfactual' depicts the hypothetical prevalence difference assuming the group with higher prevalence had the mediator levels of the group with lower prevalence. For instance, within the gender category using the mediator 'Impaired Driving Perception,' the 'Natural Course' denotes the existing difference between males and females, whereas the 'Counterfactual' illustrates the projected difference if males had the same level of perception as females. The bottom panel B quantifies each mediator's proportional impact on the group prevalence disparity, such as the perception of impaired driving accounting for a 40% contribution to the observed prevalence difference between genders. The error bars denote 95% confidence intervals.

Using a classification and regression tree output to understand the likelihood of fentanyl presence among people who use drugs in Rhode Island Leah Shaw* Leah Shaw Brandon Marshall Katie Biello Jane Buxton Jacqueline Goldman Scott Hadland Susan Sherman Alexandria Macmadu

Background: The United States is characterized by an unregulated and rapidly changing drug supply. In 2022, approximately 75% of overdose deaths in Rhode Island (RI) involved fentanyl. We sought to characterize sub-populations of people who use drugs (PWUD) at highest risk of fentanyl exposure.

Methods: We utilized baseline data from the Rhode Island Prescription and Illicit Drug Study, a randomized control trial of PWUD from 2020 to 2023. We evaluated sociodemographic and drug use-related covariates from the baseline survey and examined fentanyl presence in urine drug testing (UDT). Our classification and regression tree (CART) analysis highlights subpopulations at the greatest likelihood of fentanyl presence in UDT.

Results: Those with fentanyl present in UDT tended to be younger, non-Hispanic white or Latine, had recently injected drugs, and enrolled during 2022-2023 (N=446; $p<0.05$ for all). Preference for fentanyl was strongly associated with fentanyl in UDT ($p<0.001$). The CART analysis demonstrated that participants who suspected fentanyl exposure in their drugs were more likely to have fentanyl present in UDT. Preference for fentanyl also increased the likelihood of fentanyl in UDT, especially in younger participants (see Figure). Participants who were not confident that they had been exposed to fentanyl recently and who had not injected drugs in the past month were unlikely to have fentanyl present in UDT (estimated probability = 0.091). The CART model misclassified 18.31% of observations.

Conclusions: There was substantial variation in the presence of fentanyl in UDT among PWUD in RI and evidence to suggest that PWUD knew if they had recently been exposed to fentanyl. Harm reduction services for people actively injecting drugs and drug checking programs based on capacity building and empowerment targeted towards younger adults and those not yet using other services are urgently needed to support PWUD in navigating the current volatile drug supply.

Figure 1. Understanding the likelihood of fentanyl presence in urine drug testing using a classification tree.

Notes: Model trained with 300 observations and subsequently tested on remaining 142 observations. Four observations were dropped due to missing data. Model misclassification rate is 18.31%.

Substance Use

Venous thromboembolism among people with opioid use disorder: a retrospective data linkage study Myanca Rodrigues* Myanca Rodrigues Keerat Grewal Glenda Babe Tea Rosic Brittany B. Dennis Richard Perez Lehana Thabane Claire de Oliveira Zainab Samaan Kerstin de Wit Sameer Parpia

Background:

Research in other jurisdictions has demonstrated a higher incidence of venous thromboembolism (VTE) in people with opioid use disorder (OUD) compared to controls. Other studies have found that more males than females are at risk of thrombosis. However, there is a paucity of evidence in examining VTE among people with OUD in Canada, with no study conducted in Ontario to date.

Objective:

Our primary aim was to determine the prevalence of VTE among people receiving treatment for OUD over an eight-year period in Ontario, Canada. We also assessed whether there were sex-specific differences in VTE.

Methods:

We linked observational cohort data collected from 3,430 people receiving treatment for OUD between 2011 and 2021 in Ontario, Canada to health administrative databases for individuals enrolled in Ontario's public health insurance program. Commencing on the day of cohort enrolment, we included health records five years prior to study entry, and three years post-recruitment. Our primary outcome was overall prevalence of VTE over the eight-year period, which we identified using ICD-10-CA diagnostic codes and the diagnostic codes of physician billing claims. A Poisson regression model with VTE as the dependent variable was used to explore the association between sex and thrombosis.

Results:

The prevalence of VTE over the eight-year period was 4.8% (n=166, 95% confidence interval (CI)=4.1,5.6%). We did not find an association between sex and VTE (Prevalence Ratio=0.85, 95%CI-0.63,1.14), with a similar prevalence of thrombosis among both males (n=86/1916, 4.5%) and females (n=80/1514, 5.3%).

Limitations:

Since we lack a control group, we are unable to infer the incidence of VTE among this clinical population.

Conclusions:

The prevalence of VTE is high among people with OUD in Ontario, with both males and females susceptible to thrombosis. Clinicians responsible for the care of people with OUD should consider the impact of VTE on treatment course.
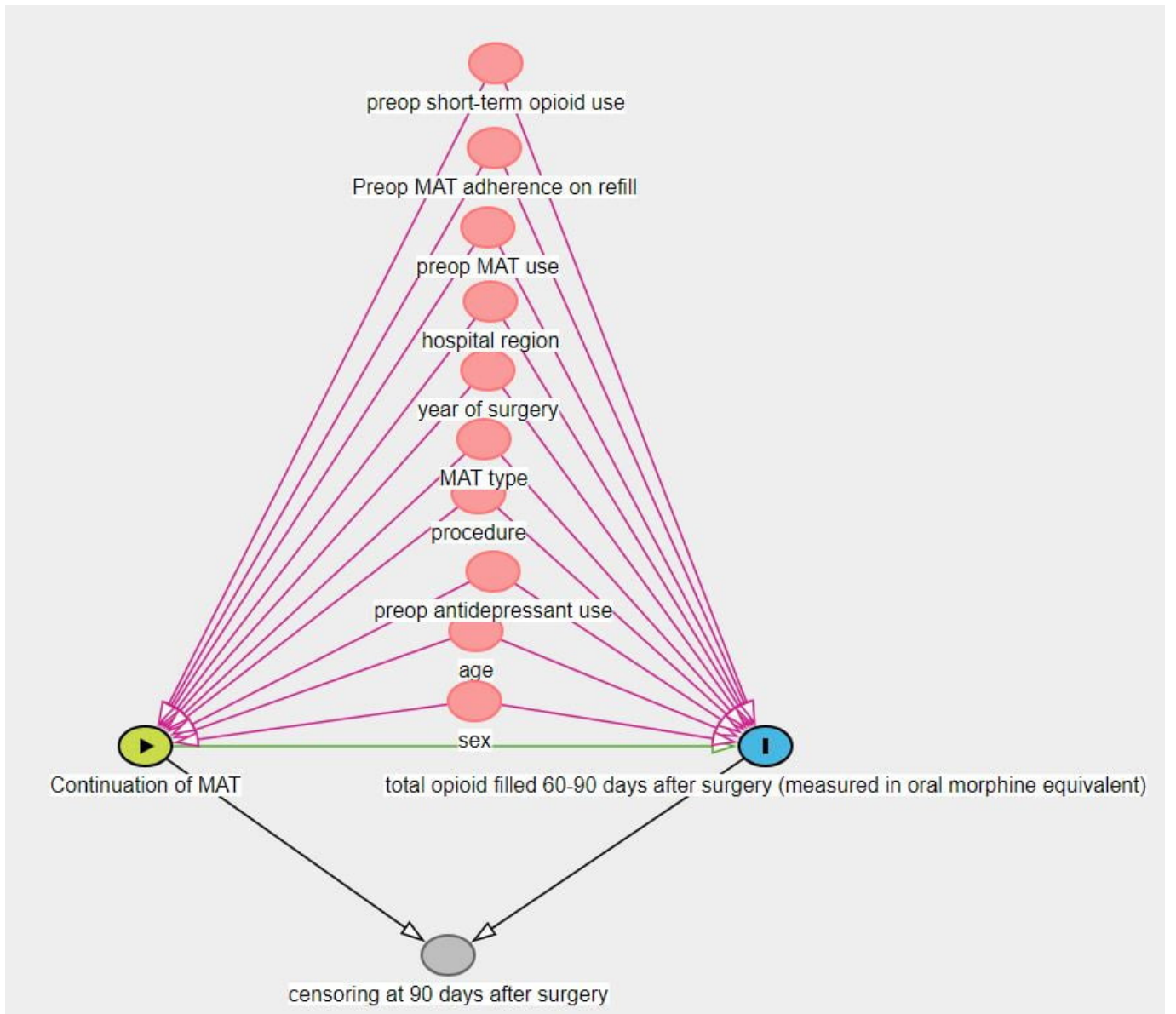
Continuation of Medication-Assisted Treatment Following Hip and Knee Total Joint Surgery in Patients with Opioid Use Disorder

Haoyan Zhong* Haoyan Zhong Zachary Shahn Faye Rim Lisa Reisinger

Background: Total hip and knee arthroplasty often involves short-term opioid use for postoperative pain, particularly challenging for those with a medication-assisted treatment (MAT) history. Medications like methadone and buprenorphine, known for receptor binding affinity and extended half-life, may hinder traditional opioid analgesic effects, raising the risk of uncontrolled postoperative pain. However, abrupt MAT discontinuation during the perioperative period may heighten relapse risk for those with opioid use disorder. Our goal, through longitudinal analysis of Marketscan database, is to assess MAT's impact on chronic opioid use in patients with a MAT history undergoing total hip and knee surgeries.

Method: The study focused on patients having elective hip and knee surgeries (2017-2021) who received methadone or buprenorphine prescriptions within 30 days before surgery. The primary outcome was total opioid prescribed (oral morphine equivalent of MAT and short-term opioid) 60-90 days post-surgery. We examined MAT continuation post-surgery as the exposure, identifying discontinuation with a >7-day gap between the first MAT refill post-surgery and the last pre-surgery MAT consumption. Inverse Probability of Censoring Weights model was used accounting for the probabilities of both exposure and censoring within 90 days after surgery. (**Figure 1**)

Results: Our analysis incorporated a total of 321 adult patients; 58.6% of patients showed continuation use of MAT after surgery. After adjusting for confounders and censoring, the difference in total opioid filled 60-90 days after surgery between the continuation and discontinuation groups was 1621 (95% CIs: -901, 4144); and the difference in short-term opioid filled was -237 (95% CIs: -689, 215)

Conclusions: No significant difference in opioid use was observed between patients continuing and discontinuing MAT after surgery, with sizable confidence intervals in both directions. Similar studies on larger samples are needed.

preop short-term opioid use

Preop MAT adherence on refill

preop MAT use

hospital region

year of surgery

MAT type

procedure

preop antidepressant use

age

sex

Continuation of MAT

total opioid filled 60-90 days after surgery (measured in oral morphine equivalent)

censoring at 90 days after surgery

Fentanyl Concentrations in Unregulated Opioids and Blood of Drug Toxicity Decedents: A Time-Series Analysis Samuel Tobias* Samuel Tobias Aaron Shapiro Andrew Tu Sandrine Merette Evan Wood Jane A. Buxton Lianping Ti

Background

Fentanyl toxicity is the leading cause of unnatural death in British Columbia (BC), Canada, largely due to fentanyl's strong potency and highly variable concentration in community drug samples. In BC, both fentanyl concentration and its variability in community drug samples has been increasing in recent years, but it remains unknown if these same trends present in post-mortem toxicology testing of opioid overdose decedents. This study aims to identify emerging trends and the possible relationship between fentanyl concentrations in community drug samples and fentanyl concentrations in post-mortem blood in the context of an ongoing drug toxicity crisis.

Methods

Data for this study were derived from the BC Coroners Service (agency responsible for investigating all unnatural deaths in BC) and drug checking sites. We analyzed post-mortem blood concentrations of fentanyl from unintentional toxicity decedents occurring in Vancouver, BC alongside fentanyl concentrations of opioid drug checking samples collected in Vancouver. The study period was January 2018 through December 2022. Blood concentrations of fentanyl were compared with monthly median concentrations of drug checking samples over time using a generalized additive model.

Results

Monthly median fentanyl concentrations of opioid samples ranged from 4.5 to 13.7%. A time-series analysis using generalized additive model adjusted for potential confounders indicated a significant non-linear association between drug checking fentanyl concentrations and blood fentanyl concentrations (edf: 3.60, chi-square: 12.63, $p = 0.020$).

Discussion

Fentanyl concentrations in both the unregulated drug supply and post-mortem blood changed significantly with the two being mutually associated. Further research into complexities of the drug supply, changing substance use patterns, and rates of fentanyl exposure among opioid-naïve individuals may explain this non-linear trend and inform strategies to abate the ongoing loss of life.
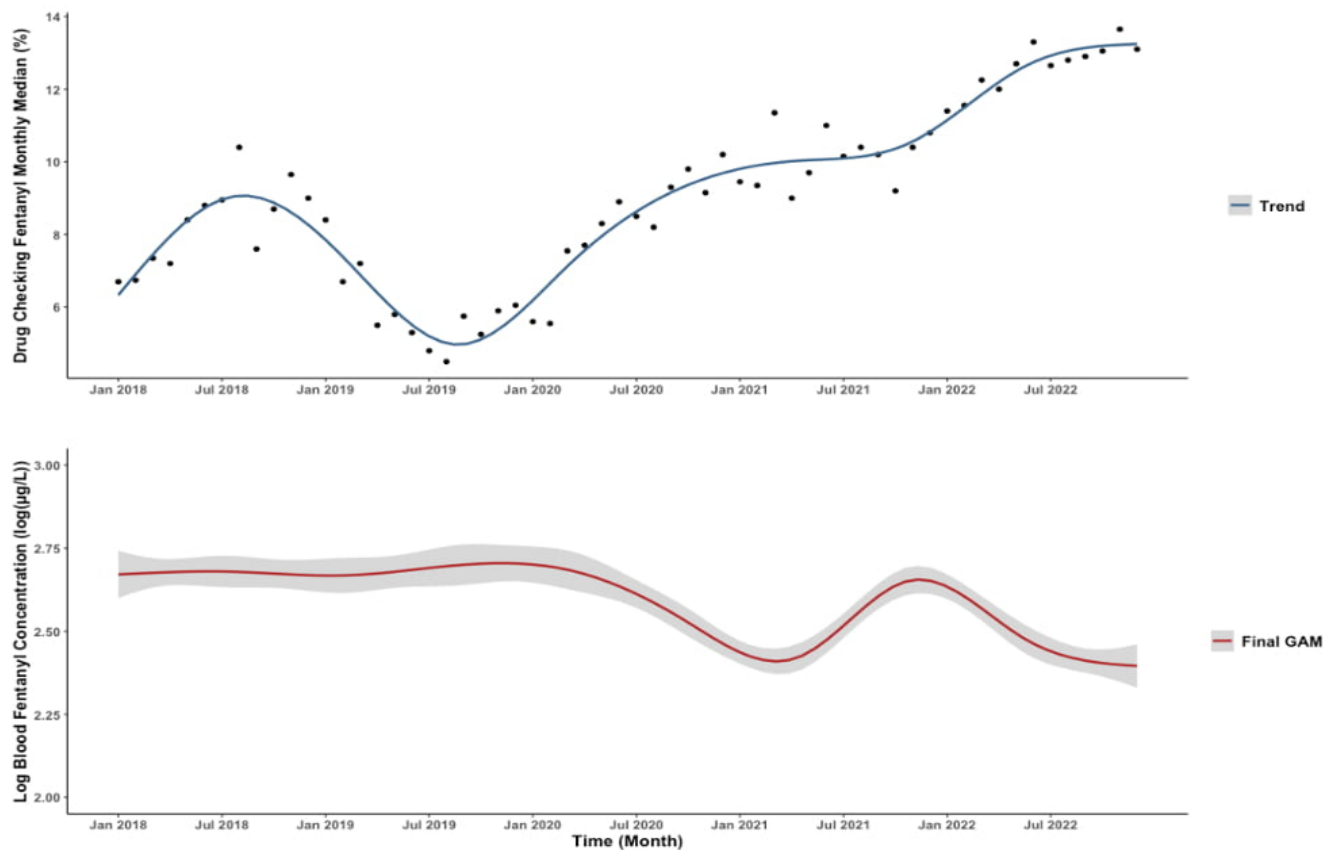
Fig 1. (Top) Monthly median fentanyl concentration of opioid samples submitted for drug checking in Vancouver, BC over time. (Bottom) A generalized additive model (GAM) of post-mortem blood fentanyl concentration over time incorporating drug checking fentanyl concentrations and adjusted for both calendar month and venous collection site.

Substance Use

Hospitalizations among people in substance use disorder treatment: a national record linkage study between 2010 and 2022 Alvaro Castillo-Carniglia* Alvaro Castillo-Carniglia Amaru Aguero Andrés González-Santa Cruza

Background. Substance use disorders are complex conditions, often requiring external triggers to evoke the need for seeking help. There is limited quantitative information on the actual incidence of negative health events influencing the decision to enter drug treatment. In this study, we analyze hospitalizations of individuals undergoing substance use disorder treatment (SUT) during 2010-2022 in Chile.

Methods. We conducted a population-based, retrospective cohort study by merging individual-level data of adults (18+) in publicly funded SUT programs with hospital discharge records from January 2010 to December 2022.

Results. Over the observed 13 years, there were about 160,000 admissions to treatment and nearly the same number of hospitalizations for individuals who underwent at least one treatment. When segmenting treatment admissions per year, the peak of hospitalizations for each sub-cohort (between 2010-2022) occurred in the same year they entered SUT.

However, this proportion decreased over the years, dropping from 20% to 8.8% in 2019 (pre-COVID-19), with an average 13.8% in the whole period. Among those who were hospitalized, the peak of treatment admissions occurred right after the discharge, with a median of 3 days in the difference between the day of SUT admission and hospital discharge (Figure 1). On average, external causes represent 4% of total hospitalizations among individuals in treatment, 3.2 times higher than hospitalizations in the general population; of these, 68% were for assault (codes X92-Y09), vs. 30% in the general population.

Conclusions. These preliminary findings showed a relative decline in hospitalizations as a trigger of drug treatment. As treatment availability increases in Chile, other sources of SUT admission (e.g., from primary health services or community outreach) are likely getting more prevalent.

Substance Use

Buprenorphine in Substance Use Disorder (SUD) Specialty Settings versus Non-SUD Settings: Trial Emulation using the Veterans Health Administration Data Haidong Lu*
Haidong Lu Thomas Thornhill Sandra Springer Ismene Petrakis Gregg Gonsalves

Background: Office-based visits involving buprenorphine prescriptions have increased significantly among non-substance use disorder (SUD) specialty and primary care clinics since 2006. We investigated whether buprenorphine prescribing in non-SUD settings and SUD specialty settings has comparable effects on retention in treatment and all-cause mortality among veterans.

Methods: We emulated a target trial using electronic health records of veterans with opioid use disorder (OUD) in the Veterans Health Administration (VHA) who initiated buprenorphine in either VHA SUD specialty clinics or non-SUD clinics between 2006 and 2019. The primary outcome was treatment discontinuation, defined as a gap of more than 30 days between the end of one prescription and the subsequent dose. The second outcome was all-cause mortality. We estimated observational analogs of intention-to-treat risk differences (RDs) and hazard ratios (HRs) while accounting for baseline confounding including patient sociodemographic factors and co-morbidities.

Results: Of 33,107 veterans meeting the eligibility criteria, 8,508 (25.7%) initiated buprenorphine treatment in non-SUD clinics, and 24,599 (74.3%) initiated treatment in SUD specialty clinics. The estimated 1-year intention-to-treat risks of buprenorphine discontinuation were 70.6% in non-SUD clinics and 63.7% in SUD clinics, resulting in a RD of 6.9% (95% CI: 5.6% to 8.1%) and a HR of 1.22 (1.18-1.26). The estimated 3-year risks of buprenorphine discontinuation were 85.9% in non-SUD clinics and 82.3% in SUD clinics, yielding a RD of 3.6% (2.6% to 4.6%) and a HR of 1.19 (1.15-1.23). The estimated 3-year intention-to-treat risks of all-cause mortality were 8.1% in non-SUD clinics and 6.9% in SUD clinics, resulting in a RD of 1.2% (0.5% to 1.9%) and a HR of 1.18 (1.07-1.29).

Conclusions: Buprenorphine prescriptions in non-SUD VHA clinics were associated with a higher risk of treatment discontinuation and all-cause mortality compared with those in SUD VHA clinics. However, both groups showed low retention on buprenorphine treatment.

Substance Use

Development and validation of the sugar-sweetened beverage addictive-like scale and its association with lipid profiles in adolescents Yun Chen* Yun Chen Pei-Wen Wu Yu-Ting Chin Chien-Hung Lee Pei-Tung Lin

The excessive consumption of sugar-sweetened beverages (SSBs) among adolescents is linked to an increased risk of obesity, type 2 diabetes, and cardiovascular disease. This underscores the importance of identifying and providing treatment for individuals with problematic drinking habits. Sugar has the ability to activate the brain's dopamine system, similar to substance addiction, leading to cravings and potentially encouraging overconsumption. The aim of this study was to develop and validate a measurement scale to assess addictive-like behaviors associated with SSB intake and investigate its relationship with lipid profiles in adolescents. Using a representative sample of 231 adolescents, exploratory factor analysis (EFA) was employed to develop the measurement scale, following the DSM-5 diagnostic criteria for substance use disorders and incorporating food addiction scales. We validated the SSB addictive-like measure utilizing confirmatory factor analysis (CFA) on another representative sample of 366 adolescents obtained from a cohort study. The association between the developed SSB addictive-like constructs and lipid profiles was analyzed using structural equation modeling (SEM). In EFA, three constructive factors, namely social impairment, impaired control, and risky use, were identified and explained 74.5% of the total variance. In CFA, the 3-factor model exhibited satisfactory internal consistency, convergent validity, and discriminant validity. In SEM, impaired control of SSB intake was positively associated higher levels of triglyceride (standardized β (sβ), 0.22) and uric acid (sβ, 0.18) after controlling for covariates. Furthermore, risky use of SSB intake showed a positive correlation with apolipoprotein B/A1 ratio (sβ, 0.20) and a negative correlation with apolipoprotein A1 (sβ, -0.25). Our study presents compelling evidence linking high-risk behavior of SSB intake to adverse lipid profiles in adolescents.

Title

Development and validation of the sugar-sweetened beverage addictive-like scale and its association with lipid profiles in adolescents

Authors

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Institute

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Abstract

The excessive consumption of sugar-sweetened beverages (SSBs) among adolescents is linked to an increased risk of obesity, type 2 diabetes, and cardiovascular disease. This underscores the importance of identifying and providing treatment for individuals with problematic drinking habits. Sugar has the ability to activate the brain's dopamine system, similar to substance addiction, leading to cravings and potentially encouraging overconsumption. The aim of this study was to develop and validate a measurement scale to assess addictive-like behaviors associated with SSB intake and investigate its relationship with lipid profiles in adolescents. Using a representative sample of 231 adolescents, exploratory factor analysis (EFA) was employed to develop the measurement scale, following the *DSM-5* diagnostic criteria for substance use disorders and incorporating food addiction scales. We validated the SSB addictive-like measure utilizing confirmatory factor analysis (CFA) on another representative sample of 366 adolescents obtained from a cohort study. The association between the developed SSB addictive-like constructs and lipid profiles was analyzed using structural equation modeling (SEM). In EFA, three constructive factors, namely social impairment, impaired control, and risky use, were identified and explained 74.5% of the total variance. In CFA, the 3-factor model exhibited satisfactory internal consistency, convergent validity, and discriminant validity. In SEM, impaired control of SSB intake was positively associated higher levels of triglyceride (standardized β (sβ), 0.22) and uric acid (sβ, 0.18) after controlling for covariates. Furthermore, risky use of SSB intake showed a positive correlation with apolipoprotein B/A1 ratio (sβ, 0.20) and a negative correlation with apolipoprotein A1 (sβ, -0.25). Our study presents compelling evidence linking high-risk behavior of SSB intake to adverse lipid profiles in adolescents.

1952 characters

E-cigarette use disparities among Virginia youth: Unraveling intersectionality of sexual orientation, race/ethnicity, and gender Mohammad Ebrahimi Kalan* Mohammad Ebrahimi Kalan Ateeqa Ijaz Aditya Chakraborty Archana Vardhan Omolayo Joy Anjorin Lisa L Lindley Rima Nakkash

Introduction:

Virginia's youth tobacco-use prevention efforts, which received an "F" grade in 2023, underscore the urgency of understanding vaping behaviors among this population. This study aims to investigate the disparities in e-cigarette use among Virginia youth considering the intersectionality of sexual orientation, race/ethnicity, and sex to inform tailored interventions and policy strategies within the state.

Methods:

Data came from the 2019-2021 Youth Risk Behavior Survey (YRBS), a nationally representative survey of high school students. The final sample comprised N=7460 Virginia high school students with valid responses to questions regarding sexual identity. Weighted logistic regression models were used to assess the association between sexual orientation (cis heterosexual, lesbian/gay, bisexual, unsure) and current vaping behavior, stratified by sex and racial/ethnic group.

Results:

Vaping e-cigarette was notably higher among most youth who self-identified as lesbian/gay, or bisexual within various race/ethnicity and sex groups compared to their cis-heterosexual counterparts. Among non-Hispanic Black students, lesbian/gay individuals showed significantly higher odds (Adjusted odds ratio(aOR)= 3.10; 95% confidence interval [95%CI]:1.34-7.15) of vaping compared to cis heterosexual students, particularly among boys (aOR=4.50; 95%CI: 1.09-18.63). Conversely, among non-Hispanic Black students, bisexual girls were more likely to vape (aOR=2.37;95%CI: 1.09-5.15) than cis-heterosexual girls. Furthermore, among non-Hispanic White individuals, bisexual students exhibited significantly higher odds (aOR=1.56; 95%CI:1.09-2.24) of vaping compared to cis-heterosexual students across all boys and girls combined. Among Hispanics, bisexual girls were more likely to vape (aOR=1.96;95%CI:1.00-3.3.83) than their cis-heterosexual counterpart girls.

Conclusions:

The findings underscore significantly higher vaping rates among lesbian/gay, or bisexual youth across diverse demographics. Notably, non-Hispanic Black lesbian/gay individuals and bisexual girls exhibited heightened vaping likelihoods compared to cis-heterosexual peers. These findings underscore the importance of considering intersectionality in understanding and addressing vaping disparities among Virginia youth.

LATEBREAKER

Substance Use

Evaluating the effect of lifting COVID-19 eviction moratoria on drug overdose death rates: an implementation of targeted learning through a modified treatment policies approach

Ariadne Rivera Aguirre* Ariadne Rivera Aguirre Giselle Routhier Ivan Diaz Kelly Doran Magdalena Cerda

During the first two years of the COVID-19 pandemic, the US witnessed 207,315 avoidable drug overdose deaths. Higher eviction rates have been associated with higher drug overdose deaths. In light of the economic turmoil caused by the pandemic, and the subsequent increased risk of eviction, 43 states and the District of Columbia implemented temporary eviction moratoria. Many of these protective measures expired between April 2020 and December 2021, leaving vulnerable households at risk of eviction. The effects of these temporary housing interventions on drug overdoses remain unexplored.

We evaluated if the expiration of state eviction moratoria was associated with higher county overdose death rates from April 2020–December 2021 in the US. We obtained mortality data from NCHS and eviction moratoria dates from the COVID-19 US State Policy Database. Additionally, we compiled a range of baseline and time-varying public health, social, economic, and policy data at the county and state level. We addressed positivity violations and time-varying confounding in this volatile period stemming from the evolution of the pandemic, using a modified treatment policies algorithm. This involved implementing a targeted minimum loss-based estimation with SuperLearner on longitudinal data to estimate the average treatment effect (ATE) and the effect of a modified treatment policy of maintaining eviction moratoria an additional month. Lastly, we accounted for clustering by estimating a state-level exposure model.

Results suggest that the ATE of lifting eviction moratoria on monthly overdose deaths is 0.2 additional deaths per 100,000 people (95%CI: 0.13, 0.27). A 1-month delay lifting moratoria could have decreased monthly deaths by 0.19 per 100,000 people (95%CI: -0.33, -0.04). These findings imply that even temporary housing measures can help curb the current overdose epidemic.

Women's Health

Oral contraceptive pill use and blood lead concentrations in U.S. premenopausal individuals: Results from NHANES 2003-2012 Kristen Upson* Arianna Foster Mandy S. Hall Nicole M. Talge Dorothy R. Pathak Renee Heffron Robert O. Wright Julio Landero Michael Yin Flavia Matovu Quaker E. Harmon Kenneth Mugwanya Andrew Mujugira Chenxi Li Kristen Upson

Oral contraceptives (OCs) are used by 151 million people worldwide for pregnancy prevention and management of menstrual disorders. Most OCs contain estrogen, which can have a bone-sparing effect by suppressing osteoclast activity. We hypothesized that lower bone turnover with current OC use decreases mobilization of toxic metal lead (Pb) stored in bone to blood. To investigate whether current OC use is associated with lower blood Pb concentrations, we conducted a cross-sectional analysis using data from the National Health and Nutrition Examination Survey (NHANES) for years 2003-2012. The study population comprised premenopausal, non-pregnant individuals ages 20-44 years with an intact uterus, at least one ovary, and not currently using injectable contraception, who had data available on current OC use and blood Pb concentrations (unweighted n=2,884). We used multivariable linear regression to estimate the percent difference in blood Pb concentrations and 95% CI between current OC users and non-users (defined as those not currently using OCs); we adjusted for potential confounding factors and accounted for the complex survey sampling design. The geometric mean blood Pb concentrations in current OC users and non-users were 0.71 µg/dl (95%CI: 0.67, 0.75) and 0.84 µg/dl (95%CI: 0.82, 0.87), respectively. After adjustment, current OC users had 11% lower blood Pb levels (95%CI: -16%, -5%) than non-users. The association persisted in analyses (i) limited to never-smokers (unweighted n=1,784) to address potential residual confounding from smoking, a substantial source of blood Pb (-10%, 95%CI: -17%, -3%), and (ii) additionally adjusting for anemia status; Pb resides in red blood cells and OCs users tend to have less menstrual blood loss (-10%, 95%CI: -16%, -5%). As no safe level of blood Pb exists, and Pb can adversely affect all organ systems, even in adulthood, further research is warranted to replicate our findings of lower blood Pb concentrations with current OC use.

Women's Health

Spontaneous abortion and ectopic pregnancy in the United States: A targeted literature review Colin Kunzweiler* Colin Kunzweiler Sandeep Basnet John Diaz-Decaro

Background: Spontaneous abortion and ectopic pregnancy are associated with myriad physical and psychological sequelae for expectant mothers and families; however, evidence describing their occurrence is limited and disparate. This study identified the rate of spontaneous abortion and ectopic pregnancy in the US.

Methods: We conducted a targeted literature review of MEDLINE and reports from obstetric/gynecologic societies. Authors reviewed titles/abstracts and full texts to determine eligibility. English-language publications of population-based or secondary data sources, surveillance efforts, or systematic reviews and/or meta-analyses, from year 2000 to September 2023 were included.

Results: 103 results from the US were identified in MEDLINE; 12 publications were included. 3 reports from the American College of Obstetricians and Gynecologists (ACOG) were included. Our review identified several definitions regarding gestational age for outcomes. Overall, spontaneous abortion/miscarriage occurs in 11%-39% of recognized pregnancies. The rate of spontaneous abortion/miscarriage is greater in women >30 years of age, and women who identify as race/ethnic minorities. In a report from ACOG, the prevalence of early pregnancy loss before 13 weeks gestation is ~10% among recognized pregnancies. Overall, ectopic pregnancy occurs in ~0.4%-2.4% of recognized pregnancies. The rate of ectopic pregnancy is greater in older women, in women who identify as race/ethnic minorities, and among Medicaid beneficiaries.

Conclusions: Among recognized pregnancies, spontaneous abortion/miscarriage is a common experience among expectant mothers and their families, while the rate of ectopic pregnancy is ~2%. Evidence is limited and professional societies cite rates from studies conducted before year 2000. Future research estimating current population-level burden of spontaneous abortion and ectopic pregnancy and examining individual and structural promotors of these outcomes is needed.

Women's Health

Emergency department utilization for mental and behavioral disorders among postpartum individuals in the context of the COVID-19 pandemic Sidra Goldman-Mellor* Sidra Goldman-Mellor Alison Gemmill Mark Olfson Jordan Jensen Shaina Sta. Cruz Claire Margerison

Pregnant and postpartum individuals faced unique challenges and uncertainties during the initial COVID-19 pandemic years, including concerns about the virus' risk to their fetus or neonate, misinformation about impact of vaccination on maternal-fetal health, and burdensome childcare responsibilities. The distinctive nature of these stressors underscores the need to examine pandemic-era mental and behavioral health in this population. Using statewide linked hospital delivery and emergency department (ED) data from California, we compared incidence of postpartum ED visits for psychiatric disorder, alcohol use disorder, drug use disorder, and assault among exposure cohorts with a delivery in "pre-pandemic" (Jan. 2016-March 2019), "transitional" (April 2019-March 2020), or "peak pandemic" (April 2020-Sept. 2021) periods. Risk ratio models accounting for cohort differences in maternal age, race/ethnicity, and insurance found that 12-month postpartum incidence of ED utilization for psychiatric disorder, alcohol, and drugs did not vary by exposure cohort. However, 12-month postpartum incidence of ED utilization for assault was substantially reduced in the transitional (RR_{adj}=0.91, 95% CI=0.86, 0.97) and peak-pandemic cohorts (RR_{adj}=0.93, 95% CI=0.86, 0.99) compared to the pre-pandemic cohort. When analyses were restricted to a 3-month follow-up period, postpartum ED utilization for psychiatric disorder increased among transitional and peak-pandemic cohorts, but RRs for other outcomes were null. Next steps are to examine heterogeneity by race/ethnicity and insurance status. Results suggest that postpartum individuals sought ED care for psychiatric and substance use problems at consistent rates during the first two pandemic years, but decreased their ED utilization for assault. Additional research is needed to understand whether these patterns result from changes in the true incidence of, vs. treatment-seeking for, these outcomes.

Women's Health

Do antibiotics help reduce hospitalizations among mastitis patients over time? Ruchir Raman* Ruchir Raman Dr Christina Ludema Ashley Judge

Background and Justification: Lactation mastitis is an inflammatory breast disease which is associated with significant maternal morbidity. The incidence of lactation mastitis has been estimated to vary between 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 very serious condition that usually requires hospitalization and treatment with intravenous antibiotics. While progression to sepsis is likely influenced by the strain of bacteria and the immune response of the individual, initial prescription of antibiotics may also influence later hospitalization. To this purpose, the current investigation aims to characterize the longitudinal association between antibiotic use among mothers with lactation mastitis and hospitalizations and whether this association is affected by socioeconomic (SES) determinants.

A cohort was constructed using claims data using sociodemographic, antibiotic use and hospitalization data available through the Optum Clinformatics Data Mart. Patients with lactation mastitis diagnosis in the dataset were identified through the ICD-10 codes O91.13 (abscesses of breast associated with lactation) and O91.23 (nonpurulent mastitis associated with lactation). Patients were followed up to check if they had any hospitalization for sepsis in the twelve months following the diagnosis. Categorical versions of the variables of interest were created, with frequencies (N) and corresponding percentages (%) tabulated at baseline.

Results: Observations for 7648 mothers with incident mastitis diagnoses have been obtained. At baseline, the population of mothers with mastitis is mostly white (5042, 65.9%), high income >=US$100K (3465, 45.3%), and have an education level of lesser than a bachelor's degree equivalent (3751, 57.1%). A longitudinal analysis of the data is currently underway.

Women's Health

Geographic Variation and Disparities in Hypertensive Disorders of Pregnancy Katherine Campbell* Katherine Campbell Lance Waller Penelope Howards Anne Dunlop Michael Kramer

Small area estimates of hypertensive disorders of pregnancy (HDP) (e.g. chronic vs gestational hypertension) are not readily available for county and local areas. Documenting local rates of disorders are of interest but generating statistically robust small area estimates can be difficult when local population and event counts are small. We use Bayesian spatial analysis to address challenges in describing county-level patterns of HDP subtypes and identifying characteristics of counties with high risk.

We abstracted birth certificate data for births to individuals ages 18 to 44 years in the US between 2009 and 2019. We model counts of each HDP subtype at the county-level via Poisson-Gamma Bayesian spatial model to estimate stable local rates of HDPs, account for spatial dependency, and identify counties exceeding the expectation of disease risk. We describe demographic and socioeconomic context based on county-specific measures to characterize counties identified as "high risk" (posterior probability of exceeding the national average) for each HDP.

Among 42 million live births in 2,869 counties, gestational hypertension rates were (7.5%) in 521 counties. Chronic hypertension rates were higher than expected (2.7%) in 513 counties and more consistently located in the southeastern US. The results revealed 204 counties exhibiting co-occurrence of high-risk for both chronic and gestational hypertension, but more than 300 counties showed subtype discordance. Differences in contextual factors were evident in counties with high-risk chronic hypertension compared to those without, whereas high-risk gestational hypertension was less strongly associated with racial density of counties and did not exhibit a clear correlation with rurality. This study underscores the question of combining HDPs for surveillance and research, given their distinct geographic distributions and the variation in their relation to place-based characteristics.

Incidence of Maternal Hemorrhage: A Systematic Analysis for the Global Burden of Disease Study Jennifer Faith* Jennifer Faith Ira Martopullo Nicholas Kassebaum Mae Dirac

Results of the Global Burden of Disease (GBD) Study 2021 are anticipated to be released in spring of 2024. As part of this study, we quantified incidence of obstetric complications, including maternal hemorrhage, for 204 countries and territories, from 1990 to 2021, and for five-year age groups from 10-54 years. We used 497 data sources to estimate incidence of maternal hemorrhage, including data from a systematic review of peer-reviewed and gray literature and from claims and hospital discharges, altogether encompassing 524 country-years from 106 countries and territories. Data included known heterogeneity in case definition, case ascertainment, denominator, and demographics, so we used Meta-Regression, Bayesian, Regularized, Trimmed (MR-BRT) to adjust sources with non-reference case definitions. Sources with aggregate age groups were disaggregated by imposing age patterns from preliminary age-specific models. We modeled maternal hemorrhage as incidence ratio, or incident cases per live birth, using a meta-regression model in DisMod-MR 2.1. Modeled estimates were multiplied by GBD-estimated age-specific fertility rates to estimate incidence rates. In 2021, we estimated 14.0 million incident cases of maternal hemorrhage, a small (1.5%) and nonsignificant decrease from the 14.2 million estimated for 1990. Incidence ratios were stable between 1990 and 2021, but incident rates decreased by 32.4%, suggesting that population increase might be a notable contributor to stable case counts over time. In 2021, incidence rates were highest in Sub-Saharan Africa, and incident cases were highest in India followed by China. We will discuss enhancements to nonfatal estimation for the upcoming round of GBD, including adding new data, enhancing adjustment of non-reference data by expanding alternative definitions and by using alternative ICD mappings of clinical data, and improving incidence ratio estimation by incorporating mortality-to-incidence ratios in the modeling process.

Women's Health

Trends in risk of pregnancy loss among US women by urban-rural residence, 2000-2018: a new tool for small domain estimation Sarah Forrest* Sarah Forrest Lauren Rossen Katherine Ahrens

Approximately 20% of pregnancies end in spontaneous loss, an outcome associated with adverse physical and psychological consequences. A previous study described increasing trends in the risk of self-reported pregnancy loss from 1990 to 2011, but it is unclear if those trends have continued or if they vary by factors such as urban-rural residence. Sample sizes of rural populations are typically small, limiting the availability of stable estimates for this population.

Data from the National Survey of Family Growth (2006–2019) were used to estimate rates of self-reported pregnancy loss (miscarriage, stillbirth, ectopic pregnancy) among US women (15–44 years) who reported at least one pregnancy conceived during 2000–2018 that did not result in induced termination (n = 17,314 women; n = 35,988 pregnancies). Trends in self-reported pregnancy loss were estimated by age group and urban-rural residence. A new small domain estimation tool, the Enhanced Modified Kalman Filter, was used to smooth estimates over groups and time. We compared relative 95% confidence interval (95% CI) widths ([upper bound-lower bound]/estimate) of model-based estimates to direct estimates.

Relative 95% CIs for model-based estimates were 35% and 53% smaller for urban and rural groups, respectively, than for direct estimates. The risk of self-reported pregnancy loss increased by a relative 3% annually for both urban and rural women 15-44 years (rate ratios [RRs]: 1.03, 95% CIs: 1.01, 1.04) from 2000-2018. The risk of loss increased among urban women aged 20-24 (RR: 1.01, 95% CI: 1.00, 1.01), 25-29 (RR: 1.01, 95% CI: 1.01, 1.02), and 30-34 (RR: 1.04, 95% CI: 1.03, 1.05) and among rural women aged 30-34 (RR: 1.02, 95% CI: 1.01, 1.03).

From 2000 to 2018, risk of self-reported pregnancy loss increased by a relative 1-4% annually among several age and urban-rural groups. A new small domain estimation tool provided substantial improvements in estimate precision relative to direct estimates.
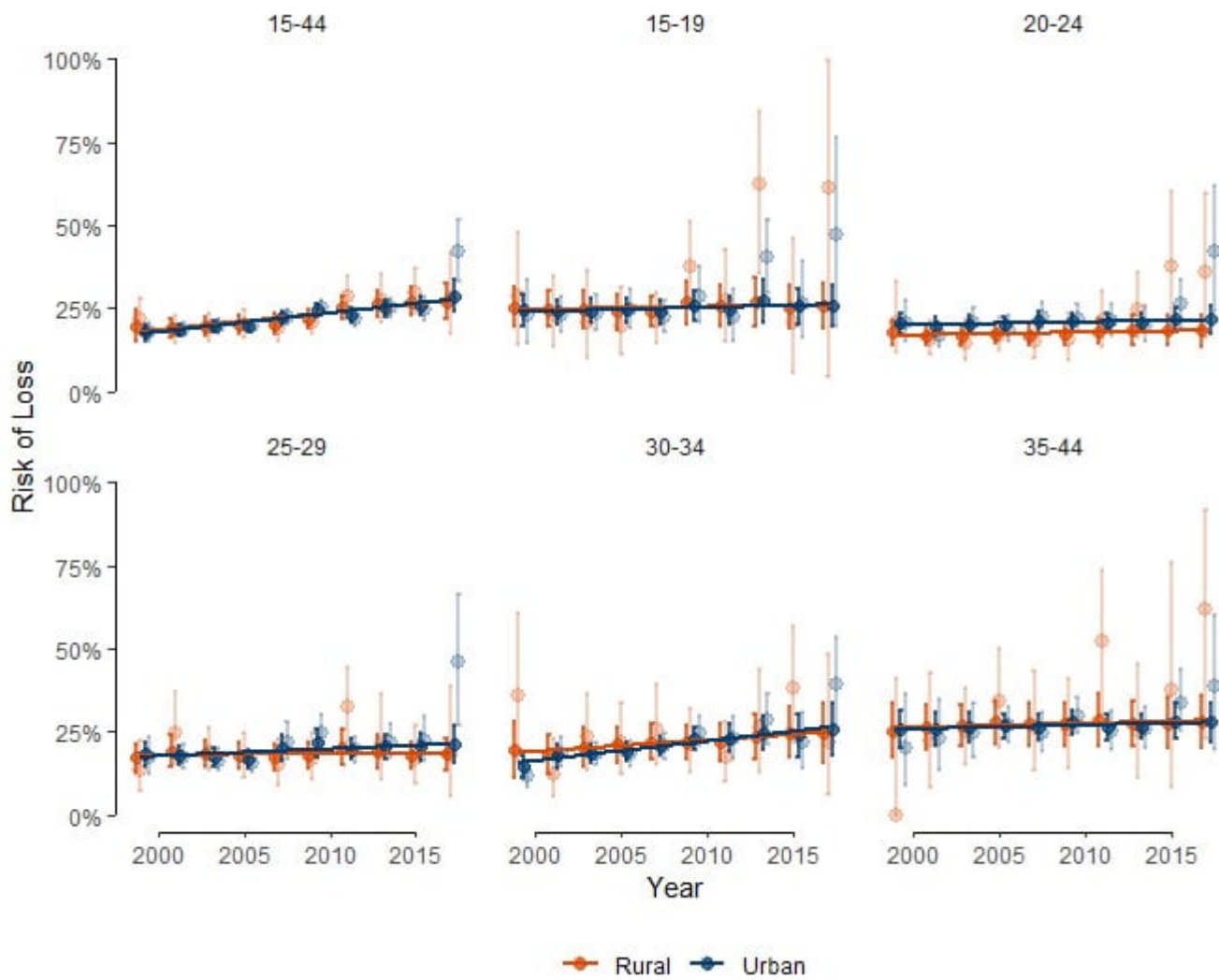
Bridging the Immunization Gap: Insights into Vaccine Coverage Among Canada's Aging Population Hussein Samhat* Hussein Samhat Arlanna Pugh Anna Maria Frescura Stephen Cule Marwa Ebrahim Julie Laroche

Background: The demographic shift towards an aging global population, coupled with immunosenescence—the weakening of the immune system with age—heightens older adults' risk of infectious diseases. Vaccination can be a crucial strategy for promoting healthy aging and preventing disease. Yet, despite vaccination's proven benefits, coverage for key vaccines like pneumococcal, tetanus, pertussis, and shingles (herpes zoster) among seniors (≥ 65 years) in Canada is notably low.

Methods: We analyzed data on 2,686 seniors from the 2023 Adult National Immunization Coverage Survey (accessed Jan 17, 2024). We adjusted survey weights for selection probability to ensure the sample's representativeness to the Canadian population. We computed weighted descriptive statistics, including frequencies and proportions for vaccine coverage. To ensure precise estimates, we utilized bootstrap weights and Wilson's method for confidence interval calculations, accounting for the survey's complex design and inherent sample variability.

Results: Preliminary findings revealed vaccine coverage rates among seniors: 54.1% [95% CI: 52.2, 56.0] for shingles, 73.9% [72.1, 75.5] for tetanus given in the last 10 years, 30.3% [28.4, 32.3] for pertussis (booster dose), and 54.7% [52.8, 56.6] for pneumococcal vaccine (one dose). Coverage varied significantly by demographics and attitudes towards vaccines, with higher estimates being reported with greater income, higher education, urban residency, being a woman, and positive attitudes. Ethnic disparities were evident, with Black seniors having the lowest coverage for tetanus and pneumococcal, Indigenous for shingles, and East/Southeast Asian for pertussis.

Conclusion: The study underscores the need for targeted public health strategies to bridge vaccine coverage gaps among seniors in Canada, emphasizing the importance of increasing awareness, improving access, and overcoming vaccine hesitancy to boost health and longevity in Canada's aging population.

Aging

Initiation of angiotensin II receptor blocker- versus angiotensin-converting enzyme inhibitor-based antihypertensive medication regimens and cognitive decline: An analysis of SPRINT Ryan M. Andrews* Ryan M. Andrews Daniel K. Addo Tom H. Greene Jordana B. Cohen Catherine G. Derington Ransmond O. Berchie Adam P. Bress

Delaying and preventing Alzheimer's disease and related dementias (ADRD) are urgent public health tasks. Both randomized controlled trials and observational studies show that lowering blood pressure with antihypertensive medications protects against ADRD; however, less is known about whether all antihypertensive medications confer the same cognitive benefits. In this study, we analyzed data from the Systolic Blood Pressure Intervention Trial (SPRINT), which randomized participants to intensive versus standard systolic blood pressure control. Our analytic sample consisted of N=1,977 participants who were followed up to 7 years and who were new users of two major classes of antihypertensive medications: angiotensin II receptor blockers (ARB) and angiotensin-converting enzyme inhibitors (ACEI). To reduce bias, we conducted our study using target trial emulation procedures, with time zero defined as the initiation of ARB or ACEI therapy and eligibility restricted to those who were not taking ARB or ACEI at the SPRINT baseline visit but initiated ARB or ACEI therapy within 12 months thereafter. Our outcome of interest was the difference in the mean rate of change in cognitive performance over time on the Montreal Cognitive Assessment for ARB versus ACEI initiators, which we estimated based on a modified intent-to-treat analysis where we fit a generalized estimating equation model with an exchangeable correlation structure and stabilized inverse probability of treatment weights to address potential confounding. Overall, we found some evidence that ARB versus ACEI therapy causes a differential effect on rates of cognitive change in Montreal Cognitive Assessment scores (B=0.018 per year, 95% CI: 0.002, 0.034). Sensitivity analyses changing our model specifications and/or using alternative measures of cognitive performance yielded similar results.

Aging

Hypothetical interventions on loneliness and memory function among middle-aged and older adults in the US Ryo Ikesu* Ryo Ikesu L. Paloma Rojas-Saunero Ashwin Kotwal Elizabeth Rose Mayeda

Background: Evidence has shown that people who experience persistent loneliness have lower memory function compared to those with transient loneliness or those who never feel lonely. However, it remains unclear whether sustained intervention on loneliness, as opposed to a one-time intervention, is more effective in preserving late-life memory function because no previous research has accounted for time-varying confounding for the association between loneliness and memory function. We aimed to examine the impact of sustained (two-time point) and one-time interventions of loneliness on memory function among middle-aged and older adults in the US.

Methods: Using the nationally-representative Health and Retirement Study in 2006–2016, we estimated the effects of [A] preventing loneliness at baseline and 4 years after baseline (sustained intervention at two time points) and [B] preventing loneliness only at baseline (one-time intervention) compared to natural course (i.e., no intervention) on memory scores 8 years after baseline. We used targeted maximum likelihood estimation to account for censoring and both baseline and time-varying confounding.

Results: The analytic sample included 16,977 participants (median baseline age, 68; 59% women). Compared to the natural course, both sustained and one-time interventions were associated with higher memory scores 8 years after baseline (0.026 standardized units [95% CI: 0.003–0.048] for the sustained intervention; 0.021 standardized units [95% CI: 0.005–0.037] for the one-time intervention).

Discussion: Our findings suggest that both sustained and one-time interventions on loneliness may be effective in preserving memory function. Future research is warranted to evaluate whether these interventions have differential impact on memory decline over a long period of follow-up.

Aging

Number of children and domain-specific cognitive function in middle aged and older adults living in the United States Meredith L. Phillips* Meredith Phillips Christina Ludema Joshua W. Brown Jaroslaw Harezlak Molly Rosenberg

Background: The number of children a person has may be associated with mid- to later-life cognitive function due to the risk and protective factors related to having and raising children, including physiological and hormonal changes, changes in sleep patterns and deprivation, stress, cognitive stimulation, and social support.

Methods: We estimated the association between number of children and cognitive function using data from the Human Connectome Project- Aging (HCP-A) (n=558, ages 36-100+). We fit linear mixed effects models with categorical number of children (0, 1-2, 3-4, and 5+) as the predictor and z-normalized cognitive scores in four domains (total cognition, memory, language, and executive function) as the outcomes, with random effects for study site. We then independently stratified models by sex and age (<60 or ≥60). We adjusted models for sex, age in years, education, employment status, and marital status.

Results: Compared to those with 0 children, men with 3-4 children had lower total cognition scores (-0.43 SD, 95% CI: -0.79, -0.07), lower memory scores (-0.40 SD, 95% CI: -0.79, -0.01), and lower language scores (-0.63 SD, 95% CI: -1.04, -0.22) but similar executive function scores. Compared to those with 0 children, women with 3-4 children had lower language scores (-0.46 SD, 95% CI: -0.91, -0.02) but similar total cognition, memory, and executive function scores. Men and women with 1-2 and 5+ children had scores similar to those with 0 children across domains. In the middle age group, total cognition was lower in those with 1-2 and 3-4 children, executive function was lower in those with 5+ children, and language scores were lower in all groups.

Conclusions: In this US sample, having a moderately high number of children was associated with decreased performance across most domains. We found this more for men than for women, with women showing lower scores only in language, while men showed lower scores in total cognition, memory, and language.
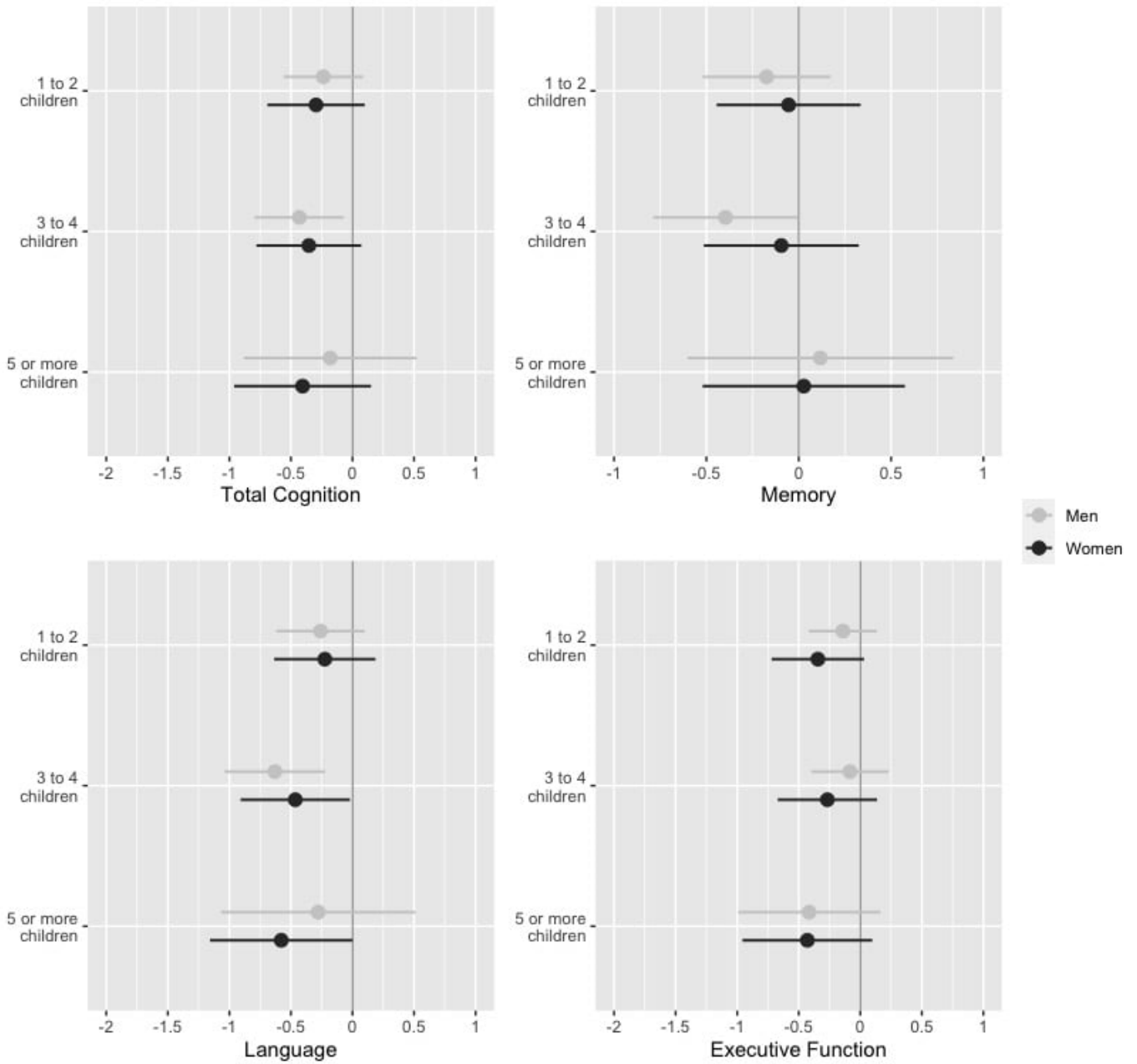
Effect Estimates for Total Cognition, Memory, Language, and Executive Function for Men and Women

Aging

Falls in the oldest old: prevalence, rate and change in rate over time in The 90+ Study
Katherine Colcord* Katherine Colcord Luohua Jiang Claudia Kawas María Corrada

Background: Falls can have serious health consequences, especially in the oldest old (individuals 90 years and older). Yet few studies have examined factors related to falls in this group. We assess fall prevalence, fall rate, and fall rate change over time by sex, living situation, and assistive device. **Methods:** Participants are from The 90+ Study, a longitudinal study of individuals 90 years and with evaluations every 6 months. Participants, or their informants, are asked how many times they have fallen in the past year (first visit) or since their last visit (follow up visits). We estimated baseline fall prevalence, longitudinal fall rate, and change in rate over time by sex, living situation, and assistive device using generalized linear mixed regression models with Poisson distribution and fixed and time-varying covariates. **Results:** In 1298 participants (mean age 92.9 years), fall prevalence at baseline was 48.6% (48.5% in men, 49.0% in women). Predicted fall rate for a 93-year-old was lower in women (0.63 falls/py) than in men (0.71 falls/py) (**Table**). Over time, fall rate remained the same in women and increased in men. Fall rate for those in nursing homes decreased over time in women and remained stable in men. In community dwellers, fall rate increased over time in men using walkers or canes, while, in women, fall rate increased over time only in cane users. **Discussion:** Individuals 90 years and older had a high rate of falls overall. Individuals in nursing homes may be less active over time or may not report falls consistently, contributing to the decrease in fall rate in this group. Individuals 90 years and older may have difficulty using a cane or may benefit from a more supportive device, contributing to the increase in fall rate in cane users. **Conclusions:** Examining falls in the oldest old is essential to establishing effective fall screening and prevention in this group.

Survival Disparities among Alzheimer's Patients in Hawaii: Exploring Racial/Ethnic Disparities and Machine Learning for Survival Prediction in the Hawaii Medicare Population Chathura Siriwardhana* Chathura Siriwardhana

Background: The survival outcomes following an Alzheimer's disease (AD) diagnosis hold significant importance for health management, caregivers, patients, and their families. Hawaii is known as the most diverse ethnic population in the US and there exist racial health disparities. This study investigates racial/ethnic disparities in survival among AD patients in Hawaii and develops Machine Learning models for survival prediction, utilizing Hawaii Medicare data.

Methods: We analyzed nine years of Hawaii Medicare data to collect information on individuals developing AD after the age of 65, tracking them until all-cause survival or censoring. We assessed the impact of race/ethnicity, in conjunction with socioeconomic status (SE), on the risk of mortality. SE status was determined using the surrogate marker: Medicare/Medicaid dual eligibility. Cox regression analysis was performed on overall survival, accounting for age at AD onset, gender, and various comorbidities. Subsequently, a Survival Random Forest was employed to predict survival within a machine learning framework, incorporating K years of longitudinal health profiles, including demographics, chronic disease profiles, observed acute conditions, and hospitalization history.

Results: The study included n = 9,393 AD subjects. Our analysis revealed that American Asians (AA) had a later age at AD diagnosis (p<.001), with an average age of 85.9, compared to 82.7 and 83.3 years for Whites (WH) and Native Hawaiians and Pacific Islanders (NHPI), respectively. SE exhibited a marginal increase in hazard (Hazard Ratio [HR]=1.36, p<.001). In comparison to AA with high SE (AA + high SE), increased hazards were found for AA + low SE (1.29, p<.001), WH + high SE (1.19, p<.001), WH + low SE (1.52, p<.001), and NHPI + low SE (1.39, p<.001). The Random Forest model with K=2 setting demonstrated a Concordance (C) Index of 0.806 via five-fold cross-validation, exhibiting robust survival predictability of AD subjects. A permutation-based study identified factors influencing subject survival.

Conclusion: The onset of AD development and survival are influenced by race/ethnicity and SE status. Machine learning, when combined with longitudinal health data, demonstrates reasonable predictability of survival.

Aging

Association between Social Participation Over Time and Cognitive Function Yu-Tien Hsu* Yu-Tien Hsu Ichiro Kawachi Jarvis T. Chen Hanno Hoven

Background

Greater social participation has been related to less cognitive decline with aging in many studies. However, there is limited understanding of how trajectories in social participation over time be associated with older adults' cognitive function in later life.

Methods

We used data from the Taiwan Longitudinal Study in Aging (TLSA), a nationally representative sample. The sample comprised participants aged 50 or above and recruited in 1989 (n = 4,400), stratified by age group (aged 50-64 years versus 65 or above). We used sequence analysis and optimal matching technique to define clustered patterns of social participation and work history in 1996, 1999, 2003, 2007, and 2011. We applied linear regression analysis to model the associations between cluster membership and level of cognitive function in 2015, measured with the Short Portable Mental Status Questionnaire (SPMSQ). We used multinomial regression analysis to explore the factors related to belong to a cluster.

Results

We identified six clusters for each subgroup. The clusters presented in the younger subgroup included: (1) socializing and helping; (2) low social participation; (3) working; (4) active in multiple states; (5) socializing; and (6) Helping. In the older subgroup, we identified the following clusters: (1) socializing; (2) helping; (3) low social participation; (4) working & low social participation; (5) helping & socializing; and (6) active in multiple states. Most participants reported changes in their pattern of social participation during the study period. However, once an individual transitioned into the low social participation cluster, they tended to stay in that cluster. In both the younger and older subgroups, we found that the working dominant cluster was associated with higher cognitive function compared to the low social participation cluster (younger subgroup: b = 0.52, 95% C.I. = 0.03 – 1.01; older subgroup: b = 2.33, 95% C.I. = 1.31 – 3.36). We also found that the multiple active social participation and working cluster was related to higher cognition (younger subgroup: b = 0.58, 95% C.I. = 0.09 – 1.06; older subgroup: b = 1.15, 95% C.I. = 0.05 – 2.26), after controlling for important covariates and accounting for censoring weights. More active patterns of social participation were found for men, at younger ages, and among non-urban residents and those without chronic disease.

Conclusion

Stable involvement in multiple types of social participation activities over time was associated with better cognitive function in older adults. Gender and urbanicity of residence were significant predictors of more active patterns of social participation.

Figure 1-1. Clusters of social participation histories, younger subgroup. (n=1,900)
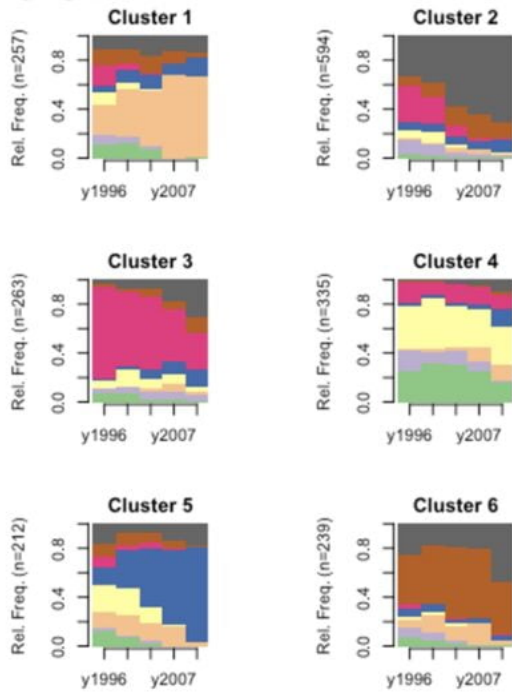
Figure 1-2. Clusters of social participation histories, older subgroup. (n=2,500)
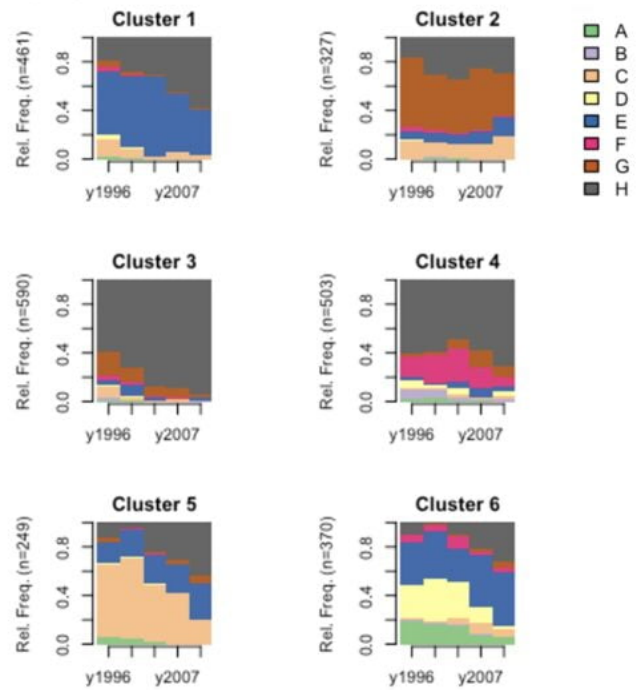
*Note: Social participation state A: helping, working, and socializing; State B: helping and working; State C: helping and socializing; State D: working and socializing; State E: socializing only; State F: working only; State G: helping only; State H: did not involve in any of the social participation types.

Aging

Effect of family caregiving on depression outcome among older European adults Sherry Hou* Sherry Hou Arijit Nandi Jee Won Park

The majority of caring for older adults is done by family members. While the conventional wisdom is that caregiving is deleterious for the caregivers' health, most studies rely on observational data and traditional regression methods, which fail to account for time-varying confounding, limiting causal inference. This analysis uses inverse probability weighting (IPW) to appropriately account for time-varying confounding in caregiving-depression relationship.

Using 7 waves (2004-2019) of the Survey of Health, Ageing and Retirement in Europe, a longitudinal survey, we estimated the effect of caregiving on depression caseness (having 4+ symptoms) comparing daily and less-than-daily caregivers to non-caregivers. We accounted for potential measured confounding and censoring by time-fixed covariates (gender, number of children, country, and education) and time-varying covariates (age, employment, marital status, income, physical limitations, psychiatric drugs, receiving help, previous caregiving, and previous depression) using IPTW and IPCW. The product of the two weights was applied to a marginal structural model to obtain the causal estimand on the prevalence difference scale. Confidence intervals were derived from bootstrapping.

Among 36,346 participants and 67,800 person-waves, compared to no caregiving in the last year, daily caregiving was associated with an 8.3 percentage point (95% CI: 6.1%, 10.5%) increase in the prevalence of depression caseness, after accounting for time-fixed and time-varying covariates. Less-than-daily caregiving was not associated with depression caseness (PD=0.8 percentage point, 95% CI=-0.9%, 2.4%).

Our results support previous findings that high levels of caregiving may increase the prevalence of depressive symptoms, while lower levels of caregiving do not. Accurate documentation of the relationship between caregiving and health outcomes is foundational in creating evidence-based policies to support healthy aging.

Table: Prevalence differences of depression caseness comparing daily and less-than-daily caregivers to non-caregivers

Caregiving status	Absolute prevalence	95% CI	Prevalence difference*	95% CI
No caregiving	32.81%	[29.74%, 35.88%]	-	-
Some caregiving	33.57%	[30.15%, 36.99%]	0.76%	[-0.88%, 2.40%]
Daily caregiving	41.09%	[37.21%, 44.96%]	8.28%	[6.05%, 10.51%]

*Compared to no caregiving

Testosterone in relation to lifespan and fertility in men and women C Mary Schooling* C
Mary Schooling Zhu Liduzi Jiesisibieke

Background: Testosterone use is controversial, with little evidence from trials. Recent genetic
evidence in humans of antagonist pleiotropy between fertility and survival suggests that testosterone
could reduce survival while promoting fertility. We used mendelian randomization (MR) to assess
sex-specific testosterone on lifespan (maternal and paternal attained age) and fertility adjusted for
relevant confounders, such as body mass index (BMI).

Methods: We identified independent (r2<0.001) genetic variants strongly (p<5e-8) associated with
testosterone and un-associated with sex hormone binding globulin, i.e., bio-testosterone (men) and
total testosterone (women) from the largest most densely genotyped genome wide association
studies (GWAS) and applied them to the largest GWAS of maternal and paternal attained age and
sex-specific participant fertility adjusted, where relevant, for sex-specific BMI from the largest
suitable GWAS

Results: Using UK Biobank GWAS, testosterone in men (n=178782), was unrelated to paternal
lifespan (n=415311) (-0.29 years per effect size, 95% confidence interval (CI) -0.69 to 0.12) but was
associated with fertility (n=209872) (0.03 children, 95% CI 0.01 to 0.06); testosterone in women
(n=230454) was unrelated to maternal lifespan (n=412937) (years -0.11, 95% CI -0.49 to 0.27) and
to fertility (n=250782) (0.01, -0.01 to 0.03). BMI from GIANT (men=152893, women=171977)
strongly decreased testosterone in men but not women. Testosterone in men was associated with
shorter lifespan -1.78 years (95% CI -0.82 to -2.77) after adjusting for BMI and remained associated
with fertility.

Conclusions: This study illustrates the importance of considering negative confounding in MR
studies. Consistent with antagonist pleiotropy, testosterone in men was associated with shorter
lifespan but more children. Whether targeting dietary and environmental drivers of testosterone
could address disparities in lifespan between men and women might bear consideration.

Midlife lifestyle factors and healthy aging in a prospective cohort of women Xiaoying Zheng*
Xiaoying Zheng Fen Wu Karen L. Koenig Yian Gu Anne Zeleniuch-Jacquotte Yu Chen

Lifestyle factors have been associated with healthy aging, however, prospective studies with long-term follow-up are limited. We aimed to examine the association between midlife lifestyle factors such as diet, BMI, physical activity (PA), and smoking status with healthy aging.

We included 4846 women who responded to the 2018 or 2021 follow-up from the New York University Women's Health Study, a prospective cohort of 14,274 women recruited in 1985-90. Lifestyle factors were assessed at baseline during midlife using standardized questionnaires. Healthy aging was determined based on absence of chronic diseases (cancer, coronary heart disease, myocardial infarction, heart failure, chronic obstructive pulmonary disease, diabetes Parkinson's, and stroke), subjective memory complaints, mental health, and physical ability at age 70 or greater, as assessed on follow-up questionnaire (2018-2021). We estimated ORs for healthy aging in relation to each lifestyle factor, controlling for other lifestyle factors and confounders.

The OR(95% CI) for healthy aging were 1.33 (1.10-1.62) and 1.33 (1.09-1.61) in relation to medium and high levels of moderate-intensity PA, compared to low level. No association was observed for strenuous or mild PA. The association between total PA and healthy aging was stronger among non-white women than white women, and for women under 45 years of age at enrollment. The OR(95% CI) for healthy aging were 1.23 (1.02-1.50) and 1.32 (1.09-1.60) in relation to medium and high levels of midlife adherence to DASH diet, compared to low level. The OR(95% CI) for healthy aging were 0.48 (0.39-0.61) and 0.27 (0.17-0.41) for women who were overweight or obese, compared to those with normal weight in midlife. History of smoking was associated with lower odds of healthy aging (OR = 0.73; 95% CI: 0.62-0.85).

Midlife lifestyle factors may be protective of cognitive function, physical ability, and absence of chronic disease later in life.

Behavior

Do New Therapies Improve Time to Diagnosis in Rare Diseases? Wesley Baisley* Wesley Baisley Betsy J. Lahue

Background

Rare disease patients often report multiple provider consultations and multi-year delays between presenting with symptoms and receiving a diagnosis (dx). The objective of this study was to explore whether newly available treatments for rare diseases contribute to earlier dx and earlier participation in research through increased general awareness of symptoms and treatments.

Methods

Three rare diseases with FDA approval 2000-2010 were selected: Gaucher's disease (GD), Fabry's disease (FD) and hereditary angioedema (HAE). Date of initial FDA regulatory approval served as a proxy for commercial availability (GD 2001, FD 2003, HAE 2010). A literature review was conducted via PubMed to identify studies published 10 years prior to commercial availability and up through to November 2023. Patient journey surveys, clinical trials, or registries reporting mean patient age at dx (primary outcome) were included. Scatter plots were used to assess reported age and study year. Linear regression assessed trends in patient age since commercial availability. Trends in volume of publications were compared pre- and post-FDA approval.

Results

Twenty-eight total studies were identified (HAE:15, GD:7, FB:6). Reported HAE age at dx (n=7 studies) decreased (R^2=0.03), while age of dx increased in GD (n=4, R^2=0.29) and was flat in FD (n=5, R^2=0.01). Age of participation increased since HAE (n=12 studies, R^2=0.20), GD (n=7, R^2=0.08) and FD (n=5, R^2=0.25) treatments became available. Results suggested 1% – 29% of variability in average age of diagnosis/participation could be explained by the increasing time since treatment availability. Most studies identified (>70%) were published within the first 10 years of availability.

Conclusion

Review of age at diagnosis and participation in studies of targeted rare diseases did not reveal that commercial availability of rare disease treatments significantly impacted age at diagnosis. Further research may be warranted to investigate this hypothesis.

Behavior

Pupillary Response as a Possible Brain Wave Analog in Children with ASD in Response to Stressful Stimulus Djellza Rrukiqi* Djellza Rrukiqi Gesulla Cavanaugh Diti Patel

Children with Autism Spectrum Disorder (ASD) have poor response to stressors and have challenges with effective stress regulation, rooted in neurodevelopmental deficits. Heightened sensory sensitivities further complicate the ability to process information during stressful events, hindering recovery and potentially impacting future interactions. The symptoms of ASD are becoming even more problematic as the rate of the disorder continues to increase nationally every year. This pilot study used a time series analysis of pupil diameter and fixation data along with electroencephalogram (EEG) data from 3 children with ASD compared to 4 children with neurotypical development (CWND). The purpose of the pilot was to assess children's response to a simulated stressor and their recovery post a relaxation phase. Data were collected using the Tobii Pro Nano, Bitbrain Versatile EEG, and the Masimo pulse oximeter. Tobii Pro lab and IBM SPSS V 27.1 were used to run multivariate analyses, including ANOVA. The results show that pupil diameter increased in both groups from baseline when exposed to stressors $F(11, 26615)= 123.43$, $p = 0.00$. While pupil responses were complementary with EEG measures and pulse rate, they varied in the ASD group even post the relaxation phase. The results from this pilot suggest that children with ASD have similar response to stressors compared to CWND but are more sensitive to stressful stimuli and have more unpredictable eye movement and physiological patterns; as such, consideration should be given to additional tools that can assess children's full recovery from stressors.

Behavior

Time Series Analysis to Decode Children's Response to Stressful Social Stimuli Shriya
Reddy* Shriya Reddy Shreeya Patel Devanshi Patel Gesulla Cavanaugh

Children with Autism Spectrum Disorder (ASD) frequently face challenges related to attention
deficits, particularly when exposed to stressful situations that hinder their ability to concentrate and
disrupt their attention spans. While numerous studies delve into the social responses of children
with ASD, a notable gap exists in eye-tracking models designed to anticipate physiological reactions
to stress within this demographic. This comprehensive two-part study adopts a time series
methodology, analyzing facial expressions, eye movement, and pupil diameter data from children
with ASD (n=17) in comparison to their neurotypical counterparts (n=13). Data in the initial stages
were gathered by using the Tobii Pro Nano, semi-structured surveys, a computer-embedded camera,
and the M-CHAT tool. For each stimulus from the generated videos, Areas of Interest (AOIs) were
created. For each of these AOIs, pupil diameter, number of saccades, and fixation were collected,
recorded, and calculated for all events of interest. To analyze this data, Tobii Pro lab and IBM SPSS
V 27.1 were utilized. From all the recordings, the results suggest that children with ASD had greater
unstable eye movement. The time series data of children with ASD revealed greater increases in
pupil diameter at the beginning of each stimulus along with considerable decreases at the onset of
stressful stimuli. No significant differences by group ($p = 0.78$) were noted for fixation duration on
objects with no social connotation (alpha 0.05, 95% CI). These findings suggest that eye-tracking
technology can be utilized to detect acute stress, attention, and disengagement in children with
ASD, offering potential support for future therapy planning tailored to their needs.

Identifying patterns of tobacco use and associated cardiovascular disease risk through machine learning analysis of urine biomarkers

Noah A. Siegel, BS* Noah Siegel Andrew C. Stokes, PhD

Tobacco use constitutes a pressing public health challenge, being the primary cause of the loss of disability-adjusted life years in the United States. The cardiovascular damage caused by tobacco is complex and nonlinear, and there is currently no dependable method for comparing exposure and harm across emerging tobacco product categories. There is a critical need to elucidate how multidimensional biomarkers of tobacco exposure influence the risk of cardiovascular harm. We employed cluster analysis, an unsupervised machine learning technique, to analyze tobacco use biomarkers drawn from the Population Assessment of Tobacco and Health (PATH) dataset with 6 waves of data from 2013 to 2021. We identified two distinctive clusters of individuals exhibiting similar patterns of tobacco exposure biomarkers. One cluster was closely associated with e-cigarettes, and another with cigarettes and dual use. We introduced a reference group composed of individuals who did not use any tobacco products and explored the connection between these clusters and clinical and subclinical cardiovascular outcomes. These clusters are visualized in figure 1. The cigarette and dual use cluster exhibited significantly higher levels of harm-related biomarkers compared to the e-cigarette cluster, which, in turn, displayed elevated biomarkers of harm in comparison to the reference group. Individuals within the cigarette and dual use cluster faced an increased risk of suffering from conditions such as myocardial infarction, stroke, congestive heart failure, or other cardiovascular diseases when compared to those in the reference group, while those in the e-cigarette cluster did not. Establishing a reliable biochemical signature for tobacco product usage holds potential for responsive, multidimensional research into the physiological effects of tobacco. Moreover, such a signature could facilitate the examination of emerging tobacco products before their effects are comprehensively understood.
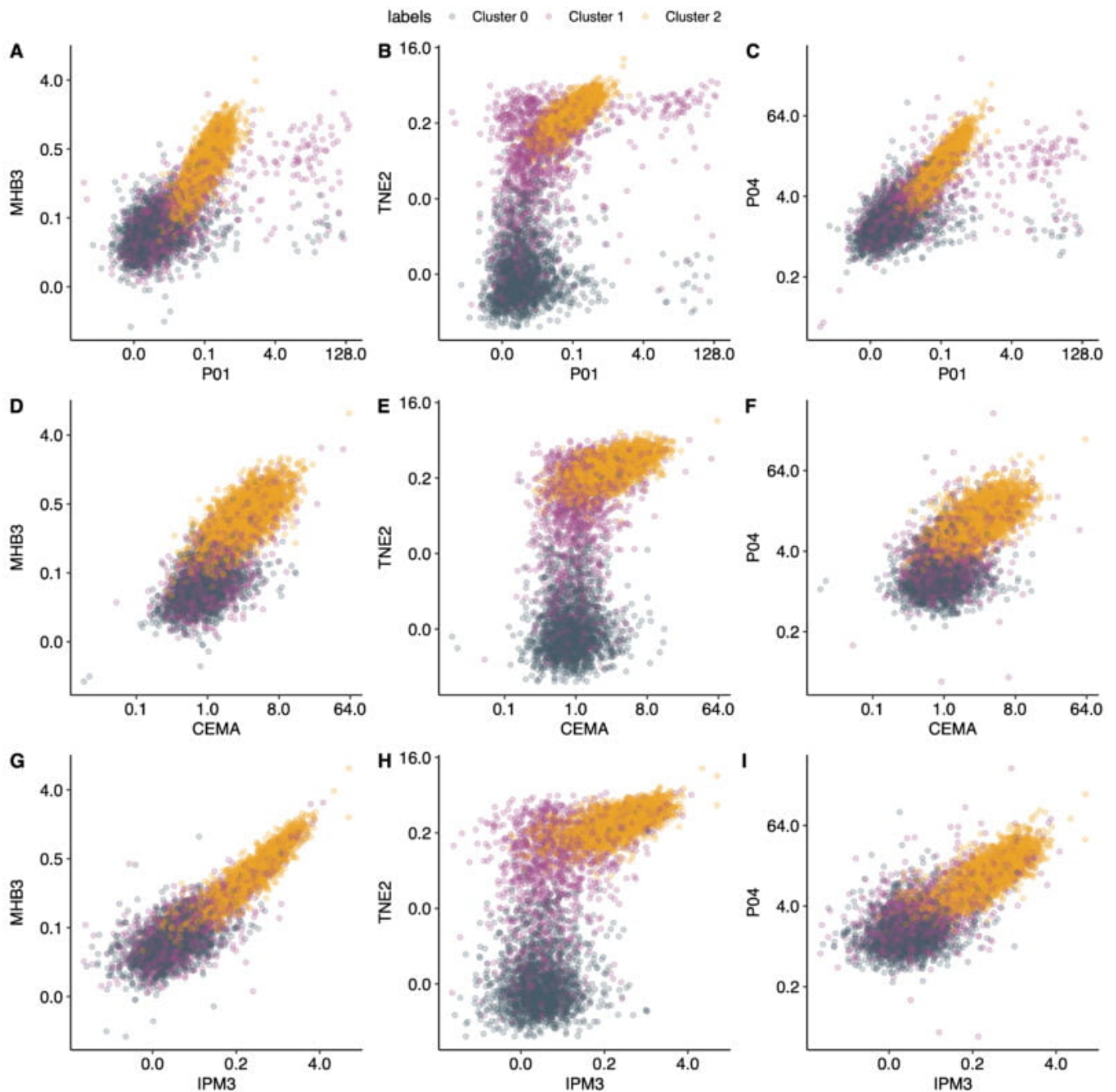
Figure 1 showing distribution of biomarkers by cluster membership. This figure demonstrates that clusters have a variety of shapes with respect to different biomarkers, and shows some of the patterns of biomarker distribution. In general Custer zero tended to have lower levels of biomarkers. Whereas Custer two had higher levels. Cluster one tended to be an intermediate cluster, and then some distributions overlapped with other clusters; this highlights the benefit of the clustering approach in its ability to elucidate these patterns and identify biomarkers of significance. Abbreviations: MHB3, (N-acetyl-S-(4-hydroxy-2-buten-1-yl)-L-cysteine (a metabolite of 1,3-butadiene; TNE2, total nicotine equivalents; P04, hydroxy fluorene (a polycyclic aromatic hydrocarbon, PAH); P01, 1-Naphthol — a PAH; CEMA, N-Acetyl-S-(2-carboxyethyl)-L-cysteine (a volatile organic compound, VOC); MHB3, N-Acetyl-S-(4-hydroxy-2-buten-1-yl)-L-cysteine — a VOC.

Estimating Heterogeneous Effects of Spousal Cardiovascular Event on Depression Toshiaki Komura* Toshiaki Komura Kosuke Inoue

Background:

Although previous studies have reported interpersonal associations between cardiovascular disease (CVD) and depression, evidence is lacking as to whether this association varies by individual characteristics. We thus aim to examine the heterogeneity in the relationship between a spouse's CVD and subsequent mental health of individuals.

Method:

Using a nationwide claims and medical database which covers approximately 40% of the working-age population in Japan, we applied target trial emulation framework to synthesize a cohort of index individuals whose spouses received first CVD diagnosis and those without the spousal CVD event between 2016 and 2019. Using 85,424 matched index individuals, we examined effect heterogeneities of spousal CVD events on depression risks of index individuals within 2 years via a novel machine learning approach, accelerated Bayesian causal forest (XBCF), adjusting for major sociodemographic characteristics, comorbidities of index individuals and spouses, health behaviors, and objectively measured physical health conditions. We built XBCF model using randomly selected 50% training sample, and evaluated the heterogeneity using the remaining 50% test sample.

Result:

During the 2 years of follow-up, a new onset of depression was observed in 1,296 index individuals (1.52%). When we applied our XBCF algorithm to the test sample, we observed a consistent increase in risk differences and odds ratios for depression due to spouse's CVD according to the ranking of estimated conditional average treatment effect (CATE; Q1 [most resilient], RD [95% CI] = -0.11pp [-0.35, 0.57]; Q2, RD [95% CI] = +0.30pp [-0.17, 0.76]; Q3, RD [95% CI] = +0.42pp [-0.07, 0.91]; and Q4 [most vulnerable], RD [95% CI] = +0.69pp [0.22, 1.17]). Individuals with high CATE were more likely to be younger, female, have fewer disease histories, and have more frequent unhealthy behaviors than those with lower CATE.

Conclusion:

The expected increases in depression risk due to spouse's CVD were heterogeneous across individuals. Vulnerable group was characterized by younger age, female, and unhealthy despite fewer prevalence of comorbidities. Future studies should elaborate on mechanisms of the spillover effect within households and targeted interventions for family members as well as a CVD patient.

The Sociome Data Commons: Pediatric asthma exacerbations on the South Side of Chicago, 2010 to 2019 Sandra Tilmon* Sandra Tilmon Sanjay Krishnan Samuel Volchenboum Jonathan Ozik Ellen Cohen Brian Furner Julian Solway
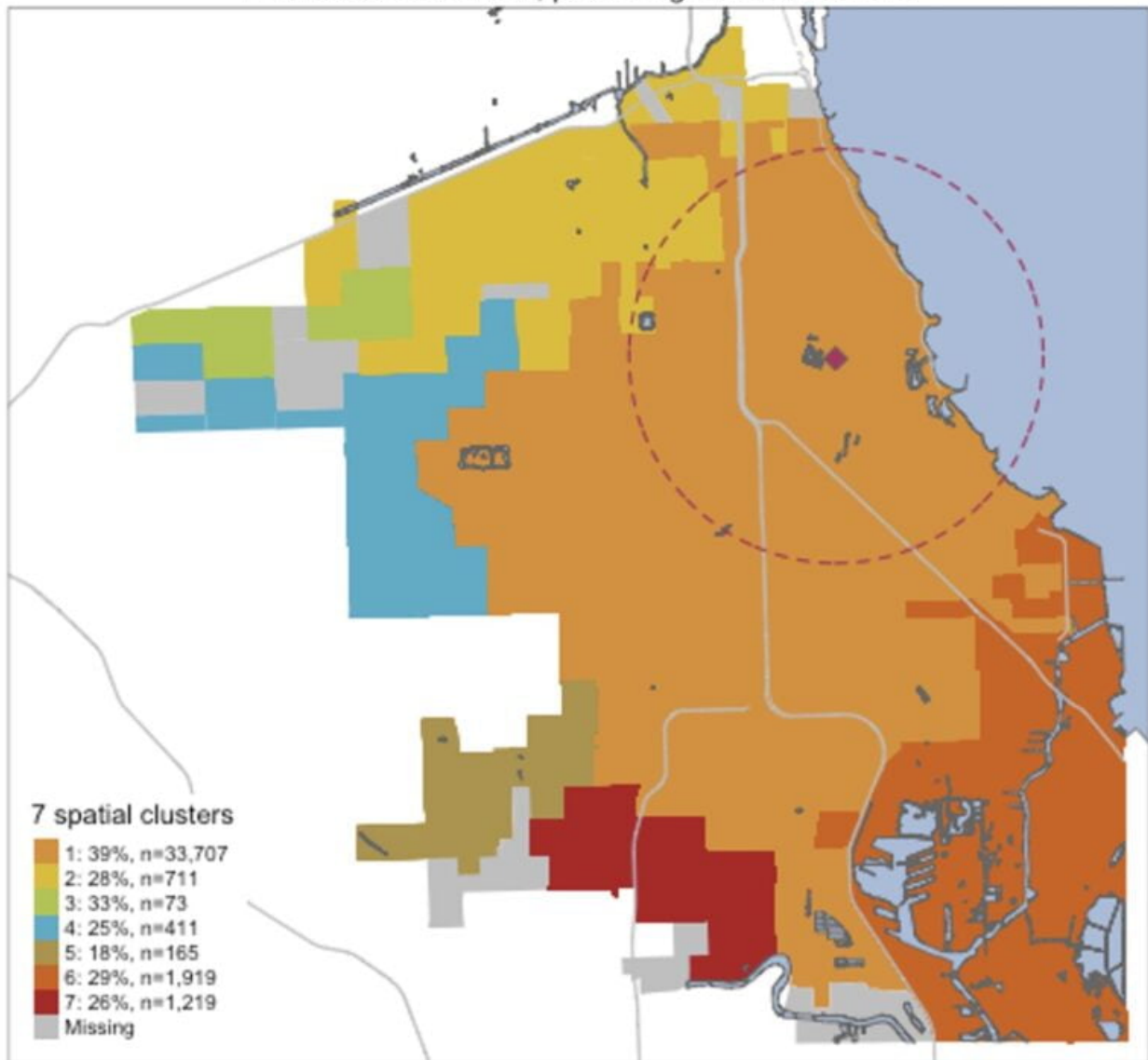
The Sociome Data Commons collects and harmonizes data about non-clinical aspects of life that affect health, from environmental to economic and social factors. By collecting a breadth of data, the Sociome aims to facilitate discovery of novel influencers of health, providing opportunities for new interventions.

In Chicago, pediatric asthma has high morbidity, persistent disparities, and has been selected as a community priority. The University of Chicago is located on the South Side of the city, serving patients mostly from surrounding communities.. For this analysis, patient race/ethnicity (largely non-Hispanic Black) was excluded to prevent overfitting on race as well as to permit later bias testing, and patient insurance (mostly Medicaid) was excluded as a proxy for poverty. Clinical covariates in the dataset include asthma phenotypes, medication, and distances to various health facilities. Non-clinical covariates include a poverty index constructed from the American Community Survey, air pollution, crime rates, tree cover, and housing conditions (including a propensity for urban flooding).

This analysis' first aim is to explore the risks associated with asthma exacerbations among pediatric asthma visits. Multiple, disparate models (logistic regression, support-vector machine, boosted decision tree, and neural network) are compared with standardized metrics of accuracy (proportion of correct predictions, positive and negative), recall (proportion of actual positives identified correctly), and R2 (proportion of variance explained). Bias is assessed on the best performing model by comparing the false negative, false omission, and true positive rates by vulnerable group status.

The second aim is to stratify by asthma exacerbation clusters (previously identified, Moran's I = 0.5958, p<.0001, see attached image) for cluster-specific risks. Implications for neighborhood or cluster-specific interventions are discussed.

Asthma exacerbations, percentage of asthma visits

7 spatial clusters

- 1: 39%, n=33,707
- 2: 28%, n=711
- 3: 33%, n=73
- 4: 25%, n=411
- 5: 18%, n=165
- 6: 29%, n=1,919
- 7: 26%, n=1,219
- Missing

Figure: Spatial clustering for asthma exacerbations as percentage of asthma visits by census tract (Moran's I = 0.5958, p<.0001), limited to tracts with at least 10 asthma visits. The University of Chicago hospital is marked by a red diamond and its 5-mile perimeter with a dashed red line. Spatial clustering showed a dominant and geographically large cluster 1 where 39% of asthma visits were for exacerbations. In contrast, only 18% of visits were for exacerbations in cluster 5. The University of Chicago hospital itself resides within cluster 1, though the cluster extends far to the south and west. Restricting clinical data to patients within cluster 1, most asthma visits were retained. However, important changes include a dramatic reduction in the South Side Hispanic population.

Methods for Deployment of a Dynamic Ecological Momentary Digital Intervention (EMI) to Improve Uptake of a 3-arm Behavioral Intervention Christian Okitondo* Christian Okitondo Angela Fertig Junia N de Brito Amanda Trofholz Jerica Berge Allan Tate

Introduction: Previous childhood obesity interventions have had limited effectiveness, partially due to inattention to competing real-time factors that influence health behaviors. Ecological momentary intervention (EMI) is a scalable, cost-effective approach to adapt to the experiences of users through real-time feedback. The ongoing Family Matters clinical trial deploys a dynamic EMI to interrupt stress processes influencing behavioral patterns shaping the family home food environment.
Objective: This study will describe an adaptive algorithm design feature of an EMI implementation, including content challenges, adaptive adjustments based on stress type and message library size, and responsiveness to user feedback, ensuring a comprehensive understanding for effective deployment.
Methodology: The Family Matters intervention study used machine learning to develop a dynamic algorithm for choosing personalized EMI messages throughout the day, aimed at enhancing family meals and reducing stress based on the stress source. The development of the algorithm was guided by two types of analyses:
1. Time-Series Analysis: Machine learning identifies and analyzes parental stress patterns influencing family meal dynamics.
2. Geospatial Analysis: Stress location (at-home vs. out-of-home) and its effect on EMI effectiveness are examined using machine learning.
Using the algorithm, morning stress report and location are then used to inform the EMI message delivered late in the day. The algorithm adapts to stress type, message library size, and user feedback. Data collected demonstrates the algorithm's adaptation, focusing on periods with consistent stress patterns.
Significance and Implications: Machine learning in EMIs facilitates adaptive interventions. Tailoring messages based on real-time stress and location sets the stage for scalable solutions enhancing home food environments and child health outcomes.

Integrating Machine Learning in Pre-Fontan Hemodynamic Studies for Enhanced Cardiovascular Outcome Prediction Tzu-Chun Chu* Tzu-Chun Chu Yanxu Yang Lazaros Kochilas Matt Oster Jessica Knight

Single ventricle congenital heart disease is a severe birth defect with significant attrition after the initial surgical repair. In advancing personalized care, assessing the impact of hemodynamics and patient characteristics on long-term outcomes is essential. Our study aims to identify key determinants of long-term survival after the Fontan procedure, the final stage of single ventricle palliation, while navigating the complexities of high dimensionality, non-linearity, heterogeneity, and issues with censored and missing data by utilizing survival machine learning (ML) models.

We queried the Pediatric Cardiac Care Consortium (PCCC), a large US-based multicenter registry of congenital heart interventions for patients undergoing the Fontan procedure from 1982-2011. Post-discharge deaths were assessed by matching with the National Death Index through 2022. Missing data were inputted using a tree-based method before model training. We fitted a random survival forest (RSF) model comprising 1000 survival trees, constructed through log-rank splitting. A permutation importance measure was used to identify the top 20 most important variables associated with long-term survival post Fontan hospital discharge.

The study involved 1,366 patients who underwent Fontan procedure (median age at Fontan = 3.1 yrs) and survived to hospital discharge of whom 172 of them died (median time to event=12.3 yrs). The out-of-bag (OOB) performance error was 0.334, and OOB ensemble mortality yielded a c-index of 0.666. The figure shows that patient baseline characteristics were predominantly chosen as important features.

Through advanced techniques, including a RSF model and permutation importance measure, we identified key determinants of late mortality post-Fontan. Further research will focus on comparing advanced survival ML models, like boosted Cox regression and support vector machines, to identify the most effective approach in predicting Fontan long-term survival in rich and complex data.

Figure. The permutation variable importance for predicting post Fontan-discharge mortality with a random survival forest (The red bar indicates a 99% asymptotic normal confidence interval does not span across zero, while the blue bar signifies the opposite).
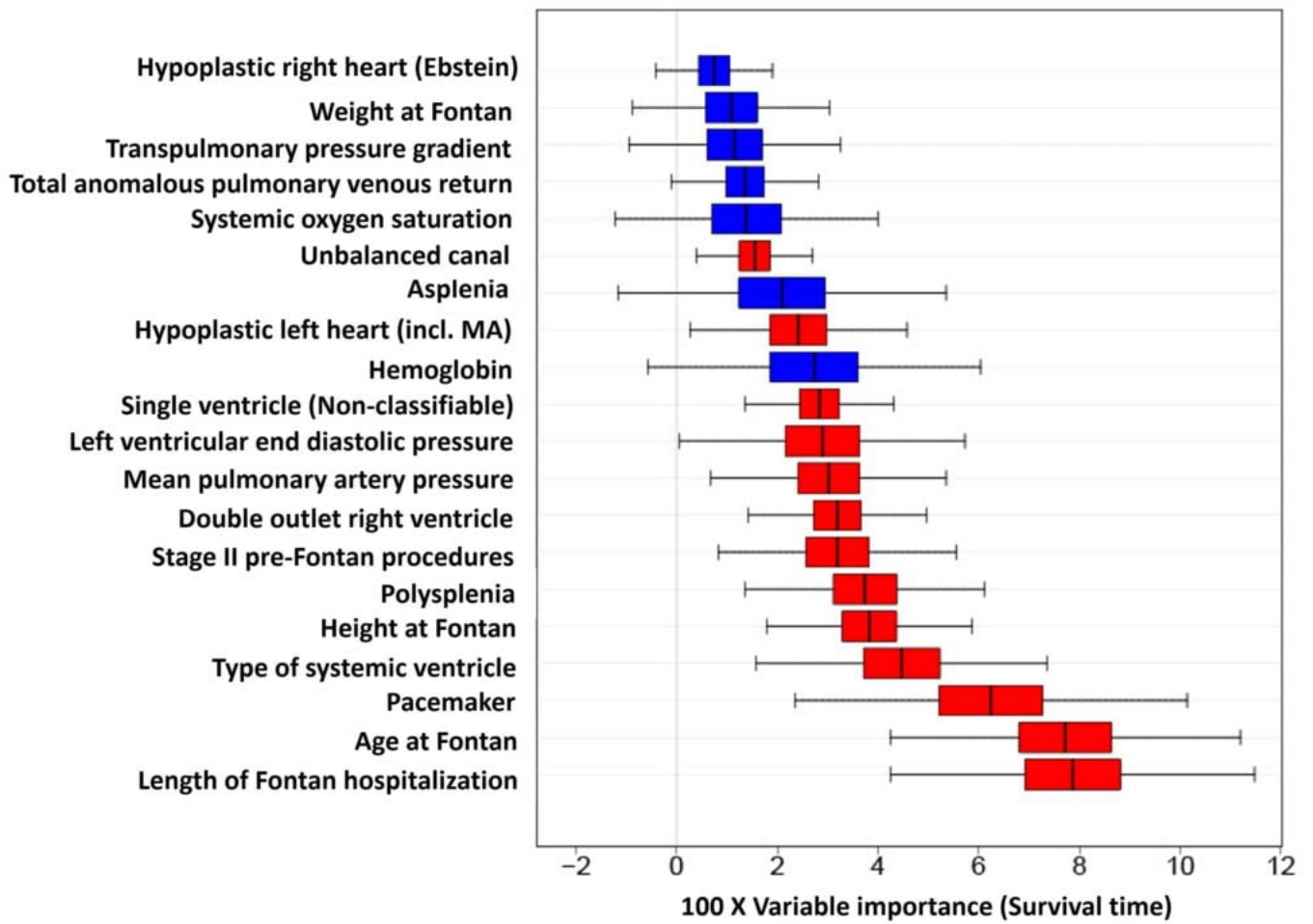
The Association of Oxaliplatin-Induced Peripheral Neuropathy, Sociodemographic, and Clinical Characteristics of Colorectal Cancer Patients with Chemotherapy Delay and Early Discontinuation Robert Hines* Robert Hines Stephanie Sutton Christopher Schoborg Shunpu Zhang Timothy Sumner

Background: The addition of oxaliplatin to the 5-fluorouracil (5FU)-based chemotherapeutic regimen in colorectal cancer patients has been shown to improve survival. However, oxaliplatin-induced peripheral neuropathy (OIPN) is the major dose-limiting toxicity with the hallmark symptom of "stocking and glove" peripheral sensory neuropathy. The purpose of this study was to assess the association between OIPN and other sociodemographic/clinical characteristics of older colorectal cancer patients with between-cycle delays in oxaliplatin administration and early discontinuation of treatment.

Methods: Colorectal cancer patients in this study were ≥ 66 years of age at diagnosis and obtained from the Surveillance, Epidemiology, and End Results database combined with Medicare claims data (SEER-Medicare). All subjects received at least two cycles of oxaliplatin. Diagnoses of OIPN and falls were defined according to diagnosis codes and were considered time-dependent exposures. Between-cycle chemotherapy delay was defined as a delay of ≥ 7 days between cycles. Early discontinuation was defined according to chemotherapeutic regimen (infusional 5-FU or oral capecitabine). Cox regression was used to obtain hazard ratios (HR) with 95% confidence intervals (95% CI).

Results: There were n = 4,566 patients available for analysis. OIPN was diagnosed during chemotherapy treatment in 4.9% (n = 225) of patients, and 1.0% (n = 45) subjects experienced a fall. Between-cycle oxaliplatin delay occurred for 57.7% of subjects (n = 2,633). OIPN was associated with a 36% increased rate of delay (HR = 1.36; 95% CI, 1.18-1.56) and having a fall was associated with a two-fold increased rate (HR = 2.02; 95% CI, 1.59-2.57). Female sex, high poverty, rural residence, and renal disease were also associated with an increased rate of delay. Early discontinuation was experienced by 24.6% of subjects (n = 1,124). OIPN was associated with a 90% increased rate of early discontinuation (HR = 1.90; 95% CI, 1.45-2.49). Female sex, older age, high poverty, noncolon tumors, and receipt of radiation all increased the rate of early discontinuation.

Conclusions: Fall prevention and therapeutics to prevent and treat OIPN are needed to decrease the likelihood of between-cycle chemotherapy delay and severe early discontinuation.

Carcinogenic Air Pollutants and Breast Cancer Risk in the Arkansas Rural Community Health Study: A Nested Case-Control Study Edgar Ellis* Edgar Ellis Sean Young Rachel Carroll Shelbie Stahr Gail Runnells Elizabeth Grasmuck L. Joseph Su Yong-Moon Mark Park Ping-Ching Hsu

Purpose: Previous epidemiological studies on the associations between outdoor air pollutants and breast cancer (BC) have not focused on rural areas in the United States, which differ in disparities and exposures compared to urban areas. We aimed to examine carcinogenic hazardous air pollutants (HAPs) and BC risk in a rural population.

Methods: Using a nested case-control design, 602 cases and 2,407 incidence density-sampled controls matched 1:4 on index age and race were included from the Arkansas Rural Community Health Study. Twelve census-tract level HAPs from the 2005 National Air Toxics Assessment were geocoded to participants' baseline addresses. HAPs were categorized into tertiles based on the control distributions. Multivariable conditional logistic regression analyses were used to estimate associations between HAPs and overall BC, and within cancer subgroups. Weighted quantile sum (WQS) regression was used to assess HAP mixtures.

Results: Adjusted models resulted in significantly decreased risk of overall BC for cadmium (ORT3 = 0.76; 95% CI 0.57-0.96), and increased risk for polycyclic aromatic hydrocarbons (PAH) (ORT2 = 1.28; 95% CI 1.03-1.59) and chromium (ORT3 = 1.26; 95% CI 1.01-1.58). Interaction analysis revealed having family history of BC positively modulated the association (Pinteraction PPD x family history = 0.14). Subgroup analyses resulted in higher risk for trichloroethylene (ORT2 = 1.68; 95% CI 1.01-2.80) among early-onset cases (≤50 years), and PAH (ORT2 = 1.31; 95% CI 1.03-1.68) and chromium (ORT3 = 1.28; 95% CI 1.00-1.65) among later-onset cases (>50 years). The WQS term was not significantly associated with BC, but chromium was weighted the most.

Conclusion: Future research is needed to obtain individual exposures and information on genetic susceptibility in this cohort to address gene-environment interactions that may be contributing to BC in rural populations.

Multimarkers of metabolic vulnerability and inflammation and risk for metabolic-associated liver cancer Ampem Darko Siaw* Samuel Antwi Ampem Darko Siaw Nicholas Johnson

Background: Metabolic dysfunction-associated steatotic liver disease (MASLD) is a rapidly growing public health problem, and a leading cause of liver cancer (hepatocellular carcinoma, HCC) in the U.S. and many parts of the world. Given the rising incidence of MASLD and the potential for many patients to progress to HCC, there is a pressing need to identify biological markers of disease progression to enable patient risk stratification and early intervention. We performed a pilot study assessing associations between three multimarker indexes; metabolic vulnerability index (MVX), metabolic malnutrition index (MMX) and inflammation index (INFX), and risk for HCC development.

Methods: A nested case-control study was performed among 52 MASLD-HCC cases and 52 MASLD controls, individually matched on age, sex, race/ethnicity, date of MASLD diagnosis, date of sample collection, and length of follow-up. Baseline, pre-malignant samples were used to measure plasma biomarkers simultaneously using nuclear magnetic resonance MetaboProfile (e.g., valine, leucine, isoleucine, citrate, high-density lipoproteins, etc.), and then aggregated into MVX, MMX, and INFX scores. These indexes were treated as continuous variables and logistic regression was used to calculate odds ratios (ORs) and 95% confidence intervals (CIs), adjusting for age, sex, race, body mass index, type II diabetes, and smoking history.

Results: Higher MVX (OR=1.06, 95% CI: 1.02-1.10) and INFX (OR=1.05, CI: 1.02-1.09) scores were associated with higher risk for HCC. No association was found between MMX and HCC risk (OR=1.04: 95% CI: 0.99-1.10).

Conclusion: These findings suggest that elevated multimarker index scores for metabolic vulnerability and inflammation contribute to HCC development in MASLD patients. These indexes could be integrated with other clinical information and genetic markers for HCC risk prediction in the setting of metabolic abnormalities.

Evaluation of dose-response between serum PFOA and testicular and kidney cancer

Alexander Riordan* Alexander Riordan Michael Anthony Capello Elizabeth Best

Introduction: In 2017, IARC classified perfluorooctanoic acid (PFOA) as a possible carcinogen for testicular and kidney cancer. Since then, two studies attempted to meta-analyze risk of these cancers by dose of PFOA (i.e. serum concentration), but only did so qualitatively or via simple methodology. We re-analyzed the dose-response relationships with a more thorough method, meta-regression, while also incorporating data from a newly published study. **Methods:** A systematic literature search was conducted to identify epidemiological studies examining the association of PFOA concentrations and risk of testicular and kidney cancer, specifically with quantitative dose estimates and associated risks. Upon retrieval, categorical dose estimates were converted to continuous estimates, using the midpoint of each category. Subsequently, doses and corresponding risk estimates were meta-regressed, using random effects methods. **Results/Conclusion:** A total of seven studies each for testicular and kidney cancer were identified, with variation on how dose was reported. Meta-regression for testicular cancer yielded a beta (slope) of 0.034 (p=0.03) per 100 ng/mL-year increase in serum PFOA concentration, incorporating a 10-year lag. For doses reported as ng/mL, the meta-regression beta was 0.0087 (p=0.05) per 1 ng/mL increase in PFOA serum concentration. Meta-regression of cumulative doses associated with kidney cancer yielded betas of 0.0032 (p=0.48), 0.0052 (p=0.47), and 0.028 (p=0.89) per 100 ng/mL-year increase in serum PFOA concentration, accounting for no lag, 10-year, and 20-year lag, respectively. Lastly, a beta of 0.0014 (p=0.21) was observed per 1 ng/mL increase of serum PFOA and increase risk of kidney cancer. All regression models demonstrated low evidence of heterogeneity as all I2 were below 22%, except one model. Our results demonstrate overall flat dose-response trends between increasing serum PFOA concentrations and risks of testicular and kidney cancer. These results are consistent with conclusions from other qualitative trend evaluations, in that associations between serum PFOA and kidney/testicular cancer are tenuous.

Cancer

Association between physical activity and quality of life among gynecologic cancer survivors in North Carolina Mu Jin* Mu Jin Jordyn A. Brown Taylor Ellington Rina A. Yarosh Yung-Fang Deng Adrian A. Gerstel Laura Farnan Hazel Nichols

Background: Physical activity (PA) can be beneficial for cancer survivors who may experience quality of life (QoL) impairments due to reduced physical function, treatment-related side effects, and psychological burdens. This analysis aims to examine the association between PA and QoL among female gynecologic cancer survivors in North Carolina (NC).

Methods: We performed a cross-sectional analysis of NC women with a registry-confirmed gynecological cancer diagnosis enrolled in the University of North Carolina Cancer Survivorship Cohort. PA levels were assessed using the Global Physical Activity Questionnaire, and QoL was measured via the Patient-Reported Outcomes Measurement Information System (PROMIS) Global 10. PROMIS scores were centered on the general U.S. population, with a mean of 50 and a standard deviation of 10. Multivariate linear regression models were used to assess the mean differences between cancer survivors with different PA levels, adjusting for covariates, including age at enrollment, race/ethnicity, BMI, education, cancer type, time since diagnosis, and any cancer treatment.

Results: The analytical sample included 669 women with a mean age of 59.9 years (SD=12.2). The mean global mental health (GMH) score was 50.1, similar to the general U.S. population, while the global physical health (GPH) score (46.2) was slightly lower than the broader population. Overall, ~74% (N=493) of survivors reported a Leisure-Time Physical Activity (LTPA) less than the Physical Activity Guidelines for Americans recommended 150 min/wk and were categorized as inactive or insufficiently active. Compared to inactive or insufficiently active survivors, active survivors (N=176) had significantly higher QoL scores (beta=2.5, P<.001 for GMH and beta=3.1, P<.001 for GPH), adjusting for all covariates.

Conclusion: Inactiveness or insufficient PA was common among gynecological cancer survivors living in NC and was associated with worse self-reported mental and physical health status.

Cancer

Acculturation, fatigue, and stress in Hispanic/Latino colorectal cancer survivors Nicole C. Lorona* Nicole Lorona Stephanie L. Schmit Jane C. Figueiredo

Background: Acculturation is associated with poorer psychosocial health and greater colorectal cancer (CRC) burden in the Hispanic/Latino population. We examined the effect of acculturation on fatigue and stress in Hispanic/Latino CRC survivors.

Methods: The present study included 964 men and women aged 21 and older, self-identifying as Hispanic, and newly diagnosed with CRC in Los Angeles, California, beginning in 2008. Validated measures of fatigue and stress were collected using English and Spanish versions of the Multidimensional Fatigue Symptom Inventory–Short Form (MFSI) and the short Depression Anxiety Stress Scales (DASS-21). Items from each measure were summed to create discrete summary scores and were further categorized into quartiles. We fit ordinal logistic regression models to quantify the association between proxies of acculturation (language preference and US/foreign-born status) and fatigue and stress scores. We fit multinomial logistic regression models to examine the associations for score quartiles.

Results: Participants whose preferred language was Spanish had a higher median age at diagnosis, were more likely to have rectal tumors, and were less likely to smoke cigarettes or drink alcohol. Adjusting for age, sex, body mass index, alcohol, smoking, education, and work-related physical activity, Spanish language preference was associated with lower fatigue scores (OR:0.63; 95%CI:0.47-0.83) and lower stress scores (OR:0.82; 95%CI:0.62-1.09). Most notably, Spanish speakers had 56% lower odds of being in the highest quartile of fatigue score (95%CI:0.28-0.73) than English speakers. Foreign country of birth was associated with lower fatigue (OR:0.78; 95%CI:0.60-1.03), but not stress scores (OR:0.97; 95%CI:0.74-1.27).

Conclusions: Hispanic/Latino CRC survivors with higher levels of acculturation report higher levels of fatigue and stress post-diagnosis.

Cancer

The Association Between Persistent Poverty and Pediatric Cancer Survival: An Analysis of SEER Data Emma Hymel* Emma Hymel Krishtee Napit Josiane Kabayundo Shinobu Watanabe-Galloway

Objectives: Cancer is the leading cause of death by disease among children under 15 in the US. Pediatric cancer outcomes are impacted by multilevel exposures, however the full extent to which the social determinants of health impact pediatric cancer survival is not well understood. The objective of this study was to examine the association between persistent poverty and pediatric cancer survival in the US.

Methods: In this population-based longitudinal study, we used data from the Surveillance, Epidemiology, and End Results (SEER)-22 registries database. All primary cases of malignant cancer diagnosed among children aged 0-19 at diagnosis from 2006-2020 were included. Cox proportional hazards modes were used to compute crude and adjusted hazard ratios (aHRs) for the association between persistent poverty and survival. Models were adjusted for age, sex, race/ethnicity, cancer type, and rurality.

Results: 97,132 children were included in our study; 12.63% resided in a persistent poverty census tract at the time of diagnosis. The 5-year relative survival rate was lower among children in persistent poverty census tracts (81.25%, 95% CI: 80.48-81.99%) compared to children living in non-persistent poverty census tracts (85.35%, 95% CI: 85.09-85.60%). In the adjusted model, living in a persistent poverty census tract was associated with a higher risk of cancer death (aHR=1.15, 95% CI: 1.10-1.21). Persistent poverty was associated with survival for children with leukemias (aHR=1.20, 95% CI: 1.09-1.31), central nervous system tumors (aHR=1.14, 95% CI: 1.04-1.26), and hepatic tumors (aHR=1.37, 95% CI: 1.01-1.85). There was no significant interaction between persistent poverty and rurality.

Conclusions: Our study observed lower cancer survival rates among children in persistent poverty neighborhoods. Further research is needed to identify multilevel interventions to mitigate disparities in pediatric cancer outcomes and to examine geographic differences in these disparities.
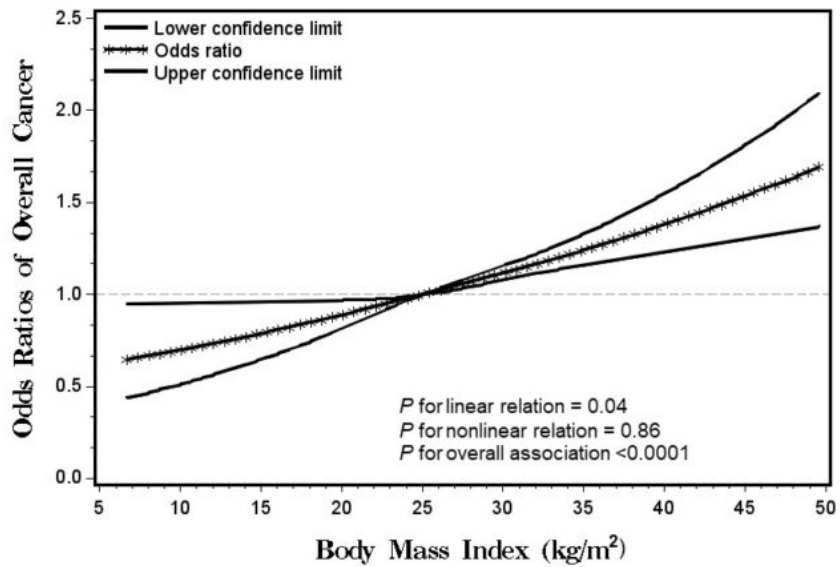
Cancer

Body Mass Index is Positively Associated with Overall Cancer Risk Among College Students in the United States: Results from the National College Health Assessment Shenghui Wu*

Shenghui Wu

Background: To understand the dose-response relation between body mass index (BMI) and cancer, as well as the associations between overweight/obesity and overall cancer risk in US college students, we conducted the first epidemiologic study to examine these associations using data from the American College Health Association-National College Health Assessment (ACHA-NCHA).

Method: The ACHA-NCHA provided self-reported data on demographic information, physical activity, BMI, smoking status, and overall cancer during 2019-2022 (n=275,185; 0.08% cancer cases). A cubic spline model and logistic regression analyses were used to evaluate associations between BMI and cancer risk adjusting for covariates.

Result: The cubic spline observed that BMI (kg/m2) was positively associated with the odds of overall cancer risk after adjusting for age, sex, race, ethnicity, education level, physical activity, and smoking status (P for linear relation=0.02 and P for overall association<0.0001); a one kg/m2 increase in BMI was associated with a 1% increased overall cancer risk. Multivariable-adjusted logistic regression analyses showed that overweight (30>BMI≥25 kg/m2)) [odds ratio (OR): 1.20 (95% confidence interval (CI): 1.08-1.34)], and obesity (BMI≥30 kg/m2) [1.48 (1.32-1.65)] were positively associated with cancer risk.

Conclusion: BMI, especially overweight/obesity, may be positively associated with overall cancer among college students in the US. To reduce cancer risks, targeted interventions to keep healthy weight among college students are warranted.

Figure 1. Smoothed Plot for Odds Ratios (ORs) of the Overall Cancer Risk According to Body Mass Index (BMI) (kg/m^2). The ORs were estimated by using the restricted cubic-spline logistic regression models with knots placed at the 5th, 50th, and 95th percentiles of BMI. The model was adjusted for age, sex, race, ethnicity, education, physical activity, and smoking status.

Cancer

Community Cancer Incidence Evaluations Near Ethylene Oxide Sterilization Facilities

Hannah Mazzotta* Hannah Mazzotta Tony Cappello Alex Riordan

Introduction: Ethylene oxide (EtO) is a highly reactive alkylating agent and gas used as a sterilizing agent in medical equipment and food, among other uses. Exposure to EtO has been associated with lymphoma, leukemia, stomach, and breast cancers, and recent literature has indicated that EtO emissions from commercial sterilization facilities could contribute to elevated cancer risks in nearby communities. However, much research to date has been focused on calculated risks with little to no information available on actual EtO-related cancer incidence rates experienced by residents living near sterilization facilities. **Methods:** A literature search was conducted to identify state or local health department reports that assessed EtO-related cancer incidence in locations near sterilization facilities. Reports which only assessed EtO exposure or were not located near sterilization facilities were excluded. Eight state health department cancer assessment reports across five states published between 2018 and 2023 were selected and assessed by location, years evaluated, cancer type, latency period, and standardized incidence ratios (SIRs). **Results/Conclusion:** The number of calculated SIRs assessed in each report ranged from 10 to 52. The proportion of statistically significant SIRs per each report was calculated to provide a means of comparison between locations, ranging from 0% to 13.3% for each report with an average of 8.3% [10 out of 120 total reported SIRs] across all reports. As such, communities living near sterilization facilities were largely found not to have experienced significantly increased EtO-related cancers relative to their respective regional or state data. These results are consistent with the available peer-reviewed environmental EtO exposure literature, which have generally reported non-significant to weak associations between environmental EtO exposure and cancer rates in their assessed spatial regions. While these community reports represent a small sample size and did not attempt to control for confounding variables such as SES or occupation, they remain a valuable tool for assessing the burden of EtO-related cancer in communities surrounding sterilization facilities until further data can be collected.

State-specific and Socio-demographic Disparities in Breast Cancer Screening Among US Women

mOHAMMAD eBRAHIMI kALAN* Mohammad Ebrahimi Kalan Ateeqa iJAZ Aditya Chakraborty Brett J. Sierra Mohan D. Pant Glenn A. Yap Brian C. Martin

Introduction

Breast cancer remains a leading cause of cancer death among American women. Early detection of breast cancer through screening plays a crucial role in facilitating more manageable and effective treatment. Here, we examined state-specific and socio-demographic disparities in adherence to the US Preventive Services Task Force (USPSTF) guidelines for breast cancer screening.

Methods

Data came from 105,833 US women aged 50-74 years who participated in the 2022 Behavioral Risk Factor Surveillance System and self-reported biennial mammography screening adherence as USPSTF recommended. Weighted frequencies were calculated to assess breast-cancer screening rates by US states, territories, and demographic factors. Multivariable log-binomial regression models were employed to estimate the factors associated with meeting USPSTF breast-cancer screening guidelines. Adjusted OR (AORs) with 95% CI were reported.

Results

Among women at average risk for breast cancer, 76.5% (estimated 36.7 million) met the breast cancer screening guidelines, with Rhode Island (85.9%) having the highest prevalence and Wyoming (65.2%) lowest prevalence among US states (Figure 1). Among those who met screening guidelines, 62.1% were in the age range of 50 to 64, 67.4% identified as non-Hispanic white, and 84.3% resided in metropolitan counties (urban vs rural). The regression model revealed that Hispanic (AOR=1.39; 95%CI:1.16-1.66; p=0.0004) and non-Hispanic Black (AOR=1.70; 95%CI:1.50-1.93; p<.001) women demonstrated greater adherence to USPSTF guidelines compared to their non-Hispanic White counterparts. Women with high school or above education (vs <high school; AORs ranged 1.43-1.78; ps<.05), those with an annual income of 35k and above (vs <35k; AORs raged 1.25-1.82; ps<.05) and insured (vs uninsured; AOR=3.95; 95%CI:3.23-4.83; p<.001) were more likely to adhere to the USPSTF guideline. Women who were American Indian or Alaska Native (AOR=0.61; 95%CI:0.42-0.89; p=0.01), had self-reported disability (AOR= 0.80; 0.73-0.88; p<.001) and avoided medical care because of cost (AOR= 0.61;95%CI:0.52-0.71; p<.001) were at greater risk of not adhering to the guideline. While retired (vs unemployed: AOR=1.27; 95%CI:1.04-1.54; p=0.01) women were more likely to adhere to the guideline, there were no significant differences among employed women or by their metropolitan counties (ps>0.05).

Conclusions

Over 75% of US women between ages 50-74 met breast cancer screening guidelines but with notable disparities. Hispanics and non-Hispanic Black women showed higher adherence, while lower education, income, cost-related medical care avoidance, and disability were linked to lower guideline adherence. Essential policy interventions are needed to ensure equitable access, early diagnosis, and, ultimately, to save lives through improved breast cancer screening.

Figure 1. Breast Cancer Screening based on USPSTF* guidelines among US states and territories, BRFSS* 2022
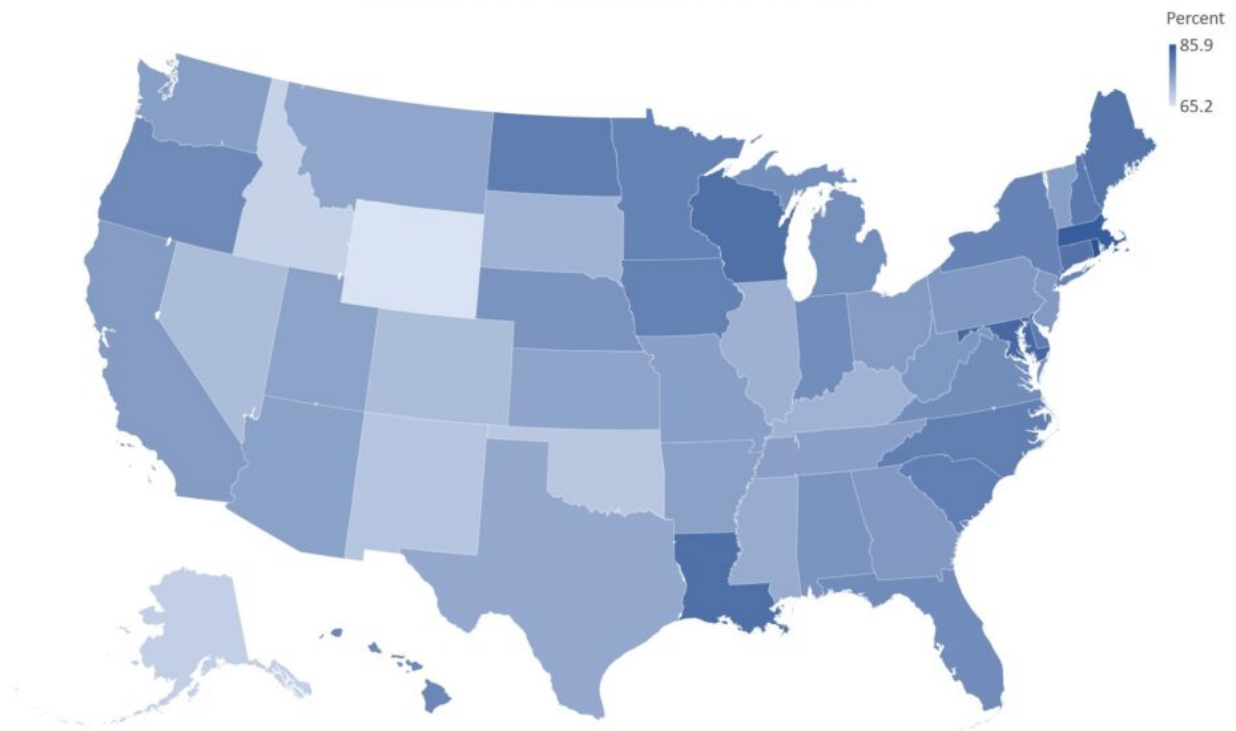
*USPSTF=US Preventive Services Task Force; BRFSS=Behavioral Risk Factor Surveillance System

Cancer

Tertiary prevention in leukemia patients: a literature review Nikita Manyak* Nikita Manyak Mingyi Chen Su Yon Jung

Background: After an extensive search, a literature gap in the tertiary prevention of leukemia patients and discussions on prognosis was identified. To address this, we conducted a comprehensive literature review, focusing on the last decade's publications.

Method: Utilizing MEDLINE and PubMed electronic databases, we performed a thorough search using key terms "progression-free survival (PFS) leukemia," restricting results to the English language within the last decade. From the initial 1,083 papers, relevant data and treatment recommendations for leukemia patients were extracted.

Results: Standard treatments like Daunorubicin, Doxorubicin, or Asparaginase for children, adolescents, and young adults (18 to 24 years) showed high relapse rates and complications within 5 years post-treatment. Notably, Blinatumomab and Ibrutinib-Rituximab demonstrated higher success rates in PFS and overall survival compared to other chemotherapy options. Two-year disease-free survival was 39.0% with intensive chemotherapy, whereas it rose to 54.4% with anticancer drugs. Additionally, patients treated with radiotherapy after relapse exhibited better long-term prevention of relapse and higher overall survival rates of 77.7% in comparison to the 11.3% in patients not treated with radiotherapy. For most pediatric leukemias, allogenic stem cell therapies have been found to be the most effective treatment with a higher rate of remission. In particular, Tisagenlecleucel, a chimeric antigen receptor (CAR) T-cell therapy, has been approved to treat pediatric leukemias when they have relapsed after initial or tertiary remission with a 5 or 10 year survival rate of 50%.

Conclusion: In the decade-long study of standard leukemia treatments for children and adolescents, CAR T-cell immunotherapy emerges as the most effective post-relapse option. Further research is warranted on immunotherapies across diverse age groups from a tertiary prevention perspective.

Cancer

Rural-Urban Differences In Timing of Medicaid Enrollment Among Cancer Patients: An Analysis of SEER-Medicaid
Anjelica Elizondo* Anjelica Eliondo Dr. Gabriel Benavidez

Background: Previous work has shown that among Medicaid enrollees, those enrolled prior to their cancer diagnosis, compared to after, have better cancer outcomes (i.e. stage at diagnosis and survival). No research has examined whether there are rural/urban disparities in early vs late Medicaid enrollment among cancer patients.

Methods: Data came from the Surveillance Epidemiology and End Results program Medicaid linked dataset. We classified patients as being enrolled either prior to or after their cancer diagnosis. A mixed effects multivariable logistic regression model was used to examine the relationship between county of residence rurality and Medicaid enrollment timing. A state level random intercept was included in the model to account for state-to-state variation.

Results: For breast (n= 44853), colorectal (n= 21908), and lung (n= 35666) cancer patients approximately, 13.0%, 16.0%, and 20.0% lived in a rural county, respectively. For each cancer type, compared to their urban counterparts, rural patients had significantly higher odds of enrolling in Medicaid after diagnosis. Odds of being enrolled in Medicaid after diagnosis were 1.08 (95% CI: 1.01, 1.16), 1.15 (95% CI: 1.05, 1.25), and 1.20 (95% CI: 1.13, 1.28) times higher for rural breast, colorectal, and lung cancer patients than urban patients, respectively. Additionally, a significant (p<.001) state-to-state variation is explained by our random intercept for each cancer type.

Conclusions: For breast, colorectal, and lung cancer patients who are enrolled in Medicaid, those who live in rural areas have significantly greater odds of being enrolled after their cancer diagnosis as compared to being enrolled prior to their diagnosis. Research has shown early Medicaid enrollment is associated with earlier diagnosis, which may subsequently contribute to improved survival outcomes. Initiatives to increase Medicaid enrollment of rural residents may aid in beneficial outcomes for those diagnosed with cancer.

Cancer

Parental employment in bitumen-related industries in relation to childhood cancer risk

Julia Heck* Julia Heck Chisom Iwundu Beate Ritz Johnni Hansen

Objective: Occupational exposure to bitumen used for roofing is classified by IARC as "probably carcinogenic to humans" (Group 2A), while bitumen used for road paving is classified as "possibly carcinogenic" (Group 2B). Further, coal tar previously used for paving is classified as "carcinogenic to humans" (Group 1). Despite these classifications, there are limited studies on childhood cancer in the offspring of workers exposed to bitumen.

Material and Methods: Our case-control study utilized data from Danish national registers. Cases (1968-2016) were identified from the Cancer Registry and linked to their parents via the Central Person Register. Occupational exposures were identified from the Supplementary Pension Fund Register with compulsory membership for all employees since 1964, which identifies the type and dates of every job. Conditional logistic regression was used to estimate the risk of pediatric cancers in offspring of fathers employed in bitumen-exposed and coal tar industries in the year preconception or during the pregnancy, and of mothers employed at any time in life.

Results: Combining all cancer types, paternal employment in bitumen-exposed industries during preconception or during the index pregnancy [Odds Ratio (OR)=1.05, 95% Confidence Interval (CI)=0.95-1.16] or employment at any time prior to the child's cancer diagnosis (OR=1.04, 95% CI=0.98-1.11), were not related to pediatric cancer risk. With regards to specific cancer types, an increased risk was indicated for astrocytoma with paternal bitumen-related employment in the perinatal period (OR=1.64, 95% CI=0.98-2.73; N=17 exposed cases). Maternal employment prior to the child's cancer diagnosis (OR=1.22, 95% CI=1.03-1.44; N=151 exposed cases) was related to increased pediatric cancer risk (all cancer types combined) and to ependymoma (OR=3.55, 95% CI 1.57-8.05; N=7 exposed cases) and rhabdomyosarcoma (OR=3.83, 95%CI 1.85-7.96; N=9 exposed cases).

Conclusion: Although the small sample sizes must be taken into account, elevated risk for pediatric cancers may occur with parental occupational exposure to bitumen. However, additional exposure to coal tars cannot be excluded.

Cancer

Differences in accelerometer-based measures of physical activity by history of cancer Jillian Nelson* Jillian Nelson Erika Rees-Punia Alpa V Patel

Physical activity is a modifiable risk factor for several types of cancer. Cancer survivors who meet moderate to vigorous physical activity (MVPA) guidelines (>150 min/week) may have improved survival outcomes. We examined how MVPA and sedentary time differ by cancer history and treatment using accelerometer-based measurements.

The American Cancer Society's Cancer Prevention Study-3 Accelerometry Sub Study recruited 21,325 participants in 2019-2023 to wear Actigraph GT3x+ accelerometers on the waist for 7 consecutive days. The Choi/Sojourn-3 axis algorithms were used to process returned accelerometers. Participants who wore the device on ≥1 day for ≥10 hours were included in this analysis (n=21,048, including n=776 cancer survivors). Multiple linear regression modeling was used to examine how MVPA and sedentary time differed by history of cancer and, among survivors, by history of chemotherapy and time since diagnosis.

Overall, mean cohort age was 58.5 (SD=10) years and 77% were women. Cancer survivors were older (62.73, SD=8.4 years) and less likely to be (72%) women. Average MVPA among all was 47.62 (SD=29.7) min/day and average sedentary time was 556.6 (SD=88.4) min/day. Overall, MVPA did not differ by history of cancer, but survivors who received chemotherapy accumulated 34 fewer minutes/week MVPA compared to survivors who didn't receive chemotherapy (p=.041). Further, those who received chemotherapy within 5 years of participating accrued 58 fewer minutes/week MVPA (p=.021) compared to survivors who did not receive chemotherapy within 5 years of participating.

Although history of chemotherapy may be related to a significant reduction in MVPA, the potential effects likely do not last beyond 5 years post-diagnosis. These results demonstrate an opportunity for physical activity interventions close to the time of cancer diagnosis to help survivors who received chemotherapy meet physical activity guidelines to improve cancer outcomes.

Utilization of Healthcare in Children Born to Lymphoma Survivors in Sweden Joshua P Entrop* Joshua P Entrop Viktor Wintzell Caroline E Dietrich Anna Marklund Ingrid Glimelius Tarec C El-Galaly Karin E Smedby Sandra Eloranta

Background Advances in lymphoma treatment lead to a rising population of young lymphoma survivors in childbearing ages who might be concerned about the impact of their disease on their children's health. Yet, no study has explored the effect of lymphoma on disease risks in children born to lymphoma survivors. Hence, our study aims to investigate the impact of lymphoma and its treatments on birth outcomes and health of children born to lymphoma survivors.

Methods We analyzed data on in- and outpatient diagnoses up to age five from Swedish national health registers using tree-based scan statistics to identify disease clusters prompting the utilization of healthcare comparing children born to lymphoma survivors (diagnosed 2000-2015) and children born lymphoma-free parents. Children born to lymphoma survivors were identified using the Swedish Lymphoma and national population registers. Each child born to a lymphoma survivor was matched on maternal age at childbirth to five children born to lymphoma-free parents.

Results We identified a total of 1 040 children born to lymphoma survivors and 5 200 children born to matched comparators, of whom 792 and 3 834 had at least one in- or outpatient diagnosis before age five, respectively. Children born to lymphoma survivors had a 13% higher rate of healthcare utilization (Rate Ratio: 1.13, 95% CI: 1.05-1.22) than children born to lymphoma-free parents. However, the panorama of diseases requiring healthcare utilization was broad and we could not identify any specific disease cluster with significantly elevated risk (P<0.05) using tree-based scan statistics.

Conclusion Children born to lymphoma survivors have an overall increased healthcare utilization up to age five, distributed across a broad range of diseases. This increase might be due to an increased health seeking behavior of their parents. An ongoing extension of this study involves investigating excess drug utilization to also capture diseases treated in primary care.

	Children born to lymphoma survivors		Children born to comparators		Risk Ratio	Risk Difference	P-value[a]
	Events	5-year risk	Events	5-year risk			
Cuts (ICD-10 codes)							
Ch. I - *Certain infectious and parasitic diseases (A00-B99)*	327	31.44%	1 384	26.62%	1.18	4.83	0.794
B25 - *Cytomegaloviral disease*	3	0.29%	1	0.02%	15.00	0.27	0.866
F50-F59 - *Behavioural syndromes associated with physiological disturbances and physical factors*	6	0.58%	8	0.15%	3.75	0.42	0.991
G00-G09 - *Inflammatory diseases of the central nervous system*	6	0.58%	8	0.15%	3.75	0.42	0.991
Ch. VIII - *Diseases of the ear and mastoid process (H60-H95)*	212	20.38%	857	16.48%	1.24	3.90	0.758
J20-J22 - *Other acute lower respiratory infections*	97	9.33%	354	6.81%	1.37	2.52	0.793
P070 - *Extremely low birth weight*	5	0.48%	5	0.10%	5.00	0.38	0.975
P701 - *Syndrome of infant of a diabetic mother*	8	0.77%	9	0.17%	4.44	0.60	0.489
Q38 - *Other congenital malformations of tongue, mouth and pharynx*	22	2.12%	60	1.15%	1.83	0.96	0.991
R70-R79 - *Abnormal findings on examination of blood, without diagnosis*	6	0.58%	7	0.13%	4.29	0.44	0.965

Table 1 The 10 most likely clusters of health-care utilisation on the ICD-10 tree obtained from the tree-based scan statistic sorted by chapters. [a]P-values are obtained from Monte-Carlo simulations and are adjusted for multiple-testing. Abbreviations: Ch, ICD-10 chapter.

Cancer

The Prospective Association between Endometriosis and Colorectal Cancer in the Sister Study

Isabella Caruso* Isabella Caruso Katie O'Brien Katherine Reeves

Background: Endometriosis is a painful and chronic inflammatory disease characterized by the growth of endometrial-like tissue outside of the uterus. Individuals with endometriosis are more likely to have coexisting chronic conditions, including cancer, autoimmune diseases, asthma diseases, and cardiovascular diseases. Inflammation may be an important component of both colorectal cancer progression and the pathogenesis of endometriosis. However, the association between endometriosis and colorectal cancer remains inconclusive.

Methods: We evaluated the association between endometriosis and colorectal cancer among 50,357 participants enrolled in the Sister Study. The Sister Study is a long-term prospective cohort study that enrolled women aged 35 to 74 in the United States, including Puerto Rico, between the years 2003 and 2009, whose sisters were diagnosed with breast cancer. Data were gathered through self-reporting at baseline and subsequent follow-up questionnaires. Cox proportional hazards analysis was used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for the association between endometriosis and colorectal cancer.

Results: Overall, 7,740 participants in the study had a baseline diagnosis of endometriosis and 1,247 participants were diagnosed during follow-up. In addition, 339 participants had an incident diagnosis of colorectal cancer. In the age-adjusted model, we did not observe associations between endometriosis and colorectal cancer (adjusted HR 0.96 95% CI 0.81-1.14).

Conclusions: This study will substantially contribute to the current literature on endometriosis by incorporating a large prospective analysis with several important covariates to address potential confounding. The age-adjusted results do not provide support for a relationship between endometriosis and colorectal cancer. More research is needed to fully understand the root cause of endometriosis and how it may contribute to increased inflammation in the body.

Cardiovascular

Association Between COVID-19 and Cardiovascular Disease Across Income Levels: Analysis of BRFSS Annual Survey Data 2022 Kareem Khairy* Kareem Khairy Amirah Ellis-Gilliam Jee Won Park

COVID-19 may be associated with cardiovascular disease (CVD) as both conditions share critical risk factors. Further, socioeconomic status (SES) (e.g., income) strongly predicts premature morbidity and mortality, with lower SES linked to higher CVD mortality and poorer CVD risk factor profiles. Thus, this study assesses the relationship between COVID-19 and CVD overall, and by income levels.

This cross-sectional study employed secondary data analysis using the 2022 Behavioral Risk Factor Surveillance System (BRFSS) dataset, with a sample size of 445,132 participants (age ≥18 years, 51.4% female, and 61.2% White adults). Multivariable logistic regression analyses, incorporating survey weights, were performed while adjusting for potential confounders. We also assessed for effect measure modification (EMM) by income levels (low: <$25,000, middle: $25,000-$75,000, high: >$75,000).

The adjusted OR (95% CIs) for CVD among those who tested positive versus did not test positive for COVID-19 was 1.07 (95% CI: 1.00-1.14). EMM assessment by income levels indicated that strong positive associations between COVID-19 and CVD among those who reported low and middle income were observed (ORs (95% CIs): 1.18 (1.03-1.35) and 1.13 (1.03-1.24), respectively). However, a negative association was most compatible among those who reported high income (OR (95% CI): 0.92 (0.83-1.02)).

We found that income is an effect modifier in the relationship between COVID-19 and CVD. Positive associations in lower income groups and the negative association in the high income group underscores the influence of SES factors on the COVID-19-CVD relationship. Our findings may indicate the vulnerability of economically disadvantaged populations to the CVD consequences of a positive COVID-19 diagnosis. Additional prospective studies should be conducted to identify if there are underlying health conditions among lower income groups that influences adverse CVD outcomes among those who are susceptible to COVID-19.

Figure. Adjusted Odds Ratios (95% CIs) for Cardiovascular Disease Comparing Those Who Tested Positive Versus Those Who did not Test Positive for COVID-19 by Income Levels.
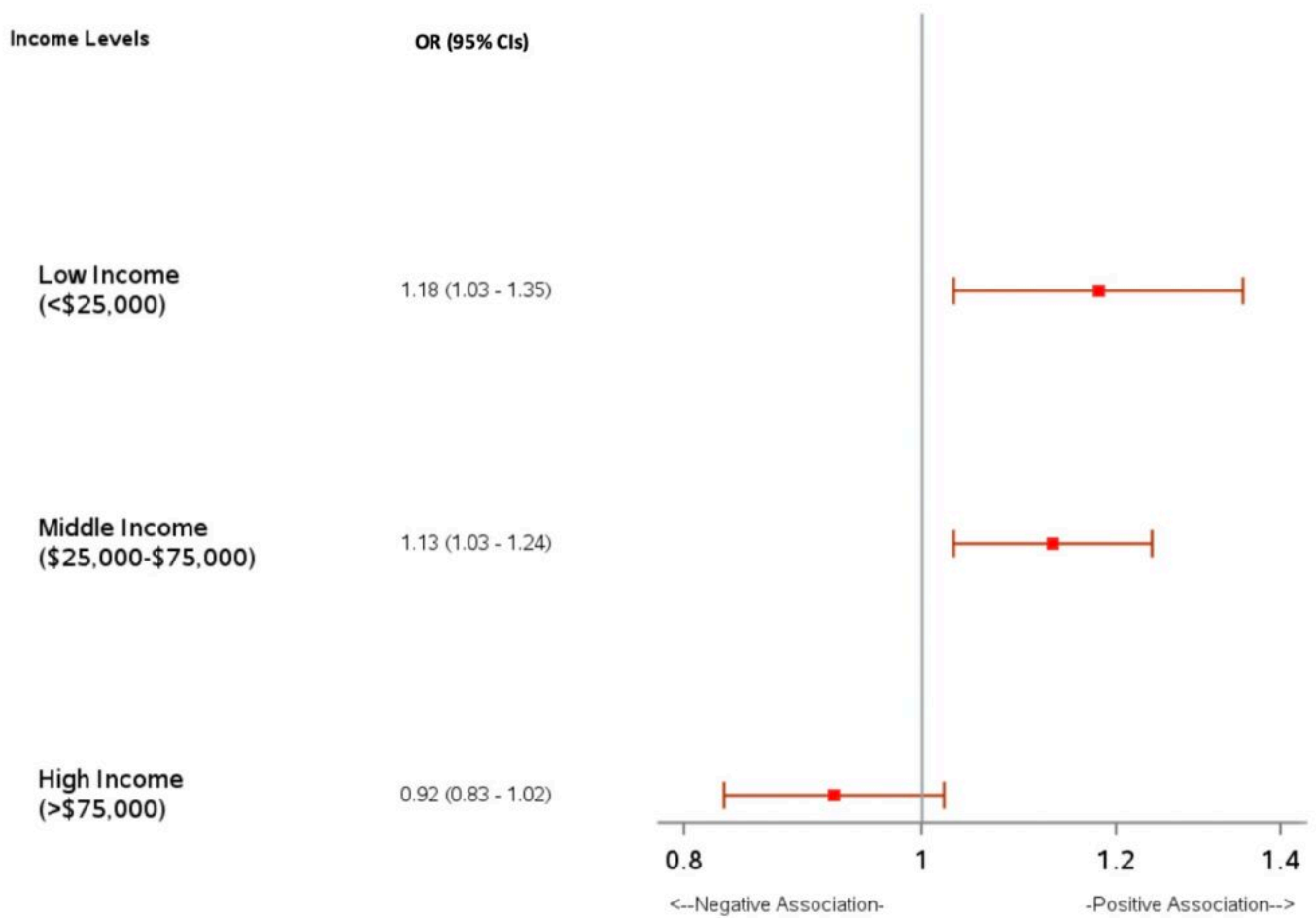
Chronotype, rotating night shift work, and cardiovascular disease risk in U.S. women: a prospective cohort study Sina Kianersi* Sina Kianersi Yue Liu Tamar Sofer Isha Agarwal Marta Guasch-Ferré Susan Redline Eva Schernhammer Kathryn Rexrode Tianyi Huang

Introduction: Rotating night shift work is associated with chronic circadian misalignment, and may contribute to cardio-cerebrovascular diseases (CVD) risk. The potential impact of rotating night shift work on CVD may be modified by chronotype, particularly if personal circadian preference and work schedules are mismatched.

Methods: In 2009, 75509 women (avg. age=55 years) with no history of CVD from the Nurses' Health Study II reported their chronotype. Information on duration of rotating night shift work has been collected biennially since 1989. Participants were prospectively followed for incident CVD (myocardial infarction or stroke), from 2009 until June 2019. We used time-varying Cox proportional hazards models to estimate the HR for CVD according to chronotype and night shift work. We conducted interaction analysis to assess if the association of night shift work with CVD differed by chronotype.

Results: We recorded 754 CVD cases over 673,534 person-years of follow-up. Compared with non-night shift workers, the demographically adjusted HR for CVD was 0.98 (95% CI: 0.82, 1.17) for night shift work of <5 years, and 1.23 (1.01, 1.49) for ≥5 years (P-trend=0.07). Compared with "morning" chronotypes, the demographically adjusted HR for CVD was 1.15 (0.98, 1.35) for "intermediate", and 1.41 (1.12, 1.76) for "evening" chronotypes (P-trend=0.004). The association comparing ≥5 years vs. no night shift work was stronger in morning chronotypes (HR: 1.45; 95% CI: 1.03, 2.05), which was attenuated after adjusting for traditional CVD risk factors (HR: 1.30; 95% CI: 0.91, 1.84). No association of rotating night work and CVD risk was found in intermediate or evening chronotypes (P for multiplicative interaction=0.09).

Conclusion: Our results suggest that female nurses with a morning chronotype may be more susceptible to the hazardous effects of rotating night shift work on CVD risk.

Risk of Heart failure in Patients With Rheumatoid arthritis: A Systematic Review and Meta-analysis of Cohort Studies Parkin Paramiraksa* Parkin Paramiraksa Metavee Boonsiri Poramin Patthamalai Amarit Tansawet

Objective
Rheumatoid arthritis (RA) is reported to be associated with an increased risk of incident cardiovascular diseases (CVD) including heart failure. However, the inconsistency remains among studies. Several systematic review and meta-analysis of cohort studies were conducted to estimate the risk of CVD in RA but did not include heart failure in the analysis. We aim to determine the risk of incident heart failure in RA patients.

Methods
A systematic search of MEDLINE, Scopus, EMBASE, Cochrane Library, and medRxiv was performed to identify relevant studies from inception to January 2024. The search terms were modified by each database. The eligible criteria are cohort studies reporting the risk of incident heart failure among populations with RA, compared with healthy control. Quality assessments were performed according to the Newcastle-Ottawa Scale (NOS). Screening, data extraction, and quality assessment were independently conducted by two reviewers. If consensus is required, the third reviewer will be consulted. The PRISMA and Meta-analysis of Observational Studies in Epidemiology (MOOSE) reporting guidelines were followed. To minimize the effects of confounders, only adjusted hazard ratio (aHR), not crude HR, were pooled using the random-effects meta-analysis. Publication bias was evaluated by funnel plot.

Results
A total of 8 studies with 8 cohorts (n = 15,096,737 participants) met the eligibility criteria. The pooled aHR in the meta-analysis revealed a significant association between RA and risk of incident heart failure (pooled aHR, 1.41; 95% CI, 1.25-1.58). No evidence of publication bias was observed. Quality assessments of the included studies were high.

Conclusion
Patients with RA were at an increased risk of developing heart failure. RA patients with baseline risk of heart failure may require screening to early diagnosis and early treatment. Research exploring underlying mechanisms for the association of RA and incident heart failure is warranted.

Cardiovascular

Transformative Impact: Evaluating Cardiovascular Health through Mississippi's Chronic Disease Quality Improvement Initiative (CDQII) – A 2019-2023 Analysis Sudheer Koutha*

Sudheer Koutha Chandana Namburi Kaithlyn Hawkins Sai Kurmana

Background:

Cardiovascular disease is the leading cause of death in the United States and Mississippi with mortality rates in Mississippi surpassing the national average. Hypertension and high blood cholesterol are prominent risk factors for cardiovascular disease, affecting a significant prevalence percentage of the adult population in Mississippi (43.9%: high blood pressure;38.3%: high blood cholesterol). Mississippi State Health Department's (MSDH) Chronic Disease Quality Improvement Initiative (CDQII), initially designed to target heart disease and stroke. This study evaluates the impact of CDQII from 2019 to 2023 across 13 healthcare systems in Mississippi.

Methods:

For this study, thirteen healthcare systems collaborated with the MSDH, reporting data securely through platforms such as dashboards and Redcap from 2019 through 2023, focusing on the total number of participants with hypertension and trends in hypertension control. Disease burden and healthcare systems are studied with Geo-Spatial Technology using Arc GIS Pro.

Discussion:

Approximately out of 90,000 individuals each year from CDQII health care systems, about 30% reported hypertension. Among those with hypertension, a significant increase in the percentage of individuals who achieved hypertension control was observed (2020: 48.15%; 2023: 61.94%). The percentage increase among individuals with hypertension in control significantly increased by 4.6 %, 15% and 6.9% for three consecutive years (2021, 2022, 2023). Overall, about 62% (n=20,178) of participants had their hypertension in control during the final year of the project.

Conclusion:

The CDQII intervention demonstrated positive impacts, particularly in the identification and management of hypertension. The findings highlighted the significance of collaborative efforts in addressing cardiovascular health outcomes in Mississippi. Further research is imperative to refine strategies and enhance health outcomes related to cardiovascular disease.

Prevalence of Cardiovascular-Kidney-Metabolic Syndrome in the United States: National Health and Nutrition Examination Survey 2011-2018 Jieun Kim* Jieun Kim Joseph J. Shearer Maryam Hashemian Kayode O. Kuku Carolina Downie Jungnam Joo Veronique L. Roger

Introduction

Cardiovascular-Kidney-Metabolic (CKM) syndrome is the result of a complex interplay between metabolic risk factors, chronic kidney disease, and cardiovascular disease. The American Heart Association (AHA) recently published definitions for CKM syndrome highlighting its progressive pathophysiology; however, the prevalence and patterns of these stages across key demographic factors in the United States remains to be fully described.

Objective

To assess the prevalence and patterns of CKM syndrome among adults in the United States.

Methods

We studied adults aged 20 years or older who completed the National Health and Nutrition Examination Survey between 2011-2018. Eligible adults (N=8,474) were classified by CKM stage using AHA criteria: stage 0 (no risk factors), stage 1 (excess or dysfunctional adiposity), stage 2 (other metabolic risk factors or chronic kidney disease), and stage 3-4 (subclinical or clinical cardiovascular disease). Weighting and sampling strata were used to generate population-based prevalence estimates and 95% confidence intervals for CKM syndrome stages, and stratified by age group, gender, and race/ethnicity.

Results

The median age of the population was 46.8 (32.8-60.3) years, 49.1% were male, and 65% were Non-Hispanic White. The prevalence of CKM syndrome by stage was as follows: stage 0 (10.5%, 95% CI: 9.4-11.7%), stage 1 (27.2%, 25.7-28.6%), stage 2 (52.8%, 51.0-54.5%), and stage 3-4 (9.5%, 8.6-10.4%). Compared to stage 0, adults in stage 3-4 were more likely to be older, male, and Non-Hispanic Black. The prevalence of stage 0 significantly decreased between 2011-2018.

Conclusion

Nearly 9 out of 10 adults in the United States live with or are at elevated risk of CKM syndrome emphasizing the striking public health burden of CKM syndrome in the United States. These results also identify critical disparities which in turn delineate pathways for urgent interventions aimed at slowing or reversing the progression of CKM syndrome.

The Metabolic Vulnerability Index as predictor of Major Cardiovascular Adverse Events in the ELSA-Brasil Cohort William R. Tebar* William Tebar Vandrize Meneghini Marcio S. Bittencourt Raul D. Santos Giuliano Generoso Alexandre C. Pereira Steven R. Jones Michael J. Blaha Peter P. Toth Paulo A. Lotufo Isabela M. Bensenor

Introduction: The Metabolic Vulnerability Index (MVX), derived from the Metabolic Malnutrition (MMX) and Inflammation Vulnerability (IVX) indices, has been a novel biomarker associated with mortality prediction in patients with cardiovascular (CV) disease. However, it is still unclear if these indices predict risk for Major Adverse CV Events (MACE).

Objective: To analyze the association of MVX, MMX and IVX levels with MACE in the ELSA-Brasil cohort.

Methods: Data from 4893 participants (50.0 [45.0-57.0] years, 54.6% of women) were analyzed. Baseline serum samples were collected between the years 2008-2010. Components of MVX (leucine, isoleucine, valine, citrulline, GlycA and small HDL particles) were analyzed by nuclear magnetic resonance spectroscopy (LipoProfile® 4 test spectra, LabCorp) and the indices were stratified into quintiles and standard-deviation (SD) increase of z-scored values. Non-fatal MACE (myocardial infarction, stroke, admission for unstable angina, revascularization) were computed within a 5-year follow-up, while fatal MACE (cardiovascular death) were computed up to 31 December 2022. Kaplan-Meier curves of cumulative hazard for MACE were compared by log-rank test and the hazard ratio (HR) for MACE was analyzed by Cox regression adjusted for sociodemographic, risk factors and CV disease.

Results: A total of 189 MACE (40 fatal and 149 non-fatal) were adjudicated. Log-rank test was significant for all three indices (Figure 1). The HR of MACE was higher in participants with ≥2 SD of the three indices (HR: 2.57, 1.36 – 4.86 for MVX; HR: 2.06, 1.11 – 3.81 for MMX; and HR: 2.48, 1.32 – 4.66 for IVX). The highest quintile of all indexes was associated with higher HR of MACE when compared to the lowest quintile (HR: 2.06 [1.27; 3.37] for MVX; HR: 1.91 [1.12; 3.23] for MMX; HR: 1.82 [1.12; 2.95] for IVX).

Conclusion: The highest quintile and 2-fold increased z-score of MVX, MMX and IVX indices are predictors of MACE among ELSA-Brasil cohort participants.
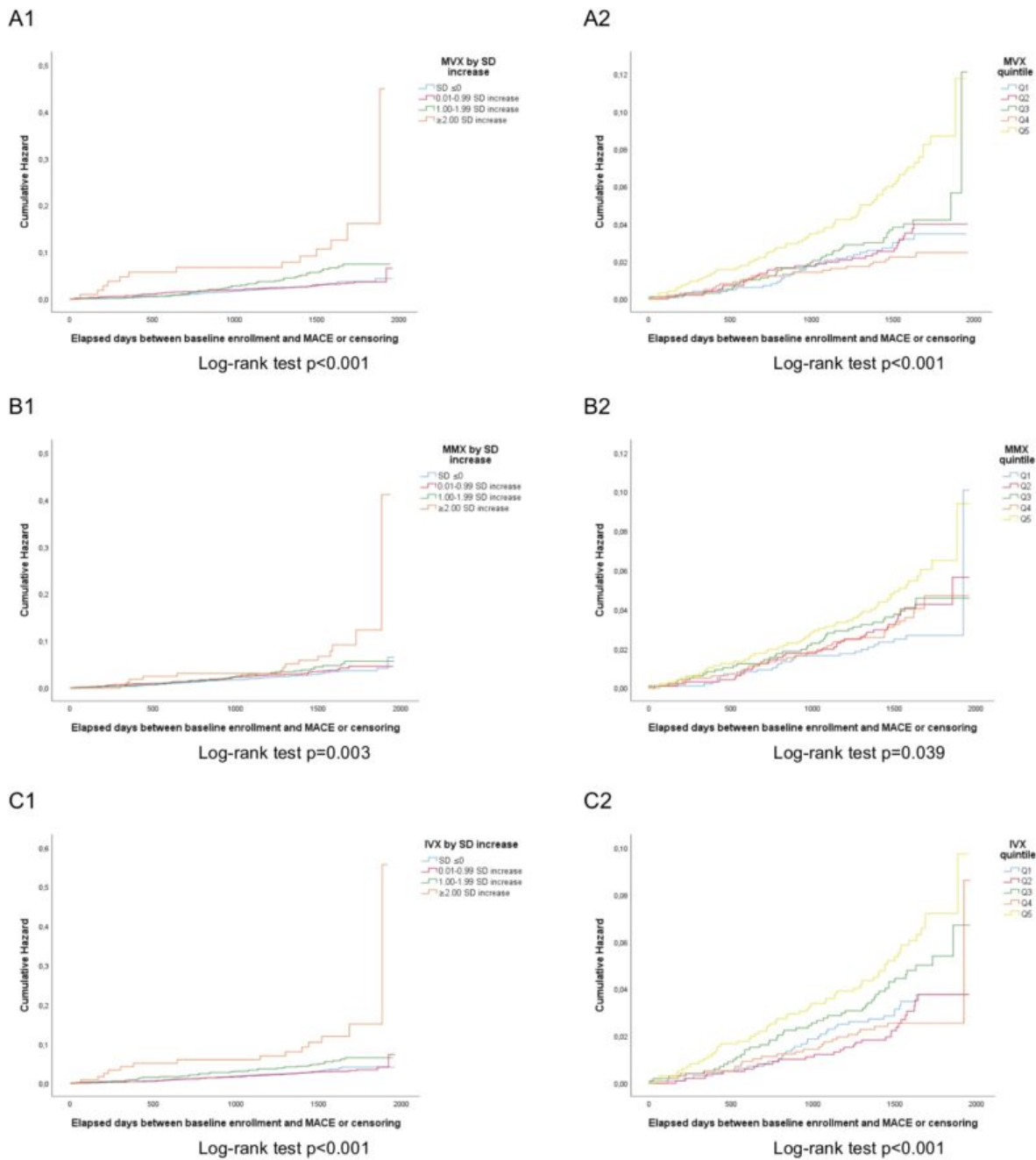
Figure 1. Kaplan-Meier curves of cumulative hazard for Major Adverse Cardiovascular Events among ELSA-Brasil cohort participants (n=4893).

Cardiovascular

Outcomes of Real-world Adults with Chronic Kidney Disease Who Are Excluded from Hypertension Clinical Trials June Li* June Li Maria E. Montez-Rath Mengjiao Huang Vivek Charu Jaejin An Michelle C. Odden John J. Sim Manjula Kurella Tamura
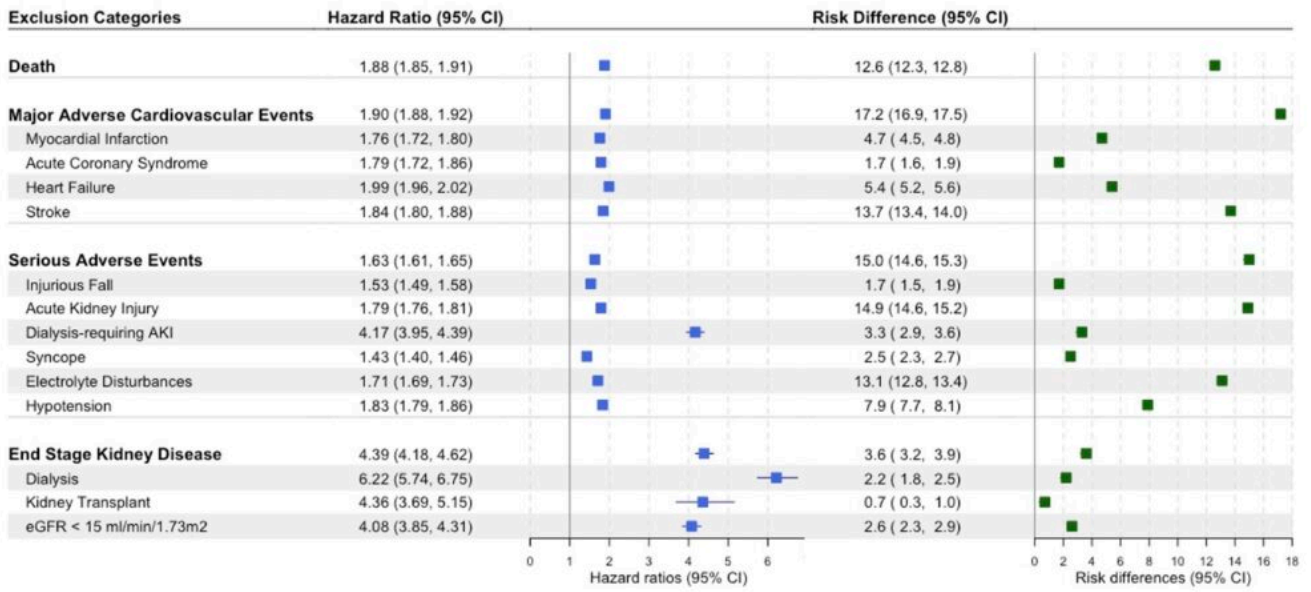
Background – Real-world adults with chronic kidney disease (CKD) are not well represented in major blood pressure (BP) target trials. Uncertainty remains around the efficacy and safety of intensifying treatment in excluded populations with different clinical characteristics. We assessed whether clinical outcomes differed between trial eligible and ineligible adults with CKD.

Methods – In a retrospective cohort study, we identified patients with CKD and hypertension in the Veterans Health Administration (VA) in 2019 who were eligible for at least one of three BP target trials, the Systolic Pressure Intervention Trial, the Action to Control Cardiovascular Risk in Diabetes trial, and the African American Study of Kidney Disease. We examined the association between trial eligibility and outcomes of death, major cardiovascular events (MACE), serious adverse events (SAEs), and end stage kidney disease (ESKD). Follow-up was censored at death, end of database linkage, or September 30, 2022. We ascertained the incidence rates, RDs, and HRs using cause-specific analysis for competing risk of death.

Results – We identified 120,038 trial eligible and 383,442 trial ineligible adults with CKD and hypertension in 2019. Trial ineligible adults had a moderately elevated risk of death (HR, 1.88, 95% CI, 1.85–1.91), MACE (HR, 1.90, 95% CI, 1.88–1.92), and SAEs (HR, 1.63, 95% CI, 1.61–1.65), and a markedly elevated risk of ESKD (HR, 4.39, 95% CI, 4.18–4.62) compared to trial eligible adults. The corresponding absolute risk differences were largest for death, MACE and kidney related SAEs, and smallest for ESKD.

Conclusion – Trial ineligible adults with CKD and hypertension had higher relative and absolute risks for all outcomes compared to trial eligible adults, but the pattern of risk differed by outcome, suggesting that the benefit-risk profile of hypertension treatment may differ from that of CKD patients included in trials.

Figure 1. Adjusted hazard ratios and risk differences for all outcomes in trial eligible versus ineligible adults with CKD and hypertension in the VA in 2019.

Exclusion Categories	Hazard Ratio (95% CI)		Risk Difference (95% CI)	
Death	1.88 (1.85, 1.91)		12.6 (12.3, 12.8)	
Major Adverse Cardiovascular Events	1.90 (1.88, 1.92)		17.2 (16.9, 17.5)	
Myocardial Infarction	1.76 (1.72, 1.80)		4.7 (4.5, 4.8)	
Acute Coronary Syndrome	1.79 (1.72, 1.86)		1.7 (1.6, 1.9)	
Heart Failure	1.99 (1.96, 2.02)		5.4 (5.2, 5.6)	
Stroke	1.84 (1.80, 1.88)		13.7 (13.4, 14.0)	
Serious Adverse Events	1.63 (1.61, 1.65)		15.0 (14.6, 15.3)	
Injurious Fall	1.53 (1.49, 1.58)		1.7 (1.5, 1.9)	
Acute Kidney Injury	1.79 (1.76, 1.81)		14.9 (14.6, 15.2)	
Dialysis-requiring AKI	4.17 (3.95, 4.39)		3.3 (2.9, 3.6)	
Syncope	1.43 (1.40, 1.46)		2.5 (2.3, 2.7)	
Electrolyte Disturbances	1.71 (1.69, 1.73)		13.1 (12.8, 13.4)	
Hypotension	1.83 (1.79, 1.86)		7.9 (7.7, 8.1)	
End Stage Kidney Disease	4.39 (4.18, 4.62)		3.6 (3.2, 3.9)	
Dialysis	6.22 (5.74, 6.75)		2.2 (1.8, 2.5)	
Kidney Transplant	4.36 (3.69, 5.15)		0.7 (0.3, 1.0)	
eGFR < 15 ml/min/1.73m2	4.08 (3.85, 4.31)		2.6 (2.3, 2.9)	

Hazard ratios (95% CI)

Risk differences (95% CI)

Confounding or bias amplification? Clues for the researcher seeking causal inference.
Krista Christensen* Krista Christensen Michael Leung Elizabeth Radke Michael Wright Tom Bateson Marc Weisskopf

In epidemiology studies, associations between exposure and outcome could be affected by confounding, but also by amplification of bias due to the presence of unknown or unmeasured confounders and correlation between the exposure of interest and co-occurring exposures. However, determining which of these types of bias – or both! – may exist is not straightforward. An example where both 'traditional' confounding and bias amplification may occur, is examination of health effects due to perfluoroalkyl and polyfluoroalkyl substances (PFAS), where correlation between PFAS is usually present, and sources (and therefore potential confounders) are not always well understood. As an example, several epidemiological studies have reported associations between PFAS biomarker levels and immune endpoints including vaccine response. In one of these studies, correlations between PFAS were moderate to high (range: 0.22 to 0.78), and results were presented for both single PFAS and multi-PFAS models. In some cases, adjusting for other PFAS changed point estimates (e.g., a 37% attenuation of the point estimate of PFDA in multi-PFAS models, compared with the single-PFAS model) while in other cases (e.g., PFOA), results were similar. We performed a simulation exercise with a dataset constructed to mimic the data from this study and examined how point estimates were changed with different causal assumptions. We found that when amplification bias was present the 'better' choice is the single PFAS model. However, if the direction of the amplification bias, strength of associations and/or degree of correlation were changed, the balance could shift such that the multi-PFAS model yielded lower bias. Furthermore, we show that it may be possible to detect bias amplification if there exists a PFAS in the mixture that is not causally related to the outcome. *Disclaimer: The views expressed in this abstract are those of the authors and do not necessarily reflect the views or policies of the U.S. EPA.

The Ethics of Causal Claims Douglas Weed* Douglas Weed

This paper examines the ethical responsibilities of epidemiologists when the issue is causation, i.e., its determination rather than the application of causal knowledge in public health or the ethics of carrying out studies. While the ethics of applying causal knowledge has received considerable attention in past discussions of the policy-making roles of epidemiologists and environmental justice, the ethics of causal claims has received little attention. This paper examines the ways ethics is used to explore professional issues in general and causal claims in particular. A review of recent ethics guidelines provides little or no guidance on causal claims themselves. One remedy can be found in the topic of obligation, a central ethical concept with close ties to responsibility. With regard to causal claims, our obligation extends beyond the abstract pursuit of knowledge to the need to use the best method for assessing causation—the systematic narrative review and others—as well as an obligation to commit any causal claim to peer review and publication. This is especially important when the claim is contrary to the current consensus. Discussed are examples in current practice where causal claims have appeared that have broad public health and policy implications and yet had not passed peer review nor appeared in print. Practical recommendations for education and practice are discussed.

Causal Inference

Assessment of unmeasured confounding in the association between perceived discrimination and mental health in a predominantly African American cohort using g-estimation Jiajun Luo* Jiajun Luo Briseis Aschebrook-Kilfoy Loren Saulsberry

Background: Perceived discrimination in healthcare settings can have adverse consequences on mental health in minority groups. However, the association between perceived discrimination and mental health is prone to confounding because of difficulty to measure. The study aims to quantitatively evaluate the influence of unmeasured confounding in this association using g-estimation.

Methods: In a predominantly African American cohort, we applied g-estimation to estimate the association between perceived discrimination and mental health, adjusted and unadjusted for measured confounders. Mental health was measured using clinical diagnoses of anxiety, depression, and bipolar disorder. Perceived discrimination was measured as the number of patient-reported discrimination events in healthcare settings. Measured confounders included demographic, socioeconomic, residential, and health characteristics. The influence of confounding was denoted as α_1 from g-estimation. Particularly, the α_1 for measured confounding was denoted as α_1^*. We compared α_1 for measured and unmeasured confounding.

Results: Strong associations between perceived discrimination in healthcare settings and mental health were observed. For anxiety, per one more patient-reported discrimination events, the OR (95% CI) unadjusted and adjusted for measured confounders were 1.30 (1.21, 1.39) and 1.26 (1.17, 1.36), respectively. The α_1^* for measured confounding was –0.066. Unmeasured confounding with $\alpha_1=0.200$, which was over three times that of measured confounding, corresponds to a relative rate of 1.12 (1.01, 1.24). Similar results were observed for other outcomes.

Conclusion: Compared to measured confounding, unmeasured confounding that was over three times was not enough to explain away the association between perceived discrimination and mental health, suggesting that this association is robust to unmeasured confounding. This study provides a novel framework to quantitatively evaluate unmeasured confounding.
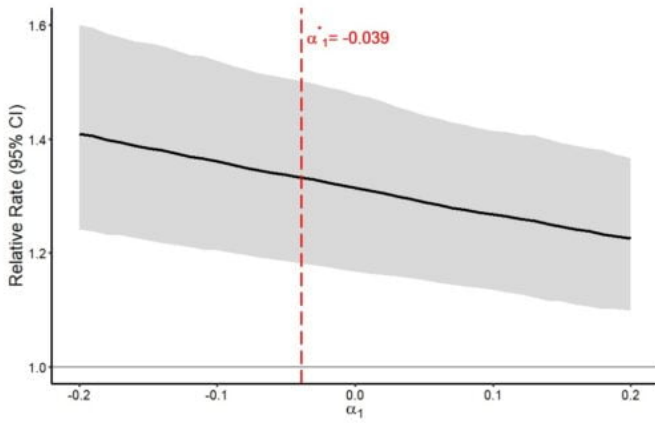
(1) Association between Perceived Discrimination and Anxiety under Different Unmeasured Confounding
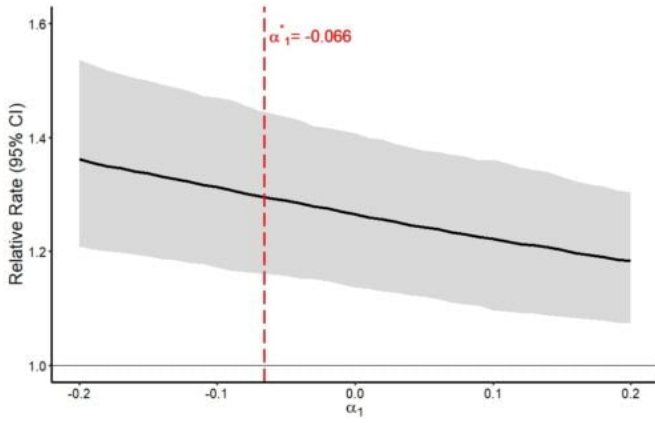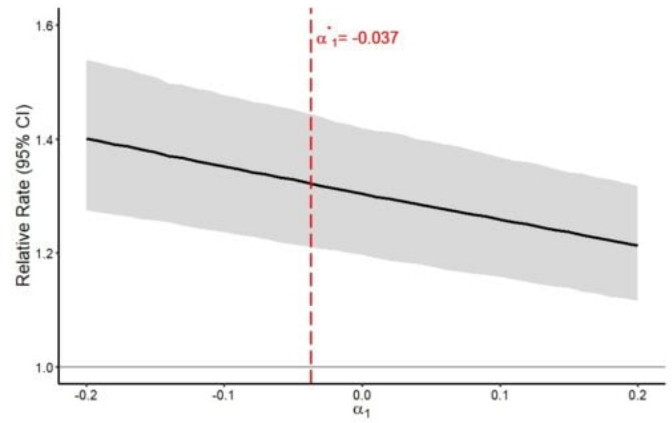
(2) Association between Perceived Discrimination and Depression under Different Unmeasured Confounding
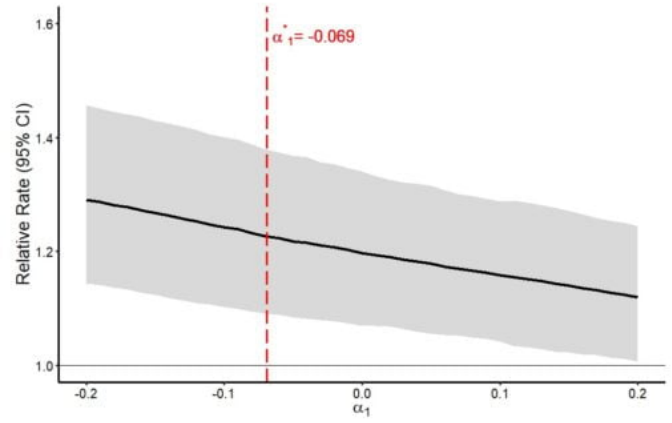
(3) Association between Perceived Discrimination and Bipolar Disorder under Different Unmeasured Confounding

(4) Association between Perceived Discrimination and Any Mental Health Disor under Different Unmeasured Confounding

Causal Inference

The problem of interpretational errors in epidemiology Aaron* Aaron Sarvet

The "causal revolution" promises to aid in the translation of data into public good. In this talk I illustrate that merely doing a "causal" analysis is not enough if it provides "the right answer to the wrong question". I present practical case studies in organ transplantation, and intensive care triage. These examples illustrate interpretational errors commonly arising in settings with scarce resources. As a constructive solution, I present work designed to prevent interpretational errors by allowing an investigator to explicitly target policy-relevant questions in these settings. More broadly, I contrast the principles of this work with contemporary trends in statistical methods development. I argue that methods can undermine public health when they prioritize statistical properties over faithfulness to real-world public health problems.

Single World Intervention Graphs (SWIGs): A Practical Guide Dana Bezuidenhout* Sarah Forthal Dana Bezuidenhout

Recent decades have witnessed substantial advancements in methodologies for estimating causal effects. In particular, the potential outcomes approach now dominates most scholarship on causality. However, despite the growing popularity of this approach, the uptake of compatible graphical methods such as Single World Intervention Graphs (SWIGs) remains limited. SWIGs are causal graphs that explicitly depict the potential outcomes of interest, thus allowing users to clearly identify the independencies required to identify the causal effect of interest. We aim to increase understanding of SWIGs and demonstrate how they can be a useful resource for epidemiologists and researchers engaged in causal research. We reviewed existing literature to create a comprehensive and user-friendly guide to using SWIGs. First, we discuss the limitations of Directed Acyclic Graphs (DAGs) under the potential outcomes framework. Then, we introduce SWIGs as a simple but powerful tool for integrating potential outcomes explicitly into causal diagrams. We provide a step-by-step guide on transforming DAGs into SWIGs that includes practical insights into constructing SWIGs under various scenarios such as confounding, mediation, and sequential randomization. Highlighting the utility of SWIGs in practice, we illustrate their application in identifying the g-formula, showcasing their capacity to make causal estimands visually explicit. This project serves as a resource for epidemiologists and researchers interested in expanding their causal inference toolkit.

Causal Inference

Mediation analysis with time-varying mediators and time-to-event outcomes accounting for competing risks
Arce Domingo* Arce Domingo Yuchen Zhang Ana Navas-Acien Kiros Berhane Brent Coull Linda Valeri

Background: In survival settings, competing events refer to any event that makes it impossible for the event of interest to occur. Not accounting for competing events by death can lead to biases caused by the fact that individuals that die do not have the opportunity to develop the event of interest. In this work, we propose a framework to deal with competing events in the causal mediation setting in presence of longitudinal mediators and time-to-event outcomes.

Methods: We used the path-specific effects framework to adapt the mediational g formula to consider the competing event as a nested mediator with our mediator of interest. Thus, we consider two indirect effects: the indirect effect through the history of the mediator of interest, and the indirect effect through the history of the competing event. We used additive hazards models to obtain effects estimates in an attributable risk scale. We applied our algorithm to real data from the Strong Heart Study, a prospective cohort of American Indians. We evaluated the potential mediating role of systolic blood pressure on the association between urinary cadmium and arsenic (in separate models) and cardiovascular disease (CVD), accounting for competing events by death. Metals were measured at visit 1 (1989-1991). Blood pressure was measured at three time points: visit 1, visit 2 (1993-1995) and visit 3 (1998-1999).

Results: 148.58 (-81.25, 376.41) CVD cases per 100,000 person-years were attributable to an interquartile range (IQR) increase in urinary cadmium. Of those, 28.16 (4.13, 56.72) cases were mediated by the blood pressure trajectory, and 28.87 (-69.59, 141.12) cases were avoided due to the individual dying before CVD happened. For urinary arsenic, 274.98 (8.58, 537.57) CVD cases were attributable to an IQR increase. Of those, 45.27 (21.68, 77.05) cases were mediated by the blood pressure trajectory, and 12.92 (-39.42, 65.28) cases were avoided by death.

Conclusion: We introduced, for the first time, a framework using path-specific effects to define causal mediated effects in presence of competing risks. Our algorithm estimates causal effects in terms of attributable cases per a number of person-years, which is a measure of public health impact. We found mediated effects of blood pressure on the association between urinary arsenic and cadmium and CVD.

LATEBREAKER

Causal Inference

Assessing the contribution of obesity to trends in diabetes across U.S. birth cohorts using a causal decomposition approach Rafeya Raquib* Andrew Stokes Meghan Podolsky

Obesity prevalence in the U.S. has increased since at least 1960. Environmental factors have been cited as drivers of this trend, but the relative effect of exposure in different birth cohorts has yet to be established. We used a counterfactual causal decomposition model combining the age-period-cohort approach with g-computation to examine how changing body mass index (BMI) distributions across birth cohorts impacted diabetes prevalence. Using data from the National Health and Nutrition Examination Survey (NHANES) III (1988-1994) and continuous waves (1999-2020) (N=33,386), we compared the observed prevalence of diabetes in the natural course to a counterfactual scenario where all one-year synthetic birth cohorts had the same distribution of BMI as the 1930 birth cohort, taking into account age, sex, race, ethnicity, and education. Diabetes status was established as having measured Hemoglobin A1c (HbA1c) ≥6.5% or HbA1c <6.5% with self-reported diabetes treatment. BMI was calculated as a lagged variable that combined weight 10-years prior to survey with height at survey to reduce the risk of reverse causality between the mediator and outcome variables. Holding age (50) and period (2008) constant, the prevalence of obesity (BMI 30+) increased from 13.4% (7.6-18.1) in the 1930 birth cohort to 34.9% (22.8-56.5) in the 1975 birth cohort. We found that diabetes prevalence would be on average 2.0 (1.0-3.9) percentage points lower for the 1960 birth cohort and 4.2 (2.7-6.7) percentage points lower for the 1970 birth cohort with the BMI distribution of the 1930 birth cohort. These results suggest that increasing obesity rates contributed significantly to rising diabetes prevalence across U.S. birth cohorts. Additional research is needed to elucidate the factors contributing to increases in obesity across birth cohorts, including early life social factors and accumulated exposure to obesogenic factors over the life course.

Figure 1: *Adjusted BMI distribution by birth cohort and natural course and counterfactual diabetes prevalence*

A | Adjusted BMI distribution by birth cohort
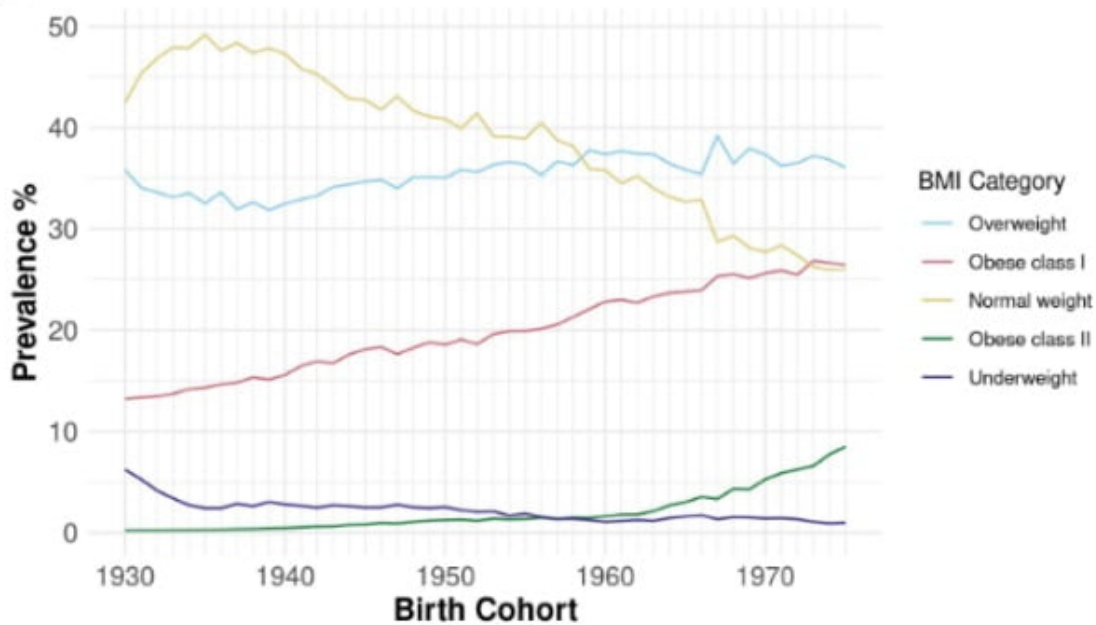
B | Natural course and counterfactual diabetes prevalence
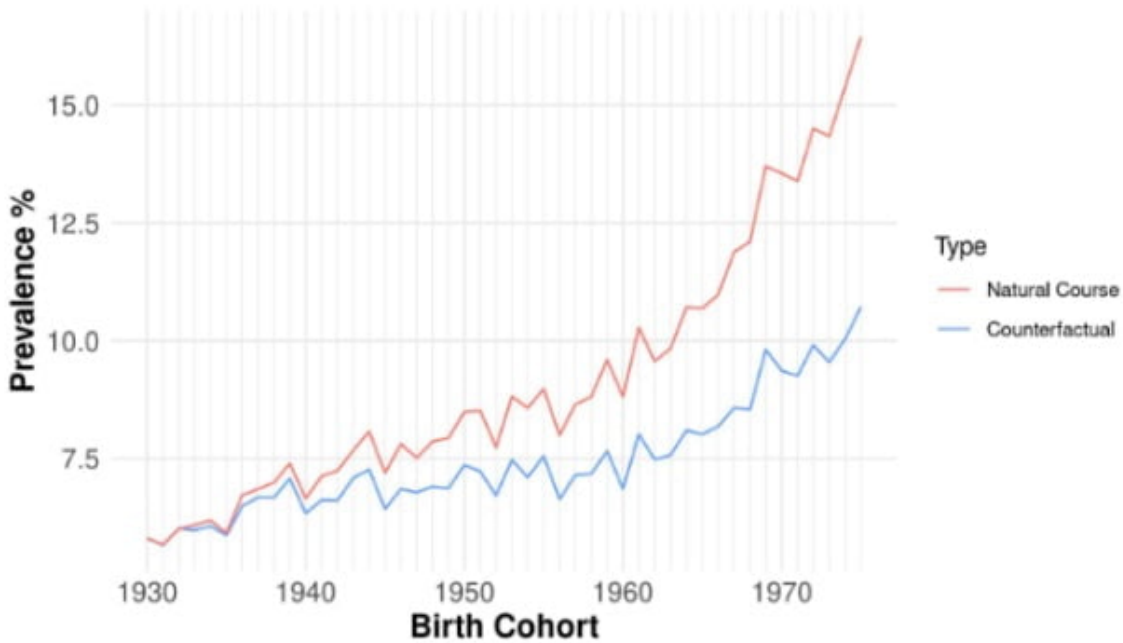
Source: National Health and Nutrition Examination Survey (NHANES) III (1988-1994) and continuous waves (1999-2020) (N=33,386). Reference cohort for the counterfactual simulation was the body mass index distribution of the 1930 cohort. Age and period were held constant at 50 years and 2008, respectively.

Are you positive? Outcome-dependent positivity violations in small populations: an example study of substance use by gender identity Dominique Heinke* Dominique Heinke Ryan P Kyle Joseph AC Delaney Bridget Whitney Sarah Mixon Robert J Fredericksen Michelle Kipke Catherine Lesko Kenneth H Mayer Michael J Li Brian Mustanski Luis Parra Geetanjali Chander Heidi Crane Lydia N Drumright

Accurately describing the health burdens of small populations is important yet challenging; many adjustment methods fail with sparse data and knowledge of best practices are limited. We evaluated the performance of two adjustment methods appropriate to small and complex samples when estimating substance use prevalence among transgender women relative to cisgender men and women.

We estimated prevalence ratios (PRs) for self-reported use of specific substances comparing trans women to cis men and trans women to cis women in an HIV collaborative with data from multi-site HIV clinical cohorts (CNICS, JHHCC) and a community cohort (RADAR). To adjust for age, race/ethnicity, study site, and year of cohort entry and of most recent self-report, we calculated PRs using 1) stabilized IPW: weighting gender groups to be similar on these factors; and 2) matching: selecting ≤2 cis men or women that was similar to each trans woman on these factors.

In the combined CNICS/JHHCC cohorts, 275 of 277 trans women matched to ≥1 one cis man and 241 matched to ≥1 cis women. In the RADAR cohort, 231 of 232 trans women matched to 1 cis man. Among more commonly used substances (nicotine, cannabis, crack/cocaine) IPW and matching provided consistent estimates in all analyses (Figure). While for less commonly used substances, both methods yielded consistent estimates for trans women vs cis men, in some instances positivity violations in the IPW analyses for trans vs cis women induced substantially divergent estimates. For example, IPW and matched estimates for methamphetamine use in trans women vs cis men were consistent in all cohorts (Figure), but there was a >2-fold difference between IPW (PR=4.48, 95%CI: 1.52-10.03) and matched (PR=1.58, 95%CI: 1.04-2.40) estimates for trans vs cis women.

Both matching and IPW can be effective adjustment approaches in small and complex samples, but IPW requires checking each outcome for positivity violations, while matching may result in loss of data.

Figure. Comparison of matched and IPW estimates: relative prevalence of substance use among transgender women compared to cisgender men and women in CNICS and JHHCC cohorts and the RADAR cohort.

Prevalence Ratios and 95% Confidence Intervals
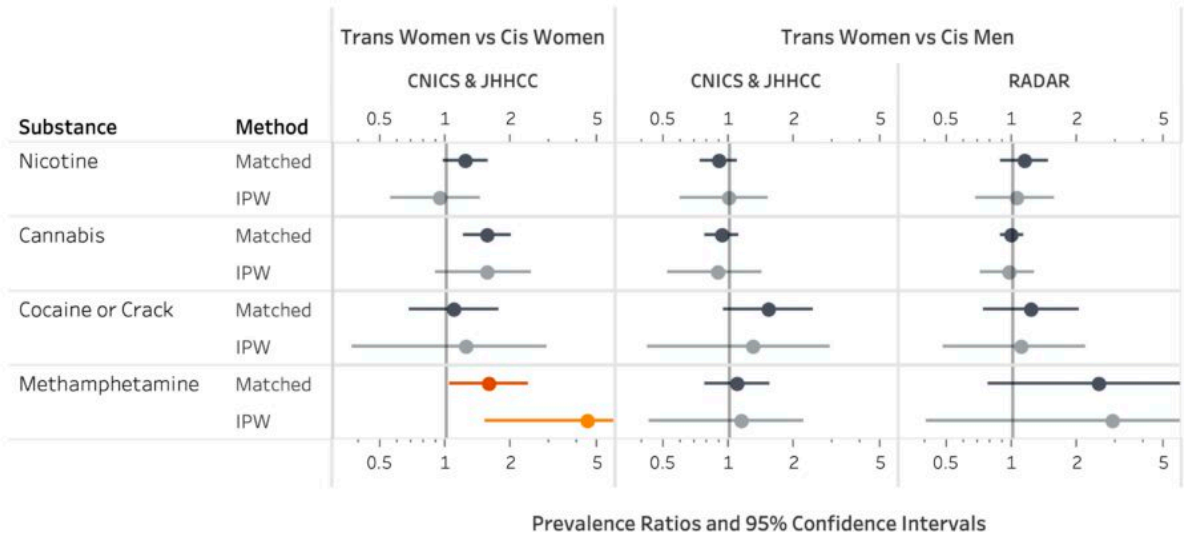
Causal Inference

Bridging Binarization: Causal Inference with Dichotomized Continuous Treatments Kaitlyn Lee* Kaitlyn Lee Alejandro Schuler Alan Hubbard

The average treatment effect (ATE) is a common parameter estimated in causal inference literature, but it is only defined for binary treatments. Thus, despite concerns raised by some researchers, many studies seeking to estimate the causal effect of a continuous treatment create a new binary treatment variable by dichotomizing the continuous values into two categories. In this paper, we affirm binarization as a statistically valid method for answering causal questions about continuous treatments by showing the equivalence between the binarized ATE and the difference in the average outcomes of two specific modified treatment policies. These policies impose cut-offs corresponding to the binarized treatment variable and assume preservation of relative self-selection. Relative self-selection is the ratio of the probability density of an individual having an exposure equal to one value of the continuous treatment variable versus another. The policies assume that, for any two values of the treatment variable with non- zero probability density after the cut-off, this ratio will remain unchanged. Through this equivalence, we clarify the assumptions underlying binarization and discuss how to properly interpret the resulting estimator. Additionally, we introduce a new target parameter that can be computed after binarization that considers the status-quo world. We argue that this parameter addresses more relevant causal questions than the traditional binarized ATE parameter. Finally, we present a simulation study to illustrate the implications of these assumptions when analyzing data and to demonstrate how to correctly implement estimators of the parameters discussed.

The Relationship Between Housing Types and the Risk of COVID-19 Infection in a University Student Population: A Pilot Convenience Sample Study . Akpevwe Amanda Ojaruega* Akpevwe Amanda Ojaruega Edmore Madondo

Background: The COVID-19 pandemic has presented unprecedented challenges, emphasizing the need to comprehend factors contributing to infection risk for effective public health management. University campuses, with diverse housing options, provide a unique setting to investigate the potential impact of different housing types on COVID-19 transmission within student populations.

Objective: This study aimed to explore the relationship between housing types and the risk of COVID-19 infection among university students, providing insights into the role of housing environments in COVID-19 spread within academic communities.

Methods: Data was collected using convenience sampling at Missouri State University from August 2020 to May 2021. Weekly PCR-based testing assessed over 1437 students who completed questionnaires with information on demographics and housing types categorized as on-campus dormitories, off-campus apartments, self/apartment with a mate(s), fraternity/sorority housing, and single-family houses. Crude and multivariable logistic regression models were used to assess associations.

Results: After adjusting for covariates, university students in fraternity/sorority houses and apartments with roommates were associated with greater odds of COVID-19 infection. The highest risk of COVID-19 infection was observed in students residing in frat/sorority houses (AOR=2.73 [95% CI: 0.177-42.043]), followed by those in apartments with roommates (AOR=2.705 [95% CI: 0.189-38.778]). Students in single-family homes, on-campus dorms, and apartments by themselves were associated with lower odds of contracting COVID-19.

Conclusion: Our findings reveal that the odds of COVID-19 infection in university students living in fraternity/sorority houses were 2.73 times higher compared to students with other housing arrangements. These findings can guide evidence-based strategies for mitigating the virus's impact on academic communities and enhancing overall public health response measures.

Assessment of Inaugural COVID-19 Vaccine Allocation Among Critical Populations in Nebraska Julia (He)* Julia (He) Bai Patrick Maloney David Brett-Major Kendra Ratnapradipa Yi Du Sai Paritala Ed Peters

The first phase of the COVID-19 vaccine distribution strategy initiated on December 2020 prioritized critical populations, defined by the Nebraska COVID-19 Vaccination Plan as healthcare personnel, critical infrastructure workforce, elderly populations, and vulnerable populations based on minority status, congregate living, and disabilities. We aim to evaluate vaccination equity and assess potential disparities in the initial rollout of the COVID-19 vaccine in Nebraska.

We conducted a cross-sectional supply-demand study covering 1 Dec 2020 – 28 Feb 2021. Statewide vaccination inventory data and immunization data from the Nebraska Department Health and Human Services (DHHS) as well as DHHS news releases detailing initial participating retail pharmacies were used to identify addresses and calculate supply quantities of state provider sites (PS) and CDC-associated retail pharmacy PS. The proportion of vaccine eligible critical population was estimated using the 2016-2020 ACS dataset. The supply to demand ratio (SDR) for each PS was determined by the supply quantity and the critical population of the census tract (CT). The county vaccine allocation score (CVAS) was created using the sum of SDR from each PS residing within the county. County level CDC reported COVID-19 death and case prevalence, USDA rurality designation, and CDC/ATSDR social vulnerability variables related to socioeconomic status, minority status, and household/housing characteristics were utilized as covariates in predicting CVAS through a multivariate linear regression model.

Our results observed a 0.21 point decrease in CVAS with each percentage increase in minority populations (CI: -0.23 – -0.02) when adjusted for COVID-19 death prevalence (Parameter estimate: 0.62, CI: 0.58-0.66) and percent in poverty (Parameter estimate: 0.27, CI: 0.02-0.52).

The evaluation of early allocation efforts will serve as a baseline to appraise future vaccination strategies in disparity reduction and equity improvement.

Table 1. Association between county COVID-19 vaccine allocation scores and county-level vulnerability factors, Nebraska, 1 Dec 2020 – 28 Feb 2021

Variable	Unadjusted		Adjusted	
	Parameter Estimate	95% Confidence Limit	Parameter Estimate	95% Confidence Limit
Percent minority	0.31	$0.01 - 0.62^{**}$	-0.12	$-0.23 - -0.02^{**}$
Percent below 150% poverty	-0.10	$-0.85 - 0.65$	0.27	$0.02 - 0.52^{**}$
COVID-19 death prevalence	0.60	$0.56 - 0.64^{***}$	0.62	$0.58 - 0.66^{***}$
COVID-19 case prevalence	0.01	$0.01 - 0.01^{***}$		
Percent multi-unit housing	3.02	$2.29 - 3.75^{***}$		
Rurality	-8.85	$-16.38 - -1.31^{**}$		
Percent mobile homes	-0.65	$-1.38 - 0.09^{*}$		
Percent with no vehicle	1.63	$-0.11 - 3.37^{*}$		
Percent with no health insurance	0.09	$-1.05 - 1.22$		
Percent with limited English language proficiency	0.52	$-0.73 - 1.77$		
Percent housing with crowding	0.59	$-1.66 - 2.84$		
Percent group quarter housing	0.59	$-0.94 - 1.39$		

*   Indicates statistical significance at the $\alpha = 0.1$ level
**   Indicates statistical significance at the $\alpha = 0.05$ level
***   Indicates statistical significance at the $\alpha = 0.0001$ level

Determinant of covid-19 vaccination coverage and post-vaccination adverses effects among at-risk people in DRCongo Remy Mpulumba Badiambile* Remy MPULUMBA BADIAMBILE Jean-claude Musasa kasongo Patrick Mukendi Kalonji Crispin Tshishimba Kamwandjemba Jean-Marcel Manongo Bakenge Guy Sakaji Ikomba Musau Sebastien Njila Tshipamba Criss Koba Mjumbe

Contexte. vaccination against Covid-19 is considered as an effective way to reduce the spread of the SARS-CoV-2 and prevent severe complications among the people at risk. however, for vaccination to be effective, it is crucial to have sufficient vaccination coverage within a population. The objective was to determine the factors influencing the COVID-19 vaccination coverage and the occurrence of post-vaccination adverse symptoms among people at risk in Mbujimayi. **Methods**. A cross-sectional study was employed. The data were obtained via an electronic questionnaire supplied by smart phone between October 2023 and December 2023, where a total of 560 people at risk from the Bonzola health zone were recruited. Logistic regression analysis was used using SPSS version 25.0 to analyze the factors associated with COVID-19 vaccine uptake and occurrence of post-vaccine symptoms. **Result**.Overall, 560 people at risk (173 females (30.9%), 387 males (69.1%) with a median age and standard deviation of 30.0 years ± 16.9. The overall vaccine coverage was 77 % and 57.7% had post-vaccine symptoms. profession, sex, age, information, raison taking vaccine were the factors that influenced the COVID-19 vaccine uptake. Profession,vaccine dose ,vaccine type were the factors that influenced the post-vaccine symptoms among people at risk in Mbujimayi. People at risk informed for covid-19 vaccination (odds ratio-OR = 0.89; confidence interval-CI: 0.82, 0.96, p < 0.000) were more likely than People at risk not informed to be fully vaccinated. **Conclusion**. These results emphasize the importance of continuing to raise awareness among at-risk populations on the importance of vaccination to reduce the effects of the pandemic, while considering individual factors that may influence vaccination coverage and post-vaccine symptoms. Additional efforts to enhance vaccination uptake are needed to improve the COVID-19 vaccination coverage.

Keywords: COVID-19 vaccination; Coverage; post-vaccination; adverse symptoms; DRCongo

Examining the Effects of Physical Environment and Social Structural Factors on Racial Disparities in COVID-19 Mortality Suresh Nath Neupane* Suresh Nath Neupane

Exploring the relationship between urban environments and population health from an urban health perspective offers a comprehensive understanding, recognizing that both are linked to urban living. This study uses several datasets, including CDC's COVID-19 mortality data and EPA's environmental justice tool, EJSCREEN, to examine the influence of physical and social environments on racial disparities in urban COVID-19 mortality across the U.S. from January 1, 2020, to April 15, 2021. Focusing on urban and suburban areas, hierarchical logistic regression models reveal the complex interplay between demographic factors, environmental exposures, and social determinants of health.

The study shows that racial disparities in COVID-19 mortality cannot be understood without considering the socio-economic and environmental context that individuals live in. Key findings include the impact of air pollution, such as particulate matter (PM2.5) levels and hazardous air pollutants (HAP), and proximity to traffic and hazardous waste facilities on increasing COVID-19 mortality risk. The study also underscores the role of social vulnerability and housing problems in exacerbating health disparities.

This study highlights that Black and Hispanic populations face lower mortality odds compared to Whites when environmental and social factors are accounted for, suggesting that addressing COVID-19 health disparities requires a multifaceted public health strategy. It calls for comprehensive interventions targeting healthcare access, environmental justice, and the improvement of living conditions to mitigate the unequal impact of COVID-19 on different racial and ethnic groups. In conclusion, the study contributes to a deeper understanding of how physical and social environments shape racial disparities in COVID-19 mortality, advocating for policy responses that address the root causes of these disparities.

Changes in psychological disease incidence patterns during the COVID-19 pandemic: A study using the nationwide health insurance data of Korea Changwoo Han* Changwoo Han

Background

The psychological impact of the coronavirus disease (COVID-19) pandemic on a comprehensive set of psychological conditions has rarely been examined. Here, we aimed to use Korea's universal health insurance data to evaluate changes in psychological disease incidence patterns during the pandemic.

Methods

Hospital visit data related to psychological diseases (January 2013–February 2023) were retrieved from the National Health Insurance Database. Using primary diagnostic codes, first-ever hospital visits for specific psychological diseases were identified, and monthly age-standardized incidence rates were calculated. An interrupted time-series analysis, adjusted for seasonality and long-term trends, was used to estimate counterfactual disease incidence rates. Observed and counterfactual rates were compared to estimate the disease incidence pattern changes during the pandemic.

Results

Compared to pre-pandemic rates, there was a decrease in the incidence [percentage changes in monthly age-standardized rate (95% confidence intervals)] of organic mental disorders (F00-F09) [-14.6% (-18.4, -10.9)] and psychoactive substance use-related disorders (F10-F19) [-12.9% (-17.5, -8.3)]. However, there was increase in anxiety-related disorders (F40-F48) [8.8% (3.1, 14.6)] and behavioural syndromes associated with physiological disturbances (F50-F59) [8.1% (4.2, 11.9)]. Additionally, the incidence of mental retardation (F70-F79) [8.6% (3.0, 14.2)], psychological developmental disorders (F80-F89) [19.6% (11.5, 27.7)], childhood- and adolescent-onset behavioural and emotional disorders (F90-F98) [45.1% (28.4, 61.8)], and unspecified mental diseases (F99) [51.8% (39.8, 63.8)] increased.

Conclusions

Psychological disease incidence patterns changed substantially during the pandemic in South Korea with important heterogeneity across specific conditions. Various pandemic-related stressors, such as disrupted lifestyles, social isolation and primary care accessibility, may explain these changes. The causes and public health consequences of these changes require further evaluation.

LATEBREAKER

COVID-19 Pandemic

Folic Acid Fortification and COVID-19 Incidence and Mortality: An International Study

Lydia Famuyide* Lydia Famuyide Ruofei Du Namvar Zohoori Benjamin Amick III Wendy N. Nembhard

It is hypothesized that SARS-CoV-2 utilizes folate for replication in humans. Prior studies demonstrated that folic acid supplementation protects against SARS-CoV-2 infection but may increase the risk of post-infection mortality in humans. Our study evaluated these findings in an ecologic study by assessing the association between country-specific folic acid intake levels and COVID-19 incidence and mortality rates.

We obtained folic acid fortification legislation status (mandatory, voluntary or none), fortification levels of grain flours, and potential folic intake (mg/day) for each country (n=196) as of December 2019 from the Global Fortification Data Exchange. COVID-19 incidence and mortality data, December 2019–April 2023, for countries were obtained from the World Health Organization (WHO). Countries were categorized into six WHO-regions and four income groups using World Bank categories. Rate ratios and 95% CI were estimated from negative binomial regression analyses to estimate the association between folic acid fortification/potential intake (mg/day) and COVID-19 incidence and mortality rates per 100,000 population stratified by WHO region and World Bank income categories.

For middle- income countries, those that had mandatory folic acid fortification policies had a 30% lower COVID-19 incidence than those that did not fortify with folic acid (unadjusted RR=0.7; 95% CI: 0.5, 1.1). There was a significant association between mandatory folic acid fortification policies and COVID-19 incidence among countries in Africa and Europe. We found no significant association between mandatory folic acid fortification policies or potential intake and COVID-19 mortality in countries by income category or WHO region.

Folic acid fortification is associated with lower incidence of COVID-19 even after adjusting for income and region but does not appear to be associated with mortality. Additional studies are warranted to further investigate this possible association.

Application of the Actor-Partner Interdependence Model to Quantify Teen-Parent COVID-19 Vaccine Decision-Making Annette Regan* Annette Regan Marie-Claude Couture Timothy Callaghan Brianna Agnew Jillian Baker Onyebuchi Arah

Although adolescents are likely to play a role in vaccine decision-making and US states are increasingly allowing adolescents (teens) to self-consent to vaccination, few studies have considered teens' role in COVID-19 vaccine decision-making. We apply the Actor-Partner Interdependence Model (APIM) to understand actor (teen) and partner (parent) effects of vaccine hesitancy on teen COVID-19 vaccination uptake. We conducted a nationally representative survey of teens aged 12-17 years old and their parents (n=764 teen-parent dyads). Parents completed a 20-minute online survey and provided consent for their teen child to participate. Teen participants separately assented to participate and completed a similar survey. Parental and teen surveys measured self-reported COVID-19 vaccination and vaccine hesitancy using a modified version of the Vaccine Hesitancy Scale for teen COVID-19 vaccination (tVHS), with higher scores indicating greater hesitancy (range 18 to 90). We used structural equation modeling to examine actor and partner influences on COVID-19 vaccination uptake. Teen and parental COVID-19 vaccine hesitancy was strongly correlated ($r = 0.85$) and this was consistent across teen ages. Structural equation modeling indicated for every one unit increase in parental COVID-19 vaccine hesitancy, teen COVID-19 vaccination decreased by 1.2% (SE 0.002) and parental COVID-19 vaccination decreased by 1.5% (SE 0.002). For every one unit increase in teen COVID-19 vaccine hesitancy, teen COVID-19 vaccination decreased by 1.1% (SE 0.002) and parental COVID-19 vaccination decreased by 0.4% (SE 0.002). Through this novel application of the APIM, we show that vaccine hesitancy expressed by teens and their parents have a negative influence on teen COVID-19 vaccination. COVID-19 vaccination rates remain lower among teens compared to adults, and these findings suggest that public health intervention should target both teens and their parents.

SEM for Parent-Teen Dyads
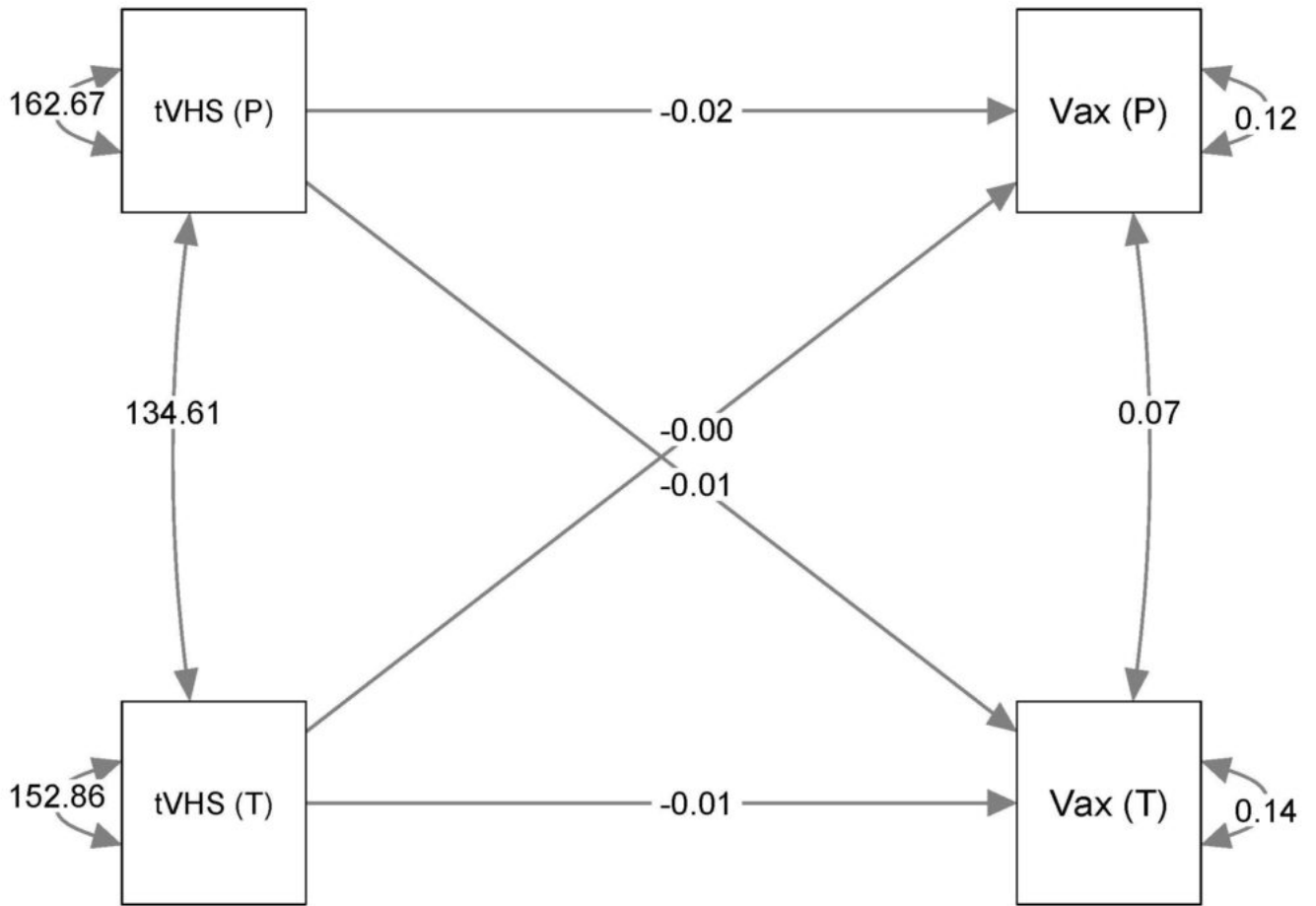
tVHS, vaccine hesitancy expressed by parent (P) or teen (T); Vax = Receipt of COVID-19 vaccine for parent (P) or teen (T)

Racial and ethnic differences in the associations between COVID-19 stigma and mental health in a population-based study of adults with SARS-CoV-2 infection Soomin Ryu* Soomin Ryu Paula Guro Jana L. Hirschtick Robert Orellana Nancy L. Fleischer

Introduction: Many individuals with COVID-19 faced stigmatization, which may contribute to poor health. However, few studies have explored the relationship between COVID-19 stigma and health and even less is known about intersectional stigma, which means having multiple stigmatized social identities simultaneously. This paper examines associations between COVID-19 stigma and mental health overall and by race and ethnicity.

Methods: Using a population-based probability sample of Michigan adults with confirmed SARS-CoV-2 infection between March 2020 and February 2022, we captured COVID-19 stigma based on (1) perceived COVID-19 stigma, (2) fear of COVID-19 disclosure to friends or family, and (3) fear of COVID-19 disclosure at work. We assessed associations between the three COVID-19 stigma measurements with symptoms for depressive and anxiety symptoms using modified Poisson regression with robust standard errors and adjusting for confounding factors.

Results: Individuals who perceived COVID-19 stigma had a higher prevalence of depressive (aPR: 1.38, 95% CI: 1.17−1.62) and anxiety symptoms (aPR: 1.41, 95% CI: 1.22−1.62) than individuals who did not perceive stigma. Moreover, individuals who were afraid to disclose their COVID-19 diagnosis to friends or family or at work had a higher prevalence of depressive and anxiety symptoms than those who were not. These associations were more pronounced among racial and ethnic minoritized individuals than among non-Hispanic White individuals.

Discussion: COVID-19 stigma was associated with higher prevalence of depressive and anxiety symptoms. This association was greater for racial and ethnic minoritized individuals, possibly due to the intersection of disease stigma and race and ethnicity. Continuing to monitor the long-term effects of COVID-19 stigma on mental health, particularly among racial and ethnic minoritized populations, will provide useful insight and lessons for future pandemics.

The role of housing infrastructure in facilitating SARS-CoV-2 infection in the carceral environment, California State Prisons, March 2020-2022 Helena Archer* Helena Archer Sandra McCoy David Sears Ada Kwan

Background:

Environmental vulnerability through congregate, crowded housing places incarcerated people at higher risk of acquiring COVID-19, and may limit effective response policy. However, the relative importance of housing type and housing features within prisons (e.g., dormitory vs cell living, open door or bars) on COVID-19 risk is poorly described.

Methods:

Using daily housing and healthcare records, we identified a longitudinal cohort of 150,633 California state prison (CDCR) residents between March 2020 and March 2022. We collected facilities and administrative data to evaluate density of residential buildings and their features relating to transmission of respiratory pathogens, categorizing units by relative occupancy within rooms (cells, multi-room dorms ("pod"), or standalone, single room dorms), and door type (solid door or barred/partial door ("open")). We assessed daily housing location and type, COVID-19 outcomes, and other relevant covariate data. We estimated the relative rate of testing positive for SARS-CoV-2 in different housing types using generalized estimating equations for Poisson regression.

Results:

At baseline, more than half of residents lived in solid-door celled housing. Across the study period, residents of solid-door pod dorms, open-door cells, open-door pod dorms, and standalone dorms had 1.49 (95% CI: 1.45,1.52), 1.59 (95% CI: 1.54,1.64), 2.54 (95% CI: 2.48,2.6), and 1.86 (95% CI: 1.82,1.9) times the rate of testing positive respectively when compared to residents of solid-door cell housing and after adjustment for individual risk factors (e.g. age, sex, underlying health conditions, vaccinations) and out-of-housing activities (e.g. classes, legal or medical appointments).

Conclusion:

Differences in infection rates across housing types can inform the safe movement of people who are incarcerated between and within facilities, and in maximizing safety and minimizing the consequences of COVID-19, even in high risk settings such as prisons.

The Prevalence and Gender Differences of Unhealthy Drinking During the COVID-19 Pandemic: Insights from a Longitudinal Cohort Study of Adults in the US Surabhi Yadav*

Surabhi Yadav Katarzyna Wyka Denis Nash Angela M Parcesepe

Objective: To investigate the prevalence and correlates of unhealthy drinking among US adults during the COVID-19 pandemic.

Methods: Data came from the CHASING COVID Cohort study, a prospective longitudinal community-based cohort of US adults. We included participants who completed the baseline questionnaire (March-April 2020) and at least one follow-up by May 2023 (N=5777). Unhealthy drinking was categorized as AUDIT-C ≥3 for women and ≥4 for men. We examined unhealthy drinking over time and its associations with sociodemographics and symptoms of depression or anxiety (GAD-7 and PHQ-8 ≥10), overall and by gender. We conducted descriptive analysis and made comparisons using Fisher's exact and Chi-squared tests.

Results: The prevalence of unhealthy drinking early in the pandemic (April-July 2020) was 36.9%, with slight gender differences (males 35.6% vs. females 38.1%). The prevalence of unhealthy drinking declined in the next six months to 28.5% (November-December 2020) and remained relatively stable thereafter. Gender differences were around 2-3%, with female adults continuing to report slightly higher prevalence. Early in the pandemic, younger age, higher education, higher income, employment, lack of loss of income due to COVID-19, fewer pre-existing health conditions, and higher levels of anxiety and depression symptoms were significantly associated with unhealthy drinking. Among adults with unhealthy drinking, gender differences were associated with younger and older age (age 18-29 males 19.4% vs. females 23.9%; age 60+ males 12.8% vs. females 18.4%), employment (employed males 75.5% vs. employed females 65.7%), lack of loss of income due to COVID-19 (males 59.3% vs. females 61.6%), anxiety (males 34% vs. females 44.3%) and one pre-existing health condition (males 28.2% vs. females 33.9%).

Conclusion: The findings underscore the need for gender-specific considerations to address unhealthy drinking, particularly during challenging times like the COVID-19 pandemic.

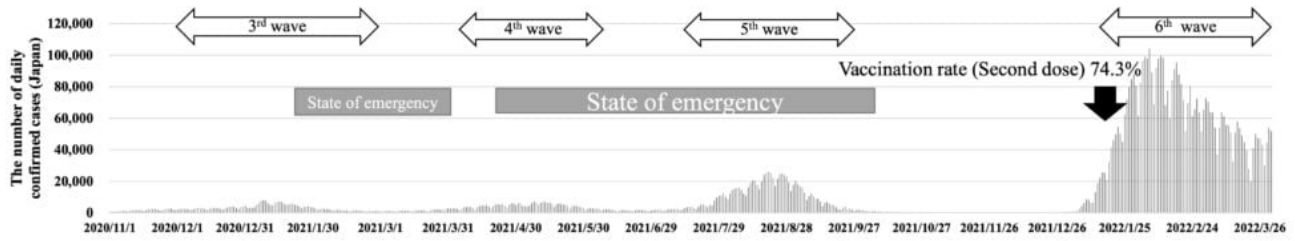Gender-Specific Unhealthy Alcohol Consumption Across Survey Time Points
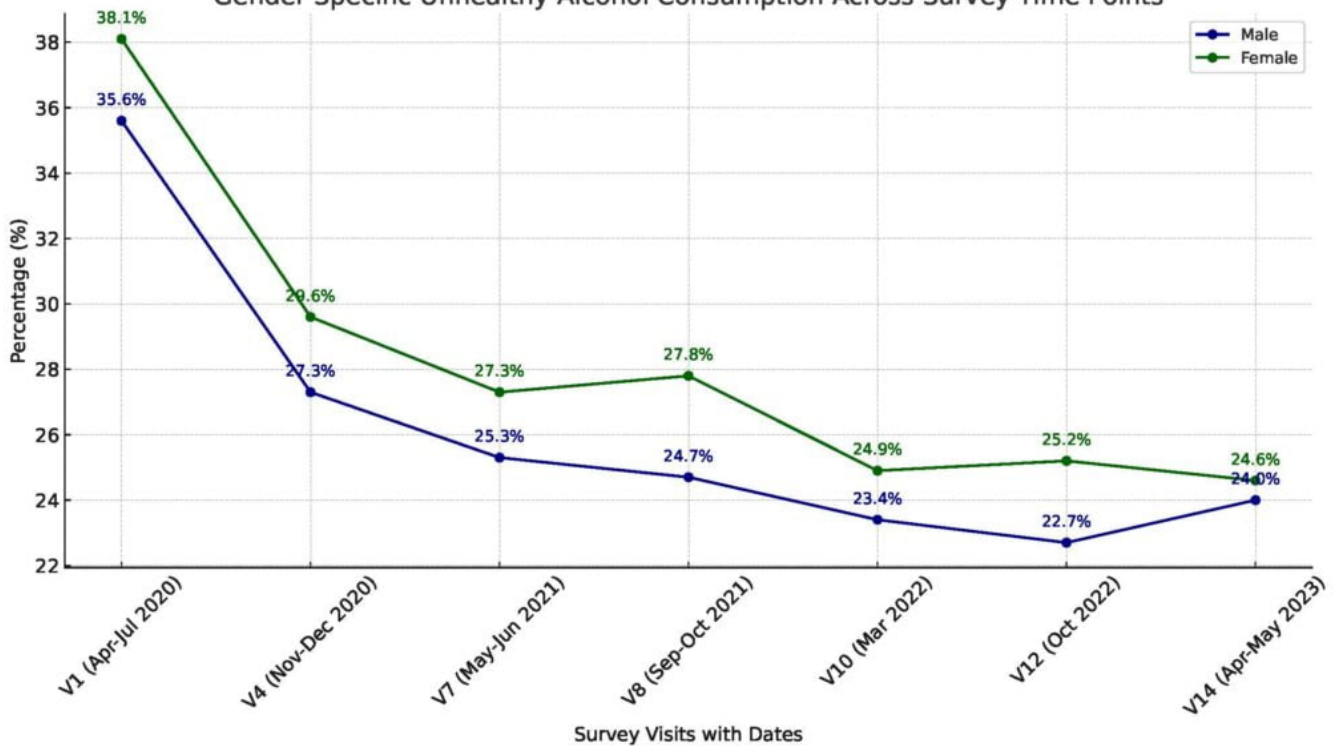
Individual feedback on behavioral risk assessments did not change future risk behaviors during the COVID-19 pandemic in Japan Shuko Takahashi* Shuko Takahashi Naomi Takahashi Masaru Nohara Ichiro Kawachi

Background: We examined prospectively whether feedback of behavioral risk assessments to individuals changed their behavioral risks across five sequential surveys during the COVID-19 pandemic in Japan.
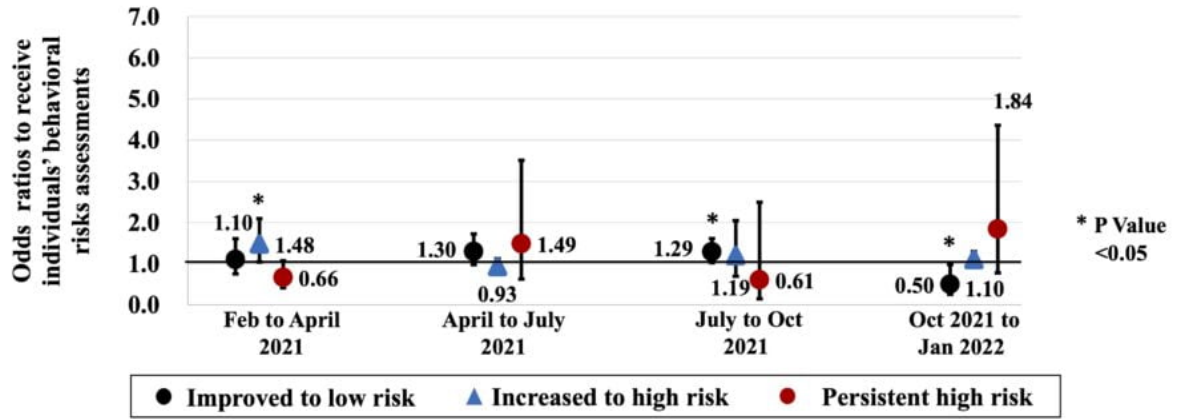
Methods: Five waves of rapid online surveys of residents in Iwate Prefecture were conducted from late 2020 to early 2022. Each individual's risk of acquiring SARS-CoV-2 infection was calculated using a quantitative assessment tool (the microCOVID) which classified each individual's risk level into low, middle, and high risk for acquiring infection. We provided feedback to individual respondents who requested information about their behavioral risks for acquiring COVID-19. After grouping individual risk levels into two groups: low risk versus middle/high risk, we calculated trajectories of behavior change between survey waves. Multinominal logistic regression was used to determine whether individual feedback was associated with behavior change, i.e., transitioning from high risk to low risk.

Results: We received responses from 9190, 11907, 9635, and 10636 individuals over follow-up survey waves. Contrary to our hypothesis, individuals who requested and received feedback on their risk of contracting COVID showed significantly higher ORs of transitioning to high risk between the 2nd and 3rd surveys conducted in February and April 2021 (OR 1.48, 95% CI: 1.04, 2.09). Although subsequently individuals who received feedback were more likely to improve to low risk between the 4th and 5th survey conducted in July to October 2021 (OR 1.29, 95% CI: 1.03, 1.62), they were again less likely to improve to low risk between the 5th and 6th survey conducted in October 2021 and January 2022 (OR 0.50, 95% CI: 0.26, 0.98).

Conclusion: Overall, feedback of individualized risk assessments was not associated with improvements in individual behavioral risk behaviors during the pandemic, and in some cases appeared to have the opposite effect.

Diabetes

Methodological approaches for addressing medication usage in studying exposure to volatile organic compounds and HbA1c among oil-spill cleanup workers Hanna Jardel* Hanna Jardel Alex Keil Chantel Martin David Richardson Patricia Stewart Mark Stenzel Larry Engel Dale Sandler

Background Oil spill cleanup workers are exposed to volatile organic compounds including benzene, toluene, ethylbenzene, xylenes, and hexane (BTEX-H). BTEX-H may disrupt glycemic regulation processes, detectable with high glycosylated hemoglobin (HbA1c) concentrations used to diagnose diabetes mellitus. This study aims to characterize how BTEX-H exposure among oil-spill cleanup workers affects HbA1c change over time. However, this change can be obscured in participants who use HbA1c-lowering medications.

Methods Data are from the Gulf Long-term Follow-up Study– a prospective cohort of workers who participated in oil spill cleanup following the 2010 Deepwater Horizon disaster. Participants provided interview data, biological specimens, and anthropometric and clinical measurements at two time points (enrollment, 2011-2013 and follow-up exam, 2014-2016).

Participants could have started HbA1c-lowering medication before either time point and continued through followup. Excluding medication users would obscure trends in HbA1c levels; we sought analytic solutions that would use all participants' data and censor HbA1c values under treatment. We evaluated two approaches: a) g-computation to predict HbA1c values, absent treatment, and linear regression and b) Tobit regression with inverse probability weighting (IPW), both after imputation to address covariate missingness. Both approaches assess the impact of quantile increases in exposure to the BTEX-H mixture and each individual chemical in relation to change in HbA1c over time.

Discussion We will present results of both strategies and discuss their strengths and limitations. Compared to Tobit regression with IPW, G-computation is computationally demanding; initial work suggests that it yields more stable point estimates. The lack of prior research addressing HbA1c-lowering medication usage in analyses necessitates formulation of strategies suitable to the available data, research question, and available computational power.

Diabetes

Spatial analysis of healthcare access and diabetes in Pennsylvania Jessica Berman* Jessica Berman Jong Cheol Shin

Previous research has ascertained that the Healthcare Data Information Set quality measures with the lowest compliance rates and highest care gaps among a diabetic population based out of Pennsylvania (PA) were within the Eye Exams for Patients with Diabetes and Kidney Exams for Patients with Diabetes quality measures. This study examined to what extent are healthcare facilities and services pertaining to eye care (EC) and kidney care (KC) accessible to diabetics in PA. Implications of this study include: 1) increased awareness of resources to boost compliance and health outcomes and 2) increased stakeholder knowledge of geographical context leading to informed decision making and resource allocation.

This study employed ArcGIS Pro for spatial analyses and RStudio for statistical analyses on the following variables: diabetes prevalence (prev), chronic kidney disease prev, diabetic retinopathy prev, median household income, zero access to a household vehicle and medically underserved areas. Locations of hospitals, dialysis facilities, endocrinologists, nephrologists, ophthalmologists and optometrists were geocoded into XY coordinates and served as the healthcare facilities and services pertaining to EC and KC. The ArcGIS Pro tools used were: Geocode Addresses, XY Table to Point, Buffer, Thiessen Polygons and Calculate Geometry Attributes. Pearson Correlation Coefficient tests were run to determine significance and r values.

The results depict a relationship between high diabetes prev and high access to healthcare services and facilities pertaining to EC and KC: hospitals (r=-0.11, p< .001), EC (r=-0.11, p< .001) and KC (r=-0.11, p< .001). This was evidenced by Allegheny, Delaware, and Philadelphia County depicting both high diabetes prev and high densities of hospitals, EC, and KC facilities and services. The additional variables mentioned were spatially and statistically analyzed with 75% of the bivariate analyses yielding significant results.

Medically Underserved Areas in PA vs. Location of Eye Care and Kidney Care Facilities/Services

Medically Underserved Areas vs. Locations of Eye Care and Kidney Care Facilities/Services in Pennsylvania

Diabetes Prevalence vs. Medically Underserved Areas in Pennsylvania
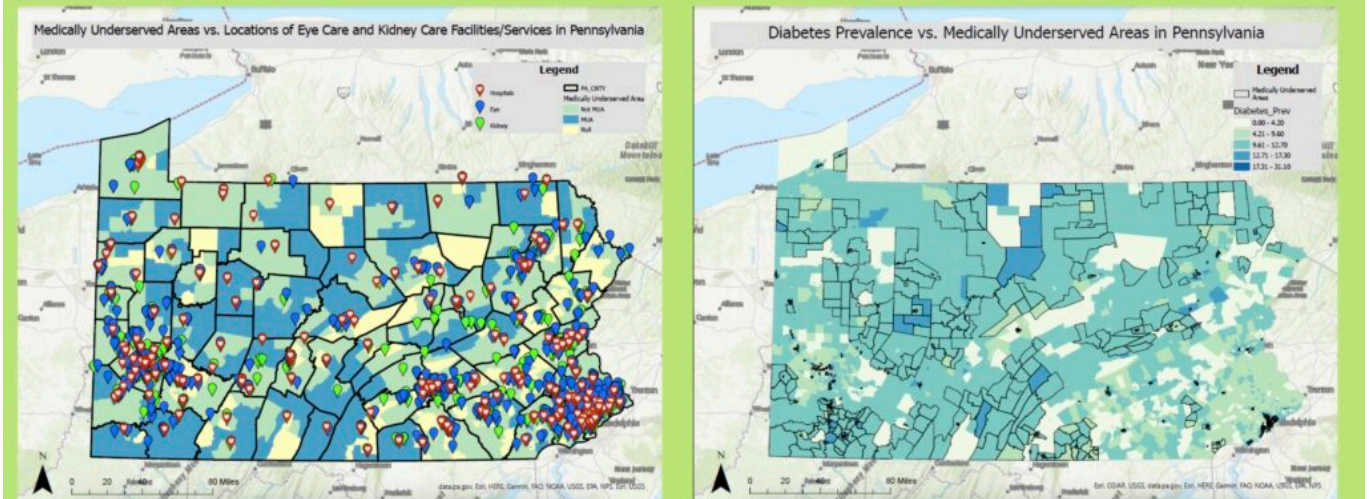
The left map depicts areas within PA that are considered to be "medically underserved" or "not medically underserved". The HRSA states that medically underserved areas (MUAs) "have a shortage of primary care health services for a specific population subset within a geographic area. These groups may face economic, cultural, or language barriers to health care" (p.1). Examples of barriers include homelessness and low income. The majority of MUAs are in the western region of PA. The right map depicts diabetes prevalence and the black outlined tracts are MUAs. It appears that PA tracts where there is high diabetes prevalence are also considered to me MUAs.

Health Resources & Services Administration, 2020

Diabetes

Social Determinants of Health and Their Association with Self-Reported Diabetes and Prediabetes Among Adults Aged ≥18 Years Paul Eke* Guixiang Zhao Machell Town Yiling J. Cheng

Introduction: Diabetes remains a major health concern in the US. This study assessed the associations of social determinants of health (SDOH) measures with self-reported diabetes and prediabetes among US adults aged ≥18 years.

Methods: The 2022 Behavioral Risk Factor Surveillance System collected SDOH and diabetes data in 42 states (including DC and US territories), and prediabetes data in 26 states. Social risk factors assessed based on SDOH measures included life dissatisfaction, lack of social/emotional support, loneliness, employment instability, food insecurity, housing insecurity, utilities insecurity, lack of transportation access, mental stress, and cost barrier for needed care. For adjusted prevalence ratios, we conducted log-linear regression analyses adjusting for demographic characteristics and health-related behavioral risk factors.

Results: Overall, the prevalences of diabetes and prediabetes were 12.0% and 14.5% among US adults, respectively. After adjustment for study covariates, adults with 10 of the 11 social risk factors (except employment instability) were 10%-27% (P<0.05) more likely to report having diabetes, and adults with 8 social risk factors (except employment instability, food insecurity, and utilities insecurity) were 14%-38% (P<0.05) more likely to report having prediabetes compared with adults without corresponding social risk factors. Adults with increasing number of social risk factors were significantly more likely to report having diabetes and prediabetes compared to adults with none of the social risk factor.

Conclusions: Social risk factors are associated with higher risk of diabetes among US adults, independent of traditional diabetes risk factors. Diabetes prevention and intervention programs may be prioritized to individuals with social risk factors.

Urinary polycyclic aromatic hydrocarbon metabolites and their association with oxidative stress among pregnant women in Los Angeles Qi Meng* Qi Meng

Introduction Polycyclic aromatic hydrocarbons (PAHs) have been linked to adverse birth outcomes, but few epidemiological studies to date have evaluated associations between urinary PAH metabolites and oxidative stress biomarkers in pregnancy.

Methods We measured a total of 7 PAH metabolites and 2 oxidative stress biomarkers (malondialdehyde (MDA), 8-hydroxy-2'-deoxyguanosine (8-OHdG)) in urine samples collected up to three times during pregnancy in 159 women enrolled at antenatal clinics at the University of California Los Angeles during 2016-2019. Using multiple linear regression models, we estimated the percentage change (%) and 95% confidence interval (CI) in 8-OHdG and MDA measured at each sample collection time per doubling of PAH metabolite concentrations.

Results Most PAH metabolites were positively associated with both urinary oxidative stress biomarkers, MDA and 8-OHdG, but the associations were stronger in early and late pregnancy. Women pregnant with boys exhibited larger increases in both MDA and 8-OHdG in association with PAH exposures in early pregnancy, while for pregnancies of girls we found stronger associations between PAH exposures and MDA in mid-pregnancy.

Conclusion Urinary OH-PAH biomarkers are associated with increases in oxidative stress during pregnancy, especially in early and late pregnancy. Sex differences in associations between PAH exposures and oxidative stress in the future need to be further explored.

Associations between neighborhood green space, quality of life, and perceived sleep satisfaction during the COVID-19 pandemic: Findings from a nationwide survey Jong Cheol Shin* Jong Cheol Shin Fathima Wakeel

Background: Sleep satisfaction, a critical contributor to overall well-being, is influenced by myriad factors including health conditions and environmental factors. The COVID-19 pandemic, with its heightened stressors and lifestyle disruptions, may have exacerbated poor sleep satisfaction. The potential benefits of neighborhood green spaces, a facet of environmental health, have not been extensively studied in this context.

Objectives: This study aimed to investigate the association between neighborhood green space, quality of life, and sleep satisfaction during the COVID-19 pandemic.

Methods: The analysis is based on data from 872 U.S. individuals who completed an online survey in August 2021. The modified 23-item WHOQOL-BREF instrument was used to assess perceived physical, psychological, social, and environmental health during the pandemic. Neighborhood Green space was measured using Normalized Difference Vegetation Index (NDVI) images captured from eMODIS imaging spectrometers at 250m resolution, mapped to participants' zip codes. Ordinary Least Squares (OLS) regression was utilized for analysis, controlling for confounders such as race, education, income, sex, and occupation.

Results: There was a significant positive association between the presence of neighborhood green spaces and sleep satisfaction. Furthermore, higher self-reported quality of life, including better physical health, psychological health, and neighborhood environment, corresponded with improved sleep satisfaction.

Conclusions: This study provides compelling evidence of the positive associations of both higher quality of life and more green space on sleep satisfaction during the COVID-19 pandemic. These findings emphasize the necessity for maintaining and enhancing urban green spaces as a public health strategy for improving sleep satisfaction, particularly during crisis situations.

Swimmers are at higher risk of gastrointestinal illness when human-associated genetic markers of human fecal contamination are present Timothy Wade* Timothy Wade Elizabeth Sams Stephanie DeFlorio-Barker Alfred Dufour Richard Haugland Kevin Oshima Edward Hudgens Orin Shanks

Numerous epidemiological studies have found associations between the level of fecal contamination in recreational waters and the risk of gastrointestinal illness among swimmers. This association, however, is likely affected by the source of fecal contamination (e.g., human, avian, dog, etc.) and has been hypothesized to be strongest when humans are the primary source of the fecal contamination. We conducted an epidemiological study in 2015 at a Lake Michigan beach to evaluate the association between fecal contamination and swimming-associated gastrointestinal illness. A total of 533 beachgoers were enrolled and 10-14 days later completed a survey about symptoms experienced since the beach visit. Water samples were collected each study day and tested for both general indicators of fecal contamination (e.g., Enterococcus spp., E. coli, and coliphage) and human-associated Bacteroides genetic markers HumM2 and HF183/BacR287. One or both human markers were detected on 7 of the 13 study days. On days when human makers were detected associations between general fecal indicators and diarrhea among body-immersion swimmers were considerably stronger than days when human markers were absent. For example, among body-immersion swimmers, the odds ratios for diarrhea associated with a log increase in Enterococcus spp. CCE /100 ml and somatic coliphage PFU/L was 6.5 (95% CI 1.5-27.76) and 6.15 (95% CI 1.66-22.76), respectively. When human markers were absent these associations were not significant. Similar patterns were observed with the other general fecal indicators. These findings provide additional evidence that exposure to human-derived fecal contamination results in higher risks of swimming-associated illness.

Ambient temperature during susceptible windows of spermatogenesis and impact on hCG+ pregnancy in an infertility treatment population Lindsey M. Russo* Lindsey M. Russo J. Richard Pilsner Timothy P. Canty Pauline Mendola Kaniz Rabeya Karen S. Schliep May Shaaban Akanksha Singh Allison M. Ring Rachael Hemmert Neil J. Perkins James A. VanDerslice C. Matthew Peterson Erica Johnstone Carrie Nobles

Background: Male preconception exposure to temperature remains a critically under-addressed area of family planning. Animal studies have found spermatogenesis susceptible to heat stress; therefore, we examined ambient temperature and hCG+ pregnancy in the Folic Acid and Zinc Supplementation Trial (2013-2018) among couples seeking infertility treatment in Salt Lake City.

Methods: In the FAZST Trial (n=2,015 men), we evaluated four susceptible windows of ambient air pollution exposure during spermatogenesis (mitosis, meiosis I-II, spermiogenesis, spermiation) for semen samples provided during couple-level intrauterine insemination (IUI, n=505 couples and 1,223 cycles) or in vitro fertilization (IVF, n=221 couples and 280 cycles) treatment cycles over nine months of follow-up. Daily ambient temperature was abstracted from weather monitoring stations for Salt Lake City and averaged across each susceptibility window. Treatment-cycle probability of pregnancy was assessed for IUI and IVF cycles separately using generalized linear mixed models adjusted for fine particulate matter, ozone, age, and income, as well as interaction with warm (Apr – Sept) versus cold season (Oct – Mar).

Results: Overall, there were 133 (10.9%) IUI and 171 IVF hCG+ pregnancies (61.1%). For a 2° C increase in average ambient temperature in the warm season, we observed no clear association in models adjusted for age, income, and fine particulate matter [e.g., RR: 1.01, 95% CI: 0.95, 1.07 during meiosis]. Upon addition of ozone, a seasonal confounder, we observed a higher likelihood of IUI pregnancy during mitosis and meiosis [e.g., RR: 1.13, 95% CI: 1.03, 1.23 for meiosis]. We observed minimal impacts among IVF participants. No associations were observed during the cold season.

Conclusion: Overall, we observed few associations, but found an unexpected association when adjusting for ozone, which may suggest potential mediation or other complexity.

Environment/Climate Change

The rise of unconventional natural gas development and the fall of coal-fired power plants: Associations with pediatric asthma onset in Pennsylvania Nina M. Flores* Nina Flores Gabriella Meltzer Heather McBrien Kara E. Rudolph Lucas RF Henneman Xin Fang Dione Mercer Jordan Law Brian S. Schwartz Stephanie Lovinsky-Desir Mary Willis Joan A. Casey

As a result of regulation, lower prices, and technological advances, in 2015, natural gas surpassed coal as the primary US electricity source. During the transition from coal to natural gas, many children lived in communities dually exposed to coal-fired power plants and unconventional natural gas development (UNGD). Although previous analyses have identified associations between exposure to coal-fired power plants or UNGD and asthma exacerbation, none have considered relations with incident asthma, these fossil fuel exposures in tandem, or the role of individual-level socioeconomic status.
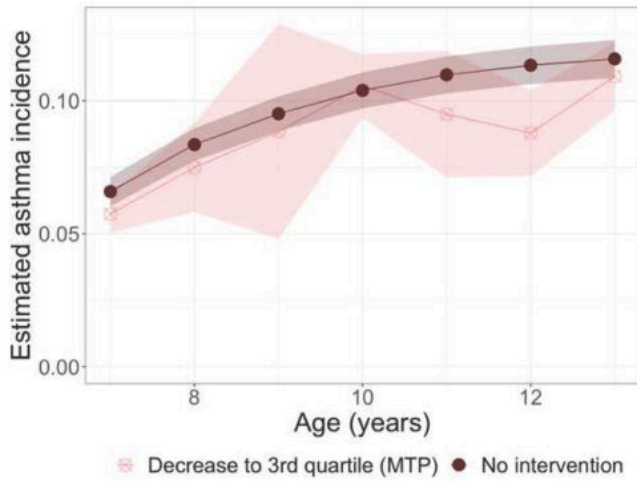
We used 2006-2020 electronic health record data from Geisinger in Pennsylvania and longitudinal modified treatment policy methodology to estimate asthma incidence under hypothetical coal or UNGD interventions. Each hypothetical intervention reduced exposures during the first 3 years of life for those with exposure above the 75th percentile to the 75th percentile. Models adjusted for date of birth and sex, Medical Assistance, race/ethnicity, maternal age, household tobacco smoke, residential latitude/longitude, county-level population density and community socioeconomic deprivation, annual average nitrogen dioxide concentration, and seasonal greenspace. We examined whether the use of Medical Assistance modifies these relationships.

Among 10,808 children, the estimated asthma incidence at age 12 under no intervention on coal exposure was 11 per 100 (95% CI 11-12); under the hypothetical intervention incidence was 9 per 100 (7-10). The estimated asthma incidence at age 12 under no UNGD intervention was 10 per 100 (9-11), and 9 per 100 (8-11) with the hypothetical intervention. We show estimated incidences from year 7-13 in Figure 1 overall (top) and among Medical Assistance users (bottom).
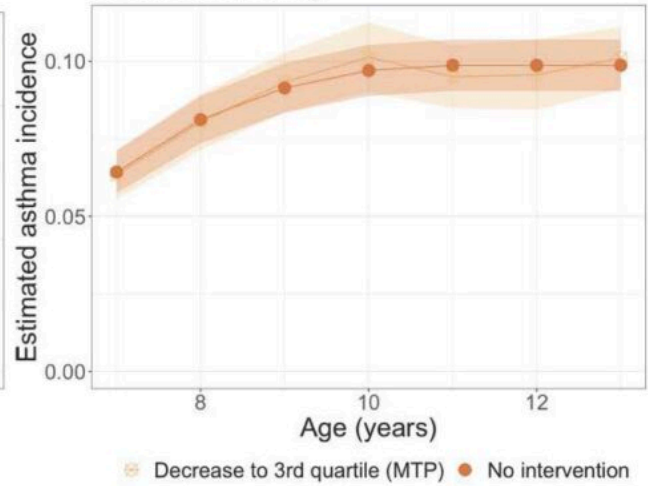
Intervention to reduce coal and UNGD exposures could reduce asthma incidence, especially among low-income individuals, who are disproportionately burdened by adverse health effects of such exposures.
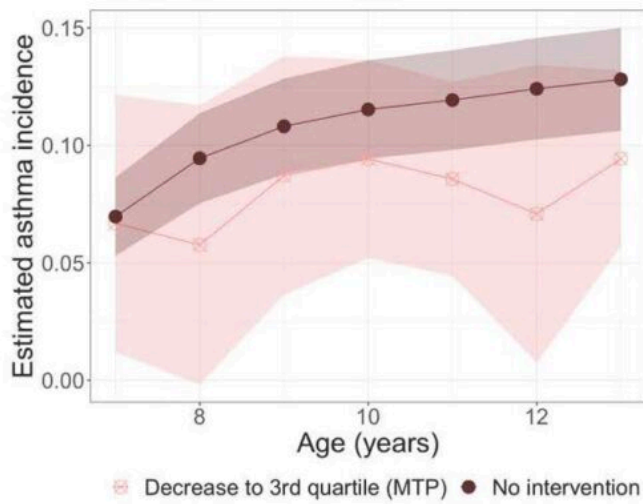
Overall (n = 10,808)
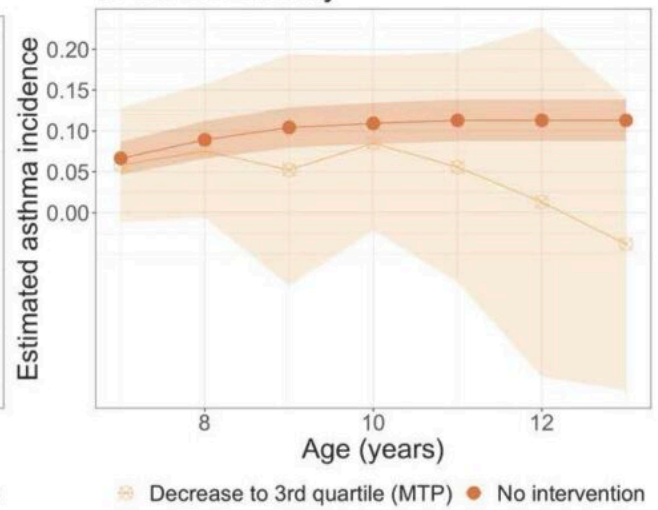
a. HyADS coal PM$_{2.5}$

⊗ Decrease to 3rd quartile (MTP) ● No intervention

b. UNGD activity

⊗ Decrease to 3rd quartile (MTP) ● No intervention

Medicaid users only (n = 1,249)

a. HyADS coal PM$_{2.5}$

⊗ Decrease to 3rd quartile (MTP) ● No intervention

b. UNGD activity

⊗ Decrease to 3rd quartile (MTP) ● No intervention

Environment/Climate Change

Characterizing Health-Related Quality of Life Risk Factors in the Fernald Community Cohort

Sara Burcham* Sara Burcham Wei Wen Hsu Sharon Larson Susan Pinney

Background: Four self-reported Health-Related Quality of Life (HRQoL) outcomes were analyzed from persons who lived in Fernald, Ohio surrounding the former U.S. Department of Energy uranium processing facility as part of the Fernald Community Cohort (FCC).

Methods: Participants in the FCC completed the initial examination between January 1990 and December 1995 (N=7,957). Descriptive statistics were computed to examine differences among sociodemographic factors and well-being measures among the groups categorized by residential distance in the form of mile rings (0-5 miles) from the facility borders. Adjusted logistic regression analyses were performed to evaluate the relationship between residential distance and well-being measures in the cross-sectional study design.

Results: Residents within 0-1 miles of the contamination site reported a more negative outlook ("partly" or "not" satisfied) for the variable, life satisfaction, compared to those participants residing in the 4–5-mile ring. Notably, factors such as recent misfortune, environmental hazard awareness, social ties, job satisfaction, and physical activity levels emerged as common determinants of HRQoL in the separate regression models: feelings of life satisfaction, life in control, life perspective, and overall physical health.

Conclusions: Residential distance was a significant predictor of self-reported life satisfaction in the fully adjusted model. The study findings warrant further exploration in future studies investigating the long-term health outcomes of residents near environmental contamination sites.

Keywords: HRQoL, environmental contamination, Superfund, health risk appraisal, life satisfaction

Life Satisfaction

Life in Control

Life Perspective

Overall Physical Health
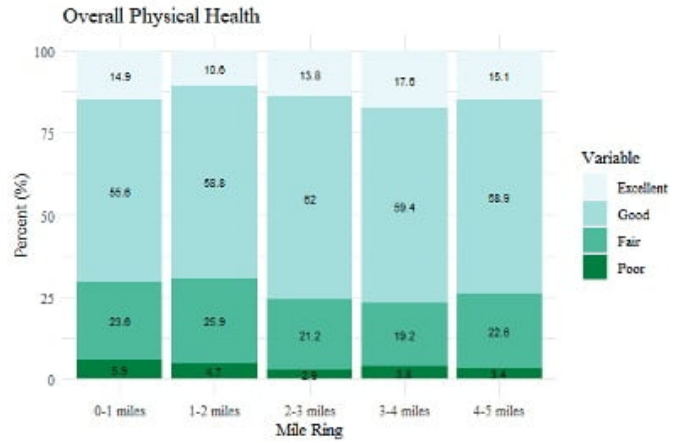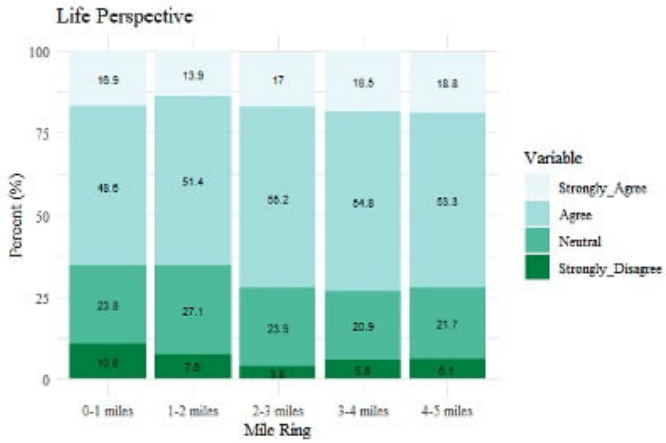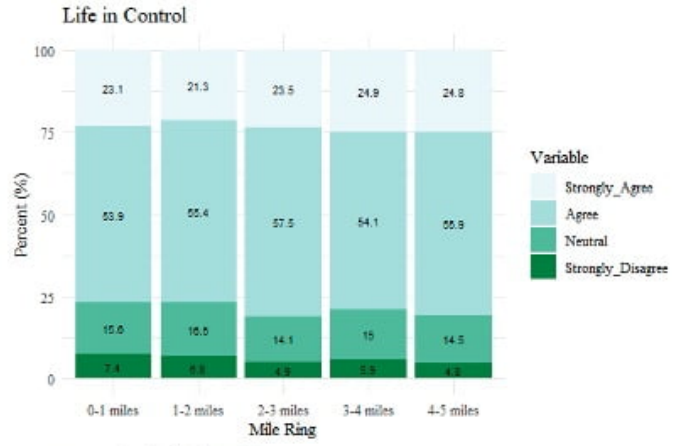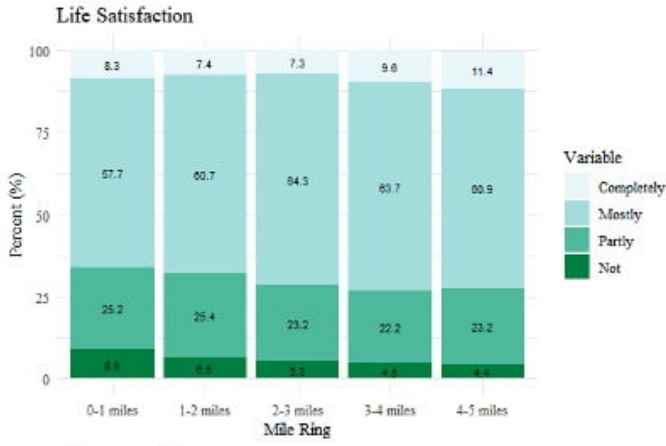
Association between noise pollution exposure and incident breast cancer in the Sister Study Brittney Gedeon* Brittney Gedeon Che-Jung Chang Rena R. Jones Peter James Dale P. Sandler Alexandra J. White

Background: Noise exposure may negatively impact sleep and the autonomic nervous system, potentially influencing the risk of developing cancer. European studies have observed modest positive associations between anthropogenic noise exposure and breast cancer incidence. Studies have not evaluated this in the United States, where sources and levels of noise may differ.

Objective: To examine the association between residential noise exposure and incident breast cancer.

Methods: We included 49,405 participants enrolled between 2003-2009 in the Sister Study, an ongoing prospective cohort of women 35-74 years of age at baseline living in the United States. Median daytime and nighttime anthropogenic noise at the participants' baseline residence were estimated by a U.S. National Park Service noise model. We used Cox proportional hazards models to estimate HRs and 95% CIs for the association between an interquartile range (daytime IQR=5.2dB, nighttime IQR=4.0dB) difference in noise and incident breast cancer. Models were adjusted for age as the timescale, socioeconomic status, race/ethnicity, area deprivation, and urbanicity-related variables.

Results: During an average of 12.4 years of follow-up, 4,507 breast cancers were diagnosed. We observed no association between an IQR increase in daytime (HR: 1.02, 95% CI: 0.97, 1.07) or nighttime (HR: 1.00, 95% CI: 0.97, 1.04) noise and breast cancer incidence. However, we found an association between the 4th quartile of daytime noise and elevated breast cancer incidence (HRQ4 vs Q1:1.12, 95% CI: 0.99, 1.27).

Conclusions: In this large prospective cohort of U.S. women, we observed no overall associations between noise and breast cancer incidence except a possible association with the highest exposure level of daytime noise. More research incorporating improved exposure assessment is needed to determine whether noise is related to breast cancer incidence.

Table 1. Relationship between anthropogenic L_{50} daytime and nighttime and incident breast cancer in the Sister Study

	Number of Cases (n)	Age-Adjusted HR (95% CI)[a]	Fully Adjusted HR (95% CI)[b]
L_{50} Daytime Noise			
IQR Increase[*]	4507	1.03 (1.00, 1.06)	1.02 (0.97, 1.07)
5.92 < Q1 ≤ 43.8	1063	Ref.	Ref.
43.8 < Q2 ≤ 47.1	1156	1.10 (1.01, 1.19)	1.08 (0.98, 1.18)
47.1 < Q3 ≤ 49.0	1134	1.08 (0.99, 1.17)	1.05 (0.95, 1.17)
49.0 < Q4 ≤ 62.6	1154	1.11 (1.02, 1.21)	1.12 (0.99, 1.27)
		P-for-trend: 0.03	P-for-trend: 0.13
L_{50} Nighttime Noise			
	Number of Cases (n)	**Age-Adjusted HR (95% CI)[a]**	**Fully Adjusted HR (95% CI)[b]**
IQR Increase[**]	4507	1.02 (0.99, 1.05)	1.00 (0.97, 1.04)
2.40 < Q1 ≤ 41.4	1089	Ref.	Ref.
41.4 < Q2 ≤ 43.6	1157	1.07 (0.98, 1.16)	1.03 (0.94, 1.13)
43.6 < Q3 ≤ 45.4	1154	1.08 (0.99, 1.17)	1.02 (0.93, 1.12)
45.4 < Q4 ≤ 54.2	1107	1.04 (0.96, 1.14)	1.00 (0.90, 1.11)
		P-for-trend: 0.30	P-for-trend: 0.93

[*]L_{50} (the noise level that is exceeded 50% of the time) daytime interquartile range (IQR) = 5.2dB
[**]L_{50} (the noise level that is exceeded 50% of the time) nighttime interquartile range (IQR) = 4.0dB
[a]Age used as the time scale
[b]Adjusted for age as the time scale, educational attainment, income, race/ethnicity, area deprivation index (ADI), light at night, population density, greenspace, and $PM_{2.5}$ concentrations.

Modifying factors and temporal trends of adverse health effects of short-term exposure to PM2.5 in Canada (2001-2018) Hwashin H. Shin* Hwashin Shin Hwashin H. Shin James Owen Anna O. Lukina Muzeyyen Kabasakal Stéphane Buteau

Background: Considerable evidence has been accumulated on acute health outcomes associated with short-term exposure to ambient fine particulate matter (PM2.5). However, spatial and temporal variations (eg, climate changes) and modifying factors of those associations need further analyses.

Methods: PM2.5-related adverse health effects were estimated, covering 80% of Canadians for 18 years (2001-2018). We considered cause, region, season, age, and sex as potential modifying factors of PM2.5-related adverse health effects. Using daily averages of PM2.5 and temperature, and daily counts of hospitalizations and mortality (non-accidental all-cause, circulatory, and respiratory), we estimated city-specific associations, and then national and regional associations. Considering climate changes by time and region, we examined trends in national and regional associations obtained by dynamic models and tested if the trends were linear.

Results: Nationally, PM2.5 exposure was associated with both hospitalizations and mortality with differences by modifying factors. In particular, circulatory mortality and respiratory hospitalization were more attributable to PM2.5 exposure. Eastern Canada was the main source of the significant association with all-cause hospitalization, whereas Western Canada bolstered the association with all-cause mortality. PM2.5 appeared to increase respiratory hospitalization during the warm season, and circulatory hospitalization during the cold season. Circulatory mortality risk was significant for seniors and females.

Conclusions: This study found the adverse health effects of PM2.5 exposures depend on PM2.5 concentrations and other factors (region, cause, season, age, sex). National estimates for the baseline (≥1 year, both sexes) cannot be interpreted without consideration of the differences by modifying factors. Seniors and females appeared more vulnerable to short-term exposure to ambient PM2.5, and linear trends in risk varied by the factors.

Foodborne disease outbreaks caused by ciguatoxin and scombroid toxin — Foodborne Disease Outbreak Surveillance System, United States, 2011–2022 Sonny Hoang* Son Hoang Cassie Hartley Virginia Roberts Anna Chard

Background: Ciguatoxin and scombroid toxin are among the top five etiologies of foodborne disease outbreaks linked to fish in the United States each year. Ciguatoxins produced by algae can accumulate in reef fish through the food chain; scombroid toxin poisoning occurs when fish are consumed after being held at improper temperatures. Climate change disruptions to marine ecosystems and critical cooling infrastructure may exacerbate the challenges of preventing these fish poisonings.

Methods: We analyzed ciguatoxin and scombroid toxin outbreaks reported to CDC's Foodborne Disease Outbreak Surveillance System from 2011 through 2022, and characterized them by location of outbreak, importation status, location of food preparation, and implicated food vehicle.

Results: There were 165 confirmed ciguatoxin outbreaks (541 illnesses; 56 hospitalizations) and 172 confirmed scombroid toxin outbreaks (537 illnesses; 5 hospitalizations). Among ciguatoxin outbreaks, all were reported by a coastal state or territory, 87% did not implicate imported fish, and 82% were attributed to food prepared in private homes. The top three fish types linked to ciguatoxin outbreaks were barracuda (35%), grouper (13%), and amberjack (12%). Among scombroid toxin outbreaks, 98% were reported by a coastal state or territory, over 50% implicated imported fish, and 57% were attributed to food prepared in sit-down dining restaurants. Most scombroid toxin outbreaks were linked to tuna (80%).

Conclusions: Prevention measures for ciguatoxin and scombroid toxin poisonings should account for both environmental conditions and consumer behaviors. While reducing harvesting from high-risk areas and consumption of specific reef fish will prevent ciguatoxin poisoning, attention to temperature control of unprepared seafood is necessary from catch to consumption to prevent scombroid toxin poisoning.

Associations between historical redlining and climate-related exposures in the Texas Flood Registry Rashida Callender* Rashida Callender Carlos Calvo-Hernandez Katherine B. Ensor Marie Lynn Miranda Jaime Madrigano

Background: Previous research has shown greater environmental burdens and worse health outcomes in historically redlined areas, but few studies have linked redlining to exposures and outcomes from climate-related events. This study examines associations between historical redlining and Hurricane Harvey-related exposures and outcomes.

Methods: In the aftermath of Hurricane Harvey, the Texas Flood Registry (TFR) deployed a survey to residents of areas affected by the storm. Home Owners' Loan Corporation (HOLC) polygons were obtained from the University of Richmond. Polygons were categorized according to the HOLC classification, using grades A (good) to D (poor). A weighted average of overlapping polygons was calculated to assign a redlining score to each census tract so that higher scores represented tracts with more "D" rated neighborhoods. Univariate and multivariate (controlling for demographics) logistic regression were used to examine the relationship between historical redlining and self-reported exposures and outcomes.

Results: A total of 965 survey respondents lived in census tracts with historical redlining data. Living in tracts in the highest quartile of redlining scores versus the lowest quartile was associated with increased odds of reporting home flooding [OR (95% CI): 4.71 (2.77, 8.42)], home damage [OR (95% CI): 2.48 (1.70, 3.66)], skin contact with floodwater [OR (95% CI): 1.70 (1.18, 2.47)], shortness of breath [OR (95% CI): 1.72 (1.11, 2.70)], and skin rash [OR (95% CI): 2.41 (1.21, 5.08)]. After adjustment, associations between redlining score and Harvey-related exposures were attenuated but remained statistically significant, while associations between historical redlining and physical health impacts were null.

Conclusions: We found associations between historical redlining and Harvey-related exposures and outcomes. Further research will examine if historical redlining modifies the association between Harvey-related exposures and outcomes.

LATEBREAKER

Environment/Climate Change

Neighborhood pollution burden associated with newborn's accelerated biological aging in MADRES, a predominately low-income, Hispanic cohort Zhongzheng Niu* Zhongzheng Niu Helen B. Foley Rima Habre Theresa M. Bastain Carrie V. Breton Shohreh F. Farzan

Background: Mitochondrial DNA contents (mtDNAc) and telomere length (TL), markers of biological aging, have been associated with environmental pollution. People are usually simultaneously exposed to multiple pollutants from multiple media (e.g., air or water), but little is known about the cumulative pollution burden on aging biomarkers in newborns.

Methods: We used qPCR to measure relative mtDNAc and TL (compared to a reference gene as a ratio) from 166 cord blood samples from the ongoing Maternal and Developmental Risks from Environmental and Social Stressors (MADRES) cohort. Residential address histories during pregnancy were assembled for each participant and used to link CalEnviroScreen 4.0 scores, a tool developed by the California Office of Environmental Health Hazard Assessment to identify census tract-level cumulative environment pollution and vulnerability impacts. CalEnviroScreen scores include a cumulative pollution burden score and 13 individual pollution scores, such as long-term exposure to ozone, diesel PM emissions, traffic density, toxic release from facilities, drinking water contaminants, and proximity to solid waste sites. We analyzed the association of the cumulative pollution burden score and each individual pollutant score (in their tertiles) with mtDNAc and TL using linear regression adjusted for participants socioeconomical status, parental age, maternal health status, birth weight and gestational age.

Results: Compared to its lowest tertile, higher cumulative pollution burden score was associated with lower mtDNAc (2nd tertile β: -0.38, 95% CI: -0.65, -0.11; 3rd tertile β: -0.21, 95% CI: -0.48, 0.06). For individual pollution, long-term ozone levels, an air quality indicator, was associated with both lower mtDNAc (2nd tertile β: -0.05, 95% CI: -0.32, 0.23; 3rd tertile β: -0.34, 95% CI: -0.63, -0.05) and lower TL (2nd tertile β: -0.08, 95% CI: -0.21, 0.04; 3rd tertile β: -0.16, 95% CI: -0.29, -0.03), while most other types of individual pollution variables were not significantly associated with mtDNAc or TL.

Conclusion: Neighborhood cumulative environmental pollution burden and ozone individually were associated with lower newborn's mtDNAc and TL, indicating accelerated biological aging.

Association Between Artificial Light at Night and Blood Pressure Among Ghanaian Adults

Kwadwo Boakye* Kwadwo Boakye

Artificial light at night is a growing environmental issue and has been associated with negative health consequences. Yet evidence concerning the effects on blood pressure remains dearth especially in sub-Saharan Africa. In this study, we examined the associations between artificial light at night and both blood pressure and hypertension among Ghanaian adults. We use data from 13784 participants in the 2014 Ghana Demographic and Health Survey. VIIRS Nighttime Day/Night Band Composites Version 1 dataset35 within the google earth engine platform was used to assess artificial light at night. Data on blood pressure measurements were obtained from the 2014 Demographic and Health Survey. Linear and logistic mixed effects models were used to analyze the data. We performed effect modification analysis on age and gender. Our findings showed that higher artificial night at light was associated with higher systolic blood ([β =0.10 mm Hg (95% CI: 0.01 – 0.18)], diastolic blood pressure ([β =0.14 mm Hg (95% CI: 0.07 – 0.21)], and higher odds of hypertension ([OR=1.02 (95% CI: 1.00 to 1.05)]. There was no evidence of the effect modification on age and gender. Our findings indicate negative associations between artificial light at night and blood pressure among Ghanaian adults.

Sensitive childhood window of long-term exposure to air pollution on adult bronchitic symptoms Futu Chen* Futu Chen Zhongzheng Niu Sahra Mohazzab-Hosseinian Steve Howland Frederick Lurmann Nathan R. Pavlovic Rob McConnell Shohreh F. Farzan Theresa M. Bastain Rima Habre Carrie V. Breton Erika Garcia

Childhood exposure to air pollution appears to have long-term effects on adult bronchitic symptoms. However, the critical window of exposure is understudied. Using data from the Southern California Children's Health Study (CHS), we assessed sensitive childhood ages for NO2 and O3 exposure associated with self-reported adult bronchitic symptoms.

We included 3 CHS cohorts (2 recruited at age ~9-10 years in 1992-93; 1 at age ~5-7 years in 2002-03) followed until high school graduation and included a follow up study in adulthood. Self-reported bronchitic symptoms in past 12 months was evaluated at adult assessment (mean age±SD=33±3 years) by questionnaire. Yearly average 24hr mean NO2 and 8hr max O3 exposure from in-utero to age 16 years was estimated using inverse-distance squared spatial interpolation and participants' residential history. Log Poisson Distributed Lag Models adjusted for childhood and adult confounders were fitted to examine childhood exposure associations with adult bronchitic symptoms.

We included 823 (NO2) to 844 (O3) participants with complete yearly exposure data. 21% reported adult bronchitic symptoms in the past 12 months. Higher NO2 exposure during ages 1-4 years was associated with higher risk of adult bronchitic symptoms, with the largest associations observed at ages 2 (RR per 10ppb=1.09 [95% CI: 1.03, 1.16]) and 3 (RR=1.09 [1.02, 1.16]), with some suggestive evidence of increased risk at ages 11-13 years. Findings remained consistent after adjusting for O3. For O3, we observed increased risk at ages 13 (RR=1.14 [1.02,1.29]) and 14 (RR=1.12 [1.02,1.23]) in the two-pollutant model. Sensitivity analyses using imputed exposure and covariate data (n=1,319) produced similar results, but shifted toward the null.

We found evidence early life (1-4 years) might be a particularly sensitive window to NO2 exposure for bronchitic symptoms in adulthood. Puberty (11-14 years) might be a sensitive window for both NO2 and O3, but results were less consistent.

Figure 1. Risk Ratios of adult bronchitic symptoms per 10 ppb increase in yearly average 24 hour average NO2 (left) and 8 hour maximum O3 (right) from in-utero to age 16 from single pollutant models and two-pollutant models that mutually adjusted for two pollutant cross bases, Children's Health Study

Environment/Climate Change
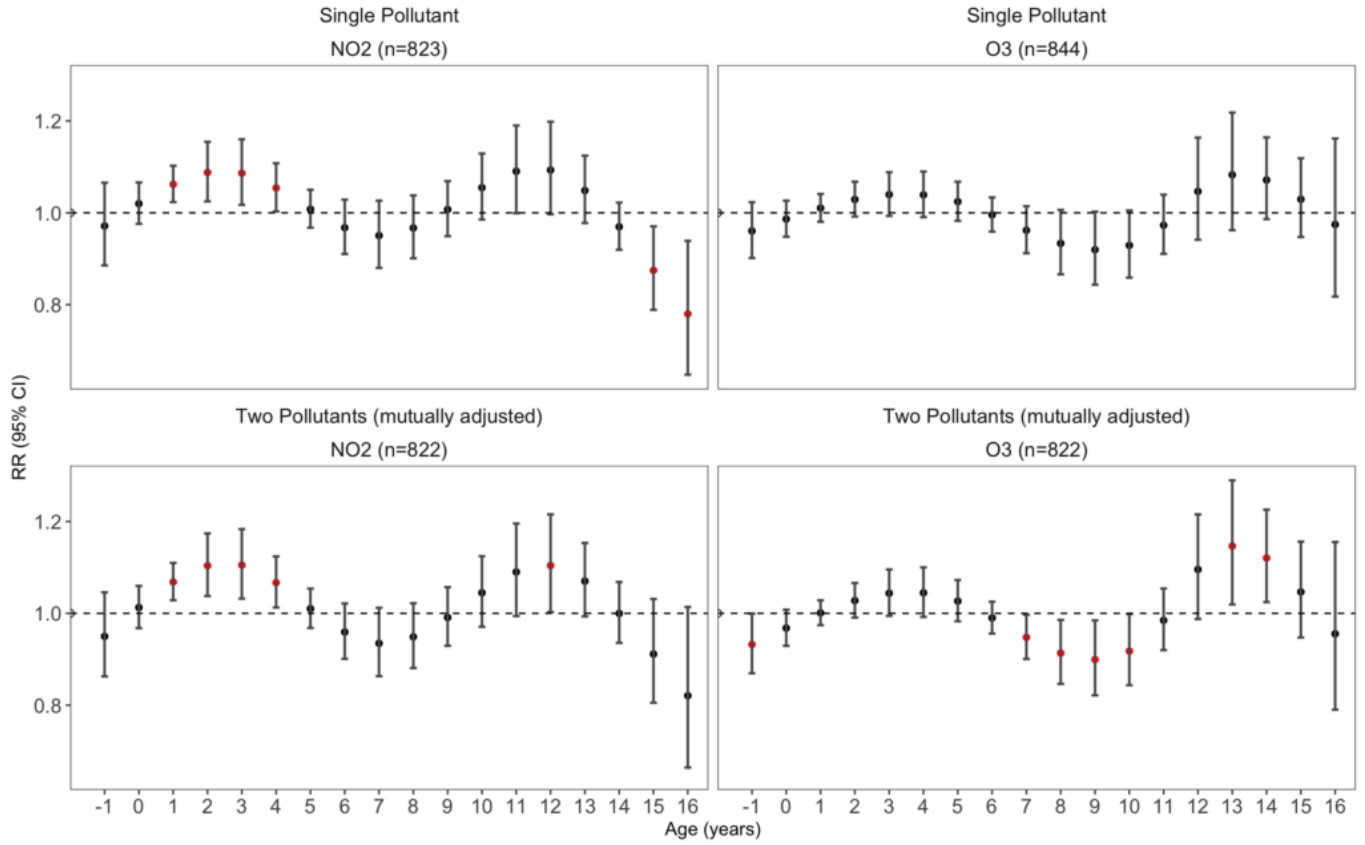
Air pollution and hypertensive disorders of pregnancy: do omega-3 fatty acids modify the association? Meghan Angley* Meghan Angley Yijia Zhang Uma Reddy Ka Kahe

Objective: Exposure to air pollution during pregnancy has been shown to be associated with hypertensive disorders of pregnancy (HDP). Several recent studies have suggested that intake of omega-3 fatty acids may mitigate the association between air pollution and adverse health outcomes. We investigated if the association between air pollution and HDP is modified by intake of omega-3 fatty acids.

Methods: We used data from the Nulliparous Pregnancy Outcomes Study: Monitoring Mothers-To-Be (nuMoM2b), a multi-center prospective cohort study. Average mean daily levels of PM2.5, PM10 and O3 during pregnancy were assigned to participants by linking participant addresses to air pollution monitoring data. HDP included gestational hypertension and preeclampsia, determined from chart abstraction. Total intake of omega-3 fatty acids and separately fish oil (EPA, DPA, and DHA) were determined from the Block 2005 Food Frequency Questionnaire, which asked participants to recall their frequency and portion size of certain foods and supplements in the three months prior to pregnancy. From these responses, we dichotomized total intake of omega-3 fatty acids and fish oil at the median as <1.3 g/day vs. ≥1.3 g/day and <0.08 g/day vs. ≥ 0.08 g/day, respectively.

Results: We excluded participants with pre-pregnancy hypertension and those whose pregnancies ended prior to 20 weeks gestation. Of the 9,221 women included in the analysis, 23.2% developed HDP. After adjustment for confounders, PM2.5 (OR: 1.66 [95% CI: 1.41, 1.96], per 5 μg/m3 increase) and PM10 (OR: 1.34 [95% CI: 1.21, 1.49], per 10 μg/m3 increase), but not O3 (per 10 ppb increase) were associated with HDP. Neither total intake of omega-3 fatty acids nor intake of fish oil appreciably modified the association between air pollution and HDP.

Conclusions: There remains a need to identify if overall dietary patterns attenuate the adverse associations between air pollution and pregnancy outcomes.

Character count (including spaces): 1961/2000

Genetics

Telomere length and all- and specific-cause mortality among U.S. adults and the role of age and race/ethnicity

Hanish Kodali* Hanish Kodali Heidi E. Jones Katarzyna E Wyka Linda Valeri Luisa N. Borrell

Background: Studies of the relationship between telomere attrition and mortality risks, all and/or specific-causes, among U.S. adults has shown inconsistent findings. Additionally, the combined effect of age group and race/ethnicity on this association has rarely been investigated.

Methods: Using two publicly available datasets, the National Health and Nutrition Examination Survey (1999-2002) and the 2019 Linked Mortality File, we analyzed 6,516 adults (aged 25 years or older) with 2,163 deaths. We employed Cox proportional hazards regression to examine the association between TL (standardized as kilo base-pairs, kbp, and assessed continuously and categorically in quartiles), and all-cause, CVD- and cancer-specific mortality before and after adjusting for selected characteristics. We also tested for effect modification by age group and race/ethnicity.

Results: In the adjusted model, a one kbp decrease in TL was associated with 1.36 higher hazard rate of all-cause mortality (95%CI:1.17,1.58). Adults with the shortest TL (first quartile, Q1) had a 1.57 times higher all-cause mortality than their peers with longest TL (Q4, 95%CI:1.25,1.98). Similarly, CVD-specific mortality risk increased 1.49 times per kbp TL decrease (95%CI:1.17,1.91), increasing to 1.72 times in the shortest vs. the longest TL (95%CI:1.18,2.50). For cancer-specific mortality, Q1 had 1.85 times higher rates than Q4 (95% CI:1.15,2.98). No significant modifications of these associations were observed due to age or race/ethnicity.

Discussion: TL emerges as a promising biomarker for predicting all-cause, CVD-, and cancer-specific mortality risks among U.S. adults, particularly highlighting its inverse association with premature death. The consistent and strong links between shorter TL and higher mortality underscore its potential role in targeted interventions and preventive strategies for all ages and race/ethnicity.

Duration of effectiveness of preventive treatment for tuberculosis: an individual-participant meta-analysis of 34 contact tracing studies Lauren Linde* Lauren Linde Meredith Brooks C. Robert Horsburgh Leonardo Martinez

Background

Tuberculosis (TB) is an infectious respiratory disease with enormous global impact. Treatment of individuals after TB exposure is widely recommended to prevent disease, however the duration of protection achieved from TB preventive treatment (TPT) is debated. Protection may vary by setting, with shorter protection hypothesized in higher-burden areas. We aimed to assess the effectiveness of TPT over time and among settings of varying TB burden.

Methods

For this individual-participant meta-analysis, we assembled multiple cohorts from TB contact tracing studies published between January 1998 and April 2018. Studies were restricted to those with at least one year of follow-up and individual-level data available for a set list of covariates. We generated Nelson-Aalen cumulative hazard plots to examine comparative hazard by TPT status. Using mixed-effects Cox regression models, we estimated adjusted hazard ratios (aHRs) for incident TB in six-month intervals from six months to four years post-exposure, then for the period from four to 11 years.

Results

We identified 432,589 contacts from 34 studies in 28 countries, with median follow-up time of 2.9 years (range: 0-11 years) and 5,063 incident TB cases. The overall TB incidence rate was 3.7 per 1,000 person-years (PY); 2.0 per 1,000 PY in those who initiated TPT, and 4.0 in those who did not. Receiving TPT was associated with reduced risk of TB for at least 3.5 years (aHR, .31; 95% CI .11-.86 at 36-42 months) overall, with considerable heterogeneity by background TB burden (Fig.). Reduced TB risk was seen among TPT recipients for at least two and three years in low- and medium-burden settings, but only up to the first year of follow-up in high-burden. Contacts given TPT had lower cumulative incidence of TB over follow-up regardless of background burden.

Conclusion

TPT provided sustained protection against TB for at least 2-3 years in low and medium-burden settings, but waned considerably faster in high-burden areas.
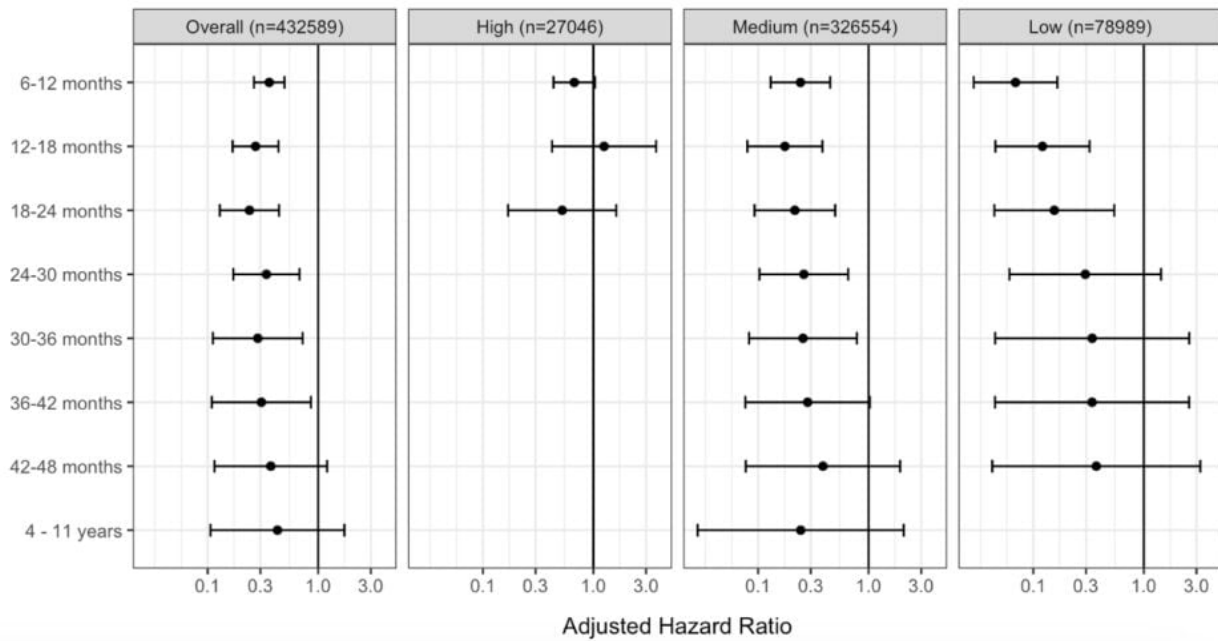
Figure. Adjusted hazard ratios for incident tuberculosis among contacts who were versus were not given TB preventive treatment, overall and by background tuberculosis burden.

Notes: X-axis displayed on log scale. Models were adjusted for contact age, sex, HIV status, and tuberculosis infection at baseline, with random effects for each individual study and study design (prospective versus retrospective data collection). Background burden was defined as low (<20 cases per 100,000 population), medium (20-100 cases per 100,000 population), or high (>100 cases per 100,000 population).

Global Health

Initiation of bedaquiline-containing regimens and risk of treatment failure among persons on treatment for multidrug resistant-tuberculosis Sarah Brumfield* Sarah Brumfield Pawandeep Kaur Afranio Kritski Valeria Rolla Sanjay Gaikwad Sonali Sarkar Tester Ashavaid Padmapriyadarsini Chandrasekaran Amrose Pradeep Timothy Sterling C Robert Horsburgh

Multidrug resistant-tuberculosis (MDR-TB), which is resistant to the two most effective first-line TB medications, is a threat to global TB control. Historically, MDR-TB treatment has been characterized by long duration and substantial toxicity. In recent years, shorter and more tolerable regimens have been developed; bedaquiline is a cornerstone of these newer regimens. We examined whether bedaquiline initiation at the start of treatment was associated with improved treatment outcomes among those with MDR-TB.

Participants were enrolled at TB treatment sites in India and Brazil from January 2019 through December 2022. Treatment regimens were selected by local clinical providers. Baseline visits occurred within 14 days of treatment initiation, and participants were followed through one year after treatment completion. We compared regimens in which bedaquiline was initiated within 28 days of the baseline visit to those that did not initiate bedaquiline within 28 days, regardless of whether bedaquiline was initiated later. Sputum smear and culture were performed at week 16 and subsequently. Treatment failure was defined as a positive culture at the last on-treatment visit or after treatment completion, TB recurred after treatment completion, death occurred before the end of treatment, or a treatment failure was reported by study staff. We performed a Cox proportional hazards analysis adjusted for country of residence, age, HIV status, presence of lung cavitation at baseline, and self-reported treatment adherence.

A total of 312 participants completed 26,780 weeks of follow-up, during which 57 (18%) participants experienced treatment failure. The adjusted hazard ratio for treatment failure comparing bedaquiline at initiation to non-bedaquiline baseline regimens was 0.59 (0.30, 1.16).

Our findings suggest that initiating bedaquiline at baseline was associated with a modest but not significant improvement in treatment outcomes in this population.

Maternal Mental health and cognitive abilities in children of the MAASTHI cohort in urban India Giridhara Rathnaiah Babu* Giridhara Rathnaiah Babu Deepa R Debarati Mukherjee

Introduction: Over 65 million children in India are at risk of suboptimal development due to various adversities. Within the MAASTHI cohort, we aimed to delineate the relationship between maternal mental health and cognitive abilities and the mental health of children.

Method: We extended the follow-up of the MAASTHI cohort in Bengaluru; N = 640; Age = 3-7 years. Literacy and numeracy were tested using the Annual State of Education Report (ASER) tool using flipbooks for stimuli presentation. We administered a Strength and Difficulty questionnaire (SDQ) to parents. The mother's mental health was assessed using the Edinburgh Postnatal depression scale.

Results: The mean age of children is 5.09 ±0.24 years, with 327(51.1%) males and 313(48.9%) females. ASER tool was administered among children aged over 4 years (N=572); 442(77%) of these children attended private school and 124(21%) attended government school. We found that 54% of children could read letters,16% read words and 13% could read a paragraph. On the mathematical portion of the test, 57% recognized single digit, 30% recognized double digit, 18% could add and 12% could subtract single-digit numbers. The mean SDQ scorings were, for emotional symptoms (2.5±1.88, 0-10), conduct disorders (3±1.77, 0-9), hyperactivity (4±2.13, 0-10), peer problems (2±1.5, 0-8), prosocial scale (9±1.84, 0-10) and the total difficulty scores were (11±4.61, 1-33). Maternal mental health, as indicated by EPDS score is associated with child SDQ Score (β=0.171, 95% CI (0.08, 0.21), P-0.00).

Conclusion: In the five scales of SDQ, children scored the highest in the pro-social scale reflecting a strong capacity for positive social interaction in this age group. ASER results suggest that a considerable proportion of the surveyed children have some foundational skills in literacy and mathematics. Mother's mental health status had a significant impact on child's mental health in the MAASTHI cohort.

Mortality following substance use disorder treatment: population-based record-linkage retrospective cohort design Andrés González-Santa Cruz* Andrés González-Santa Cruz Alvaro

Background. In Chile, the Government funds substance use disorder treatment (SUD) for all individuals with public health insurance (approximately 81% of the population). There is limited information regarding short-term, medium-term, and long-term mortality risks. We described the standardized mortality ratios (SMRs) for all adult patients in publicly funded SUD treatments from 2010-2022.

Methods. We conducted a population-based, retrospective cohort study by merging individual-level records of adults (aged 18-65) enrolled in Chilean publicly funded SUT programs with national mortality data from 2010 to 2022. We calculated SMRs by comparing the observed number of deaths to the expected number within specific age groups (18-29, 30-44, 45-59, and 60-65), periods (annually), and across different sex categories. Stratum-specific population estimates were obtained from the Ministry of Health's mortality data, supplemented by population projections from the National Institute of Statistics' open data portal. The 95% confidence intervals (CIs) were calculated using Vandenbroucke's method.

Results. There were 100,322 people with at least one admission to treatment during 2010 and 2022. Seventy-four percent were male, and the average age at admission was 39 (standard deviation= 10.5). The SMR in the SUT population was 15.5 (95%CI 15.0, 16.1) times higher than expected based on the general population. Women aged between 30-44 had a mortality risk up to 29.6 times (95%CI 26.0, 33.5) higher than expected (See Figure 1).

Conclusions. These descriptive results show a large cumulative mortality risk among people in SUT, compared to the general population, particularly among women, and with the largest sex gap at younger ages. The specific contribution of substance use in explaining this elevated risk and the effect of SUT as a public health strategy to mitigate these disparities will be further explored.

Figure 1. Standardized mortality ratios for people in SUT, by age group and sex

Y-axis was log-transformed. Dashed black lines represent the null value.
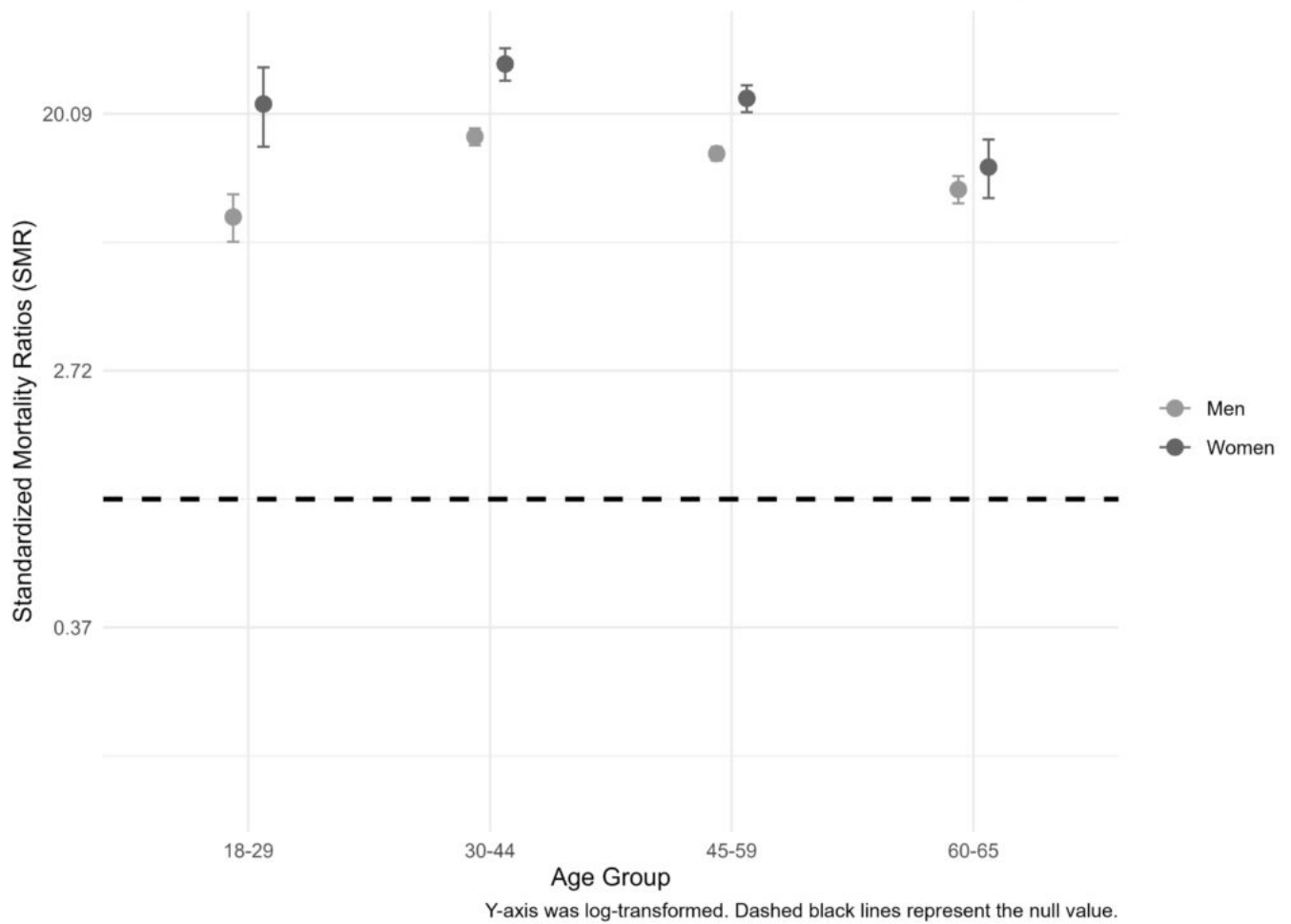
Impact of Vacant Lots on Adolescent Neighborhood Perceptions and Mental Well-being

Marina C. Jenkins* Marina Jenkins Jon Kawatachi Rebecca Skinner Beth Marshall Kristin Mmari

There are currently over 20,000 vacant lots across Baltimore City. Unmaintained, urban vacant lots have been found to impact adult mental well-being and local violence rates; however, little is known about impacts of adolescents. We aimed to compare adolescent perceptions about their neighborhood and mental health indicators between those who live near unkept vacant lot and those that did not.

A survey was conducted in 2022-23 among a geographically and socioeconomically representative sample of adolescents ages 13-18 residing in Baltimore. Variables included demographic characteristics, perceptions of neighborhood quality, and stressors: violence, safety and food insecurity. Post-traumatic stress disorder (PTSD) was indicated with a binary indicator based on DSM-5 criteria. Our exposure was indicated by agreement with the statement "In my neighborhood, there are a lot of vacant lots that haven't been cleaned." We used chi-square tests of proportions to compare neighborhood perceptions, stressors, and PTSD, and a t-test was used to compare number of experiences with violence between exposure groups.

We analyzed a sample of 364 adolescent surveys, of whom 86.7% were African American, 49.2% were male and the mean age was 15.6 (SD=1.7). Among Baltimore adolescents, 40.3% reported living near unkept vacant lots. Adolescents who lived near vacant lots were more likely to report food insecurity, witness drug use and perceive their neighborhood to be dangerous, unclean, and have higher rates of crime (p<.05). Adolescents who lived near unkept lots reported more experiences with violence (Mean diff.=4.3, p<.01) and increased rate of PTSD which neared statistical significance (p=.06)

The presence of uncleaned vacant lots may be detrimental to youth perceptions of neighborhood quality and safety in urban settings and may impact well-being. Greening and maintenance of vacant lots may improve adolescent perceptions of their neighborhoods and promote thriving.

Association of Discrimination in Medical Settings and Preeclampsia among Pregnant Women in All of Us Study Olivia Kapera* Olivia Kapera Baojiang Chen Jaime P. Almandoz Courtney Byrd-Williams Sarah E. Messiah

Background. Factors contributing to the increasing prevalence of United States maternal mortality are complex and not well understood. While studies have highlighted the impacts of racism and discrimination on well-being and health, to date, no studies have examined how the role of discrimination in maternal mortality varies by race and ethnicity. To address these gaps, we analyzed the association of discrimination and preeclampsia among a racially and ethnically diverse national sample of pregnant women participating in the All of Us study.

Methods. This cross-sectional study analysis of the All of Us program data included 2,303 pregnant women ages 18-to-44 years. Discrimination was measured by proxy using a 7-item survey to assess courtesy, respect, service quality, being treated as competent, acting afraid, being treated as inferior, and being listened to during a healthcare visit. Adjusted logistic regression models generated odd ratios (aOR) of preeclampsia by discrimination in medical settings controlling for race/ethnicity, body mass index (BMI), gestational hypertension, gestational diabetes, and urinary tract infection.

Results. Mean sample age was 36.7 years (SD 5.01). The sample was 67% (n=1466) non-Hispanic White, 52% (n=1191) college graduate or higher, 42% (n=963) with annual income >$75K, and 58% (n=1336) married. Non-Hispanic Black (NHB) women were ~1.8 to 2.1 times more likely to develop preeclampsia if they experienced discrimination in medical settings compared to those who did not report these experiences controlling for other variables (p-value <0.05 for all items).

Conclusion. Findings here show that discrimination in medical settings is associated with increased odds of preeclampsia in NHB women. These results underscore the need for a comprehensive strategy to address these inequities, encompassing reforms in the healthcare system and broader societal shifts to challenge discrimination to eliminate healthcare disparities.

Investigating Practice-Level Surgery Tendency: Racial/Ethnic Differences among Premenopausal Hysterectomy Patients Joacy Gerard Mathias* Joacy Gerard Mathias Natalie A Rivadeneira Lauren G Anderson Michael Green Annie Green Howard Mollie E Wood Erin Carey Timothy S Carey Wanda Nicholson Til Sturmer Kemi Doll Whitney R Robinson

Intro: In the US, benign premenopausal hysterectomy is disproportionately common in the South and among Black women. Much research investigates provider factors associated with hysterectomy approach and outcomes. Little research investigates practice-level factors associated with greater hysterectomy rates. Methods: We characterized practices by proportions of hysterectomy patients with low pre-surgical symptom severity, indicating practices' High Surgery Tendency (HST). Then, we investigated whether Black, White, and Hispanic patients were differentially likely to be treated by HST practices. The Carolina Hysterectomy Cohort used electronic health record (EHR) data from premenopausal benign hysterectomy patients (aged 18-44 years) treated in the South from 2014-2017. EHR data were linked to state physician licensing data to obtain surgeon and practice demographics. We ranked practices by % of patients below the study median on measures of pre-surgical symptom severity (bulk, bleeding, and pain). Practices with >18% of patients below median on all 3 symptoms were called HST. In multivariable-adjusted (MV-adj) Poisson regression models, dichotomized HST was modeled as a function of patient race/ethnicity (Non-Hispanic White [referent], non-Hispanic Black, Hispanic). Covariates were patient age, BMI, Charlson Comorbidity Index, symptom severity scores, and insurance payor (public, private, and uninsured). Results are presented as MV-adj PR (95% CI). Results; The analytic dataset included 1640 patients, 100 providers, and 20 practices. The 6 HST practices treated 531 patients. Hispanic patients were most likely to be treated at academic centers and least likely to be treated by HST practices (PR: 0.60 [0.40, 0.91]). Black and White patients were similarly likely to be at HST practices (PR=1.08 [0.95, 1.23]). After excluding academic practices because they were unlikely to operate on low-severity patients, in non-academic practices, Black and Hispanic patients were twice as likely to be treated at HST practices: PRs=1.86 (1.19, 2.89) and 1.53 (1.15, 2.04), respectively. Conclusion: Outside of academic centers, Black and Hispanic patients were more likely than White patients to be treated at practices with a lower threshold for performing surgery.

Revisiting the theory of "deaths of despair": a causes of cases and causes of incidence approach Luis E Segura* Luis Segura Seth J Prins Rodrigo Zepeda-Tello Silvia S Martins

Background: Since its publication, the theory of "deaths of despair" has been widely accepted. However, the central claim of this theory—whether increasing prevalences of despair (ΔDespair) led to increased all-cause mortality rates (ΔDeaths), between 1999 and 2014, only among NH white individuals in midlife, higher among those with high education—remains untested. Using Rose's causes of cases and causes of incidence framework, we outline and test the individual and between-group claims made by the authors of this theory. **Methods:** We used Cox proportional hazard models to test the individual-level claim: despair increasing the risk of death using data from the NHIS. For the between-group claim, we fitted bootstrapped race- and education-specific autoregressive models with all-cause mortality rates per 100,000 individuals as our outcome adjusted for a 1-year lagged indicator of all-cause mortality rates, changing despair prevalence, and 2-year lagged indicators of confounder rates. We obtained yearly prevalences of despair from the NHIS, yearly rates of all-cause mortality from the CDC detailed mortality files, and confounder rates from the Current Population Survey. **Results:** At the individual-level, we found that despair increases the risk of death (HR= 1.24 [1.16; 1.31]) for individuals of all race and ethnic backgrounds. At the between-group level, was associated with a yearly increase of 0.17 (-0.75; 1.09) deaths per 100,000 among NH white individuals with high education, and a yearly decrease of -0.25 (-0.87; 0.38) deaths from all causes per 100,000 among NH white individuals with low education. Moreover, these associations were imprecise and not exclusive for NH white individuals in midlife. **Conclusion:** This study challenges the theory's central claim, emphasizing the need to explore alternative explanations for the observed mortality increase among white Americans in midlife, such as racial resentment and anxieties.

Does Health Care Access Mediate the association between Material Deprivation and Contraceptive Non-use in Female Ontarian Youth. Derek Akateh* Derek Akateh Jason Were Roman Pabayo

Background: In Canada, about 15% of sexually active youths do not use birth control, with a substantially high rate of abortions and STIs among this group in the last decade. Research has explored predictors of contraceptive non-use, but there is a lack of research regarding social and environmental factors and mechanisms through which they are associated with contraception use.

Objectives: This study aimed 1) To examine the association between material deprivation and contraceptive non-use and 2) to determine whether this association was mediated by healthcare access.

Methods: We conducted a cross-sectional study using data from the 2013/2014 Canadian Community Health Survey, a population-representative survey that collects health data at the Public Health Unit (PHU) level. The CCHS dataset was linked to the 2011 Ontario Marginalization Index data. The analytic sample included 1098 sexually active females (15-24 years) across 34 PHUs in Ontario. We conducted a multilevel path analysis to determine if the relationship between PHU-material deprivation and contraceptive non-use was mediated by healthcare access.

Results: Female youth living in PHUs with higher material deprivation were significantly more likely not to use contraceptives (unstandardized ß = 0.77, 95% CI: 0.08, 1.45). Higher material deprivation was also associated with reduced healthcare access (unstandardized ß= -0.06; 95% CI: -0.12, -0.01). However, healthcare access did not mediate the relationship between material deprivation and contraceptive non-use (indirect path β =0.004; 95% CI= -0.03, 0.04).

Conclusion: Findings from this study indicate that material deprivation is associated with contraceptive non-use among female youth in Ontario and that healthcare access did not mediate the relationship. The findings suggest that addressing structural deprivation by way of lowering area-level material deprivation has the potential to impact both youth access to services and improve contraceptive use.
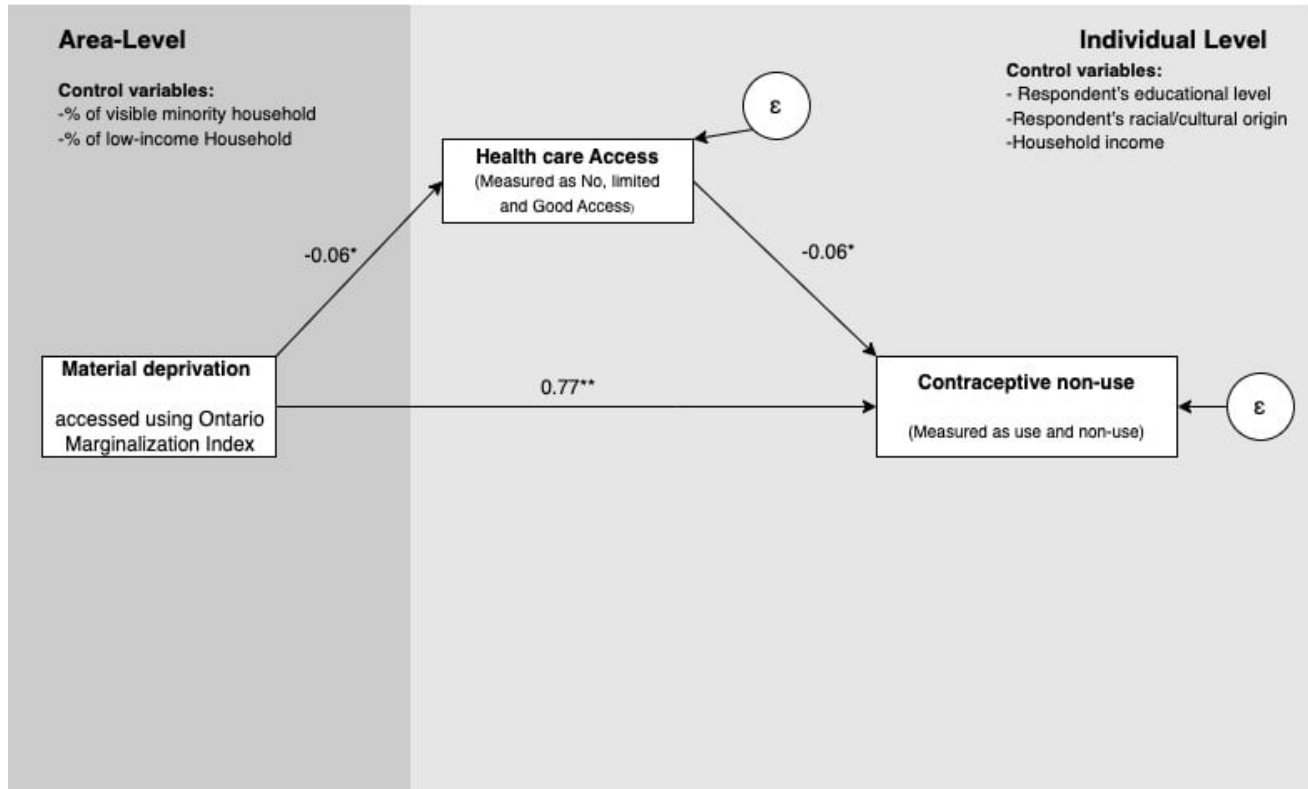
* = p < 0.005, ** = p <0.001

Figure: Path diagram and unstandardized coefficients of the multi-level path analysis between area level material deprivation and Ontarian youth contraceptive status as mediated by Health care access.

Unveiling Disparities: Examining Differential item functioning's Impact on Racial Health Equity Among White and Black Populations

Ester Villalonga-Olives* Ester Villalonga-Olives Abdolvahab Khademi Yun-Yi Pan Yusuf Ransome

Introduction: Due to persistent structural oppression against Black individuals in the United States, the relationship between social capital and health for Blacks differs compared to Whites. Results from cross-sectional data analyses suggested that social capital indicators are not psychometrically equivalent by race. Our aim is to test longitudinal measurement invariance (MI) and differential item functioning (DIF) of social capital indicators by race and education.

Methods: Longitudinal data were collected from the Midlife in the United States study (n= 7700; years 1995-2016). Scales included social capital indicators measuring Contributions to Community and Community Involvement. We used structural equation modeling (SEM) and item response theory (IRT) to test longitudinal MI and DIF by race and education.

Results: We found violation of longitudinal and multi-group MI at configural and metric levels in both scales, where factor structure and indicator loadings failed to sustain over time. IRT results showed DIF in both scales in specific indicators, such as 'Many people come for advice,' indicating a consistent advance of one racial group over the other even if both groups had the same levels of social capital ($P(\chi 2,2) = 0.00$). When we investigated race and education interaction, all items in the Contributions to Community and some of the Community Involvement items showed DIF.

Conclusion: We found lack of invariance in several social capital items. These findings suggest that attempts to compare social capital between Black and White people may contain biases that should be acknowledged in research. To correct the issue, future work on social capital measures should involve processes that evaluate the assumptions behind each question (for existing data) and involve key stakeholders from racial and underrepresented communities when creating new items.

Racial and ethnic disparities in sleep health – evidence from the United States (US) Behavioral Risk Factor Surveillance System (BRFSS), 2020 Wendy W. Dlamini* Rebecca J. Howett Wendy W. Dlamini Rashmi Maharjan Alyson J. Littman Amanda I. Phipps

Background: Inadequate sleep is associated with several poor health outcomes. It is unknown whether there are disparities in sleep by racial or ethnic group. We evaluated the association between race and ethnicity and inadequate sleep.

Methods: We conducted a secondary analysis of cross-sectional data from 388,639 US adults (aged ≥18 years) from the 2020 BRFSS. The exposure was self-reported race and ethnicity, aggregated into 8 groups: 7 race groups of non-Hispanic ethnicity (American Indian or Alaskan Native, Asian, Black, Multiracial, Native Hawaiian or Other Pacific Islander, White, Race Not Listed), and 1 Hispanic ethnicity group of any race. The analytic outcome was self-reported daily sleep duration (inadequate <7 hours, adequate ≥7 hours). We calculated weighted descriptive statistics and estimated weighted adjusted-prevalence ratios (aPRs) using log-quasibinomial regression. Sex and age were specified a priori as adjustment variables. Further, we explored effect modification by rural or urban residency.

Results: The overall prevalence of inadequate sleep was 32.7%. Compared to White participants (prevalence 30.6%), the prevalence of inadequate sleep was significantly greater among most non-White participant groups, with the exception of those who identified as Asian (30.5%, aPR=0.95, 95% CI: 0.88, 1.02) or Hispanic (32.3%, aPR=1.01, 95% CI: 0.97, 1.05). Inadequate sleep was most prevalent among those who identified as Black (43.6%, aPR=1.39, 95% CI: 1.35, 1.43) or Native Hawaiian or Other Pacific Islander (47.0%, aPR=1.47, 95% CI: 1.32, 1.64). There was no meaningful difference in associations when stratified by rural or urban residency.

Conclusion: US residents from most minority racial and ethnic groups have a higher prevalence of inadequate sleep compared with White non-Hispanic residents. Interventions are warranted to address structural factors that increase racial and ethnic minorities' susceptibility to inadequate sleep.

The association between total social exposure and incident multimorbidity Ingrid Giesinger*
Ingrid Giesinger Emmalin Buajitti Arjumand Siddiqi Peter Smith Rahul G. Krishnan Laura Rosella

Background

The social determinants of health are associated with multiple chronic diseases including multimorbidity, the co-occurrence of two or more conditions. There is a paucity of literature that examines the combined influence of multiple social determinants within an individual i.e., the totality of social exposures. Using comprehensive linked population-representative data, we aimed to evaluate the effect of the totality of social exposures on the incidence of multimorbidity in Ontario, Canada.

Methods

Social exposures were obtained from Ontario respondents aged 18 to 74 to the Canadian Community Health Survey between 2000 to 2011 (females n=56,656; males n=48,611). Totality of social exposure (TSE) was generated through additive and weighted approaches. Additive TSE was generated by summing 12 binary measures of social exposure. Weighted TSE included 15 binary measures of social exposure summed within 5 equally weighted domains (community and social context, material circumstances, economic stability, education and population group). Both additive and weighted TSE measures were categorized into four groups reflecting the spectrum of social disadvantage.

Incident multimorbidity was identified through data linkage to healthcare data (1992 to 2021) using validated algorithms for congestive heart failure, chronic obstructive pulmonary disease, diabetes, lung cancer, myocardial infarction, and stroke. The cumulative incidence function of age to multimorbidity was calculated by each TSE measure. The association between TSE and age to multimorbidity was estimated using cause-specific Cox proportional hazards models. All analyses were sex-stratified.

Results

Totality of social exposure was associated with risk of multimorbidity in both additive and weighted models with a strong social gradient (Figure 1). Those experiencing the most social disadvantage had an over 2-fold increase in the risk of multimorbidity, compared to those with the least social disadvantage (Weighted TSE: AHR females, 2.75; 95%CI 2.73, 2.77; AHR males, 2.23; 95%CI 2.21,2.24).

Conclusions

Our findings highlight the importance of considering the cumulative effect of multiple social determinants of health on multimorbidity.

Figure 1: Sex-stratified cumulative incidence function of age to multimorbidity with death as a competing risk, by additive and weighted total social exposure

a. Females - additive total social exposure

b. Females - weighted total social exposure

c. Males - additive total social exposure

d. Males - weighted total social exposure

Group 4 – Most social disadvantage | Group 3 | Group 2 | Group 1 – Least social disadvantage
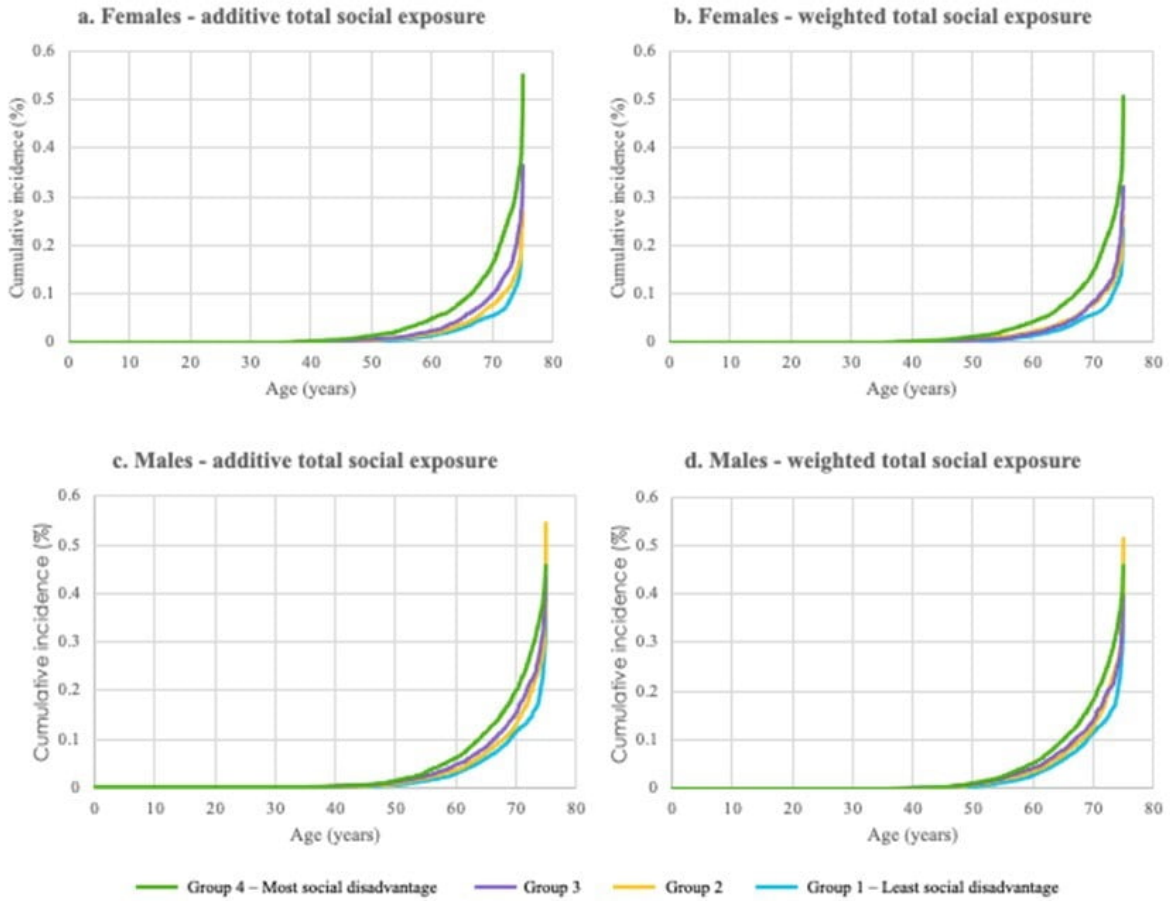
Exploring clinically meaningful change in health-related quality of life and heart problems in a Black population: A Coronary Artery Risk Development in Young Adults Study (CARDIA) Isabelle Pierre-Louis* Isabelle Pierre-Louis Chengwu Catarina Sarah

Background: Health-related quality of life (HRQoL) measures quantify the impact of heart problems on HRQoL changes over time. Previous research has shown Black individuals are more likely to have negative HRQoL changes over time, compared to their White counterparts. However, little research has clarified how sex differences within Black populations and heart problems play a role in HRQoL changes using the minimal clinically important difference (MCID).

Methods: We used data from the longitudinal, multicentered study of 853 Black participants attending the years 15, 20, 25, and 30 CARDIA examinations. Perceived heart problems were self-reported; HRQoL was measured through the 12-Item Short Form Survey consisting of mental (MCS) and physical (PCS) components. For the MCID, we used 0.5 standard deviation of the change score between Year 15 and 30, and then created a binary clinically meaningful decline variable. Mixed effects logistic regression models assessed the impact of race and heart problems on HRQoL changes.

Results: At year 30, 66% of women and 34% of men had a clinically meaningful decline in MCS. In PCS, 64% of women and 36% of men had a meaningful decline at year 30. After adjusting for heart problems and sociodemographic factors, Black men have a higher odds of a clinically meaningful decline between years 20 and 25 compared to years 15 and 20 (OR: 1.81, 95% CI: 1.10, 2.99), but this significance was not found in women (OR: 1.00, 95% CI: 0.68, 1.46). We found no significance after adjustment for either men or women in PCS model.

Discussion: Previous studies found Black women report lower HRQoL compared to Black men, but few adjust for the impact of heart problems, which are known to impact Black men more frequently. Finding heart problems impact HRQoL changes overtime in Black men, could signify greater issues including lack of care for their heart conditions, and other psychosocial factors. More research may be necessary to understand this association.

Contextualizing racial/ethnic disparities in obstetric anal sphincter injury in the United States Maya Rajasingham* Maya Rajasingham Parnian Hossein-Pour Rohan D'Souza Roxana Geoffrion Cande Ananth Giulia Muraca

Introduction

Racial disparities in obstetric anal sphincter injury (OASI) across parity, mode of delivery, and immigration status are poorly understood; their investigation may provide valuable insight into individuals at greatest risk of OASI.

Methods

We designed a cohort study of 15,964,178 vaginal births in the United States (US) using CDC Natality Files (2016–2021). Cox proportional hazard models, adjusted for confounders with gestational age as the underlying timescale, were fit to evaluate the association between self-reported race/ethnicity and OASI. Models were stratified by parity (nulliparous/parous), obstetric history (previous cesarean delivery), and mode of delivery (spontaneous vaginal [SVD], forceps, vacuum).
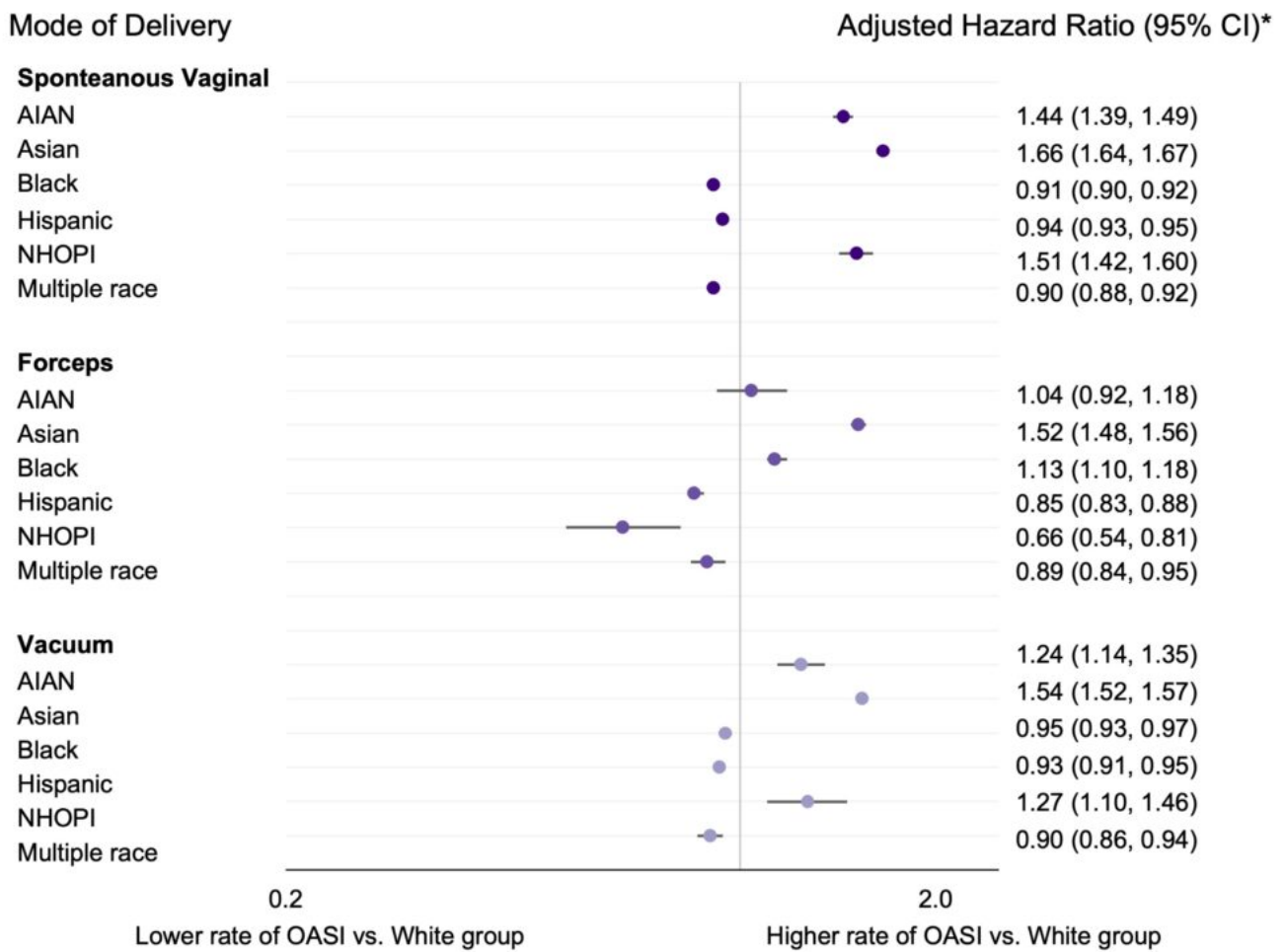
Results

In nullipara, OASI rates varied by mode of delivery with the highest rate among forceps (SVD: 2.0%, forceps: 14.7%, vacuum: 6.6%). Non-Hispanic Asian individuals experienced the highest rates of OASI across all modes of delivery. Compared to non-Hispanic White individuals, OASI rates among Asian individuals with SVD were 3.3% vs. 1.9% (aHR 1.66; 95% CI 1.64, 1.67), 21.9% vs. 15.1% with forceps (aHR 1.52; 95% CI 1.48, 1.56), and 10.9% vs. 6.9% with vacuum (aHR 1.54; 95% CI 1.52, 1.57). OASI rates varied between Asian subgroups, with the highest rate in Indian individuals (SVD: 4.1%, forceps: 27.2%, vacuum: 13.1%). Among forceps, higher OASI rates were observed in non-Hispanic Black vs. White individuals (Fig 1). OASI rates were higher among foreign- vs. US-born residents within each race. Similar trends were apparent in the parous population.

Conclusions

In the US, Asian individuals, particularly those who identify as Indian, have higher OASI rates than White individuals, irrespective of parity and mode of delivery. Rates of OASI are higher among foreign-born US residents. These findings underscore the importance of training birth attendants in best practices, and a tailored counselling approach that is culturally sensitive and trauma informed.

Fig 1. Obstetric anal sphincter injury (OASI) by race/ethnicity and mode of delivery among nulliparous individuals, United States, 2016-2021.

Mode of Delivery		Adjusted Hazard Ratio (95% CI)*
Sponteanous Vaginal		
AIAN		1.44 (1.39, 1.49)
Asian		1.66 (1.64, 1.67)
Black		0.91 (0.90, 0.92)
Hispanic		0.94 (0.93, 0.95)
NHOPI		1.51 (1.42, 1.60)
Multiple race		0.90 (0.88, 0.92)
Forceps		
AIAN		1.04 (0.92, 1.18)
Asian		1.52 (1.48, 1.56)
Black		1.13 (1.10, 1.18)
Hispanic		0.85 (0.83, 0.88)
NHOPI		0.66 (0.54, 0.81)
Multiple race		0.89 (0.84, 0.95)
Vacuum		
AIAN		1.24 (1.14, 1.35)
Asian		1.54 (1.52, 1.57)
Black		0.95 (0.93, 0.97)
Hispanic		0.93 (0.91, 0.95)
NHOPI		1.27 (1.10, 1.46)
Multiple race		0.90 (0.86, 0.94)

0.2   2.0

Lower rate of OASI vs. White group   Higher rate of OASI vs. White group

CI, confidence interval; AIAN, American Indian or Alskan Native; NHOPI, Native Hawaiian and Other Pacific Islander.
*Adjusted for maternal age, marital status, education, payer, WIC, pre-pregancy body mass index, assisted reproductive technology, multiple gestation, pre-pregancy diabetes, pre-pregancy hypertension, gestational diabetes, preeclampsia/eclampsia, induction of labor, augmentation of labor, high infant birth weight.

LATEBREAKER

Health Disparities

Risk factors underlying racial/ethnic disparities in tuberculosis diagnosis and treatment outcomes, 2011-2019: a multiple mediation analysis of national surveillance data Mathilda Regan* Mathilda Regan Terrika Barham Yunfei Li Nicole A Swartwood Garrett R Beeler Asay Ted Cohen C Robert Horsburgh, Jr Awal Khan Suzanne M Marks Ranell L· Myles Joshua A Salomon Julie L Self Carla Winston Nicolas A Menzies

There are persistent racial/ethnic disparities in tuberculosis (TB) outcomes in the United States. This study examines the extent to which inequalities in health and socioeconomic status mediate these disparities. We extracted data from the US National TB Surveillance System on TB patients during 2011-2019. We used a sequential multiple mediation approach to evaluate eight potential mediators: three comorbid conditions (HIV, end-stage renal disease [ESRD], diabetes), homelessness, and four census-tract-level measures (poverty, unemployment, insurance coverage, and racialized economic segregation). We estimated the marginal contribution of each mediator using Shapley values. During 2011-2019, 27,788 US-born persons were diagnosed with active TB. Black and Hispanic persons had higher risks of not completing TB treatment during this time period, relative to White persons (aRR 1.27, 95% CI 1.19-1.35; aRR 1.22, 95% CI 1.11-1.33, respectively). In multiple mediator analysis, the eight measured mediators explained 72% of the disparity for Black persons and 69% for Hispanic persons. The biggest contributors to these disparities for both Black and Hispanic persons were concomitant ESRD, concomitant HIV, census-tract-level racialized economic segregation and census-tract-level poverty. Our findings underscore the need for initiatives to reduce disparities in TB outcomes among US-born persons, particularly in highly racially and economically polarized neighborhoods. Mitigating the structural and environmental factors that lead to disparities in the prevalence of comorbidities and their case management should be a priority.

Housing instability is associated with decreased viral suppression among people with HIV in the United States Birdget M Whitney* Bridget Whitney Lydia N Drumright Stephanie A Ruderman L Sarah Mixson Robin M Nance Amanda L Willig Sonia Napravnik Kenneth H Mayer Laura Bamford Edward Cachay Jeffrey M. Jacobson Joseph A Delaney Heidi M Crane

Background

People experiencing houselessness have ~5-10-fold higher prevalence of HIV compared to stably housed individuals. Among people with HIV (PWH), lack of stable housing contributes to impaired access to, and continuity of, care.

Methods

Analyses include adult PWH in clinical care at 6 Centers for AIDS Research Network of Integrated Clinical Systems (CNICS) sites who completed a self-reported assessment on housing between 2019-2023 and had a viral load measured within 18 months prior to their housing assessment. Housing stability was assessed using a single item: "In the past month, how would you describe your living situation?"; response options: 'Homeless,' 'Unstable,' 'Stable,' 'Don't know'. HIV viral suppression was defined as <50 copies/ml HIV1-RNA. Associations between housing stability and HIV viral suppression were estimated by relative risk regression adjusted for age, sex, race/ethnicity, and site.

Results

Among 6,406 PWH (median age: 52; 83% male; 44% White, 39% Black, 12% Hispanic), 9.1% reported housing instability: 4.6% 'Unstable,' 2.8% 'Homeless,' 1.7% 'Don't know'. Self-reported antiretroviral therapy use was high overall, 96.2%, but varied by housing status: 96.7% 'Stable,' 92.5% 'Unstable,' 85.5% 'Homeless,' 92.7% 'Don't know.' Compared to their stably housed counterparts, PWH reporting an unstable living situation were 9% less likely to be virally suppressed (RR=0.91, 95%CI:0.86-0.96), PWH reporting houselessness were 24% less likely to be virally suppressed (RR=0.76, 95%CI:0.67-0.82), and PWH who reported 'Don't know' in response to the stability of their living situation were 11% less likely to be virally suppressed (RR=0.89, 95%CI:0.81-0.98).

Conclusion

Housing instability was associated with a 9-24% lower likelihood of HIV viral suppression among PWH in care in the US. These results suggest that a growing lack of access to stable, affordable housing may be deleterious to successful management of HIV and a barrier to ending the HIV epidemic.

Associations between Housing Instability and HIV Viral Suppression
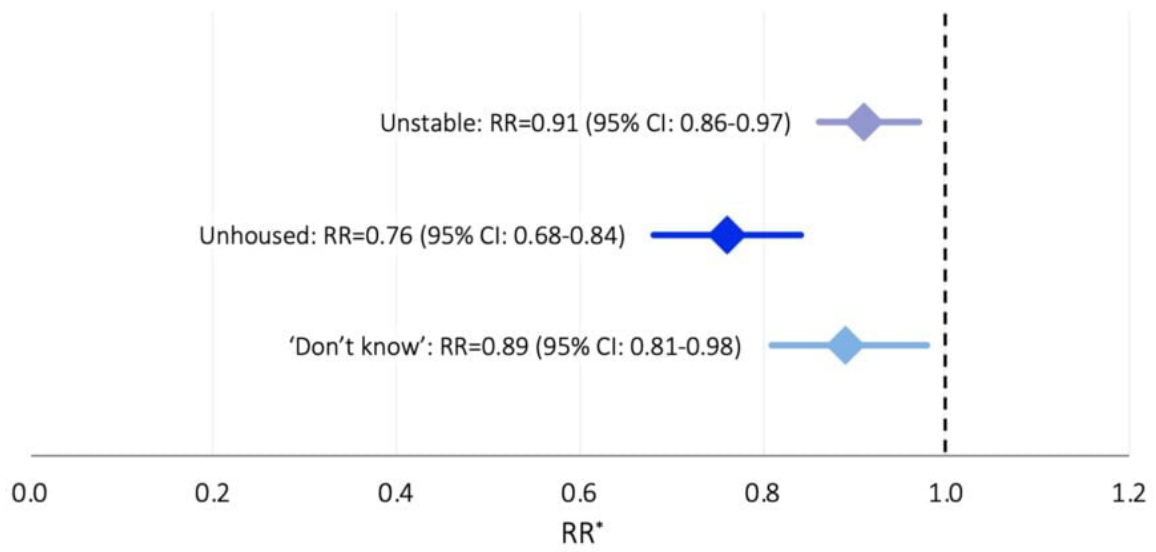
*Relative risk regression estimates adjusted for age, race/ethnicity, birth sex, and site; reference group: stable housing.

Impact of health seeking behavior on Pulmonary TB care in Raipur District of Chhattisgarh province India: Community based study Dr ASHISH SINHA* DR ASHISH SINHA

Introduction: Patients with undiagnosed pulmonary TB act as reservoirs for transmission and will result in 10-15 secondary infections in 1-5 Yrs. Health seeking behavior plays important role in early diagnosis and prompt treatment in TB care. Identification of factors influencing TB care could help in better programmatic impact and overall outcome of TB care.

Material and Methods: This cross sectional study was conducted among 262 Pulmonary TB Pt during Nov – Oct 2022. In-depth interviews were done among study subjects. After informed consent we assessed patient's experiences and documented their journey from initial symptoms until they reached public health facility.

Results: Overall, 198 (78.57%) index cases 21.42% caretakers were interviewed. Mean age of study participants was 36.7 ± 16 years; 87% belonged to the backward class and 56% were from rural areas, 25.39% were illiterate, approximately half (46%) of them were laborers and 29.36% belonged to the joint family. Cough >2wks (55.6%) and evening rise of temperature (32.1%) were the first symptoms followed by chest pain and loss of appetite. Most (97.2%) participants didn't know earlier sign & symptoms of TB; 91.7% didn't know which health care facility to be accessed for the same while 85% had accustomed to visit private health facilities for common illnesses. About one third (32%) participants got appropriate treatment on 1st contact followed by 55%, 71.4%, 81.82% and 100% in subsequent health facility contacts (i.e. 2nd 3rd, 4th and & 5th). Very few (14.3%) had a fear of TB. Waiting time to access TB care at Public health facility was for 31 days (31 ± 45 days) and 57 days (± 60 days). Male, self-medication, ignorant to classical symptoms of TB were significant determinants for health seeking behavior. Participants who contacted private health facility, not aware of signs and symptoms of TB were **4 times** at higher risk, adopted self-medication were **3 times**, more than two consultations were **12-13 times** higher risk of experiencing waiting time (≥ 30days) for diagnosis (Odds ratio 3.056, 4.086 and 14.617 respectively . [p-value ≤ 0.05]. Study participants who were residing in a rural area, middle & lower socio-economic class and visited private health facility first, were significant predictors for increase waiting time (≥ 30days) for diagnosis in study area. aOR 2.176[95% CI (1.017-4.659)]. aOR2.627[95% CI (1.114-6.196)].

Conclusions: Poor health-seeking behavior among study subjects due to ignorance of the sign and symptoms of pulmonary TB, more than two consultations, seeking care from a private health facility and not getting appropriate referral from formal as well as informal health facilities in study area. The common determinants were self-medication, illiteracy, middle and lower-class status and ignorance about classic signs and symptoms.

Health Disparities

Negative external experiences increase risk for suicide attempt in transgender adults
Katherine Medina* Katherine Medina Nishanthi Anthonipillai

Existing research has explored possible risk factors associated with increased risk for a suicide attempt. Some of these have pointed towards lack of social support increases risk and increased support acts as a buffer against suicidality. However, few studies have examined the relationship in transgender adult population. Through an analysis of the TransPop dataset, transgender population only, the association between social support and negative external experiences, and risk of suicide attempts. Utilizing step-wise logistic regression, model 1 revealed disability status as significant in increasing odds for suicide attempt (OR=1.98, 95% CI: 1.18, 3.36). Whereas in model 2, disability was not significant nor was social support; ACE score (OR=1.30, 95% CI: 1.11, 1.51) and everyday discrimination (OR=1.94, 95% CI: 1.31, 2.88) increased odds for suicide attempts. Therefore demonstrating the negative effect of discrimination and early adverse experiences.

Inequities in youth mortality in the rural United States: The role of firearms Allison Lind*

Allison Lind Susan M Mason Elizabeth Wrigley-Field

Background: Rising mortality in children and adolescents ("youth") in the United States is driven by an increase in firearm deaths. Black youth have been disproportionately affected, accounting for half of all youth firearm fatalities in 2021. Rural youth have consistently faced an elevated risk of mortality compared to their urban peers. Historically, however, rural residence was advantageous for Black youth.

Objective: To assess the persistence of the "rural advantage" in mortality rates for Black youth amid the recent increase in firearm deaths.

Methods: We leveraged CDC WONDER data for our study. Our outcome of interest is youth mortality, defined as the death of a child or adolescent 1 to 19 years of age. We categorized deaths into firearm and non-firearm-related. We calculated crude mortality rates per 100,000 and stratified by race (non-Hispanic Black & non-Hispanic White) and rurality (population <50,000 rural & ≥ 50,000 urban). We descriptively examined the contribution of firearms to youth mortality and explored time trends.

Results: 4350 youth died by firearms in 2020, comprising 20.3% of all youth deaths that year. Preliminary data for 2022 suggests this trend has remained consistent. In contrast, in 2014, when all-cause child mortality was at its lowest (23.8 deaths per 100,000), firearms accounted for 13.6% of deaths. While there was an overall increase in the proportion of deaths attributed to firearms over time, striking variations were observed across demographic groups (**Figure 1**). The firearm mortality rate for Black rural youth in 2022 (20.2 deaths per 100,000) was nearly five times the 2012 rate (4.2 deaths per 100,000), playing a substantial role in the simultaneous rise in all-cause mortality. The vast majority of these deaths occurred in the southern United States.

Conclusions: Rising youth mortality in the United States, driven by firearms, is a public health crisis. It profoundly impacts Black youth, including those residing in rural areas.

Contribution of Firearms to All-Cause Youth Mortality, 1999-2022
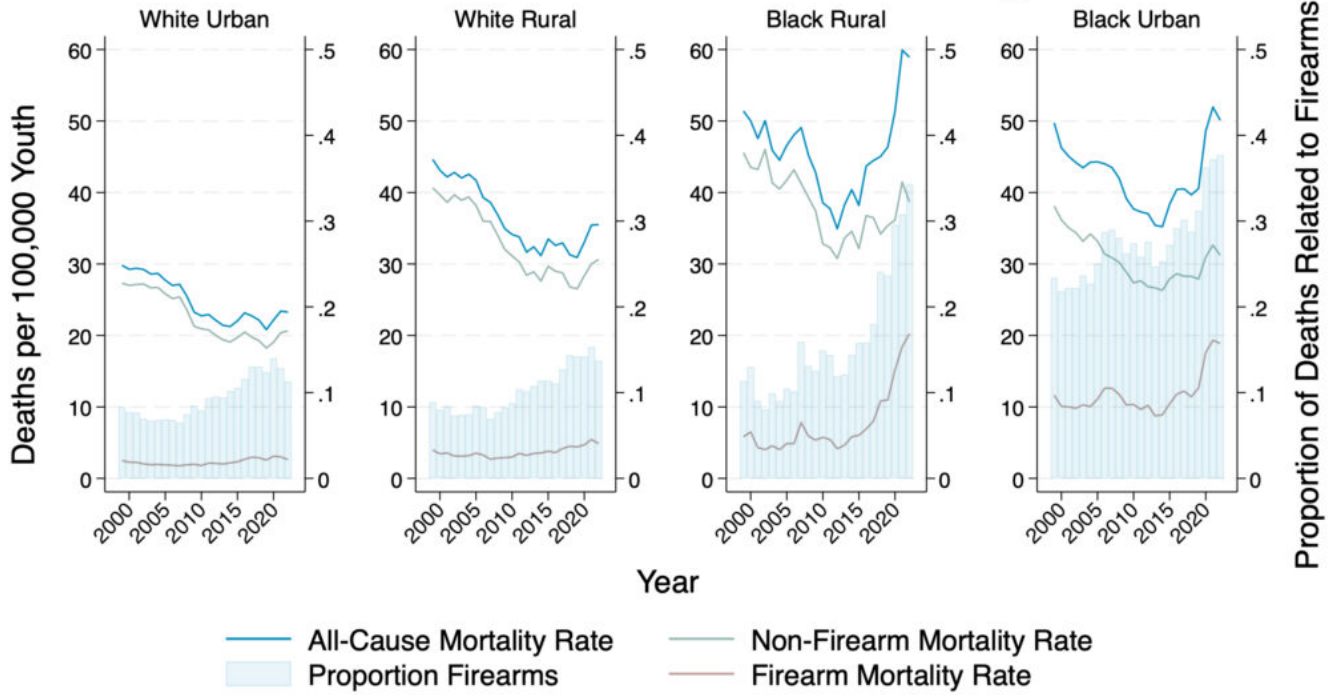
Youth are defined as persons 1 to 19 years of age

Sociocultural stressors and asthma among adults in the Hispanic Community Health Study / Study of Latinos (HCHS/SOL) Juan C. Celedón* Yueh-Ying Han Wei Chen Eric Forno Krista M Perreira Eyal Oren Martha Daviglus Olga Garcia-Bedoya Robert Kaplan Carmen Isasi

Hispanic/Latino adults experience high levels of psychosocial stress; however, little is known about sociocultural stressors and asthma in Hispanic adults.

Cross-sectional study of 4,736 adults aged 18 to 74 years who participated in the Hispanic Community Health Study/Study of Latinos (HCHS/SOL) Sociocultural Ancillary Study. All participants completed an interview-administered sociocultural assessment within 9 months of their baseline exam. Weighted logistic regression accounting for sampling design was used for the analysis on sociocultural stressors (immigrant stress, racism/discrimination, neighborhood social cohesion and neighborhood problems) and current asthma or asthma symptoms. All models adjusted for age, sex, Hispanic/Latino subgroup, site, birthplace, acculturation, health insurance coverage, body mass index, parental history of asthma, smoking status, pack-years of cigarette smoking, dietary patterns (assessed using the alternative health eating index 2010), and three other sociocultural stressors. A mediation analysis was conducted to estimate the contributions of depressive symptoms and anxiety to the sociocultural stressor–asthma association.

Neighborhood problems were associated with increased odds of current asthma (OR for comparison of 2nd-4th quartiles vs. lowest quartile=1.62 [95% CI=1.06-2.46]) and asthma symptoms (OR for 2nd-4th quartiles vs lowest quartile=1.40 [95% CI=1.03-1.91]). Conversely, neighborhood social cohesion was associated with decreased odds asthma. In a mediation analysis adjusted for the same covariates, depressive symptoms and high anxiety explained 20% and 17%, respectively, of the neighborhood problems–asthma symptoms association.

Among Hispanic adults, neighborhood problems were associated with current asthma symptoms, and depressive symptoms and anxiety partly mediated this association. Clinicians caring for adults with asthma should be aware of potential stressors and comorbidities such as depression and anxiety.

Racial and Ethnic Disparities in Mental Health Service Utilization during COVID-19 Abena Yirenya-Tawiah* Abena Yirenya-Tawiah Catherine Cubbin

Abstract

Objective: Racial/ethnic disparities in access to and delayed mental healthcare persist and disenfranchise marginalized populations. The COVID-19 pandemic exacerbated unmet needs for improved mental health services and care. Using the Andersen's model of healthcare utilization, we examined associations between predisposing, enabling, and need factors on mental healthcare utilization among a nationally representative sample of US adults during the pandemic.

Design: This cross-sectional study examined mental healthcare seeking behaviors using cross-sectional data from the 2021 National Health Interview Survey using Andersen's healthcare utilization framework (n=19,555). Accounting for weighting and the complex sample design, and including imputed income files for missing data, we estimated logistic regression models to examine adjusted associations between predisposing (age, gender, race/ethnicity, marital status), enabling, (insurance status, income, education, geographic location), and need (anxiety and depression symptoms) factors and receiving mental healthcare in the prior year.

Results: Our findings from multivariate logistic regression models indicated significant mental healthcare disparities in every predisposing, enabling, and need factor. In adjusted models, racial and ethnic minorities used services at significantly lower odds than non-Hispanic Whites.

Conclusion: Results suggest the need for improved policies and culturally relevant evidence-based interventions in improving mental health seeking attitudes and overall care, specifically for underserved populations. There's a dire need to address access and barriers to mental health services in the US with a focus on how race and ethnicity intersect with other established barriers such as socioeconomic status and geography.

Characteristics of new residents of assisted living facilities: a case-control study Derek R. Manis* Derek Manis David Kirkwood Stacey Fisher Wenshan Li Peter Tanuseputro Zain Pasat Colleen Webber Andrew P. Costa

Background: The characteristics of older adults who transition to an assisted living facility versus who remain in the community are poorly understood. We examined the characteristics of new residents of assisted living relative to community-dwelling home care recipients.

Methods: We conducted a case-control study in Ontario, Canada. We obtained linked, individual-level health system administrative clinical, sociodemographic, and community-level data from new residents of assisted living from 04/01/18 to 12/31/19. New residents of assisted living were matched to home care recipients in a 1:4 ratio on age and sex. We obtained clinical, functional, sociodemographic, and community-level variables from InterRAI-HC assessments and other census-level datasets. We used conditional logistic regression to model associations with characteristics determinant of a transition to an assisted living facility.

Results: There were 3,088 new residents of assisted living (Mean [SD] age 86 [7.03] years, 67% female) who were matched to 12,352 home care recipients. New residents of assisted living had increased odds of two or more falls (aOR 1.37, 95% CI 1.20-1.57), a mood disorder (aOR 1.19, 95% CI 1.08-1.30), and cardiac arrhythmias (aOR 1.12, 95% CI 1.02-1.23). They were concentrated in communities with the highest income quintile (aOR 1.31, 95% CI 1.03-1.65) and less so in rural communities (aOR 0.60, 95% CI 0.51-0.71). They also had a decreased odds of having a spouse or partner caregiver versus a child (aOR 0.62, 95% CI 0.53-0.73) and a hospitalization in the last seven days versus no hospitalization in the last 90 days (aOR 0.72, 95% CI 0.59-0.87).

Conclusions: New residents of assisted living facilities have a history of falls, mood disorders, cardiac arrhythmias, and caregivers who are their children. Our findings also underscore the relationship between income and urban location for a transition to a privately financed assisted living facility.

Impact of South African child support grant on child health: longitudinal evidence from 2008-2017 Daniel Flanagan* Daniel Flanagan Alexandria Hadd Robin Richardson

Background: Established in 1998 to improve the welfare of children living in low-income households, South Africa's Child Support Grant (CSG) has grown to one of the largest cash transfer programs globally. Previous cross-sectional evaluations of the CSG have been limited in establishing long-term benefits on child health. Our objective was to evaluate the effect of receiving a CSG on child health outcomes using longitudinal data collected over a 10-year period.

Methods: We used data from the National Income Dynamics Survey (NIDS), which collected demographic, income, and health data on children and caregivers via repeat household surveys every two years from 2008-2017. Multivariable logistic regression was used to estimate the effect of grant receipt on three child health indicators: moderate-severe stunting (height-for-age z-score ≤ -2 SD), moderate-severe wasting (weight-for-height z-score ≤ -2 SD), and clinic visits in the past 12 months. For stunting and wasting, we restricted our sample to children <5 years old (n=8,876). For clinic visits, we included children up to 15 years old (n=18,545). Models adjusted for survey year, province, child race, and caregiver's age, gender, education level, and employment status.

Results: 67.5% and 66.4% of eligible children under 5 and 15 years old successfully received a child support grant. In adjusted models, we found no association between grant receipt and moderate-severe stunting (OR=1.13; CI95 0.98-1.32) or moderate-severe wasting (OR=1.12; CI95 0.87-1.45). Grant receipt was associated with reduced odds of visiting a clinic in the past year (OR=0.78; CI95 0.74-0.82).

Conclusions: Among eligible children, receiving a child support grant did not reduce moderate-severe stunting or wasting in children under 5 but did reduce annual clinic visits in children 0-15 years old. Use of longitudinal data to study CSG impact improves upon prior evaluations but highlights the challenge of quantifying long-term benefits to child health.

Approaches for complex data organization to facilitate implementation and effectiveness research on health promotion and disease prevention in health services settings Kamala Adhikari* Kamala Adhikari Gary Teare Muhammad Mughal Jawad Chishtie

Aim: The Integrating Prevention into Connect Care for Health (IPiC-Health) initiative is currently being implemented in health services settings in Alberta, Canada to modify patient's smoking and alcohol use behavior. The initiative comprises implementation and effectiveness research using mixed methods involving quasi-experimental quantitative assessments of implementation uptake and effectiveness and qualitative evaluations of implementation factors. We aimed to develop practical approaches for the seamless organization of various types of quantitative data obtained from multiple, different sources within a complex clinical implementation context.

Methods: We export in-person and telephone-based surveys, administrative health data, and EHR data and informed consent forms to the Microsoft SQL (Structured Query Language) server. We use the SQL server for data storage, formatting, linkages, filtering, checking data quality, and creating data views in real-time or periodically. We identify eligible research participants, harmonize datasets, and create a central IPiC-Health research database using a unique ID in the SQL server. We export data to various software for analyses, visualization, and reporting. We engage research and information technology team and build team's capacity to enable data organization processes.

Expected results: IPiC-Health is currently in the implementation and data collection and organization phase. The unified data organization keeps us organized to create a secure, rich, and high-quality IPiC-Health database ready for analysis. Briefly, the database allows the regular assessment of intervention uptake and effectiveness on behavior change, health services use, and cost savings associated with the initiative. It also permits those evaluations from an equity lens.

Conclusion: A unified data organization approach optimizes the efficient use of multiple data for monitoring health services initiatives and conducting unique various research.

Alcohol outlet density and adolescent drinking behaviors in Thailand, 2007–2017: A spatiotemporal mixed model analysis Polathep Vichitkunakorn* Polathep Vichitkunakorn

This study aims to explore the relationship between alcohol outlet density and drinking behaviors among Thai adolescents. We utilized the alcohol drinking behavior data from the 2007, 2011, and 2017 Tobacco and Alcohol Consumption Survey in Thailand. We analyzed the relationships between alcohol sales license figures and consumption behavior using a spatiotemporal mixed model. Our data had two levels. The upper (provincial) level featured alcohol sales license density (spatial effect), the years of survey (temporal effect), and the social deprivation index. The lower (individual) level included the demographic data of the adolescents. A total of 9,566 Thai adolescents participated in this study, based on surveys conducted in 2007 (n = 4,731), 2011 (n = 3,466), and 2017 (n = 1,369). The density of alcohol sales licenses increased the odds for the one-year current drinker category (odds ratio [OR] = 1.08, 95% confidence interval [CI], 1.04–1.45), especially in male adolescents (OR = 1.09, 95% CI, 1.04–1.14). Furthermore, it increased the odds for the heavy episodic drinker category for female adolescents (OR = 1.23, 95% CI, 1.05–1.44). Increased alcohol sales licenses are associated with higher alcohol consumption among Thai adolescents. This highlights the need for government organizations to develop and apply strategies to reduce the number of licenses for the sale of alcohol.

Pre-exposure prophylaxis (PrEP) indicators by race/ethnicity among persons who inject drugs (PWID) receiving CDC-funded HIV testing Deesha Patel* Deesha Patel Weston O. Williams Carolyn Wright

Pre-exposure prophylaxis (PrEP) program performance reduces risk of HIV acquisition. However, use among persons who inject drugs (PWID) remains low, especially for PWID of non-White race/ethnicity. We examined program performance indicators for PrEP use and PrEP-related services by race/ethnicity among PWID testing negative for HIV infection via CDC-funded HIV testing.

Using 2019-2021 HIV testing data submitted by CDC-funded health departments and community-based organizations to the National HIV Prevention Program Monitoring & Evaluation system, we analyzed the following program performance indicators for HIV-negative PWID: current PrEP use, eligibility for PrEP referral among those not currently using PrEP, referral to a PrEP provider among those eligible, and assistance with linkage to a PrEP provider among those referred. To compare by race/ethnicity, we calculated aPRs with 95% CIs and p-values in robust Poisson models, adjusting for age, gender, U.S. Census region, and year.

The prevalence of current PrEP use ranged from 0.4% to 4.0%; in adjusted models, current use was higher for Asian (4.0%; aPR=3.89), multiracial (2.2%; aPR=2.48), Black (1.8%; aPR=2.05), and Hispanic/Latino (1.5%; aPR=1.84) PWID versus White PWID (0.9%; all p<0.05). Eligibility was higher for Black (60.6%; aPR=1.06) and multiracial (60.3%; aPR=1.06) PWID versus White PWID (59.3%; all p<0.05). Referral was higher for Native Hawaiian/Pacific Islander (50.4%; aPR=1.20) and Black (50.4%; aPR=1.18) PWID, but lower for Hispanic/Latino PWID (36.2%; aPR=0.93), versus White PWID (45.4%; all p<0.05). Assistance with linkage was higher for Native Hawaiian/Pacific Islander (81.0%; aPR=1.33), Black (78.8%; aPR=1.18), and multiracial (67.5%; aPR=1.09) PWID versus White PWID (63.8%; all p<0.05).

PrEP use was low among all PWID testing negative for HIV infection. PrEP-related services generally reached a greater proportion of Black PWID; however, PrEP-related services need to reach all racial/ethnic groups to increase PrEP use and reduce HIV acquisition among PWID.

Current PrEP Use, Eligibility for PrEP Referral, Referral to a PrEP Provider, and Assistance with Linkage to a PrEP Provider by Race/Ethnicity among PWID Receiving CDC-Funded HIV Testing Services

| Race/Ethnicity	Current PrEP Use		PrEP Eligibility		PrEP Referral		Linkage Assistance to a PrEP Provider	
	%	aPR	%	aPR	%	aPR	%	aPR
White	0.9	Ref	59.3	Ref	45.4	Ref	63.8	Ref
Black/African American	1.8	2.05 (1.72 – 2.44)	60.6	1.06 (1.04 - 1.08)	50.4	1.18 (1.15 - 1.21)	78.8	1.18 (1.15 - 1.21)
Hispanic/Latino	1.5	1.84 (1.53 – 2.22)	57.3	1.01 (0.99 – 1.03)	36.2	0.93 (0.90 – 0.96)	62.4	0.95 (0.92 - 0.99)
Asian	4.0	3.89 (2.34 – 6.47)	55.9	1.00 (0.91 - 1.09)	39.5	0.92 (0.77 – 1.09)	64.4	0.98 (0.83 – 1.16)
American Indian/Alaska Native	1.0	1.34 (0.89 – 2.02)	61.8	1.02 (0.99 - 1.05)	47.9	1.04 (0.99 - 1.10)	56.4	0.97 (0.91 - 1.04)
Native Hawaiian/ Pacific Islander	0.4	0.42 (0.06 - 3.00)	51.2	0.97 (0.87 -1.09)	50.4	1.20 (1.02 - 1.41)	81.0	1.33 (1.17 - 1.51)
Multiracial	2.2	2.48 (1.70 – 3.64)	60.3	1.06 (1.01 - 1.11)	38.4	0.88 (0.80 – 0.97)	67.5	1.09 (1.0004 – 1.18)

Modeling the Mediating Effects of Multidimensional HIV-related Stigma on Antiretroviral Therapy Adherence and Viral Suppression among Diverse Racial/Ethnic Minority Women with HIV in the Miami-Dade County Ryan-White Program, Florida

Mary Jo Trepka* Ekpereka Nawfal Diana M. Sheehan Gladys Ibañez

Background. This study examined the mediating effects of HIV-related stigma types on the relationship between race/ethnicity and antiretroviral therapy (ART) adherence and viral suppression among women with HIV (WHIV).

Methods. We included a cohort of 542 racial/ethnic minority WHIV (non-Hispanic, non-Haitian Black; Haitian; and Hispanic). Structural equation modeling was conducted with the latent constructs of HIV-related stigma dimensions (anticipated, internalized, and enacted) as mediators, using diagonally weighted least squares to test the direct and indirect effects of race/ethnicity on > 95% antiretroviral adherence and viral suppression (<200 copies/ml), adjusting for covariates. All paths from race/ethnicity to the mediators and outcomes were estimated with comparison to means for all race/ethnic groups or sample proportions. Bootstrapping with 5,000 replications were used to obtain the 95% bias-corrected confidence interval (CI).

Results. Final model fit indices indicated excellent fit (Comparative Fit Index = 0.978, Tucker-Lewis Index = 0.987, Root Mean Square Error of Approximation = 0.024). The direct effect of race/ethnicity on viral suppression was significant with Haitian WHIV less likely to be virally suppressed (β = -0.48, 95%CI: -0.90, -0.14) and Hispanic WHIV more likely (β = 0.43, 95%CI: 0.15, 0.85) compared to the overall sample proportion of viral suppression. We found nonsignificant mediating effects on viral suppression for all HIV-related stigma types. However, Haitian WHIV (β = 0.33, 95%CI: 0.19, 0.46) reported increased anticipated stigma compared to average level among the race/ethnic groups.

Conclusion. Haitian WHIV experience anticipated stigma and are less virally suppressed. Concerted efforts to improve HIV-health outcomes should prioritize understanding the unique cultural beliefs and perceptions about HIV that influence HIV-related stigma prevalent in this community to inform and strengthen HIV-stigma reduction intervention
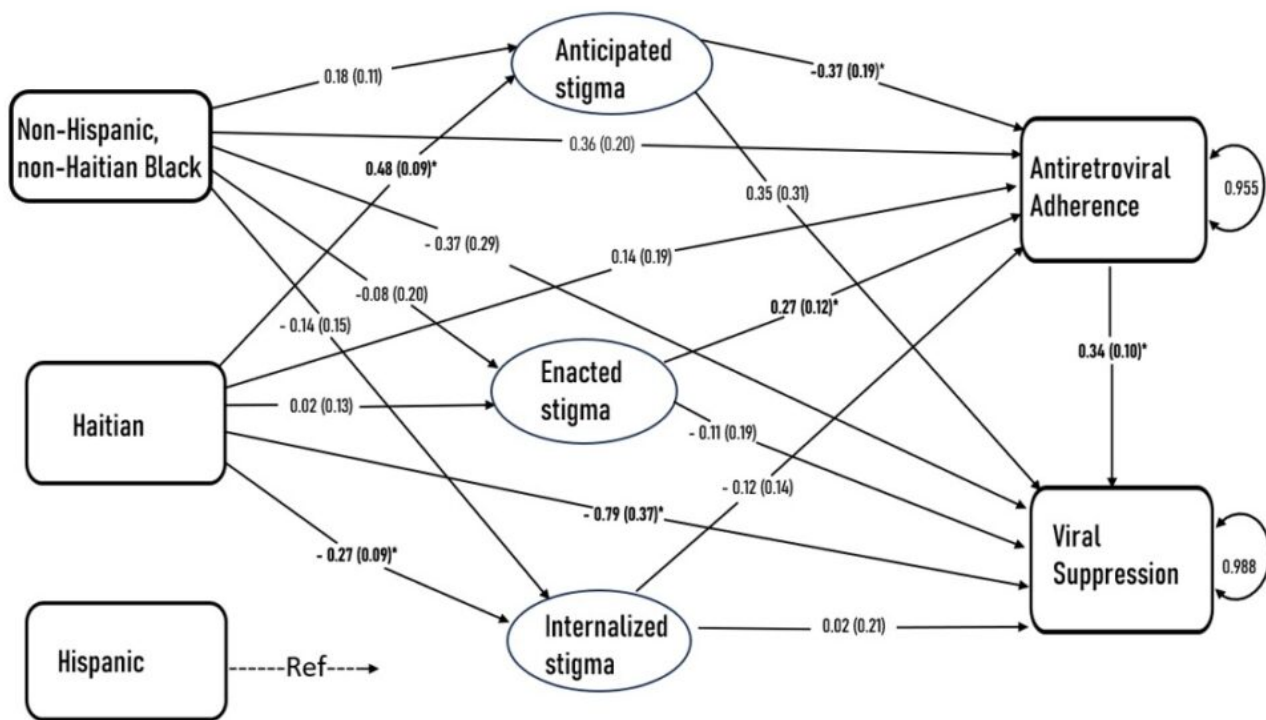
Fig. 1. Final structural equation model for race/ethnicity, latent constructs of HIV-related stigma dimensions, and ART adherence and viral suppression among women with HIV in Miami-Dade Ryan White program (N=542). Indicators of HIV-related stigma dimensions are not included in the diagram. Latent and observed variables were depicted in ovals and rectangles respectively.

Note: Associations are presented as path coefficients (unstandardized) with standard errors in parentheses. Covariates include age, U.S born, Income level, education level and years living with HIV.

*Significant 95% bias-corrected confidence intervals (does not include zero).

Characterizing the HIV care continuum among children and adolescents (<18 years old) with HIV in Eastern and Southern Africa in the era of "Treat All": A systematic review and meta-analysis Nel Jason Haw* Nel Jason Haw Marcela Banegas Sita Lujintanon Allison Agwu Catherine Lesko Derek Ng
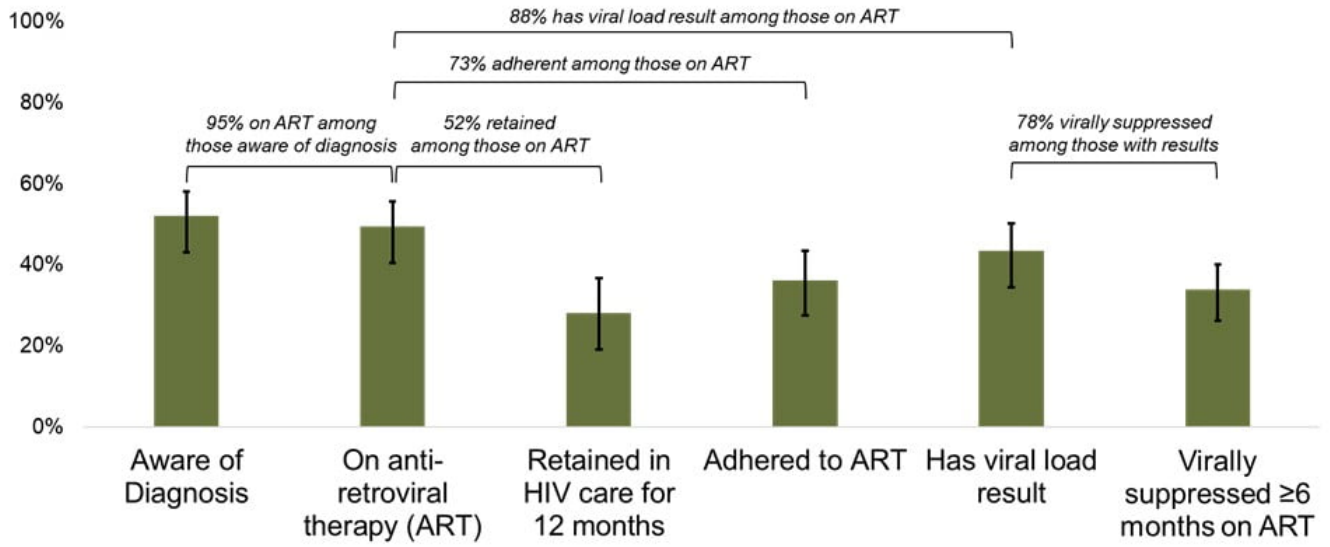
Background: The "Treat All" era for antiretroviral treatment (ART) increased HIV service delivery to children and adolescents (<18 years-old) with HIV (CAHIV). The goal is to reach ≥95% of people with HIV diagnosed, receiving ART, and virally suppressed. Data are limited for CAHIV. We conducted a systematic review and meta-analysis to describe the HIV care continuum among CAHIV during the "Treat All" era living in the UNAIDS Eastern and Southern African region, where two-thirds of CAHIV reside globally.

Methods: We searched PubMed, EMBASE, and the African Index Medicus databases for peer-reviewed articles published from 1 January 2010 to 1 June 2023. We included studies reporting ≥1 care continuum proportion among CAHIV in ≥1 country in the study region during the country's "Treat All" implementation. We extracted the numerator and denominator of the relevant care continuum proportions and pooled proportions using random-effects logistic regression.

Results: Of the 10,279 studies screened, 178 met pre-specified criteria for data extraction. Studies came from 16 countries; many were from South Africa (36) and Ethiopia (30). The most common ages were 10-19 (36) and 0-14 (32). Most studies were conducted in health facilities (150) and were cohort studies with follow-up of ≥6 months (110). The care continuum pooled proportions (95% CI) are as follows: awareness of HIV diagnosis: 52% (43%, 58%); retained in care within 12 months of ART initiation: 57% (47%, 66%); adherent on ART: 73% (68%, 78%); has viral load test after ART initiation: 88% (85%, 90%); and achieved viral load suppression after at least 6 months on ART: 78% (76%, 80%).

Conclusion: During the age of "Treat All," most children and adolescents with HIV in the Eastern and Southern African region who are diagnosed with HIV initiate ART, but other aspects of the care continuum are low, particularly HIV diagnosis, retention in care, and adherence to ART.

Care Continuum among Children and Adolescents with HIV in Eastern and Southern Africa in the Era of "Treat All"

Pooled proportions from a meta-analysis of 178 studies

88% has viral load result among those on ART

73% adherent among those on ART

95% on ART among those aware of diagnosis

52% retained among those on ART

78% virally suppressed among those with results

Aware of Diagnosis

On anti-retroviral therapy (ART)

Retained in HIV care for 12 months

Adhered to ART

Has viral load result

Virally suppressed ≥6 months on ART

Error bars represent 95% CI.

Infectious Disease

We Built This City: Changes to metropolitan TB patterns during the COVID-19 pandemic

Victoria Fisher* Victoria Fisher Nadia Abuelezam

Background: After a drop in reported tuberculosis (TB) in 2020, cases in the U.S. are on the rise. The COVID-19 pandemic changed how and where we live, which has implications for infectious diseases, like TB, commonly associated with dense living conditions. The majority of reported TB cases come from large metropolitan areas. We aim to explore if trends in TB incidence have changed in the "post-COVID" era by metro typology.

Methods: County TB case data, the outcome, was taken from the CDC; county-level demographics are from the American Community 5-Year Survey for 2017-2022. The exposure, metro typology score (lower = more "metro"), comes from the USDA. Covariates included pre- (2017-2019) and post-pandemic (2020-2022) eras, county total population, percent male, percent receiving public assistance, average household density, and percent who live below the poverty level. We assessed the relationship between typology category and TB incidence via mixed effect Poisson regression models.

Findings: Across 330 counties (2017-2022), the mean TB cases count was 29.5 (95% CI: 26.7, 32.4). Mean county typology score was 1.64 (95% CI: 1.6, 1.7). There is a weak, negative correlation between total cases and county typology score (R = -0.22, 95% CI: -0.27, -0.17). In the unadjusted model, the least metro counties were significantly associated with a post-COVID TB incidence rate ratio (IRR) of 8.6 (95% CI: 5.3, 14.3); the most metro counties were significantly associated with a 0.83 (95% CI: 0.82, 0.86) post-COVID IRR. In the fully adjusted model, the least metro counties were significantly associated with a post-COVID TB IRR of 5.0 (95% CI: 3.0, 7.0); the most metro counties were significantly associated with a post-COVID TB IRR of 0.82 (95%CI: 0.8, 0.84).

Discussion: Our results suggest that in the post-COVID era large metro counties have continued to see a decrease in TB incidence while smaller metro and micro counties are experiencing steeper incidence rates.

Assessing the Emerging Trend of Lassa Fever in Liberia (2016-2022) Bendu Sherman* Bendu Sherman Danielle Gartner

The case fatality rate (CFR) of Lassa fever in Liberia is much higher than the worldwide CFR of 1% reported by the World Health Organization (WHO). In recent years, the trend in Lassa Fever cases has also changed. To better understand this emerging trend, we described the general characteristics and seasonal variation in cases and the CFR over time. We analyzed data from 350 cases across six counties in Liberia with a high prevalence of Lassa fever cases. The data was collected through a surveillance system that includes hospitals, the National Reference Lab, and the National Public Health Institute of Liberia (NPHIL). The data included information on suspected and confirmed Lassa Fever cases between 2016 and 2022, aggregated at the county level. 74.6% (n=261) were confirmed cases by the National Reference Lab, while 25.4% (n=89) were suspected cases. Among the confirmed cases, 39.5% (n=103) were under the age of 18 years, 54.4% (n=142) were female, and 41% (n=107) died. Additionally, 55.6% (n=145) of confirmed cases were reported during the dry season, and 91.6% (n=239) were from three counties – Bong, Grand Bassa, and Nimba. The highest overall CFR (62.50%) was reported in 2016, while the highest CFRs among confirmed cases were reported in 2018 (66.67%) and 2021 (60%). The lowest overall and confirmed CFRs were reported in 2022, 29.73% and 29.58%, respectively. The highest CFRs were observed in the dry season in 2016 (69.57%) and 2018 (60%). However, the CFRs in rainy and dry seasons declined in 2022. Lassa Fever is a significant public health issue in Liberia. While the CFRs reported in this work are significantly high, it is worth noting that the high CFR could be influenced by the presence of more severe cases in the case count. Most Lassa fever cases (~80%) are often asymptomatic or mild. Therefore, people visiting the hospital may have more severe cases of the disease.

Infectious Disease

Severity of Respiratory Illness and Influenza-Associated Hospital Admissions in Kenya — January–May 2023 Elizabeth White* Elizabeth White Nzisa Liku Bryan Nyawanda Victor Opere Jorim Ayugi Joel Machuki Peter Muturi Rosalia Kalani Nancy Otieno Danielle Iuliano Gideon Emukule

Introduction: Kenya has a high burden of respiratory illness and two seasonal influenza epidemics each year (January–March and June–August). Surveillance data are used to monitor influenza activity and guide resource allocation. We established intensity thresholds (ITs) to assess respiratory illness and influenza-associated hospitalization severity during January–May 2023.

Methods: We used the Moving Epidemic Method to calculate ITs for (1) the percentage of hospitalizations for severe respiratory illness (SRI), defined as admissions with a respiratory diagnosis (e.g., pneumonia) and (2) the percentage of hospitalizations attributable to influenza, obtained by multiplying indicator (1) by % influenza test positivity. Hospitalizations and diagnoses were abstracted from admission registers at five hospitals and summarized by week. Weekly influenza test positivity was from the same hospitals. ITs were calculated using 2019, 2021, and 2022 as baseline years, excluding 2020 due to the COVID-19 pandemic. Moderate, high, and very high ITs were defined as the 50th, 90th, and 98th percentiles, respectively, of the geometric mean and standard deviation of the 30 highest weekly values in baseline years (10 values per year). We compared weekly surveillance data from January–May 2023 with ITs to assess severity of each outcome during that period.

Results: During January–May 2023, % SRI reached a peak of 31.6%, below the IT50 (32.1%), indicating low severity. The percentage of hospital admissions for influenza reached a peak of 4.7%, above the IT50 (4.1%) but below the IT90 (6.3%), indicating moderate severity.

Conclusions: This is the first analysis of respiratory illness and influenza-associated hospitalization severity in Kenya. In early 2023, respiratory hospitalizations were low and influenza-associated hospitalizations were moderate compared to baseline years. ITs will be updated annually with additional baseline data, and severity can be assessed in future epidemic periods.

Weekly percentages of hospital admissions that were for severe respiratory illness (left) and for influenza (right) during January-May 2023, compared with the corresponding IT50 (yellow), IT90 (orange), and IT98 (red).
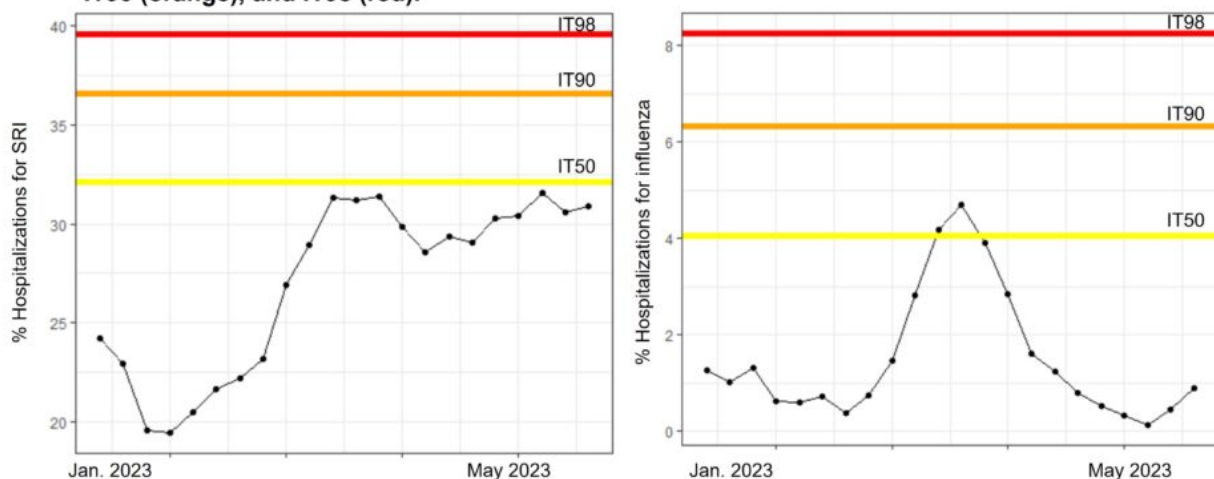
LATEBREAKER

Infectious Disease

Antimicrobial Resistant Nontyphoidal Salmonella Infections Among the US Pediatric Population: 2004-2021 Secondary Data Analysis Nhi Tran* Nhi Tran

Background: Nontyphoidal Salmonella (NTS) poses a significant public health burden in the US, causing an estimated 1.2 million annual infections. Children are disproportionately affected, with infants and young children vulnerable due to immature immune systems. This study investigates longitudinal trends in antimicrobial resistance (AMR) among pediatric NTS isolates obtained from the CDC's National Antimicrobial Resistance Monitoring System (NARMS).

Methods: We analyzed NARMS data spanning 2004-2021, focusing on NTS isolates from children aged 0-19. Descriptive statistics, t-tests, and logistic regression were employed to examine AMR patterns, associations with patient characteristics (age, region), serotypes, and changes over time. Isolates demonstrating resistance to at least one antimicrobial agent were of primary interest.

Results: Children aged 0-4 consistently comprised the majority of NTS cases (62.7% in 2004-2012, 65.4% in 2013-2021). Resistance to ampicillin, amoxicillin-clavulanic acid, ceftriaxone, and chloramphenicol significantly decreased between the two time periods (e.g., ampicillin: 0.1 to 0.09, p=0.005). Nalidixic acid resistance doubled (0.02 to 0.04, p<0.001). Logistic regression revealed factors such as later time period (2013-2021), specimen source, age group, serotype, and region significantly influenced AMR likelihood.

Conclusion: This study highlights the trend of AMR in pediatric NTS infections in the US. While progress has been made in combating resistance to certain antibiotics, emerging resistance patterns underscore the continued threat of AMR. A multi-faceted approach encompassing antibiotic stewardship, infection control, and tailored interventions remains essential to safeguard children's health.

Prevalence of TB-related Symptoms and Self-reported Disability Among Adults Post-TB Treatment in Kampala, Uganda: A Retrospective Study Adenike McDonald* Adenike McDonald Juliet Sekandi Patrick Kaggwa Asmith Joseph Esther Buregyeya Sarah Zalwango Damalie Nakkonde

Background: Growing evidence suggests that post-TB related morbidity occurs, however, limited epidemiological data exists on the burden of symptoms and disability post TB treatment. Our study evaluated the prevalence of TB-symptoms, self-reported disability and factors associated among individuals who recently completed TB treatment in Uganda.

Methods: Between January 2022 and October 2023, we conducted a retrospective cohort study of adults ≥18 years who had successfully completed treatment for drug-sensitive TB in Kampala, Uganda. We collected data on current TB-related symptoms, and we measured disability using 12 items adopted from the World Health Organization Disability Assessment Schedule (Whodas 2.0).

 Results: Of the 200 participants, the median age (IQR) was 33.0 (26- 44.5), 105 (52.5%) were male, and 46 (23%) were HIV-infected. The prevalence of any TB-related symptoms was 58%. The proportion of persons self-reporting any disability was 83.5%. The median (IQR) disability score was 16 (13-21), and the mobility and participation domains contributed 52.3% of the cumulative disability score. Being female, completing treatment 6-8 months prior to interview, and having TB-related symptoms were significantly associated with self-reporting a disability in any of the domains with the AOR being 2.37 (p=0.04), 2.87 (p=0.04) and 2.51 (p=0.03) respectively after adjusting for age, and HIV status.

Conclusions: TB-related symptoms and self-reported disability were highly prevalent in the study setting suggesting that the health and wellbeing for persons who complete TB treatment remain compromised. Further evaluation and interventions to address the quality of life for survivors during the post TB period should be considered as part of the continuum of care.

Is a COVID-19 booster dose still helpful? Association between the COVID-19 vaccine and risk of COVID-19 hospitalization during Omicron Margaret Lind* Margaret Lind Matt DT Hitchings Sameer Pandya Derek AT Cummings Wade Schulz Albert I Ko
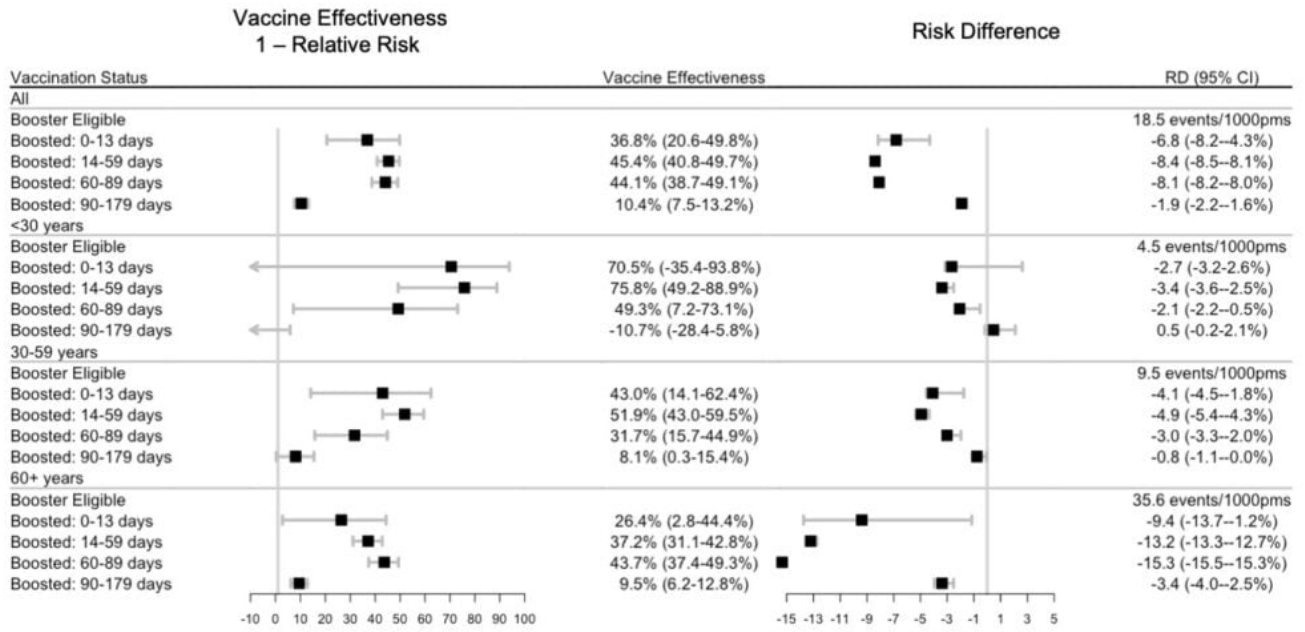
Background: COVID-19 severity diminished with the emergence of the Omicron variant. As a result, the protective effect of COVID-19 vaccine booster doses against severe disease remains unclear. Here, we examine the associations between receiving a COVID-19 booster dose and the risk of COVID-19 related hospitalization during the Omicron predominant period (12/13/2021-4/30/2023).

Methods: We performed a cohort study of people within a large US health system who completed their primary COVID-19 vaccine series. We compared the risk of COVID-19 related hospitalization between booster-eligible people (180+ days since last dose) to those recently boosted using a Poisson regression. Age stratified analyses were performed and marginal effects were estimated using G-computation.

Results: The 768,524 people who were booster-eligible or recently boosted during the study period experienced 5,324 COVID-19 related hospitalizations. Compared to booster-eligible people, people boosted in the last 14-59 days were significantly less likely to have a COVID-19 related hospitalization (Vaccine Effectiveness: 45.4% [40.8-49.7%]; Risk Difference [RD]: -8.4 [-8.5, -8.1] events/1000 person-months [pms]). The risk of hospitalization among booster-eligible people was highest for people aged ≥60 years (35.6 events/1000pms). The relative risk reduction in the 14-59 days following booster dose receipt was highest for people aged <30 years but the absolute reduction was greatest for people aged ≥60 years (RD; -13.2 [-13.3, -12.7]; Figure1).

Discussion: Booster dose receipt reduced the number of hospitalizations among people vaccinated in the last 14-59 days by ~8 events per 1000pms, corresponding to a 52% risk reduction. While there was a significant reduction for all age groups, people aged ≥60 years had the greatest underlying risk and largest absolute reduction. These findings suggest that booster doses provide protection regardless of age but that the benefit is greater for older people.

Figure 1. Association between COVID-19 booster doses and COVID-19 related hospitalizations

Vaccination Status	Vaccine Effectiveness 1 – Relative Risk	Vaccine Effectiveness	Risk Difference	RD (95% CI)
All				
Booster Eligible				18.5 events/1000pms
Boosted: 0-13 days		36.8% (20.6-49.8%)		-6.8 (-8.2--4.3%)
Boosted: 14-59 days		45.4% (40.8-49.7%)		-8.4 (-8.5--8.1%)
Boosted: 60-89 days		44.1% (38.7-49.1%)		-8.1 (-8.2--8.0%)
Boosted: 90-179 days		10.4% (7.5-13.2%)		-1.9 (-2.2--1.6%)
<30 years				
Booster Eligible				4.5 events/1000pms
Boosted: 0-13 days		70.5% (-35.4-93.8%)		-2.7 (-3.2-2.6%)
Boosted: 14-59 days		75.8% (49.2-88.9%)		-3.4 (-3.6--2.5%)
Boosted: 60-89 days		49.3% (7.2-73.1%)		-2.1 (-2.2--0.5%)
Boosted: 90-179 days		-10.7% (-28.4-5.8%)		0.5 (-0.2-2.1%)
30-59 years				
Booster Eligible				9.5 events/1000pms
Boosted: 0-13 days		43.0% (14.1-62.4%)		-4.1 (-4.5-1.8%)
Boosted: 14-59 days		51.9% (43.0-59.5%)		-4.9 (-5.4--4.3%)
Boosted: 60-89 days		31.7% (15.7-44.9%)		-3.0 (-3.3--2.0%)
Boosted: 90-179 days		8.1% (0.3-15.4%)		-0.8 (-1.1--0.0%)
60+ years				
Booster Eligible				35.6 events/1000pms
Boosted: 0-13 days		26.4% (2.8-44.4%)		-9.4 (-13.7--1.2%)
Boosted: 14-59 days		37.2% (31.1-42.8%)		-13.2 (-13.3--12.7%)
Boosted: 60-89 days		43.7% (37.4-49.3%)		-15.3 (-15.5--15.3%)
Boosted: 90-179 days		9.5% (6.2-12.8%)		-3.4 (-4.0--2.5%)

Infectious Disease

Coccidioidomycosis hospital visits in Texas, 2011-2021 Heather Mayfield* Heather Mayfield Vanora Davila

Coccidioidomycosis, or Valley fever, is a fungal disease caused by the soil-dwelling fungi Coccidioides immitis and Coccidioides posadasii. Texas is estimated to be in the endemic range of Coccidioides posadasii but does not have mandatory reporting requirements for coccidioidomycosis. The lack of surveillance in Texas limits understanding of disease dynamics and may contribute to underreporting and underdiagnosis due to decreased awareness. This study estimated the demographic characteristics and geographic distribution of coccidioidomycosis hospital visits, assessed the prevalence rates of hospital visits for coccidioidomycosis, and examined how rates vary by demographic and geographic factors. We used Texas Health Care Information Collection hospital discharges between 2011-2021 among Texas residents with a coccidioidomycosis-related diagnosis code in the record (n=6049 records). Coccidioidomycosis hospital visits increased from 348 in 2011 to 709 in 2021. Most hospital visits for coccidioidomycosis occurred in those 46-64 years old (42.6%), male (55.5%), and Hispanic (48.4%). A 96-county area designated as the Valley fever region accounted for 65.2% of visits, while only accounting for 37.8% of Texas counties. More than 75% of visits were in the Moderate/Extreme illness severity category. We used negative binomial regression to calculate prevalence rate ratios of hospital visits by demographic and geographic groups. Our results suggest that geographic region, sex, and race/ethnicity are associated with increased rates of hospital visits for coccidioidomycosis. Prevalence rates for females were lower compared to males (PR=0.36, 95% CI:0.31-0.42). Compared to Hispanics, non-Hispanic Blacks (PR=1.25, 95% CI:1.01-1.56) had higher prevalence rates, and non-Hispanic Whites (PR=0.80, 95% CI:0.65-0.98) had lower rates. These results highlight the need for increased awareness, expanded surveillance, and continued monitoring of coccidioidomycosis in Texas.

Impact of the COVID-19 pandemic on incarceration and tuberculosis notification rates among individuals who are incarcerated in Europe and the Americas Amy Zheng* Amy Zheng Lena Faust Joshua Warren Leonardo Martinez

Background

People who are incarcerated are at higher risk for tuberculosis (TB) infection and disease due to the prison environment (e.g., overcrowding and poor ventilation) as well as individual risk factors (e.g., malnutrition and substance use). COVID-19 led to major disruptions in diagnosis and care TB programs globally. However, the impact of the pandemic on prison population counts and TB notification rates among people who are incarcerated, a high-risk, vulnerable group, is unknown.

Methods

In collaboration with the Pan American Health Organization (PAHO), European Centre for Disease Control and Prevention, and European World Health Organization Regional Office, we collected tuberculosis notification and incarceration data from 2010-2022. A joint hierarchical Bayesian time-series model with a negative binomial distribution was developed to predict prison population counts and TB notification rates for each country from 2020-2022. We compared these predicted estimates to observed trends to evaluate the impact COVID-19 on incarceration and TB notification rates.

Results

Of the 101 countries in Europe and PAHO, 79 and 45 countries were included for incarceration and notification rate outcomes, respectively. The impact of COVID-19 on incarceration levels was highly heterogeneous across countries and regions (Figure 1). In Europe, most countries reported lower TB notification rates in 2020 (16/21 countries) and 2020 (17/21 countries). In the Americas majority of countries had drops in TB notification rates during the pandemic (Figure 1). Countries in the Americas with greatest decreases in TB notification rates during the pandemic were more likely to be countries with a high tuberculosis burden in prisons (e.g., El Salvador, Venezuela, Peru).

Conclusion

Our findings suggest that the COVID-19 pandemic has substantially impacted tuberculosis notification rates in prisons. Countries with larger tuberculosis epidemics in prisons were especially impacted by the pandemic.
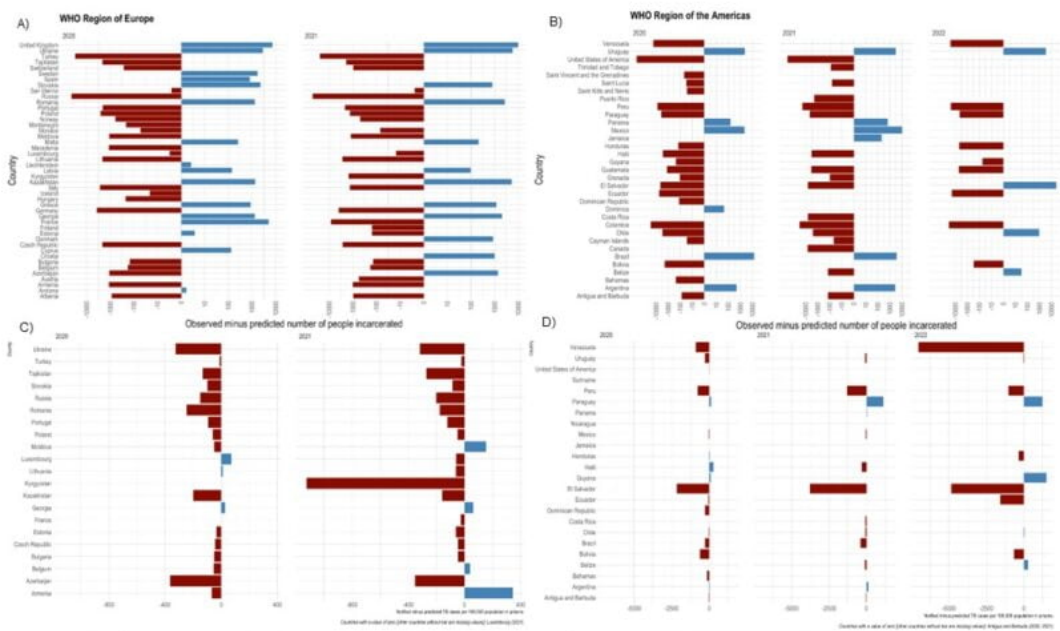
Figure 1. A) Difference between the observed and the predicted for prison population counts in the WHO European region. Red represents that the predicted was greater than the observed and blue represents that the predicted was less than the observed. B) Difference between the observed and predicted for prison population counts in the WHO Americas region C) Difference between the observed and the predicted tuberculosis notification rate per 100,000 people in the WHO European region D) Difference between the observed and the predicted tuberculosis notification rate per 100,000 people in the WHO Americas region

Infectious Disease

Determinants of Hepatitis C Virus Treatment Completion Among Los Angeles County Residents Diagnosed Between January 1, 2021 and April 30, 2022

Cassidy Hernandez-Tamayo* Cassidy Hernandez-Tamayo Chrysovalantis Stafylis Albert J Farias Lokesh Bhardwaj Riya Shah Tatiana Becerra Dara Bruce Roopkamal Saini Natalie Saremi Immanuel Thomas Krzel Manansala-Tan Arjun Vij Alison Li Nathan Sudeep Jacob Gizamba Bijan Hosseini Sabrina Navarro Sofia Ufret-Rivera Gilbert Orta Portillo Prabhu Gounder Mirna Ponce Jewell Jeffrey D Klausner

Background: Hepatitis C Virus (HCV) infection is a treatable leading cause of death in the United States. However, there is little population-based evidence to establish determinants of treatment completion. Thus, we undertook an observational study of recently reported cases and treatment outcomes in Los Angeles (LA) County.

Methods: We identified residents with a reported positive HCV RNA test result in the LA County registry from January 2021 to April 2022. We interviewed cases about their HCV infection awareness and treatment status. We evaluated bivariate and multivariable associations between demographics and clinical characteristics and treatment completion using Pearson's Chi-Square Tests and multivariable logistic regression, respectively. Prevalence odds ratios and 95% confidence intervals determined the magnitude of the multivariable associations.

Results: Among 611 cases interviewed, the majority were publicly insured (61%), male (65%), and untreated (72%). There were no statistically significant differences in the proportion of untreated respondents in the minority compared to non-minority groups (75% vs 70%, p=0.20). However, Black individuals compared to other ethnic groups had the highest proportion of untreated respondents (77%, p=0.04). A higher proportion of symptomatic compared to asymptomatic respondents were untreated (87% vs 61%, p<0.01). In the multivariable model, Black respondents had 0.4 (95% CI: 0.2, 0.8) times the odds of completing treatment compared to Whites. Asymptomatic respondents had 4.4 (95% CI: 2.3, 8.4) times the odds of completing treatment compared to those symptomatic, adjusted for liver disease diagnosis, insurance status, provider type, heritage and age group.

Conclusion: Respondents who were Black and symptomatic compared to those White and asymptomatic were less likely to be treated. Low treatment completion rates suggest the need to establish expanded public health efforts to ensure timely treatment in these populations.

Infectious Disease

Mediation Analysis for Calcium, Vitamin-D, and COVID-19 Severity Ayse Ulgen* Ayse Ulgen Sirin Cetin Wentian Li

Background: Hypocalcemia and vitamin-D deficiency are known to be associated with a worst outcome of COVID-19 patients, but their causal direction is unclear. **Methods:** In this paper, blood samples of more than 1300 COVID-19 patients from Tokat, Turkey are analyzed. A new strategy is adopted; instead of inferring a simple causal model, the task to estimating causal path proportions with a given assumed causal model is assumed. For a given causal model, if a causal path is not statistically significant and/or if a causal path has a very low proportion, a particular causal model is unlikely to be true. Therefore, choices among all possible causal models may be narrowed. With three variables: vitamin-D and calcium level, and indicator variable on if a patient is in critical state or not, standard mediation analysis is used to investigate the possible relationship among them. Since age contributes to almost every risk factors as well as to COVID-19 prognosis, age (and gender) are used as co-variates in the mediation analysis. **Results:** 1) Association between being critically-ill by COVID-19 and calcium (but not vitamin-D) is independent from osmolality: Logistic regressions show that osmolality, calcium, and vitamin-D are all significantly associated with critically ill status conditional on age and gender, with p-values 2.6E-7 (osmolality), 5.3E-10 (calcium), 2.7E-4 (vitamin-D) and 2E-6 (log-vitamin-D. 2) Reduction of vitamin-D level at different age groups: It can be seen from Fig.1 that the reduction of vitamin-D scale is less in the critical group for older age group (e.g. 80 or above), compared to a relatively younger group (e.g., in the age of 60s). **Conclusions**: Single regression analyses is not adequate for inferring causality. Assuming that cause is the independent variable and effect is the dependent variable in a regression analysis is only an assumption and may not reflect reality.

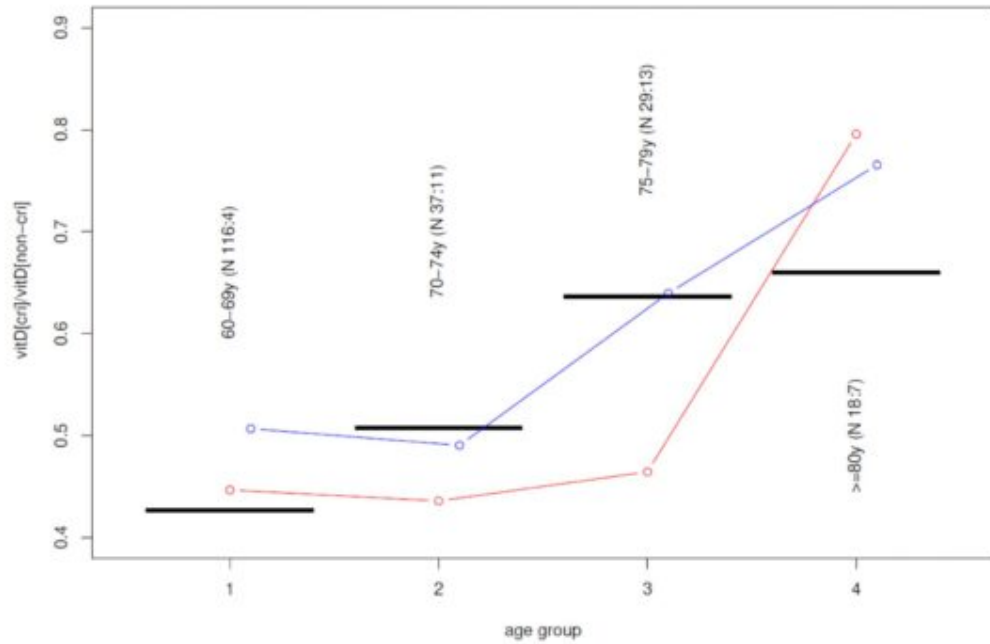## Fig 1:Reduction of Vitamin-D level at different age groups:

Figure 2:

In-season evaluation of influenza forecasts during the 2023-2024 US influenza season
Sarabeth M. Mathis* Sarabeth Mathis Rebecca K. Borchering Alexander E. Webber Matthew Biggerstaff FluSight Influenza Forecasting Consortium

Influenza-related hospitalizations are a major contributor to the disease burden in the United States with CDC estimating 100,000 to 710,000 hospitalizations annually between 2010 and 2022. Accurate predictions of influenza hospital admissions can help support public health planning and interventions. CDC coordinated a collaborative forecasting challenge for the 2023-24 influenza season beginning October 11, 2023, through April 30, 2024. Forecasting teams were asked to provide national and jurisdiction-specific probabilistic predictions for weekly laboratory-confirmed influenza hospital admissions during the 2023-24 influenza season.

Similar to previous years, FluSight prepared an ensemble and baseline model each week. The ensemble calculates the unweighted median of each quantile among eligible forecasts, and the baseline estimates the most recent observed weekly admission count as the median for all forecast horizons. A distribution of historical change around the median is used to determine prediction intervals.

Forecast skill was evaluated on absolute weighted interval score (WIS), a proper score that generates interval scores for probabilistic forecasts provided in the quantile format, WIS relative to the baseline model, and coverage, a metric that assess how often the prediction interval contained the actual observed value.

As of January 3, 2024, an average of 24 modeling teams submitted 25-30 models each week. Eight models outperformed the FluSight ensemble in terms of WIS and 27 models outperformed the FluSight baseline including the FluSight ensemble. 95% coverage was over 90% for five teams. Forecast overage and accuracy during the initial period influenza hospitalizations were increasing improved compared to results from the 2022-23 season when influenza activity increased atypically early in the season.

Accurate forecasting can help public health officials anticipate trends throughout the influenza season.

Infectious Disease

**Estimating the generation time for influenza transmission using household data in the United States** Louis Yat Hin Chan* Louis Yat Hin Chan Sinead E. Morris Melissa S. Stockwell Natalie M. Bowman Edwin Asturias Suchitra Rao Karen Lutrick Katherine Ellingson Huong Q. Mclean Edward A. Belongia Yvonne Maldonado Jessica E. Biddle Sarah E. Smith-Jeffcoat Matthew Biggerstaff Melissa Rolfes H. Keipp Talbot Carlos G. Grijalva Rebecca K. Borchering Alexandra M. Mellis

The generation time (GT), representing the interval between infections in primary and secondary cases, is essential for understanding and predicting the transmission dynamics of seasonal influenza, including the effective reproduction number (Rt). However, comprehensive GT estimates for seasonal influenza, especially post-2009, are lacking. As a substitute, the serial interval, defined as the duration between symptom onsets of successive cases, is often used due to the practicality of observing symptom onsets.

We estimated the GT utilizing data from a 7-site case-ascertained household study in the United States over 2 influenza seasons, 2021-22 and 2022-23. Over 200 individuals with influenza and their household contacts were enrolled within 7 days of the first illness in the household, and prospectively followed for 10 days of daily symptom monitoring and nasal swab collection. Households with more than one primary case, defined by date of first symptom onset in the household, were excluded. Influenza was detected through polymerase chain reaction (PCR) testing of nasal swabs collected daily from exposed household contacts. We analyzed these data by modifying a previously published Bayesian data augmentation approach that imputes infection times of cases to obtain both intrinsic (assuming no susceptible depletion) and realized (observed within household) GT. We also assessed estimate sensitivity by varying the incubation period.

We estimated a mean intrinsic GT of approximately 3.0 (95% credible interval, CI: 2.7-3.2) days, with the realized household GT marginally shorter with an estimate of 2.6 (95% CI: 2.4-2.8) days. The GT exhibited limited sensitivity to the incubation period.

Our study contributes to the ongoing efforts to refine estimates of the GT for influenza. Our estimates, derived from the recent data, fall within the uncertainty bounds of previous estimates, suggesting consistency, and will be incorporated into real-time Rt estimation efforts.

Infectious Disease
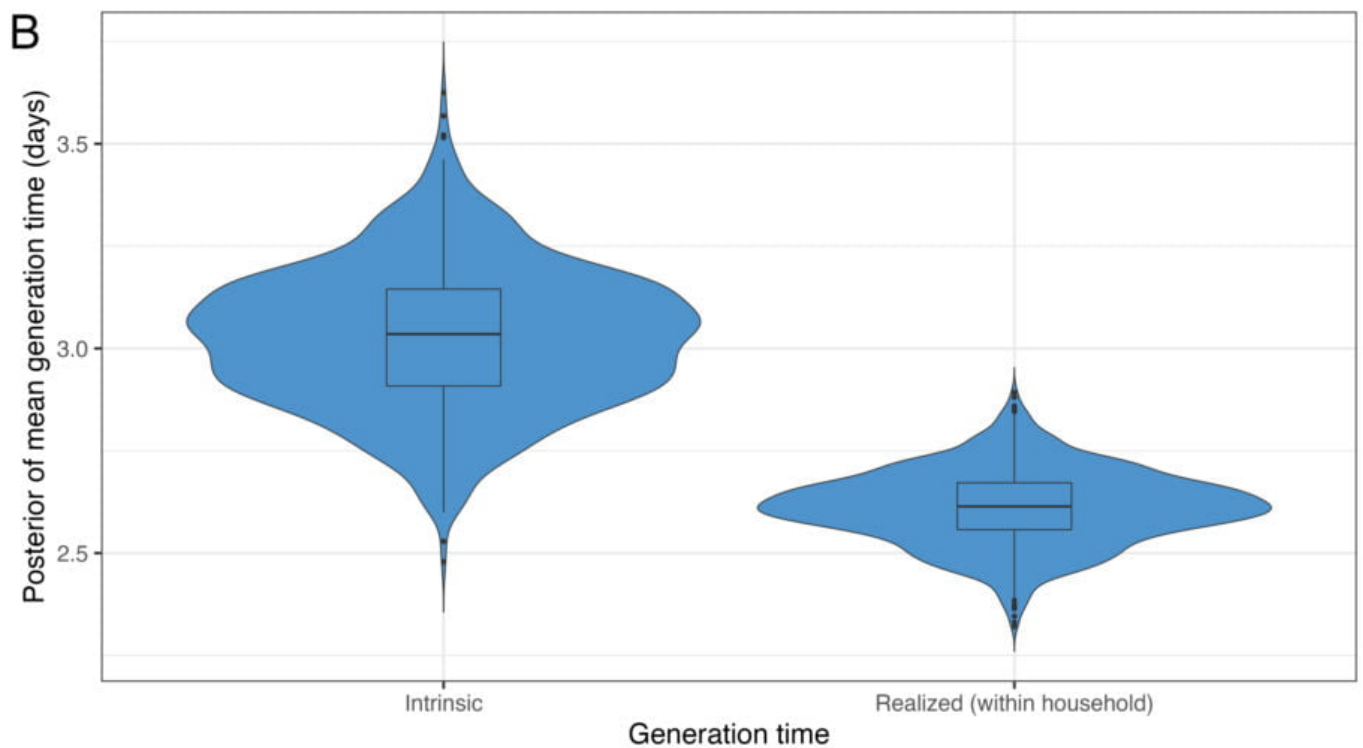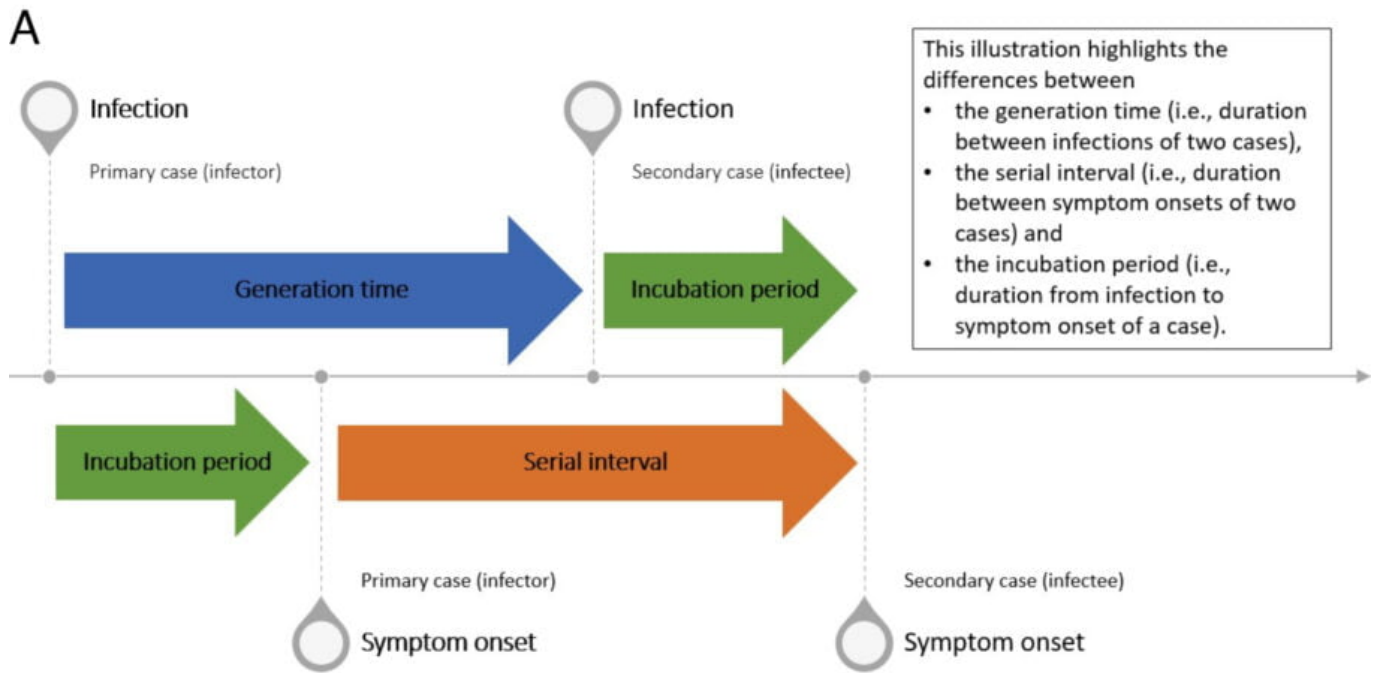
Genome wide association analysis in Asian cohorts reveal key variants for spontaneous seroclearance of hepatitis B surface antigen and associated clinical traits
Jun Tao* Jun Tao Chien-Jen Chen Zhiwei Liu Hwai-I Yang Kevin Wang Bin Zhu Chih-Jen Huang Yu-Han Huang Mei-Hung Pan Mei-Hsuan Lee

Background: Chronic hepatitis B virus (HBV) infection affects an estimated 16 million individuals worldwide and accounts for approximately 555,000 deaths per year. Seroclearance of hepatitis B surface antigen (HBsAg), which is difficult to achieve with antiviral treatment, is one of the most important clinical outcomes for chronic hepatitis B infection. A prior report has shown that hepatitis B e antigen (HBeAg) positivity, HBV DNA level, and quantitative HBsAg levels are major factors associated with spontaneous HBsAg seroclearance. However, few studies have examined the genetic determinants of spontaneous HBsAg seroclearance. We aimed to evaluate the host genetic basis for spontaneous seroclearance of HBV infection.

Methods: We performed a genome-wide association study (GWAS) of 3,240 individuals with chronic HBV infection who were enrolled between 1991 and 1992 in a community-based study in Taiwan. Serum samples collected at baseline and follow-up examinations were tested for HBsAg, HBeAg, serum HBV DNA levels, and quantitative HBsAg levels. Samples were genotyped using Affymetrix Axiom CHB1 Array arrays and imputed using TOPMed reference panel and a Taiwanese reference panel for the human leukocyte antigen (HLA) regions. A stepwise approach was used to select significant variants – those independently associated with two of the three traits – hepatitis B e antigen (HBeAg) positivity, HBV DNA level, or quantitative HBsAg levels in regression models ($P<1\times10^{-5}$ and LD pruning $R2<0.5$) – were selected for testing the association of genetic variants with spontaneous HBsAg seroclearance by log-additive analysis, adjusting for sex, age group at baseline, and principal components. To further validate our findings, we examined the impact of identified loci on early clearance of HBsAg in an independent population from the Taiwan Biobank, including 54,072 individuals with HBsAg-negative and anti-HBc-positive status and 11,340 individuals with HBsAg-positive status.

Results: Of 2,951 participants with HBsAg information during an average of 12 years of follow-up, spontaneous HBsAg seroclearance occurred in 535 participants. Four SNPs were associated with two of the three traits (HBeAg positivity, HBV DNA level, or quantitative HBsAg levels), of which three were significantly associated with spontaneous HBsAg seroclearance (i.e., $P\leq0.05$), including rs446717 (nearby gene: CTNNB1; P=0.0508), rs6906021 (HLA-DQB1; P=0.0363), and rs148385846 (CAMK1D; P=0.0047). None of the imputed HLA alleles were significantly associated with spontaneous HBsAg seroclearance. Two loci were also associated with early clearance of HBsAg in the Taiwan Biobank (rs446717; P=0.0417 and rs6906021; $P=2.53\times10^{-37}$).

Conclusion: This study identified three loci that may explain the genetic determinants of spontaneous HBsAg seroclearance through baseline HBeAg positivity, HBV DNA levels, and quantitative HBsAg levels, with two loci also associated with early clearance of HBsAg. Notably, the distinct role of HLA in both early and late HBsAg clearance was observed. These genetic findings may have important clinical implications for treating chronic HBV infections.
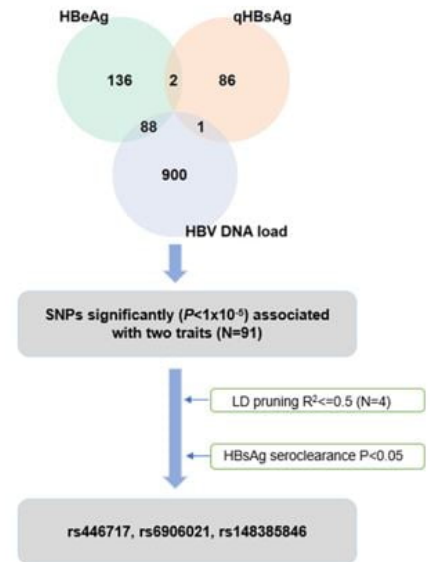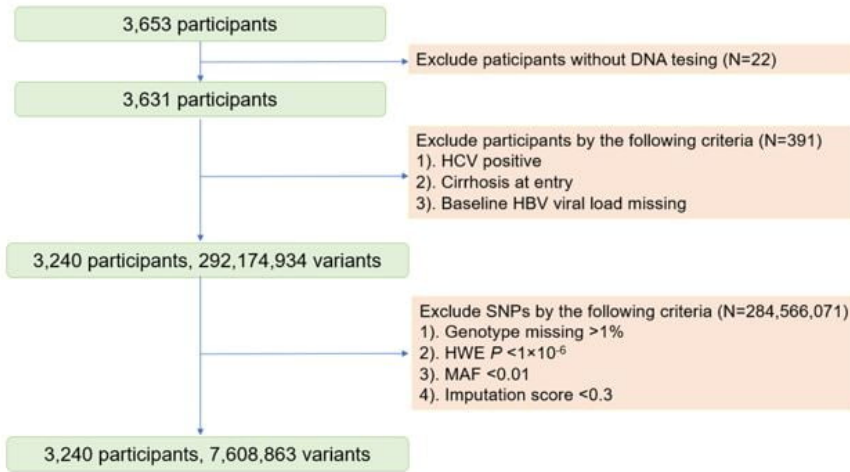
Factor structure and concurrent validity of the severity of violence against women scale in zambia and south africa Amy Zheng* Amy Zheng Anthony J. Rosellini Jeremy C. Kane Kristina Metz Srishti Sardana Ross Greener Sithabile Mngadi Pertunia Manganye Lawrence C. Long Donald M. Thea Laura Murray Matthew Fox Mwamba Mwenge Saphira Munthali-Mulemba Sophie Pascoe

Background: The Severity of Violence Against Women Scale (SVAWS), is a 46-item questionnaire developed and validated among women in the US to assess two subscales: threatening acts and physical violence. However, it has not been evaluated using gold standard scale validation approaches and little is known about its psychometric properties in other populations and cultures.

Methods: Exploratory factor analysis (including parallel analysis) was used to evaluate the structural validity and psychometric properties of SVAWS among women reporting intimate partner violence in the past year in Zambia (N=246) and South Africa (N=368). Factor loading patterns were evaluated based on their strength and conceptual interpretation (e.g., eliminating items with loadings<0.3 or large cross-loadings). Cronbach's alpha was used to evaluate the internal consistency. Concurrent validity analyses were conducted to determine whether constructs assessed by SVAWS were associated with depression, trauma, and substance use.

Results: Our findings in Zambia and South Africa indicated several non-salient factor loadings. While the original scale identified two subscales, our findings identified three underlying dimensions with good internal consistency: Threatening (α=0.90-0.96), Physical (α=0.86-0.87), and Sexual (α=0.81-0.87). In support of their concurrent validity, the three subscales were more strongly associated with trauma (Harvard Trauma Questionnaire r=0.32-0.51) and depression (Center for Epidemiologic Studies Depression Scale r=0.33-0.44) than ever reporting substance use (Alcohol, Smoking, and Substance Involvement Screening Test r=-0.03-0.28).

Conclusion: While SVAWS is an appropriate tool for assessing intimate partner violence in South Africa and Zambia, the underlying constructs may differ across cultures and require revisions to SVAWS items and highlight the importance of validating instruments in new contexts to ensure concepts are measured accurately and reduce bias.

Injuries/Violence

Losing sleep? The effects of exposure to gun violence near one's residence on self-reported sleep quantity in Chicago, 2020-2021 Suzanne G. McLone* Suzanne G McLone Chad M. Coleman Hannah Matzke Nikhil Prachand Matthew P. Fox Jonathan S. Jay

Very few studies have investigated the association between exposure to gun violence and sleep. We used data from the Healthy Chicago Survey, an annual survey with an address-based sampling scheme of adults in Chicago, IL, to address this question. Self-reported survey responses included poverty level, BMI status, health status, and sleep duration. The dates and locations of firearm shootings were accessed via the Chicago Data Portal. Exposure to gun violence was measured as shootings occurring within 400 meters of respondent's residence either 7 days before (exposed group) or 7 days after (unexposed group) taking the survey. Sleep was dichotomized into <7 hours and >=7 hours. We fitted log-linear regression models to generate RRs and 95% CIs of exposure to gun violence prior to the survey on <7 hours of sleep. We used probabilistic quantitative bias analysis to estimate the magnitude and direction of the impact of differential outcome misclassification on results; the error in classification depends on respondents' BMI status and/or health status. Overall, 741 survey respondents were included in the study, 40% of whom reported getting <7 hours of sleep. The RR (95% CI) of the impact of gun violence on sleep duration of <7 hours was 1.14 (0.95, 1.37) in the fully adjusted model with age, race/ethnicity, gender, poverty level, BMI status, and health status as covariates. A modest, positive effect between exposure to gun violence and <7 hours of sleep was observed, although with some imprecision. Results of the quantitative bias analysis indicated that our conventional results were biased away from the null, and that there was no effect of exposure to gun violence on < 7 hours of sleep (RR=1.04, 95% SI: 0.89, 1.22). These results indicate that studies investigating the effects of various exposures on self-reported sleep quantity ought to perform quantitative bias analysis on the results to account for the effect of outcome misclassification due to self-report bias.

Robb Elementary School Shooting and Mental Health Outcomes Among US Adults: An Interrupted Time Series Study Camerin Rencken* Camerin Rencken Alice Ellyson Isaac C. Rhew Carol A. Davis, EdD Ali Rowhani-Rahbar

Introduction: Mass school shootings elicit extensive media coverage; potentially heightening distress even among individuals without geographic proximity or personal connections to the event. However, there is limited research on this association. This study aims to assess the mental health impact of the May 24, 2022, Robb Elementary School Shooting in Uvalde, Texas, on adults nationwide and examined variations between parents and non-parents, crucial for guiding trauma-informed policies and interventions.

Methods: Using the 2022 CDC Behavioral Risk Factor Surveillance System, we will use a controlled interrupted time series design, comparing the number of poor mental health days pre- and post-shooting among parents (treatment group) and non-parents (control group) within 30 days preceding the interview date. Descriptive statistics with 95% confidence intervals are presented; upcoming work will include findings with complex survey weights, considering confounding, seasonality, clustering, and autocorrelation.

Results: The sample comprises 65,461 adults, with 51.3% (50.5% – 52.1%) female and 35.7% (35.0% – 36.5%) parents. Roughly 8% (7.5% – 8.2%) of participants resided in Texas, and one-fifth had a previous depressive disorder diagnosis. Pre-shooting, parents reported 5.16 (4.84 – 5.48) days of poor mental health, non-parents 4.84 (4.61 – 5.06) days. Post-shooting, parents reported 5.19 (4.85 – 5.52) days of poor mental health, non-parents 4.85 (4.60 – 5.11) days.

Conclusion: While preliminary findings suggest a limited difference in mental health outcomes between parents and non-parents, the final models will be to determine the public health significance of these distinctions. Initial results suggest the need for both rigorous empirical evidence and future policies aimed at preventing and mitigating the consequences of school shootings.

Injuries/Violence

Leveraging Legal Epidemiology for Suicide Prevention Research: An Interdisciplinary Approach to Systematically Assessing Policy Enactment Across the United States Anne E. Massey* Anne Massey Avery K. Druyon Sandra Roettgering Ali Rowhani-Rahbar

Legal epidemiology offers a standardized set of methods to conduct rigorous policy research, grounded in a public health framework. This approach addresses a historical gap in systematic methods available to directly apply public health science to policy research. We used these methods to identify all state-level policies across the United States related to training occupation groups in suicide prevention—an emerging but understudied strategy to decrease suicide rates. Our research team, including epidemiologists and law students, developed a standardized search protocol for this cross-sectional study. Using the protocol and Westlaw, a legal research database, we searched all 50 states and the District of Columbia for any policies related to suicide prevention training for occupation groups. To add rigor, each jurisdiction (n=51) was searched by two researchers. All polices identified were recorded in standardized templates to collect the citation, title, enacted date, effective date, and legal text for each policy. We met weekly to resolve any divergences in findings between the two researchers. Once data collection was complete, we reviewed all policies to remove any duplicates and collectively determine our final policy set. In total, we identified 823 policies that were effective as of July 1, 2022. There were an average of 10 policies per jurisdiction in our final policy set, with a minimum of one in Michigan and a maximum of 43 in Washington. This national assessment can be used by policy makers, advocacy groups, and researchers. It also generated a robust exposure dataset that can be used: 1) to subsequently evaluate the impact of these policies on suicide outcomes, and 2) by other researchers who want to access or update these data while maintaining consistent methodology across studies. Legal epidemiology can add significant rigor to policy research, has been underutilized in epidemiology, and is an advantageous tool for public health researchers.

Demographic and Crash Characteristics Influencing the Place of Death in Pedestrian Fatalities Yoottapichai Phosri* Yoottapichai Phosri Ethan Morgan

Introduction: In the United States, pedestrian safety is a pressing public health concern, with an increasing number of fatalities since 2010. The aim of this study was to examine the influence of crash characteristics on the place of death for pedestrians fatally injured in motor vehicle crashes.

Methods: The analysis included single-motor vehicle crashes from the Fatality Analysis Reporting System (FARS) database, 2021. Multivariable logistic regression analyses were used to assess the relationship between crash characteristics and place of death, either on-site/en route or not on-site/en route, adjusting for demographic characteristics.

Results: Among those in the sample, 3,153 perished at the scene/en route and 2,787 perished after reaching hospital care, but still as a result of crash-related injuries. Compared to fatally injured, younger pedestrian adults, older pedestrian adults had significantly lower odds of dying at the scene or en route (65 years or over) (aOR = 0.65; 95% CI: 0.43, 0.98). Conversely, the odds of dying at the scene or en route increased for crashes involving drivers under the influence of alcohol (aOR = 1.46; 95% CI: 1.13, 1.88), vehicle speeds of 56 mph or higher (aOR = 3.06; 95% CI: 1.11, 8.46), crashes occurring in dark condition with no road lighting (aOR = 2.50; 95% CI: 2.09, 2.98), and in non-intersection areas (aOR = 2.25; 95% CI: 1.67, 3.01), compared to those not under the influence of alcohol, vehicle speeds of 25 mph or less, crashes occurring during daylight hours, and intersections, respectively.

Conclusions: Among fatally injured pedestrians, older adults are less likely to die at the crash scene or en route, suggesting potentially greater survivability for this demographic. In contrast, factors such as drivers under the influence of alcohol, higher vehicle speeds, poor lighting conditions, and crashes occurring in non-intersection areas significantly increase fatality risks at the crash scene or en route. These findings emphasize high-risk scenarios that require targeted safety interventions and policy measures to ensure safer roads and communities. Future research should further explore the factors contributing to potential survivability, particularly in older adults, to help reduce fatalities.

"I wish that they understood that if a woman is being held hostage by money, she is being held hostage physically": Experiences, Impacts, and Implications of Economic Abuse on Perinatal People Sarah Scott* Sarah Scott

Background

Economic abuse is one form of intimate partner violence (IPV) intended to control a survivor's ability to make, save, or spend money in order to gain power over them. Economic abuse creates barriers for survivors to maintain employment, critical for securing health insurance, avoiding food insecurity, and sustaining stable housing. Perinatal people may be more vulnerable to economic abuse due to changes in financial and employment life such as parental leave, increased expenses, and increased healthcare costs. Yet, little is known about how economic abuse manifests within the perinatal period.

Objective

To explore: 1) how economic abuse manifests within the perinatal period; 2) what impacts economic abuse has on perinatal people; and 3) how best to support perinatal survivors.

Design/Methods

We conducted virtual semi-structured interviews with IPV survivors and IPV advocates. Participants were recruited through an online recruitment registry, national IPV organizations, and local domestic violence agencies. Interview audio-recordings were transcribed verbatim. We used a deductive-inductive thematic analysis approach. Two research team members individually coded each transcript. The codebook used apriori codes matching the interview guide and inductive codes. The coders met several times to resolve discrepancies in coding. The research team met monthly to review emerging codes, consolidate codes into themes, and make iterative changes to the interview guide.

Results

We completed 18 interviews with advocates and 20 interviews with survivors. Demographics are available in Table 1. We identified seven themes. Participants described several experiences of economic abuse, including financial control, exploitation, and employment sabotage. Participants described health, financial, and social impacts on survivors and children. Partners leveraged the criminal-legal, child welfare, and healthcare systems and cultural norms about pregnancy, including those related to gender and religion to financially harm survivors. Participants highlighted finances as a barrier to leaving the relationship. Advocates described how economic abuse impacts marginalized survivors. Dream resources described include cash assistance, healthy relationship and financial education, and employer policies. Representation quotes are presented in Table 2.

Conclusions

This study built on existing literature to highlight the ways that economic abuse specifically impacts perinatal survivors and their children. Findings emphasize the need for support for perinatal survivors of economic abuse.

Table 1

n (%)	Survivors (n=20)	Advocates (n=18)
Gender		
Woman	17 (85%)	15 (83%)
Man	0 (0%)	1 (6%)
Gender Fluid	1 (5%)	1 (6%)
Gender Queer	0 (0%)	1 (6%)
Non-binary	0 (0%)	2 (11%)
Prefer not to answer	2 (10%)	0 (0%)
Race and Ethnicity		
White	7 (35%)	12 (67%)
African American	7 (35%)	3 (17%)
Latino	3 (15%)	1 (6%)
American Indian or Alaskan Native	1 (5%)	2 (11%)
Asian or Pacific Islander	2 (10%)	1 (6%)
Other	1 (5%)	1 (6%)
Prefer not to answer	0 (0%)	0 (0%)
Age		
18-24	1 (5%)	0 (0%)
25-34	12 (60%)	10 (56%)
35-44	3 (15%)	5 (28%)
45-54	2 (10%)	3 (17%)
55-64	2 (10%)	0 (0%)
65+	0 (0%)	0 (0%)
Location		
Northeast	4 (20%)	9 (50%)
Southeast	8 (40%)	2 (11%)
Southwest	4 (20%)	3 (17%)
Northwest	2 (10%)	0 (0%)
Midwest	2 (10%)	4 (22%)
Years worked as an advocate	-	
1-2 years		2 (11%)
3-5 years		7 (39%)
6-10 years		8 (44%)
Prefer not to answer		1 (6%)
Practice setting	-	
Urban		13 (72%)
Rural		2 (11%)
Suburban		3 (17%)

Table 2

Mental Health

Association between pro-suicide website searches through Google and suicide death in the United States from 2010-2021. Nora Kelsall* Nora Kelsall Catherine Gimbrone Mark Olfson Madelyn S. Gould Jeffrey Shaman Katherine M. Keyes

The rate of suicide death has been increasing, making understanding risk factors of growing importance. While exposure to explicit suicide-related media is known to increase population suicide rates, it is not known whether pro-suicide website forums, which often promote or facilitate information about fatal suicide means, are related to change in suicide deaths overall or by specific means. The present study aimed to estimate the association of the frequency of Google searches of known pro-suicide web forums and content with death by suicide over time in the US. National monthly Google search data for names of common pro-suicide websites between January 2010 and December 2021 were extracted from Google Health Trends API. Suicide deaths were identified using the CDC National Vital Statistics System (NVSS), and three primary means of death were identified (poisoning, suffocation, and firearm). Distributed lag non-linear models (DLNMs) were then used to estimate the lagged association between the number of Google searches on suicide mortality, stratified by age, sex, and means. Months in the US in which search rates for pro-suicide websites increased had more documented deaths by intentional poisoning and suffocation, among both adolescents and adults. For example, the risk of poisoning suicide among youth and young adults (age 10-24) was 1.79 (95% CI 1.06, 3.03) times higher in months with 22 searches per 10 million as compared to 0 searches. We also observed that increased search rates were associated with fewer youth suicide deaths by firearm with a three-month time lag for adolescents. Although more analysis is needed, findings suggest an association between increased pro-suicide website searches and increased suicide deaths, specifically deaths by poisoning and suffocation, emphasizing the need to further investigate sites containing potentially dangerous information and their associations with deaths by suicide, as they may affect vulnerable individuals.

Exploring the relationship between adolescent tobacco use and mental health: national youth tobacco survey Noor Abdulhay* Noor Abdulhay Ruchi Bhandari R. Constance Wiener Bethany Barone Gibbs Sijin Wen

Introduction: Adolescent tobacco use, especially with the introduction of Electronic Nicotine Delivery Systems (ENDS), has posed a significant threat to adolescent mental health. The objective of this study is to investigate the relationship between tobacco use and mental health among adolescents.

Methods: The 2021 and 2022 National Youth Tobacco Survey assessed anxiety and depression using the four-item Patient Health Questionnaire (PHQ-4), which was recoded into two separate binary variables (<3 vs. >/=3). Tobacco use was categorized into four groups: ENDS users, Combustible Tobacco Product (CTP) users, dual users, and non-users. Descriptive statistics and weighted regression models were used to examine the odds ratio (OR) and 95% confidence intervals (CI) between tobacco use and mental health, adjusting for potential confounders. Analysis was conducted using R version 4.1.1.

Results: Among the 48,704 adolescents included in the analysis, 10,824 reported depression and 12,439 reported anxiety. Adjusted odds of depression were higher among dual users (OR:2.03, CI:1.45-3.03), ENDS users (OR:1.68, CI:1.50-1.85), and CTP users (OR:1.47, CI:1.22-1.85) compared to non-users. The adjusted odds of anxiety were higher among ENDS users (OR: 1.66, CI: 1.47-1.89), dual users (OR: 1.48, CI: 1.33-1.65), and CTP users (OR: 1.39, CI: 1.16-1.76) compared to non-users.

Conclusion: This study highlights a significant association between tobacco use and poor mental health among adolescents, particularly in those who use both CTP and ENDS. Future longitudinal research should observe the direction of this relationship, determining whether poor mental health outcomes precede tobacco use, if tobacco use intensifies mental health issues, or if a bidirectional relationship exists among this vulnerable age group.

Mental Health

Cumulative bone lead and firearm use associated with suicidal ideation and depression in Veterans. Gabrielle Groth Hoover* Christian Hoover Aaron Specht Mu-Yin Chang Camille Lanne Marquez Katelyn Elizabeth Rand Katherine Beavis

Veterans are at risk for elevated lead exposure, depression, and suicidal ideation. Suicide is associated with firearms, which may be associated with lead exposure from ammunition. Lead may also be related to symptoms of depression and suicidal ideation; this is poorly understood due to a focus on acute, rather than cumulative, measures and a failure to consider firearms in the lead-depression link. To address this gap, we leverage data from an ongoing cohort study of Veterans in psychiatric treatment using self-report measures of psychopathology (Patient Health Questionnaire, PHQ-9), clinician interviews, firearm and exposure surveys, and in vivo x-ray (Bone) scans. Preliminary analyses included 135 participants who were 79% White, 75% Male, and middle-aged (median = 43 years). A median split with fisher's exact test examined unadjusted associations between lead, suicidal ideation, and firearm ownership. A logistic ordinal regression assessed lead as a continuous variable over four levels of suicidal ideation. A linear regression examined total PHQ-9 scores as a continuous outcome, controlling for bone lead, firearms, military service history, other mental illness, and demographics. Individuals who had high bone lead levels were 2.7 times (95% CI: 1.20, 6.00) more likely to endorse suicidal ideation while gun owners had 1.7 times higher odds of having high bone lead levels. Logistic regression found increases in lead levels associated with significant increases in the odds of higher severity of suicidal symptoms at each threshold, ranging from 3.7 (none:mild) to 49.7 (moderate:severe). Linear regression found a unit increase in bone lead associated with a 10.2% increase in PHQ-9 symptoms (95% CI: 1.02, 1.2). Results suggest cumulative bone lead levels are significantly associated with suicidal ideation and depression. While there is some evidence that firearm ownership is associated with lead exposure, more research is needed in a complete sample.

Mental Health

Longitudinal association between short leukocyte telomere length and mental health during the COVID-19 pandemic Dongkyu Lee* Dongkyu Lee Sun Jae

Objective:

Shortened telomere length is a biomarker of cellular aging. This study evaluated the association between leukocyte telomere length and mental health outcomes during the COVID-19 pandemic.

Method:

A total of 215 participants with leukocyte telomere length measurements at the baseline survey (2013-2018) were sampled from a community cohort. The participants were followed-up using consecutive online mental health surveys (Wave 1: March 2020 to Wave 5: November 2022) during the COVID-19 pandemic at similar intervals. Telomere lengths were divided into tertiles as short (T1), medium (T2), and long (T3, reference) lengths. Depression (Patient Health Questionnaire-9, PHQ-9), anxiety (Generalized Anxiety Disorder-7, GAD-7), post-traumatic stress symptoms (PTSD Checklist for DSM-5, PCL-5), loneliness (UCLA Loneliness Scale, ULS-6), and resilience (10-item Connor-Davidson Resilience Scale, CD-RISC-10) were measured as mental health outcomes with continuous scales. Depression (PHQ-9≥10) and anxiety (GAD-7≥10) were also measured as binary variables. Significance levels were set at p<0.01 regarding five mental health outcomes. Generalized estimating equations were used to estimate the association between telomere length at baseline and mental health outcomes during the COVID-19 pandemic.

Result:

Short telomeric length was associated with increased PHQ-9 (β: 1.53, 99% CI: 0.23-2.83), GAD-7 (β: 1.06, 99% CI: 0.06-2.06), and PCL-5 (β: 3.11, 99% CI: 0.12-6.10) scores. Binary depression (OR: 3.27, 99% CI: 1.31-8.19) and anxiety (OR: 6.23, 99% CI: 1.25-31.09) status was also associated with short telomeric length, showing dose-response relationship (p-for-trend<0.001, respectively).

Conclusion:

Short telomeric length was associated with depression, anxiety, and post-traumatic stress symptoms. Cellular aging could increase vulnerability against mental health problems when social stress is given.

Common mental disorder improvement after a 6-week talk-therapy intervention among people with HIV on methadone maintenance treatment in Hanoi, Vietnam

Teresa R Filipowicz* Teresa R Filipowicz Ha V Tran Ha T T Nong Thuy T T Tran Kelsey R Landrum Sydney E Browder Brian W Pence Giang M Le Ruth Verhey Bradley N Gaynes

Background

Common mental disorders (CMDs), such as depression, anxiety, and stress, frequently affect people with HIV (PWH) who inject drugs in Vietnam, a country with limited mental health professionals. Task shifting mental health care to lay counselors is a response to resource constraints, but it is unclear if this economical option is as effective as mental health care from professional counselors.

Methods

VITAL was a pilot randomized controlled trial to adapt a CMD intervention (Friendship Bench [FB]) for PWH on methadone treatment in Hanoi, Vietnam. Participants were individually randomized to 1 of 3 arms: FB delivered by professional (n=25) or lay counselors (n=25) in 6 weekly sessions, or standard care (n=25). This analysis compares symptom response over the 6 sessions in the two FB arms. We defined CMD symptom response as a mean reduction of ≥50% across all CMD symptom domains elevated at baseline for ≥2 consecutive weeks. We estimated the mean difference between arms in average weekly CMD symptom change and time to CMD response via a generalized linear model and a Kaplan Meier estimator, respectively. We compared differences in survival curves using a log-rank test ($\alpha=0.05$).

Results

All lay counseled and 96% of professionally counseled participants were male with a mean age of 45 and 44 years, respectively. Ten of 25(40%) of professionally counseled participants experienced CMD response compared to 7 of 25(28%) lay counseled participants (proportion difference: 12%(-14, 28). Professionally counseled participants had a mean -30.0 CMD symptom improvement compared to -26.5 for lay counseled participants (mean difference -3.5[-23.9, 16.8]). The survival curves did not differ significantly (p-value = 0.63).

Conclusion

There is no meaningful difference in CMD response between professionally counseled versus lay counseled participants in this pilot study. Additional, larger-scale trials are needed to explore if CMD response from talk therapy differs by counselor type.

Product-Limit Survival Estimates
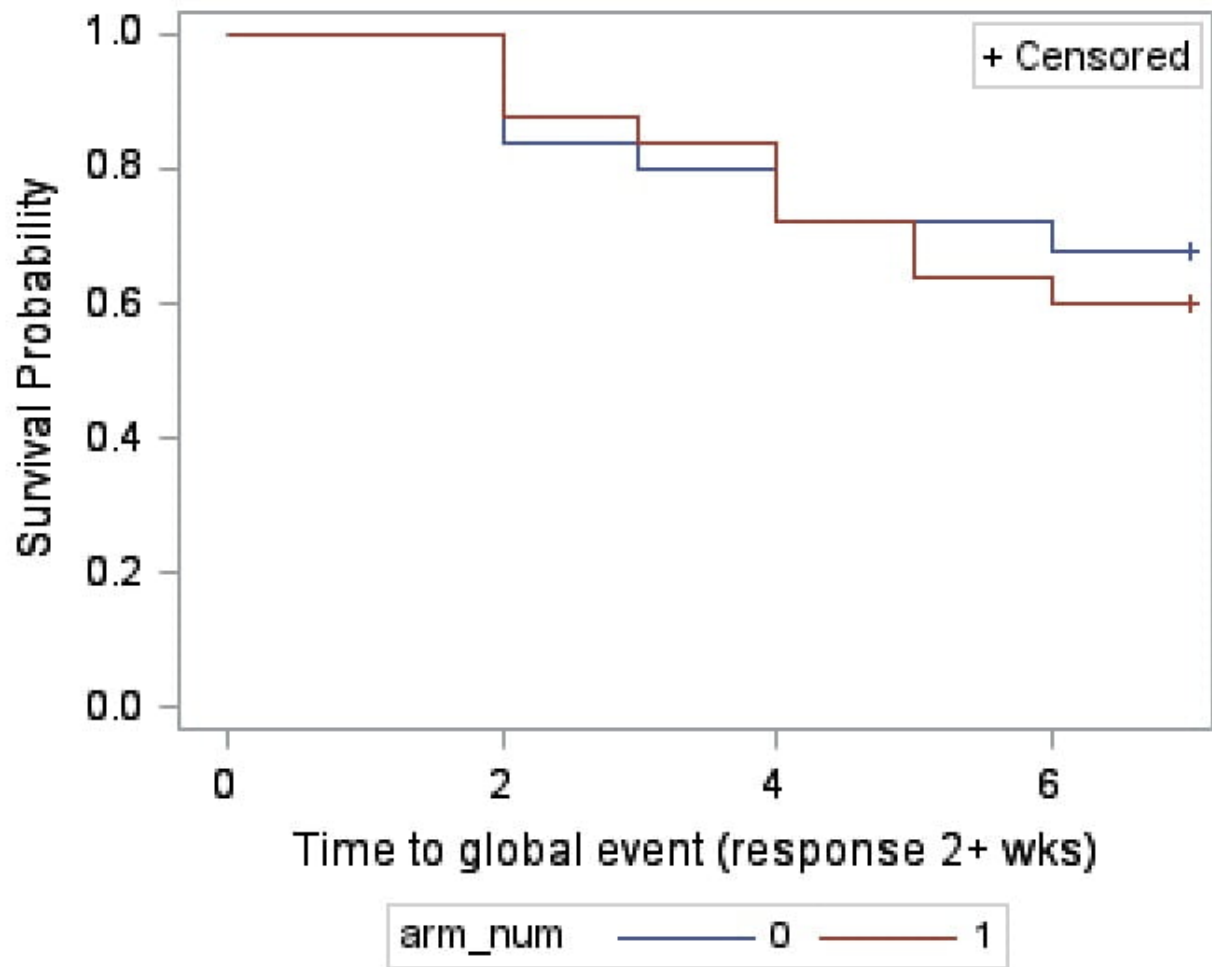
Mental Health

Gender matters for thriving: preserving young people's mental health despite poor family support Afshin Vafaei* Afshin Vafaei William Pickett Susan Phillips

Youth sometimes avoid or overcome mental health issues despite having limited access to family, peer, or community supports. In keeping with intersectionality theories, we explored circumstances that might override known social determinants of depression.

Methods: We used 2018 Canadian Health Behaviours in School-aged Children data. The outcome was self-reported good mental health i.e. no depressive symptoms. Inputs were resilience (the ability to thrive despite individual/social difficulties), subjective body image, spiritual health, food security, and life satisfaction. Via Chi-square automatic interaction detection (CHAID) decision tree models we identified key covariates that described subgroups at higher risk of depressive symptoms. A series of empty logistic multilevel regression models was constructed to evaluate clustering of depressive symptoms associated with covariates emerging from CHAID analyses (done by calculating intraclass correlation coefficient values and median odds ratios). Finally, we developed binomial regression models to quantify beneficial effects of these protective variables in high-risk populations, e.g.., those reporting low family support as the first split in CHAID.

Results: According to the CHAID model (Figure) beyond family support, teacher support, resilience and body image were the most important covariates for all, while level of social capital was important only for boys. These findings were mirrored in cluster effects. Findings from binominal multivariate regression modelling varied by sex. Among boys, only teacher support and positive body image were protective. Girls who reported normal body image had an OR of reporting good mental health of 1.36 (95%CI:1.24-1.50), whereas this effect in boys was only 6% (OR=1.06; 95%CI:1.01-1.12). Resilience was protective only among girls. Findings have clinical and policy implications for the protection of youth mental health.
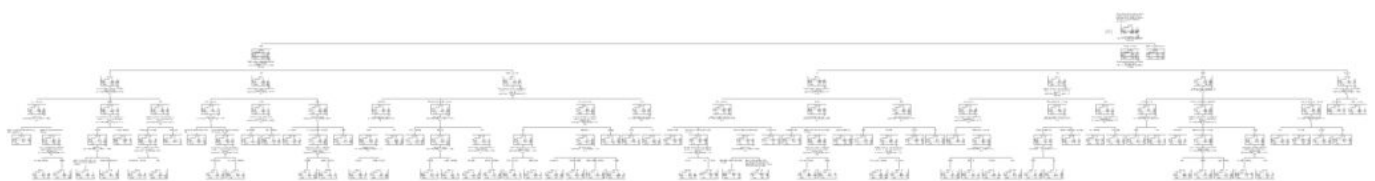
Metabolomic profiles of depression in Parkinson's disease patients Yuyuan Lin* Yuyuan Lin Kimberly C. Paul Dean Jones Douglas I. Walker Aline Duarte Folle Irish Del Rosario Yu Yu Keren Zhang Adrienne M. Keener Jeff Bronstein Beate Ritz

Objectives: Depression is a common non-motor symptom of Parkinson's disease (PD). While mechanisms for this are poorly understood, it has recently been suggested that the gut microbiome affects depression and also PD risk. Here we applied high resolution, untargeted metabolomics to explore whether there are dysregulated metabolic pathways possibly suggesting an influence from the gut microbiome in PD patients with depression.

Methods: We performed a metabolome-wide association analysis using serum samples of PD patients from a population-based case control study (total n = 635). Metabolomic profiling was done using liquid chromatography with mass spectrometry (LC-MS). We did two analyses using different depression outcomes, first depression diagnosis before baseline, and second, the Geriatric Depression Scale (GDS) score at baseline interview.

Results: 4762 metabolomic features were detected from the LC-MS after data cleaning. Using partial least square models and a threshold of VIP ≥ 2, we identified 223 metabolomic features associated with depression diagnosis and 212 with a high GDS score. Among all significant features, 127 were successfully annotated. The leading metabolite categories identified were lipids/lipid-like molecules and amino acids and derivatives. The strongest association with both outcomes was seen for 6-Hydroxy-1H-indole-3acetamide (VIP = 8.59 depression diagnosis; VIP = 3.24 for GDS score). In the pathway analysis, 10 metabolic pathways were highlighted using the Mummichog package. The majority was related to amino acids and lipids metabolism, including tryptophan and tyrosine metabolism.

Conclusions: Our study highlighted perturbation and dysregulated pathways related to gut microbial metabolism associated with depression in PD, suggesting possible links between the gut microbial flora and depression in PD patients.

Mental Health

Longitudinal association of homocysteine with depressive and anxiety symptoms among urban adults: Healthy Aging in Neighborhoods of Diversity across the Life Span study

Michael Georgescu* Michael Georgescu May A. Beydoun Christian A. Maino Vieyte Marie T. Fanelli-Kuczmarski, Jason Ashe Hind A. Beydoun Sharmin Hossain Nicole Noren Hooten Michele K. Evans Alan B. Zonderman

To examine longitudinal associations of homocysteine (HCY) with depressive symptoms scores among urban adults, before and after stratifying by sex, race and levels of anxiety. We analyzed data collected on 1,460 Healthy Aging in Neighborhoods of Diversity across the Life Span (HANDLS) participants (baseline age: 30-64y), across Visit 1 (2004-2009), Visit 2 (2009-2013) and Visit 3 (2013-2017). HCY at baseline and z-transformed probability of higher HCY trajectory were measured at baseline visit 1 and estimated across the 3 visits using group-based trajectory models (GBTM), respectively. The 20-item Center for Epidemiologic Studies Depression (CES-D) scale was utilized to compute total and domain-specific depressive symptoms scores. Mixed-effects linear regression models controlled for socio-demographic, lifestyle and selected health characteristics. We found a significant positive association between baseline Loge(LnHcy) [LnHcy] with depressive symptoms over time. A positive and significant cross-sectional association between LnHcy with depressive symptoms was also identified (β [SE]=1.825 [0.883], P=0.039). However, heterogeneity was detected across anxiety levels, with individuals below median anxiety experiencing faster increases in CES-D domain 2 scores (β [SE]=0.041 [0.018], P=0.024). A "High" LnHcy trajectory, identified using GBTM, probability was directly associated with baseline CES-D total score (β [SE]=0.64 [0.28], P=0.021), mainly driven by interpersonal problems. However, there was also a positive association between LnHcy and depressive symptoms for individuals with anxiety scores above the median. Baseline LnHcy positively correlates with depressive symptoms, with variations across anxiety. Specifically, individuals below median experiencing faster increases in the interpersonal sub-domain which was associated with "High" LnHcy trajectory probability in the overall sample.

A Descriptive Epidemiological Study on Mental Health Service Utilization in African Immigrant Students Enrolled in Universities in the United States Zeinab Baba* Zeinab Baba Heather B. Edelbute

Background: Mental health among college students continues to be of increasing concern on US college campuses. At the same time, more students are coming from abroad to the US for higher education, contributing to the diversity of universities in the US. International students from sub-Sahara African (SSA) represent a growing group of international students and also an understudied population who may have unique mental health needs.

Methods: Data on international students from SSA were obtained from the Healthy Minds Network (HMN), a yearly web-based survey conducted on US university campuses. Descriptive analyses were conducted for academic years spanning 2020-2021 (n=611), 2021-2022 (n=568), and 2022-2023 (n=1,105); 80% of them reported being a visa holder (F-1, J-1, H1-B, A, L, G, E, and TN).

Results: Across all three academic years, more international students from SSA reported being over the age of 35 when they arrived in the US, being enrolled as a full-time student, and living in on-campus housing compared to the overall international student population. Over 80% of our study population across each academic year reported not receiving counseling or therapy for mental health concerns compared to less than 70% for international students overall. The most commonly diagnosed mental health conditions for this population were anxiety and depression. Many international SSA students used informal help-seeking methods to receive support for mental or emotional health from roommates, friends, and religious counselors.

Conclusions: As the university student body in the US continues to diversify and grow, it is important to understand unique challenges faced by subpopulations of students. This study provides descriptive characteristics that will inform the provision of mental health services to this group.

Ecological momentary assessment of posttraumatic stress disorder symptoms and sleep quality among patients on medical marijuana Krishna Vaddiparti* Krishna Vaddiparti Benjamin Churba Catalina Lopez-Quintero Carly Crump Zhi Zhou Yan Wang John Williamson Robert L Cook

Background: Posttraumatic stress disorder (PTSD), results from witnessing/experiencing traumatic events. It includes sleep disturbances, nightmares, and impaired mental health. While medical marijuana (MMJ) is often used to ease PTSD symptoms, its therapeutic effectiveness lacks strong evidence.

Objective: To present the key study outcomes and showcase the viability of involving persons with PTSD using MMJ in a follow-up study, employing real-time smartphone Ecological Momentary Assessment (EMA).

Methods: We recruited fifteen individuals meeting PTSD criteria from medical cannabis clinics in North-Central Florida. Employing EMA via smartphones, we longitudinally evaluated participants four times a day for at least five days during baseline, dose-adjustment, and stable-dose phases. Surveys were conducted using PTSD checklist for DSM-5 (PCL-5), Pittsburgh Sleep Quality Index (PSQI), Positive and Negative Affect Schedule (PANAS), and PROMIS Global Health at three time points: baseline (pre-MMJ initiation), and 30- and 70-days post-initiation.

Results: Participants, averaging 44 years (SD 11.9), with 80% being white and 60% female, demonstrated significant improvements at 30- and 70-day follow-up in PTSD score $[F(2,24)=13.25]$, PSQI score $[F(2,25)=16.54]$, Sleep quality $[F(2,27)=22.57]$, Sleep duration $[F(2,27)=8.33]$, nightmares $[F(2,26)=13.87]$, negative affect $[F(2,26)=9.82]$, and mental health $[F(2,27)=8.44]$. All outcomes were statistically significant at $p<0.05$.

All participants reached the threshold of completing 90% of the EMA with a small missing response rate of 3.2%. EMA results corroborate survey data results and confirm an improvement of symptoms during follow-up.

Conclusion: This pilot shows the viability of including persons with PTSD using MMJ in a study with daily EMA assessments, surveys, and follow-ups. It indicates lasting positive effects on sleep, well-being, and reduced PTSD symptoms and nightmares for at least 70 days post-initiation.

Study Assessment Plan

Detailed EMA Regimen

New patient evaluation and apply for Medical Cannabis Card

Obtain State Medical Cannabis Card

Baseline Assessment

Face-to-face

Baseline EMA

EMA 4 times a day for ~ 4 to 5 days

Dose-adjustment phase EMA

EMA 4 times a day for 7 days

30 Day

Online

Stable dose phase EMA

EMA 4 times a day for 7 days

70 Day

Face-to-face

Pre MMJ Phase (No MJ use) ~10 -15 days

Dose-Adjustment Phase ~21 days

Stable Dose Phase

Detailed EMA Regimen labels: Waking, Morning, Afternoon, Night, Day 1, SLEEP, Day 2, SLEEP

Methods/Statistics

The power of mixtures Alexander Keil* Alexander Keil Maria E Kamenetsky Giehae Choi Rena R Jones Jessie P Buckley

Epidemiologic analysis of exposures within a mixture has numerous challenges, which has inspired many strategies for identifying mixtures as health hazards. We have observed three basic strategies, which estimate: 1) an overall association with all exposures, 2) independent associations with all exposures, and 3) an association with a reduced-dimension exposure. However, gaps remain regarding accuracy of these strategies for classifying whether a mixture is harmful to human health.

Using two published examples of exposure mixtures, we performed a plasmode simulation study of the power, type-I-error, and type-S-error (error in the sign of effect) of these strategies under different scenarios that represented varying features of the mixture (effect size, number of causal exposures, and confounding strength). The statistical approaches were: 1) overall effect estimation via quantile-based g-computation (QGC), 2) independent effect estimation for all exposures via multiple linear regression (MLR), and 3) linear regression of a 1-dimensional exposure using principal component analysis (PCA+LR). We assessed overall effect sizes ranging from null to 0.5 outcome standard deviations per quartile increase in all exposures. We also estimated "power gain" (probability of detecting an association in QGC but not MLR).

QGC yielded higher power and lower type-S error than other methods and frequently (up to 90%) found true associations when MLR failed to find any associations (**Figure**). MLR had the lowest power when using multiplicity corrections and high type-I error otherwise. PCA+LR had negligible type-S error and was intermediate in power.

When making decisions using hypothesis testing, MLR is problematic for decisions about whether a mixture is associated with a health outcome. Using dimension reduction via PCA or overall effect estimation are two more powerful options when used appropriately, though overall effect estimation is more interpretable.
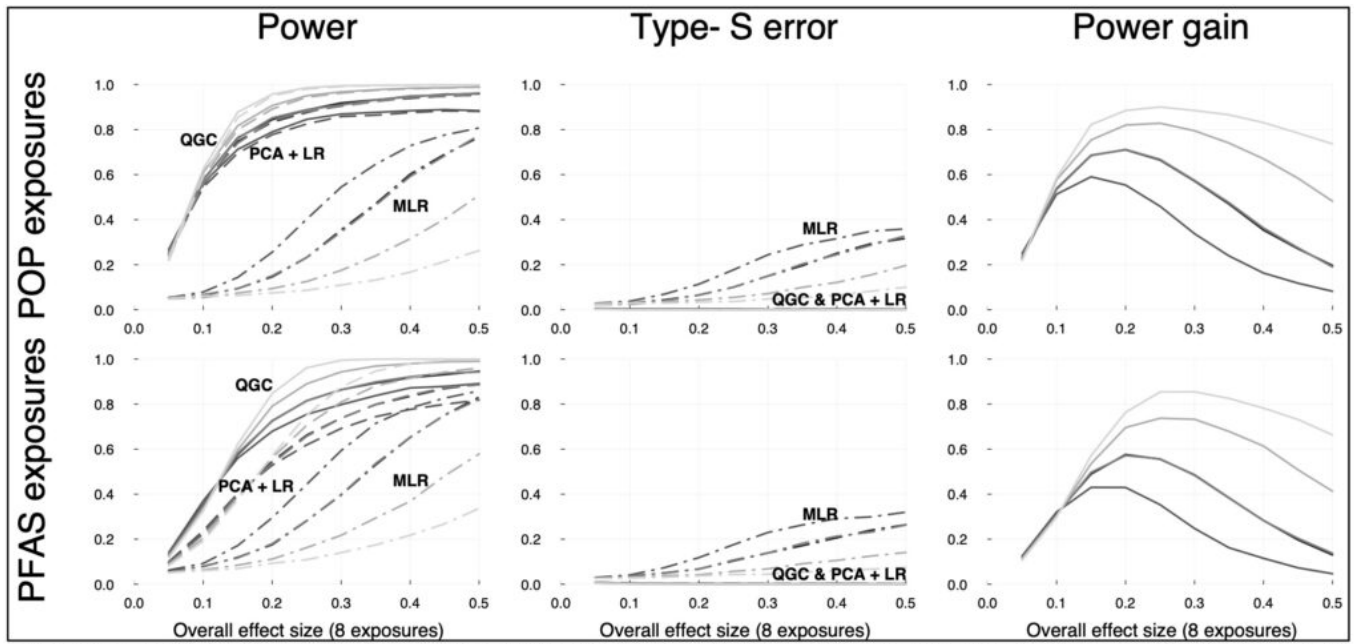
Figure: Power (**left panels**), type-S error (**middle panels**), and power gain (**right panels**) by overall effect size for quantile-based g-computation (QGC – solid lines), multiple linear regression (MLR – dot-dash lines) and principal component analysis followed by linear regression (PCA+LR – dashed lines) of the top principal component. Data are plasmode simulations from published National Health and Nutrition Examination Survey data on dioxins, polychlorinated biphenyls, and furans (POP exposures; **top panels**, 18 exposures and 14 covariates, N=979) and Per- and polyfluoroalkyl substances (PFAS exposures**; bottom panels**, 8 exposures and 6 covariates, N=499). Statistical power is two-sided for $\alpha = 0.05$ and is given for the overall effect parameter (QGC), any regression parameter for an exposure after a Bonferroni correction (MLR), and for the regression parameter of the first principal component in a regression. A type-S error is defined as a significant effect in the wrong direction. The shade of lines corresponds to the number of causal exposures in the mixture (how many exposures the joint effect was spread across), which include a single causal exposure (black) and 2,3,5 and 8 causal exposures (lightest gray). Note: Type-S error is negligible for QGC and PCA+LR. Power gain is defined as the probability of detecting an association in QGC, given a false negative finding in MLR.

Comparison of machine learning, Bayesian spatiotemporal model, and substitution approaches to estimate cause-specific mortality rates from sparse data: A simulation study

Ikhan Kim* Ikhan Kim Hyeona

In this study, we compared machine learning, the Bayesian spatiotemporal model, and the substitution approaches when calculating the suicide mortality rate according to education level in 237 districts in Korea. We acquired the population and number of suicide deaths by year (2005, 2010, 2015), district, education level (middle school or lower, high school, college or higher), and 10-year age group (30-39, …,80 or older). We set up a hypothetical situation assuming that the suicide death rate by age group in all districts in Korea was the same by year and education level and calculated the age-standardized suicide mortality rates as the reference value. 1,000 samples were randomly drawn, assuming a Poisson distribution of deaths by year, district, education level, and age group. One thousand age-standardized suicide mortality rates for years, districts, and education levels were estimated and compared with the reference value. We used five different approaches. (1) Use the observed number of deaths as is, (2) substitute the death number using the suicide death rate according to year-education level-degree of urbanization, or (3) substitute the number of deaths with 0.1 when the number of suicide deaths is 0. We also used (4) Bayesian spatiotemporal models and (5) machine learning methods (generalized linear models via penalized maximum likelihood likelihood). Root mean squared error (RMSE), mean absolute error (MAE), and mean error (ME) were used in comparison. The suicide mortality rate in low population sizes, such as middle school or lower and rural areas, differed significantly from the reference value. The substitution approach estimated the suicide mortality rate of the high-education group higher than the non-substitution approach. However, when using the Bayesian spatiotemporal model and machine learning, there was a tendency for the suicide mortality rate of groups with low levels of education to be calculated to be high.

Revisiting the modifiable areal unit problem in the era of exposome-wide association studies: Assessing the performance of the CDC/ATSDR Social Vulnerability Index at privacy-protecting spatial scales Jonathan V. Lewis* Jonathan Lewis Nathaniel MacNell Gary J. Larson Anna J. Jones Ian D. Buller Farida S. Akhtari Kyle P. Messier Alison A. Motsinger-Reif

Background: Exposome-wide association studies (ExWAS) may be sensitive to environmental exposure assessments across geographic and temporal scales. Linking de-identified geomarkers to participant locations facilitates data sharing and improves privacy protection. However, conducting analyses at different spatial scales and boundaries may yield varying estimates of epidemiologic associations.

Methods: We replicated the CDC/ATSDR Social Vulnerability Index (SVI) and its n=16 components and n=4 themes using 2015-2019 U.S. Census Bureau American Community Survey data across North Carolina census tracts (TR; n=2,195) and four aggregations: county subdivision (CS; 1,041), 5-digit Zip Code Tabulation Area (Z5; 808), county (CT; 100), and 3-digit Zip Code Tabulation Area (Z3; 20). We descriptively compared individual components, themes, and overall SVI at chosen scales and fit 67,392 logistic regression models of theoretical associations using a simulated epidemiologic cohort of one million locations.

Results: Fifteen individual components (94%; p-value<0.05) showed statistically significant differences across scales by a Kruskal-Wallis test. Moran's I (one lag) for SVI became increasingly variable and showed less evidence of spatial clustering at larger scales (ITR=0.53; ICS=0.30; IZ5=0.25; ICT=0.44; IZ3=-0.09). In models fit to simulated data, odds ratios for SVI at larger scales attenuated towards null with decreased empirical coverage as the simulated population effect size increased.

Discussion: SVI became less informative when aggregated at larger administrative units. The epidemiologic efficacy of a simulated ExWAS study to detect associations was reduced when using aggregated geomarkers.

Conclusion: Our results emphasize the importance of using data at spatial resolutions that align with hypothesized exposure-phenotype mechanisms and anticipating the potential loss of epidemiologic efficacy when participant data are limited to larger spatial scales to protect privacy.
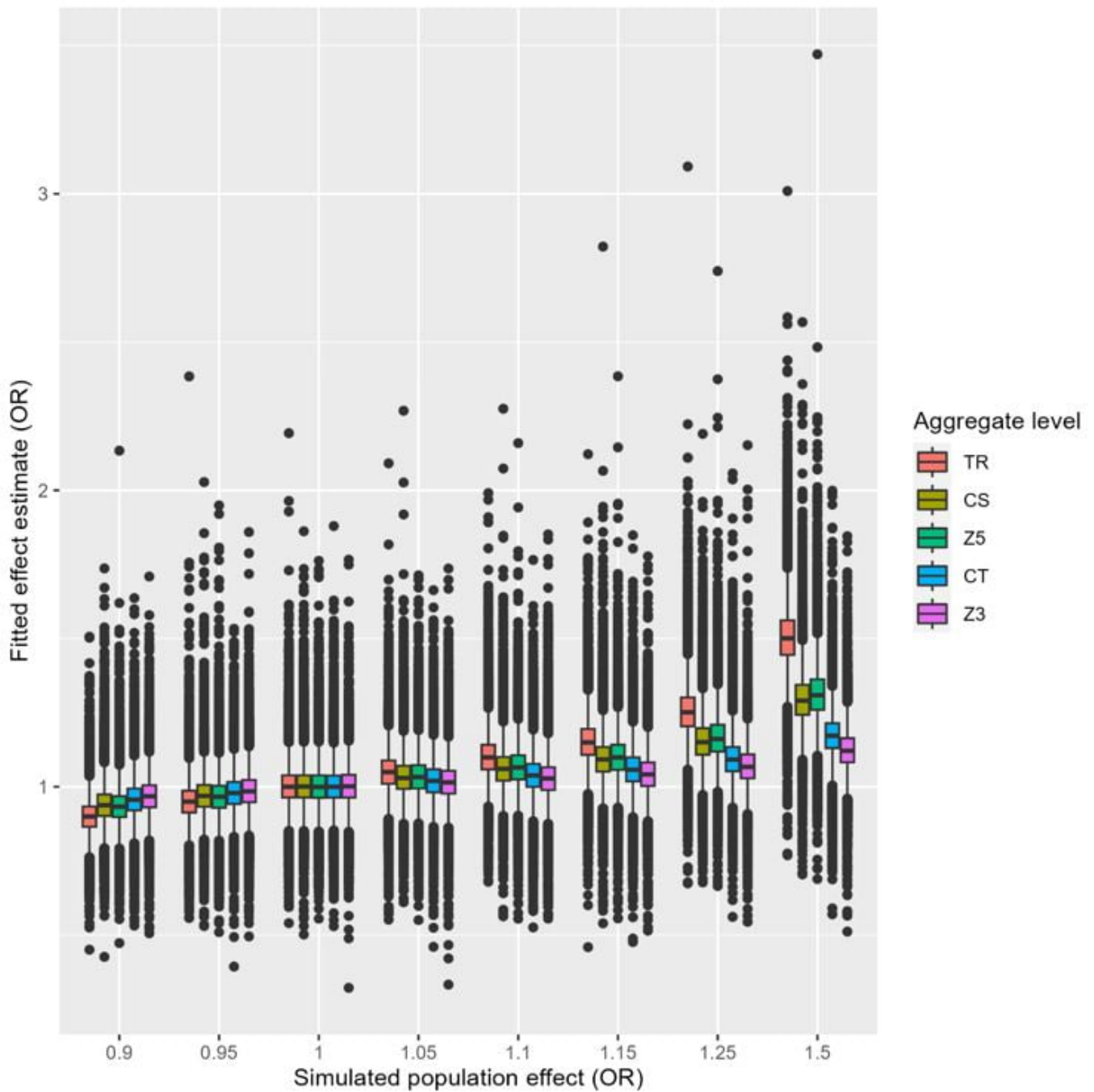
Figure 1. Estimated effects for the CDC/ATSDR Social Vulnerability Index across varying simulated population effects, by aggregate level. This figure illustrates changes in fitted effect estimates as the simulated population OR moves away from null, and the SVI is aggregated at larger administrative units.

Methods/Statistics

Application of a data fusion design to improve incidence estimates of etiology-specific diarrheal disease using hybrid study data Maria Garcia Quesada* Maria Garcia Quesada Alex Breskin James Platts-Mills Patricia Pavlinac Sean Galagan Lance Waller Benjamin Lopman Elizabeth Rogawski-McQuade

Accurate estimates of infectious disease incidence are critical for prioritizing and powering studies of public health interventions including vaccines. Because cohort studies are often cost prohibitive, hybrid studies (i.e., facility-based disease surveillance with catchment area enumeration and healthcare utilization survey) are an appealing alternative. Previously, healthcare utilization adjustments have been applied as simple proportions within one or two stratifying features, which can fail to capture the full heterogeneity in healthcare seeking behaviors by disease severity and sociodemographic characteristics. Given the potential impact of small differences in such proportions on adjusted incidence rates, proper adjustment is critical. Furthermore, commonly used methods for quantifying uncertainty around incidence estimates in hybrid designs often utilize computationally intensive bootstrapping or Monte Carlo simulations. Here, we use data from the Global Enteric Multicenter Study (GEMS) to illustrate the application of a data fusion design with M-estimation to estimate etiology-specific diarrheal disease incidence from hybrid study data, with the goal of later applying these methods in the ongoing Enterics for Global Health (EFGH) study. M-estimation enables the estimation and combination of statistical parameters from different data sources using stacked estimating functions and allows a closed-form solution for the variance. Here, four sets of estimating equations must be defined: 1) logistic regression to estimate healthcare seeking propensity weights based on the healthcare utilization survey, 2) true number of cases based on healthcare seeking and facility sampling weights, 3) total population at risk based on community sampling weights, 4) estimated true incidence. We demonstrate how this method can be implemented for any study with hybrid data, and compare our resulting incidence estimates and corresponding variance with other established methods.

Methods/Statistics

Evaluating methods for high-dimensional mediation in metabolomics data Susan Hoffman*
Susan Hoffman Donghai Liang Anne dunlop Todd Everson Audrey Gaskins Michele Marcus Ashley
Naimi

Background: The metabolome represents a biologically functional measurement of gene-environment interactions and gene transcription. Metabolomics has emerged as a sensitive analytical platform with the potential to offer novel insights into the biological underpinnings mediating exposure-outcome relationships with the appropriate application of statistical methods. This study aimed to test several high-dimensional mediation analysis techniques in simulated metabolomics data to understand the functionality and performance of different methods.

Methods: We simulated data based on the Atlanta African American Maternal Child Cohort with a specific focus on the metabolomic features to understand how changes in the high-dimensional mediator set impact estimator bias, mean-squared error (MSE), and confidence interval coverage. We evaluated high-dimensional mediation analysis methods developed by Zhang, et al. (HIMA) by Gao, et al. (HDMA), as well as a "Meet-in-the-Middle" (MITM) approach proposed by Chadeau-Hyam, et al.

Results: In our preliminary analyses, all evaluated methods demonstrated the ability to detect a mediating effect within a system devoid of correlations between mediators. However, the evaluated methods performed differently with correlations between mediators resulting from the exposure affecting mediator-outcome confounding. Under these conditions involving correlated mediators, MITM appeared to be comparatively less effective than HDMA and HIMA in identifying the correct mediating effect and would often select metabolites that were not among the true mediator set.

Conclusions: This study represents the first comprehensive evaluation of different high-dimensional mediation techniques for metabolomics applications utilizing simulated data. By comparing and evaluating existing mediation methods commonly used in fields like epigenetics, this study bridges the gap between existing methodologies and their potential applicability to metabolomics research.

Methods/Statistics

A graphical user interface tool to facilitate assessment of bias from differential pre-baseline selection Kelvin Pengyuan Zhang* Kelvin Pengyuan Zhang Sneha Mani Lindsay Kobayashi Alden Gross Jennifer Weuve Ryan Andrews

Pre-baseline selection encompasses the processes–e.g., death, illness, inconvenience–that determine who enrolls in a study. These processes can potentially bias a study's estimated effect of an exposure on an outcome if they occur differentially and jointly with respect to the exposure and outcome (or their correlates). For example, when the exposure of interest affects the risk of mortality and there is an unmeasured common influence on the outcome and mortality, the pool of eligible participants for a given study may have susceptibility to the exposure's effects on the outcome that differs from that of the referent population, thereby potentially leading to collider-induced selection bias. Because this selection bias arises from processes occurring prior to baseline, standard analytic tools like inverse probability weighting cannot be applied to address the potential bias. Tools that can help quantify the magnitude of the potential bias (e.g., simulation studies) have steep learning curves.

To address the need for easy-to-use tools to evaluate the potential for and magnitude of pre-baseline selection bias, we developed a graphical user interface via the Shiny package in R. Users can input key statistics, like cohort sample sizes, age distributions of their cohort, and the probability of mortality (unstratified or stratified by participants' sex or country of residence), along with structural assumptions about the types and strengths of pre-baseline selection processes that could be present. Users are also able to choose pre-specified values for these inputs. These input parameters are then processed by our Shiny application to produce summary statistics that quantify the potential influence of selection bias on the estimated effect of interest. Because this tool removes many technical barriers to implementing pre-baseline selection bias analyses, we hope that it assists researchers in incorporating bias analyses into their own work.

Do you think you're better off alone? Causal inference with imbalanced dependence between exposure groups Joshua Nugent* Joshua Nugent Laura Balzer

In many studies, participants are clustered into groups, such as neighborhoods or schools. In such settings, we typically assume that the clusters are the independent unit, but this is sometimes an oversimplification of the underlying dependence structure. In the SEARCH-IPT trial, for example, public health officials were (artificially) grouped together for randomization. In the intervention arm, the groups became mini-collaboratives in which an intervention for tuberculosis prevention was delivered; in the control arm, participants continued with standard practice. As a result, intervention participants were dependent, while control participants were effectively independent (Figure). For such trials, we show that targeted minimum loss-based estimation (TMLE) accounting for the imbalanced dependence structure and leveraging machine learning (Super Learner, SL) improves power while maintaining nominal confidence interval coverage. Its application in SEARCH-IPT resulted in a 20% efficiency gain. Additionally, unlike more traditional methods (e.g., GEE), our approach has the flexibility to estimate wide range of target parameters. We recently generalized our theoretical and practical results to observational studies, where imbalanced clustering is common but less frequently studied. For example, health officials choosing to participate in mini-collaboratives would be dependent, while health officials declining participation would be effectively independent. For such observational studies, we show that TMLE with SL yields meaningful improvements in precision as well as reductions in bias due confounding.
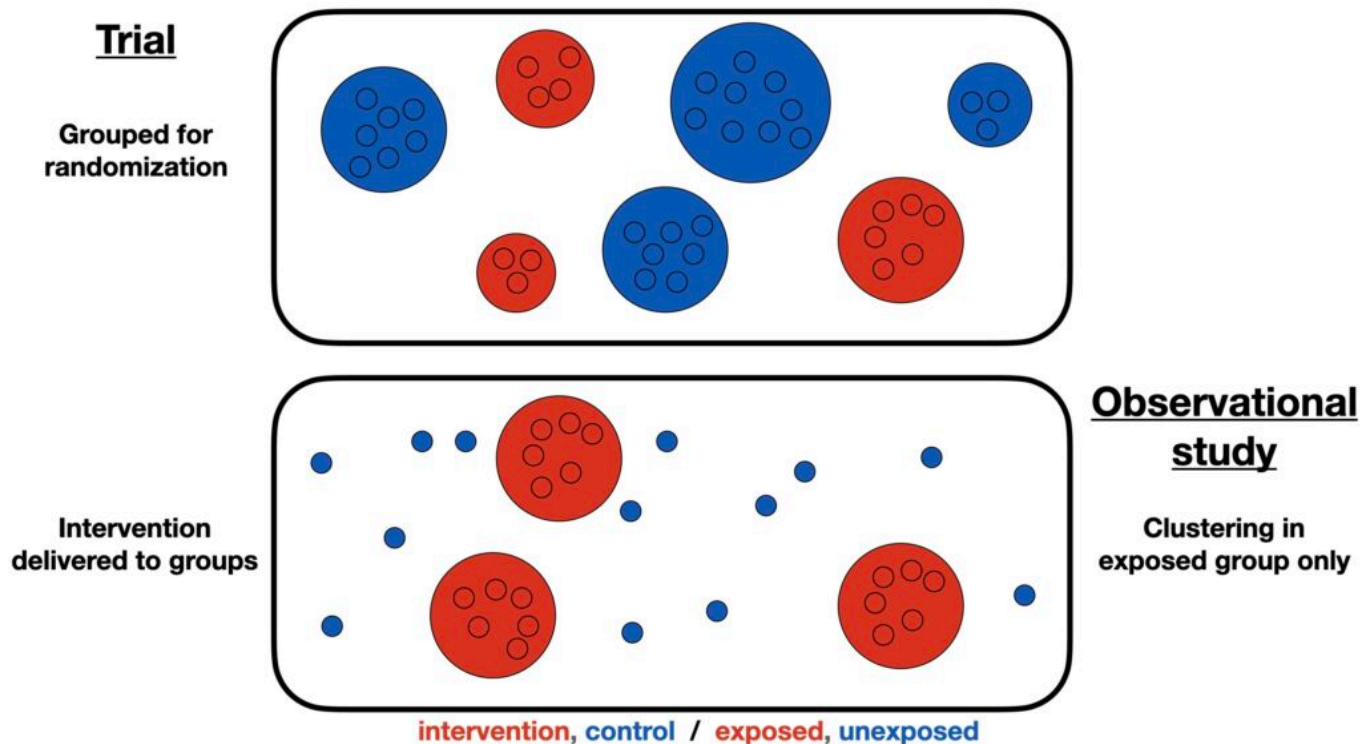
A joint analysis of simultaneous epidemics of dengue, chikungunya, and Zika in Colombia using a Poisson-multinomial spatial model Laís Picinini Freitas* Laís Picinini Freitas Alexandra Schmidt Jorge Emilio Salazar Flórez Brayan Ávila Monsalve César García-Balaguera Berta N. Restrepo Gloria I. Jaramillo-Ramirez Mabel Carabali Kate Zinszer

Dengue, chikungunya, and Zika are *Aedes*-borne diseases (ABD) that have caused large syndemics in the Americas in the 2010s. Colombia, where dengue is historically endemic, faced its first chikungunya and Zika epidemics in 2014 and 2015, respectively, when cases of dengue were also on the rise. In this ecological study, we applied a Poisson-multinomial spatial model to study simultaneously the outbreaks of dengue (n=291820), chikungunya (n=75913), and Zika (n=72031) in Colombian municipalities (n=1121). We obtained case data from the Colombian National Surveillance System (SIVIGILA) by municipality between weeks 01/2014 and 39/2016. The total number of ABD cases is fitted to a Poisson model and, conditioned on the total, we assume a multinomial model for the allocation of the number of cases of each disease across the municipalities. The model also estimates the associations with environmental and socioeconomic variables. Covariates were standardized and the model was fitted using the Stan platform in R. Mean temperature was identified as the main contributor for total ABD cases (mean 2.15, 90%CredI 1.95-2.38). Municipalities with better access to healthcare had an increased risk of ABD (1.20, 1.11-1.30). The Normalized Difference Vegetation Index (NDVI) was also positively associated with the total number of ABD (1.28, 1.18-1.39). However, the odds of a municipality having chikungunya and/or Zika compared to dengue decreased when NDVI increased (0.75, 0.67-0.84, and 0.85, 0.75-0.96, respectively). Increased odds of having chikungunya and/or Zika compared to dengue were observed in more humid municipalities (1.13, 1.01-1.25, and 1.40, 1.26-1.57, respectively). When chikungunya and Zika emerged in Colombia, dengue was widespread in the country. Chikungunya and Zika first epidemics may have concentrated in municipalities with more favorable conditions to the vector, potentially explaining the difference in factors associated with these diseases compared to dengue.

Visualizations for non-inferiority trial simulations with applications in quantile regression

Hayden Smith* Hayden Smith Geoffrey Wall

Introduction: New pharmacological agents and delivery methods can be compared to standard therapies using non-inferiority trials. Sample size and power determinations for these trials can be calculated using data simulations. Objective: to present a sample size determination with multiple visualizations for non-inferiority trial-based data simulations.

Methods: A trial was designed to compare intravenous dexmedetomidine (IV dex [standard therapy]) to IV dex plus adjunctive sublingual (SL) dex in reducing alcohol withdrawal syndrome symptoms in Intensive Care Unit patients. The estimand was the median (tau=0.5) difference in modified Minnesota Detoxification Scale (mMINDS) scores at 2- and 24-hours after treatment initiation across study arms. Differences were calculated using quantile regression. Sample size and power levels were determined based on 10,000 simulated samples, with an expected IV dex estimate of N~(12, 2) and IV + SL dex contrast estimate of N~(-2, 2). The non-inferiority threshold value was a contrast SL dex score </= 1.

Results: Simulations revealed 25 subjects per treatment arm would result in an alpha of 0.05 and beta of 0.97 for the contrasted median SL dex mMINDS score equal or below the threshold, see Figure. Also presented at the conference will be additional visualizations and statistical code (i.e., SAS and R) for simulations and interim analyses. Lastly, various quantile regression methods (e.g., conditional, Bayesian, heterogenous treatment effects, quantile treatment effects/doubly robust, and tree or neural network-based estimates) are currently available and their strengths and limitations in simulation studies will be discussed.

Conclusions: The presented simulation and visualization methods can be employed in observational and experimental study designs. Of note, the developed figures can help communicate explicit study design details to sponsoring agencies and Institutional Review Boards.
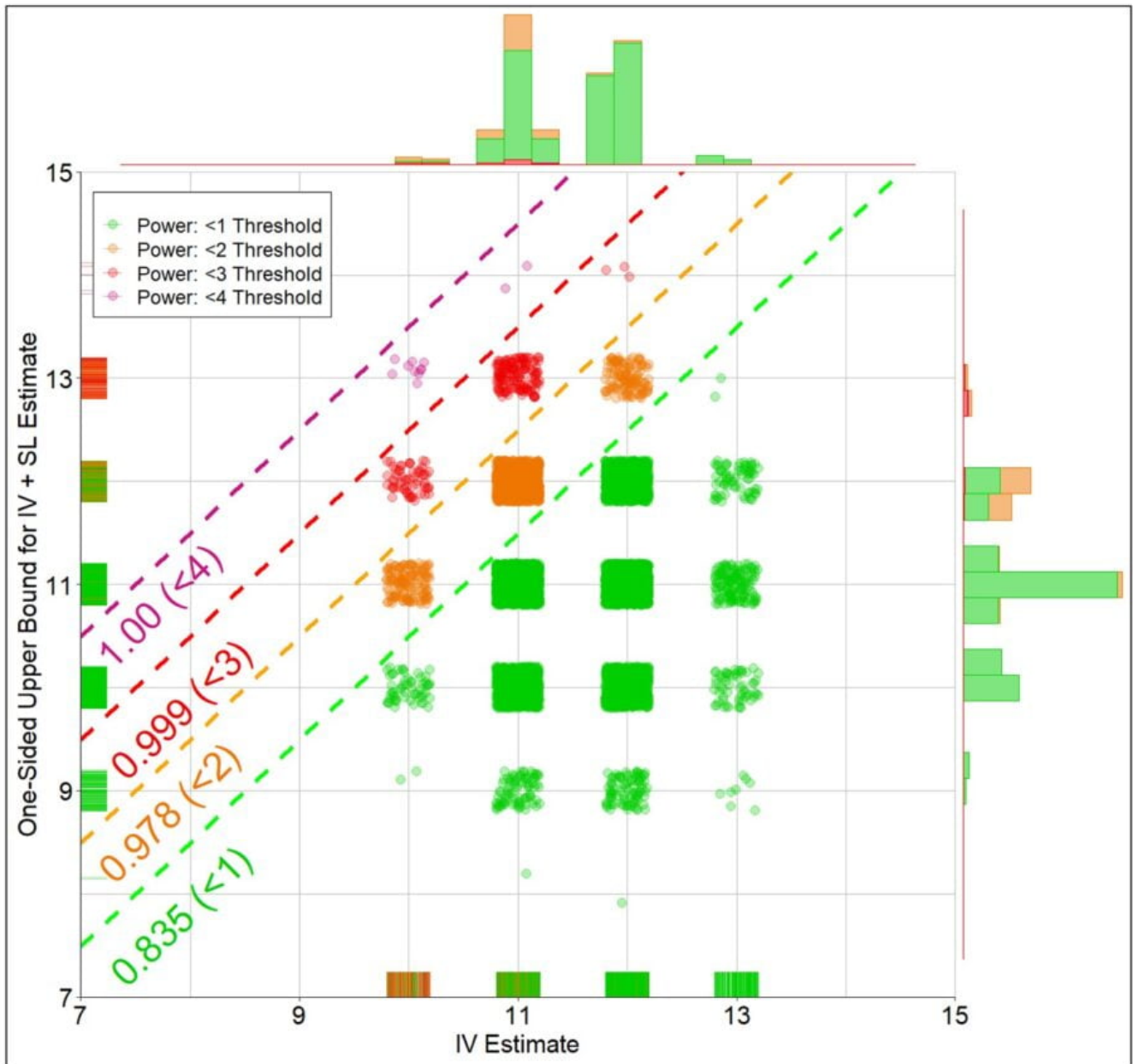
Figure. Visualization of power values for a set number of study participants (n=25) per treatment arm in a trial when examining different non-inferiority thresholds. Study was based on 10,000 simulated samples with a-b lines representing the threshold level for a unit incremental increase in the non-inferiority threshold value. Presented calculations held for both the 2- and 24-hour comparisons. Note: jitter was added to plotted values for better visualization of content. IV=intravenous; SL = sublingual.

Dynamic Updating Strategies in Assessing Hospital Performance: A State-wide Assessment of Observed-to-Expected Mortality Ratios in Surgical Aortic Valve Replacements Jackie Pollack* Jackie Pollack Wei Yang George Arnaoutakis Michael Kallan Stephen Kimmel

Background-Prediction models that determine expected outcomes are infrequently updated, despite demonstrating increasing inaccuracy over time. This can result in incorrect assessment of hospital performance. Dynamic model updating may provide a method to ensure accurate assessments and comparisons across hospitals.

Methods-Using a baseline prediction model, derived from the Pennsylvania Health Care Cost Containment Council (1999-2006), four modeling strategies were used to estimate 30-day postoperative mortality following Surgical Aortic Valve Replacement (SAVR) from 2007 to 2018: (1) A typical, non-updating (static) model, where the model remained fixed throughout the study period. (2) Applying an annual correction factor (CF), based on the methodology of the Society of Thoracic Surgeons. (3) Calibration regression (CR) to annually recalibrate the model. (4) Dynamic logistic state space modeling (DLSSM) to continuously update model coefficients. Hospitals were ranked based on observed to expected (O/E) ratios and Z-scores to assess the impact on performance rankings and to identify outliers.

Results-The test data included 29,127 SAVRs with 765 deaths among 53 hospitals. Across all updating strategies, nearly all hospitals experienced rank changes when compared to the static model. Within ranking tertiles, 18.9% (n=10) of hospitals shifted tertile tiers with CF and CR approaches, and 22.6% (n=12) changed with DLSSM. While the static model labeled 15 hospitals as having significantly better-than-expected performance, only 3 maintained this classification with CF and DLSSM, and 5 retained it with the CR methods. No hospitals demonstrated significantly worse-than-expected mortality in the static model, but CR identified 6 and DLSSM and CF both identified 7.

Conclusion-Static models may misclassify hospital performance and rankings. Regular updating to better assess O/E ratios among SAVRs can lead to large changes in estimated performance and hospital rankings.
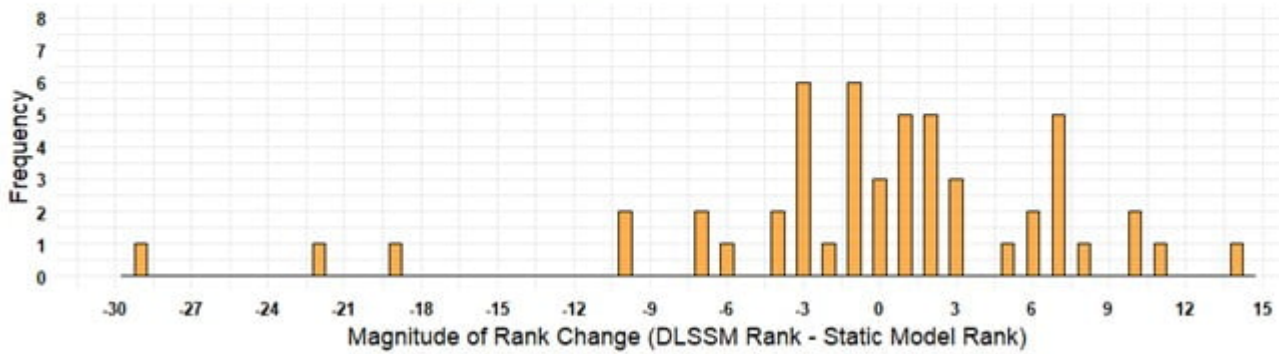
Distribution of Z-score Rank Changes
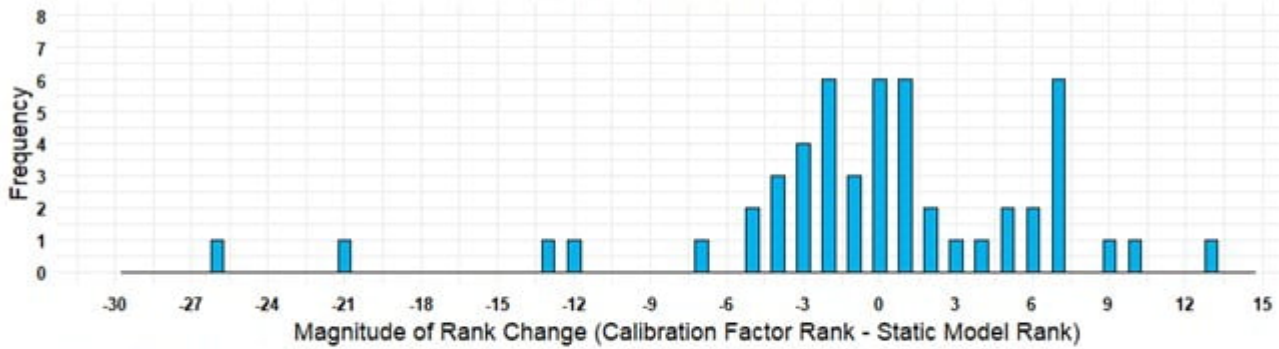
CF: Calibration Factor (Update Intercept)
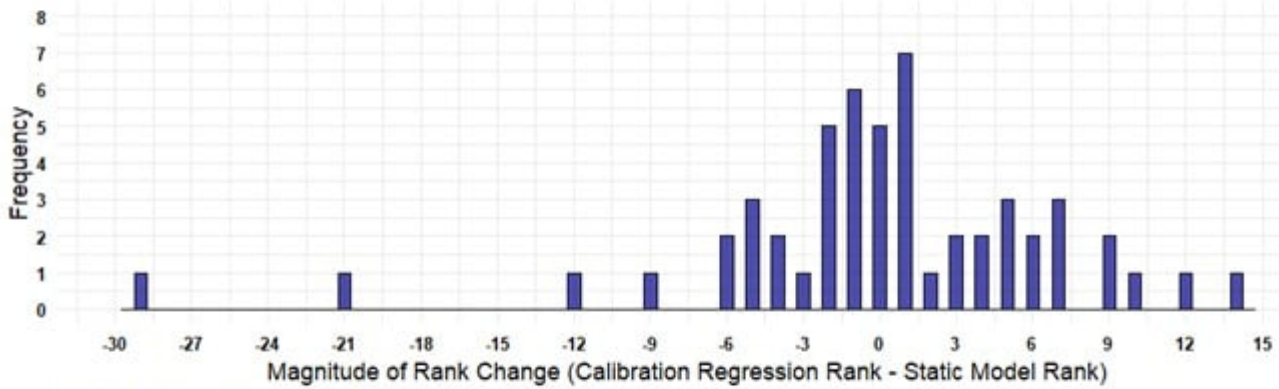
CR: Calibration Regression (Update Intercept & Slope)

DLSSM:Dynamic logistic state space model (Continuously Updates Coefficients)

Negative values indicate hospitals decreased in ranking after updating

Simultaneous Ranking and Clustering of Small Areas based on Health Outcomes Ronald
Gangnon* Ronald Gangnon Elizabeth Blomberg

A common task in public health communication is ranking and/or clustering different geographic
units (small areas), e.g. counties in the United States, based on health (or socioeconomic)
outcomes/determinants. We consider a nonparametric empirical Bayes finite mixture model for small
area health outcomes (binary, count or quantitative) that is suitable for simultaneously ranking and
clustering small areas. Small areas are ranked using optimal point estimates of the joint ranks,
which minimize the expected integrated squared error loss on the health outcome (mean or
proportion) scale. Small areas are simultaneously clustered by assigning small areas to the optimal
(minimum mean square error loss) cluster (mixture component) for their estimated rank positions.
We illustrate the utility of our approach with an analysis of percent low birth weight (<2,500g)
births for Arizona counties, 2014-2020.
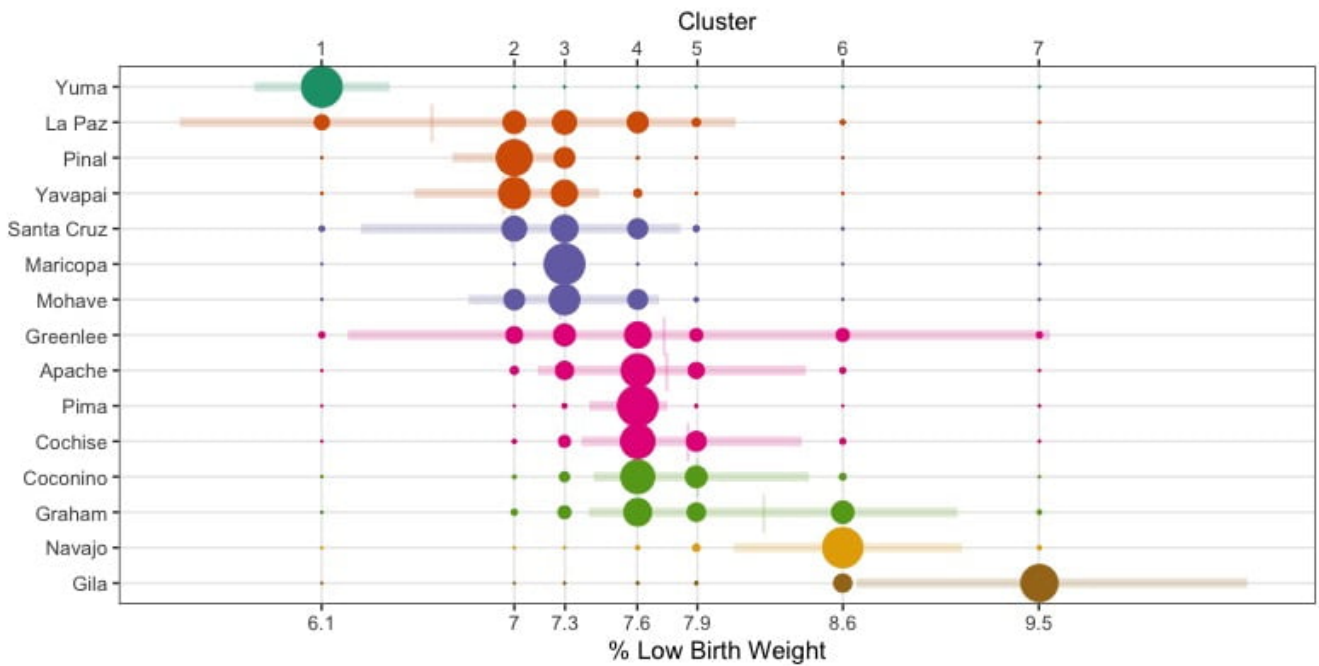
Impact Of Marijuana Legalization on Alcohol Consumption and Alcohol Use Disorder: Substitution, Complementarity, or Both? Rikki Fan* Rikki Fan Aaron White

Background. Marijuana policies are rapidly evolving. The legalization policy may potentially influence marijuana use. In addition, marijuana policies may impact use and consequences of alcohol and simultaneous use of alcohol and marijuana (SAM) due to potential spillover effects.

Methods. State-level aggregate data from National Survey on Drug Use and Health (NSDUH) 2002-1018 were used to conduct pretest-posttest control group design analysis. The nine states with passage of recreational marijuana legalization (RML) between 2012 to 2016 were the treatment group, the 32 states who had never passed RML up to 2021 served as the control group. Two years preceding and two years succeeding the institution of RML were designated as the points where pretest (baseline) and posttest (follow-up) values were extracted respectively. The following measures were considered: 30-day marijuana use; initiation of marijuana past year; alcohol use past month; and alcohol use disorder past year; recent simultaneous use of alcohol and marijuana. The analysis was stratified by three age groups, i.e., 12-17 years, 18-25 years, and 26 years or older. The mixed regression model was constructed to examine RML effects with adjustment for pretest, cohort effect, and status of medical marijuana legalization (MML).

Results. States instituting RML exhibited higher baseline of 30-day prevalence and 1-yr incidence of marijuana use which were also associated with higher proportion of states who had previously instituted MML in RML states compared to non-RML states. Although marijuana use increased in both RML-states and non-RML states, RML-states exhibited increases to a greater magnitude for all age groups. Among teenagers, the most recent SAM decreased among non-RML states over time. Among adults, the most recent SAM increased among both non-RML and RML states over time; after controlling for the baseline, the magnitude of increase was higher among RML states than that among non-RML states.

Conclusion. The further increased marijuana use after RML institution was superimposed over the effect of MML. The relatively higher rate of SAM among RML-instituted states appear to be mainly attributed to increased marijuana use. Neither complementarity nor substitution hypothesis is supported in the context of liberalization of marijuana policies.

Neurology

The effect of herpes zoster vaccination on the occurrence of deaths due to dementia in England and Wales Felix Michalik* Pascal Geldsetzer Felix Michalik Min Xie Markus Eyting Simon Heß Seunghun Chung

Background: Using a unique natural randomization, we have recently provided evidence from Welsh electronic health record data that HZ vaccination caused a reduction in new dementia diagnoses over a seven-year period. This study aimed to determine whether eligibility for HZ vaccination also caused a reduction in deaths due to dementia in England and Wales over a nine-year follow-up period.

Methods: Adults who had their 80th birthday shortly before September 1 2013 were ineligible for free HZ vaccination and remained ineligible for life, whereas those who had their 80th birthday shortly after September 1 2013 (i.e., born on or after September 2 1933) were eligible for one year. This date-of-birth threshold generated birth cohorts who are likely exchangeable in observed and unobserved characteristics except for a small difference in age and a large difference in HZ vaccination uptake. We used country-wide data from death certificates in England and Wales on underlying causes of death from September 1 2004 to August 31 2022 by ICD-10 code and month of birth. Our analysis compared the percentage of the population with a death due to dementia among the month-of-birth cohorts around the September 2 1933 eligibility threshold using a regression discontinuity design.

Results: The study population included 5,077,426 adults born between September 1 1925 and August 31 1941 who were alive at the start of the HZ vaccination program. We estimated that over a nine-year follow-up period, eligibility for HZ vaccination reduced the percentage of the population with a death due to dementia by 0.38 (95% CI: 0.08 to 0.68, p=0.012) percentage points, corresponding to a relative reduction of 4.8%. As in our prior analysis, this effect was stronger among women (-0.62 [95% CI: -1.06 to -0.19] percentage points, p=0.004) than among men (-0.11 [95% CI: -0.51 to 0.28] percentage points, p=0.574).
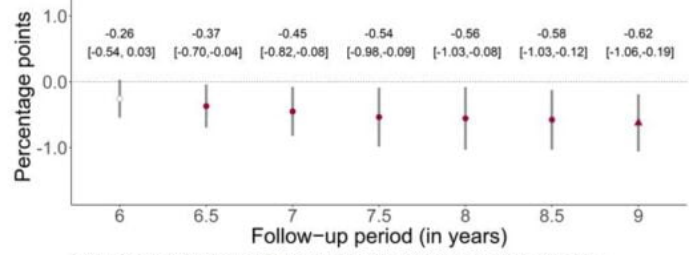
Conclusions: Our findings indicate that HZ vaccination improved cognitive function at a fairly advanced stage of the dementia disease process because most individuals whose underlying cause of death was dementia during our nine-year follow-up period were likely already living with dementia at the start of the HZ vaccination program.
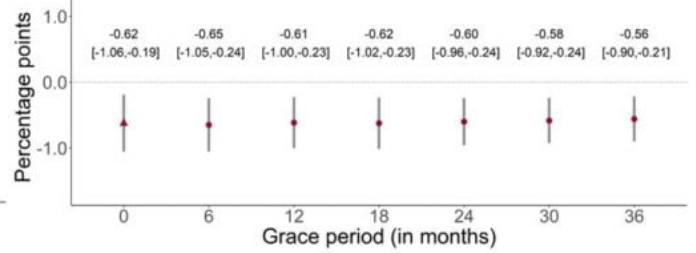
Women

A) Effect of being eligible for HZ vaccination on dementia deaths
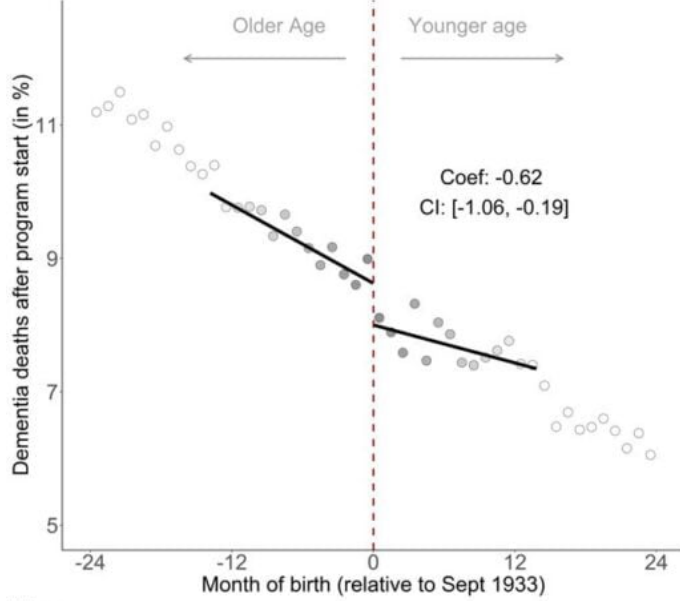
Older Age | Younger age

Coef: -0.62
CI: [-1.06, -0.19]

B) Effect of being eligible for HZ vaccination on dementia deaths across different follow-up periods

-0.26	-0.37	-0.45	-0.54	-0.56	-0.58	-0.62
[-0.54, 0.03]	[-0.70,-0.04]	[-0.82,-0.08]	[-0.96,-0.09]	[-1.03,-0.08]	[-1.03,-0.12]	[-1.06,-0.19]

C) Effect of being eligible for HZ vaccination on dementia deaths across different grace periods

-0.62	-0.65	-0.61	-0.62	-0.60	-0.58	-0.56
[-1.06,-0.19]	[-1.05,-0.24]	[-1.00,-0.23]	[-1.02,-0.23]	[-0.96,-0.24]	[-0.92,-0.24]	[-0.90,-0.21]

Men

A) Effect of being eligible for HZ vaccination on dementia deaths

Older Age | Younger age

Coef: -0.11
CI: [-0.51, 0.28]

B) Effect of being eligible for HZ vaccination on dementia deaths across different follow-up periods

0.00	0.01	0.04	0.02	0.00	-0.08	-0.11
[-0.35,0.35]	[-0.33,0.34]	[-0.33,0.40]	[-0.36,0.39]	[-0.44,0.43]	[-0.47,0.30]	[-0.51,0.28]

C) Effect of being eligible for HZ vaccination on dementia deaths across different grace periods

-0.11	-0.11	-0.10	-0.11	-0.10	-0.11	-0.14
[-0.51,0.28]	[-0.50,0.29]	[-0.47,0.27]	[-0.49,0.26]	[-0.44,0.23]	[-0.43,0.21]	[-0.43,0.15]

Neurology
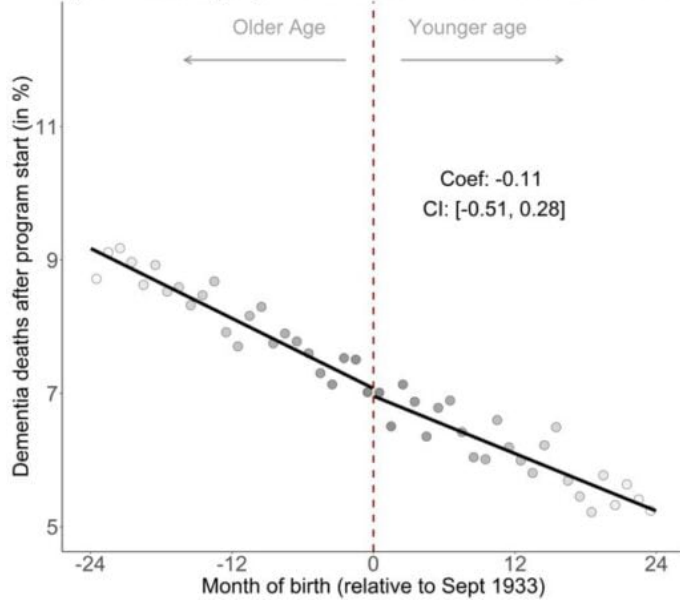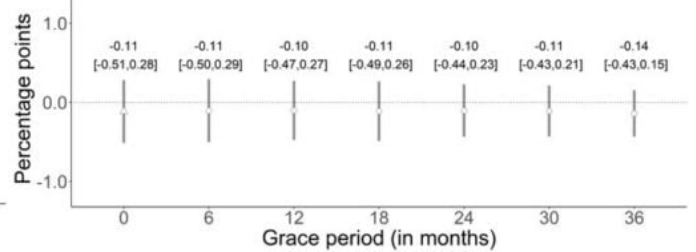
Risk of Dementia in Patients with Adulthood Atopic dermatitis: A Systematic Review and Meta-analysis of Cohort Studies

Parkin Paramiraksa* Parkin Paramiraksa Metavee Boonsiri Poramin Patthamalai Amarit Tansawet

Emerging yet contrasting evidence has reported the association between adulthood AD and the risk of developing dementia. We aim to determine the association between adulthood AD and the risk of incident dementia.

A systematic search of MEDLINE, Scopus, EMBASE, Cochrane Library, and medRxiv was performed through September 2023 to identify eligible cohort studies examining the risk of dementia among adults (age ≥18 years) with AD versus non-AD controls. Two reviewers independently extracted study characteristics and outcomes. Quality assessments were performed according to the Newcastle-Ottawa Scale (NOS). The PRISMA and Meta-analysis of Observational Studies in Epidemiology (MOOSE) reporting guidelines were followed. The adjusted hazard ratio (aHR) were pooled using the random-effects meta-analysis. Subgroup analysis were conducted according to the types of dementia and severity of AD. Publication bias was evaluated by funnel plot.

Of 3,906 identified studies, 5 studies with 5 cohorts (n = 12,543,457 populations) were eligible for inclusion and were pooled in the meta-analysis. A significant association was found between AD and risk of incident all-cause dementia (pooled aHR, 1.13; 95% CI, 1.06-1.21; I2=81%). Subgroup analysis of dementia types illustrated a significantly increased risk of Alzheimer's disease (pooled aHR, 1.13; 95% CI, 1.04-1.24; I2=80%) and vascular dementia (pooled aHR, 1.17; 95% CI, 1.11-1.24; I2 =11%). Interestingly, subgroup analysis of AD severity revealed that severe AD was associated with significantly increased risk for incident all-cause dementia (pooled aHR, 1.36; 95% CI, 1.21-1.54, I2=0%), but not in mild AD (pooled aHR, 1.52; 95% CI, 0.76-3.05, I2=85%). No evidence of publication bias was observed. Quality assessments of the included studies were high.

Patients with adulthood AD have a significantly increased risk of dementia. These findings may provide a reference for the clinical management of AD patients with baseline risk of dementia.

Cumulative Burden of Depression and Domain-Specific Cognitive Impairment in the Women's Interagency HIV Study: A Marginal Structural Model Approach Cesar Higgins Tejera* Cesar Higgins Tejera Priya Duggal Adaora Adimora Elizabeth Topper Debora Gustafson Beth Jamieson Pauline M. Maki Anjali Sharma Amanda B. Spence Kathleen Weber Andrea Weinstein Deborah Jones Weiss Pariya Wheeler Gina Wingood Linda A. Teplin Leah H Rubin Kathryn Fitzgerald

Background: Chronicity of depression correlates with memory, attention deficits, and task completion challenges, indicating that the burden of depression has broad cognitive repercussions. Large prospective studies with repeated measures of depressive symptomatology and domain-specific cognitive function are lacking. We estimated the association between cumulative depressive symptomatology and domain-specific cognitive impairment among women with HIV (WWH) and without (WWoH) in the Women's Interagency HIV Study.

Methods: Participants were followed-up from enrollment to cognitive impairment onset. Cumulative depression burden was calculated using Center for Epidemiologic Studies Depression scale (CES-D) scores: CES-D ≥33 = 1, CES-D ≤9 = 0, CES-D 10-32 interpolated to proportions between 0 and 1. We multiplied these proportions and the time elapse between visits to obtain our depression burden measure. Domain-specific cognitive impairment was defined as 1-SD below mean performance in attention, memory, executive function, learning, or speed. We used inverse probability of exposure and censoring weights to estimate incidence rate ratios (IRR) from marginal structural Poisson models.

Results: Among 2,576 participants (1,781 WWH), average age was 45.7, with 13.8% cumulative depression burden over 12.8 years. WWH had higher depression burden (14.23%) than WWoH (12.9%), and 46% of women were censored. In the overall sample, 1-SD above mean cumulative depression burden was associated with 1.56 (95%CI: 1.33, 1.83) times higher risk of attention/working memory impairment. Similar associations were found for verbal memory (IRR = 1.26; 95%CI: 1.15, 1.38), executive function (IRR = 1.45; 95%CI: 1.34, 1.73), verbal learning (IRR = 1.32; 95%CI: 1.21, 1.43), processing speed (IRR = 1.34; 1.17, 1.52), and in models stratified by HIV-serostatus.

Conclusions: Addressing high depression burden among women could positively impact cognitive health.

LATEBREAKER

Nutrition/Obesity

Association of soft drinks consumption and modifiable health behavior in a Brazilian nationally representative school-based study Luciana B Nucci* Luciana Nucci Carina C Castelucci S. Cristina Oancea

High consumption of sugar-sweetened beverages (SSBs) is associated with type II diabetes, cardiovascular disease, and various cancers. Soft drinks are a major component of daily caloric and sugar intake, and the leading SSB consumed by Brazilians. This study aimed to investigate the amount of soft drink consumption (SDC) among adolescents and its associated health risk behaviors (HRB).

Data are from a 2019 cross-sectional school-based Brazil national survey (n=142,883 students ages 13–17 years). The outcome variables were defined by five modifiable HRB related to alcohol consumption, tobacco use, physical activity, screen time, and eating habits for adolescents. Latent class analysis was used to group participants based on HRB and we identified 3 distinct classes: 1- sedentary lifestyle (45.4%); 2- alcohol/tobacco use and unhealthy eating habits (10.6%); and 3- minimal health risks (44.0%). The association of these patterns with SDC was analyzed through multinomial logistic regression, adjusting for sex, age, race, school year, and type of school (public or private).

Consumption of soft drinks on 4-6 days and every day in the last week was seen in 16.7% (95%CI: 16.1-17.2%) and 8.7% (95%CI: 8.3-9.1%) of the students. Compared to those who did not consume soft drinks the week before, the adjusted OR of SDC on 1-3, 4-6, and every day in the last week were 1.35 (95%CI: 1.28-1.43), 2.4 (95%CI: 2.2-2.6), and 3.3 (95%CI: 3.0-3.7) for those with a sedentary health style; and of 1.9 (95%CI: 1.7-2.1), 4.5 (95%CI: 3.9-5.1), and 7.6 (95%CI: 6.5-9.0) for those with higher probabilities of alcohol/tobacco use and unhealthy eating habits.

In conclusion, the studied HRBs were associated with significantly greater SDC among Brazilian adolescents. Identifying adolescents more likely to consume soft drinks regularly can inform targeted lifestyle interventions. Furthermore, policies that aim to reduce the consumption of these unhealthy beverages are justified.

Adolescent dietary patterns and risk of chronic liver disease mortality and incident liver cancer: A prospective cohort study Longgang zhao* Longgang Zhao Xinyuan Zhang Yun Chen Yikyung Park Linda M. Liao Jessica L. Petrick Peter T. Campbell Katherine A. McGlynn Xuehong Zhang

Objectives: Healthy dietary patterns in adulthood have been associated with favorable liver health, but no study has examined the role of the adolescent diet in adverse liver outcomes. We evaluated the relationship between adolescent dietary patterns and the risk of chronic liver disease mortality and liver cancer in adulthood.

Methods: We conducted a prospective cohort study using data from the NIH-AARP Diet and Health Study, comprising 241,628 adult participants who had recalled their dietary intake at ages 12-13 when they participated in the study (mean: 61 years). We employed principal component analyses to derive dietary patterns based on 37 food items from the food frequency questionnaire. We used the Cox proportional hazards regression model to estimate the multivariable HRs and 95% CIs for associations between different dietary patterns and adverse liver outcomes with adjustments for potential confounders including adult and adolescent characteristics.

Results: With a median of 15.5 years follow-up, we documented 437 chronic liver disease deaths and 419 incident liver cancers. We identified three dietary patterns: a plant-based pattern (high in fruits and vegetables), a Western modern pattern (high in ice cream and doughnuts, but low in milk and vegetables), and a Western traditional pattern (high in hot dogs and French fries, but low in milk and butter). After controlling potential confounding factors, the adolescent Western modern pattern score was positively associated with the risk of chronic liver disease mortality (HR quartile 4 vs quartile 1=1.40, 95% CI=1.06-1.86, P trend=0.05). Dietary patterns during adolescence were not associated with liver cancer risk.

Conclusions: For the first time we found a positive correlation between Western modern patterns during adolescence and mortality from chronic liver disease. If confirmed by future research, these findings crucially inform the significance of a healthy adolescent diet in preventing liver disease.

Table. Hazard ratios of chronic liver disease mortality and incident liver cancer according to quintile of energy-adjusted adolescent dietary pattern scores in NIH-AARP Diet and Health Study, 1995-2011

	Q1	Q2	Q3	Q4	P trend
		Quartiles of dietary patterns, Hazard Ratio (95% Confidence Intervals)			
Chronic liver disease mortality					
Plant-based pattern [a]					
Cases	96	109	125	107	
Age-adjusted model	1.00 (reference)	1.14 (0.86-1.49)	1.31 (1.00-1.71)	1.12 (0.85-1.47)	0.41
Multivariable model	1.00 (reference)	1.14 (0.86-1.51)	1.33 (1.01-1.76)	1.20 (0.90-1.59)	0.19
Western modern pattern [b]					
Cases	86	123	105	123	
Age-adjusted model	1.00 (reference)	1.46 (1.11-1.93)	1.27 (0.95-1.69)	1.54 (1.16-2.03)	0.008
Multivariable model	1.00 (reference)	1.40 (1.06-1.86)	1.19 (0.88-1.59)	1.40 (1.06-1.86)	0.05
Western traditional pattern [c]					
Cases	92	120	110	115	
Age-adjusted model	1.00 (reference)	1.32 (1.01-1.73)	1.23 (0.93-1.63)	1.32 (1.00-1.74)	0.08
Multivariable model	1.00 (reference)	1.25 (0.95-1.65)	1.15 (0.87-1.53)	1.21 (0.92-1.60)	0.26
Incident liver cancer					
Plant-based pattern [a]					
Cases	106	113	91	109	
Age-adjusted model	1.00 (reference)	1.07 (0.82-1.39)	0.86 (0.65-1.14)	1.03 (0.79-1.35)	0.97
Multivariable model	1.00 (reference)	1.06 (0.80-1.39)	0.88 (0.66-1.18)	1.12 (0.85-1.48)	0.53
Western modern pattern [b]					
Cases	99	105	103	112	
Age-adjusted model	1.00 (reference)	1.10 (0.84-1.45)	1.11 (0.84-1.47)	1.29 (0.98-1.69)	0.08
Multivariable model	1.00 (reference)	1.08 (0.82-1.42)	1.04 (0.78-1.38)	1.16 (0.88-1.53)	0.35
Western traditional pattern [c]					
Cases	91	104	121	103	
Age-adjusted model	1.00 (reference)	1.17 (0.88-1.55)	1.41 (1.07-1.85)	1.25 (0.94-1.66)	0.07
Multivariable model	1.00 (reference)	1.10 (0.83-1.47)	1.27 (0.96-1.69)	1.05 (0.79-1.40)	0.60

Abbreviations: CI, confidence intervals; HR, hazard ratio.

Multivariable adjusted model adjusted for age at entry into cohort, sex, education level, race, alcohol intake, body mass index, smoking, physical activity, diabetes, aspirin use, adulthood healthy eating index, father occupation, body mass index at 18, physical activity at 18, and total energy intake at 12-13 years old.

[a] Plant-based dietary patterns are characterized by a high consumption of fruits and vegetables.

[b] Western modern patterns are characterized by a high consumption of cake, cookies, pizza, and doughnuts but a low consumption of milk, eggs, and vegetables.

[c] Western traditional patterns are characterized by a high consumption of bacon, hot dog, French fries, beef and beans but a low consumption of milk, butter, and cakes.

Nutrition/Obesity

Racial-ethnic Disparities in Obesity and Mortality among Older Adults (Aged ≥50 Years) in the U.S. (1998-2020) Nader Mehri* Nader Mehri Angela M. Malek Gaurav Dave Michelle Song Ehsan Rostami

Obesity has been increasing over time in the U.S., especially among younger and older adults, the latter for whom the association with mortality is less clear. Depending on the disease, the outcome may be better for older adults with overweight and obese BMIs than healthy or underweight BMIs known as the "obesity paradox". Using 12 waves of the Health and Retirement Study (HRS, 1998-2020), we investigated racial-ethnic disparities in obesity and mortality among older women (aged ≥50 years) in the U.S. We utilized the multistate life table method to quantify the number of years that women at age 50 could expect to live in different weight states based on having healthy weight, overweight and obese BMIs (including class 1, class 2 and class 3 or severe obesity).

The results demonstrate that after adjusting for education, non-Hispanic White women at age 50 could expect to live an additional 31.1 years, of which 10.2 years are expected to be a healthy weight, 10.3 years as overweight, and 10.6 years as obese (6.1 years class 1 obesity, 2.8 years class 2 obesity and 1.8 years severe obesity). In contrast, non-Hispanic Black (NHB) women at age 50 could expect to live an additional 29.3 years of which only 4.9 years are expected to be a healthy weight. This indicates that most proportions of NHB women remaining life at age 50 are expected to be overweight (9.1 years) and obese (15.2 years) including 3.2 years with severe obesity. Hispanic women at age 50 could expect to live an additional 33.5 years of which 8.9, 12.1, and 12.5 years are expected to be a healthy weight, overweight, and obese, respectively. This includes living 7.5, 3.1 and 1.9 years of their remaining life with class 1 obesity, class 2 obesity as well as severe obesity, respectively.

Overall, the findings indicate that there are notable racial-ethnic disparities in obesity and mortality among older women in the U.S. We plan to present comprehensive results for both genders upon abstract acceptance.

Years of remaining life in different weight categories by race-ethnicity at age 50 (V
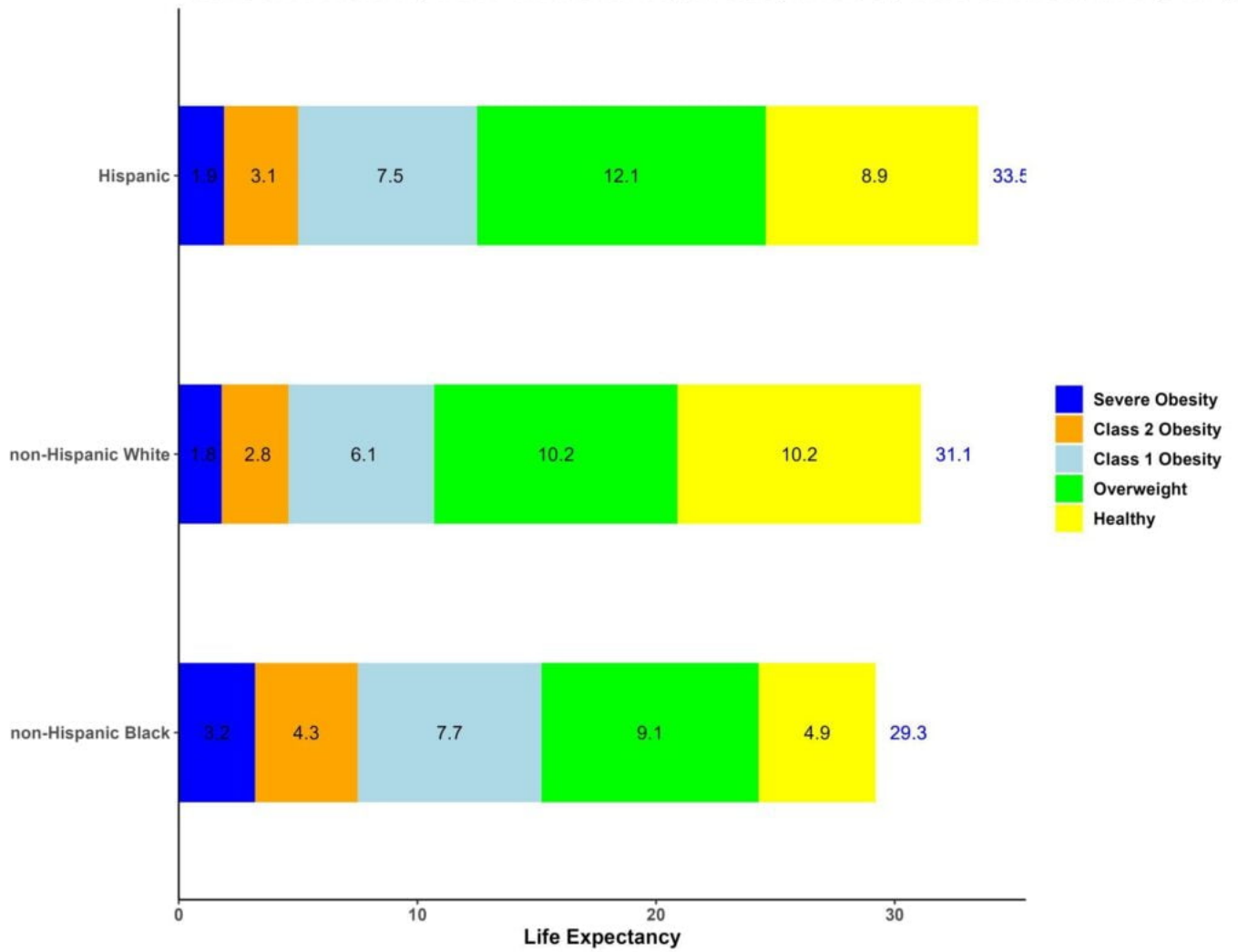
Comparing anthropometric measures from the Cancer Prevention Study II Nutrition Cohort Kierstin Faw* Kierstin Faw Emily Deubler Lauren R Teras Alpa V Patel

Introduction: Recent commentaries question whether body mass index (BMI) is a good proxy for excess body fatness in predicting disease risk. Other anthropometric measures that may better measure visceral fat such as, waist circumference (WC) or waist to height ratio (WtHR), have been postulated to better predict disease risk. This study aims to understand the relationship between BMI, WC, and WtHR in a large population of men and women.

Methods: In the Cancer Prevention Study II Nutrition Cohort, self-reported height was collected in 1992 and self-measured weight and WC were ascertained in 1997 among cancer-free individuals and used to calculate BMI, WtHR, and WC. These measures were compared continuously, using correlation coefficients (r) and categorically, using weighted kappa statistics (k, percent agreement). The WtHR categories were <0.50, 0.50-0.55, and ≥ 0.55. BMI categories were 18.5-25 (healthy weight), 25-30 (overweight), and ≥ 30 kg/m2 (obese). WC cut points were <31.25, 31.25-35.75, and ≥ 35.75 cm for women and <36.75, 36.75-40.00, and ≥ 40.00 cm for men.

Results: Among women (N= 50,618), based on BMI, 50% were healthy weight, 33% were overweight, and 17% were obese. Continuous BMI was strongly associated with WtHR and WC (r=0.81; r=0.79). The kappa statistics revealed similar results with categorical BMI having moderate agreement with WtHR and WC (k=0.54; k=0.49). Among men (N=43,783), based on BMI, 36% were healthy weight, 49% were overweight, and 15% were obese. Continuous BMI was strongly correlated to WtHR and WC (r=0.81; r=0.78). Categorical BMI had fair to moderate agreement with WtHR and WC (k=0.34; k=0.47).

Conclusion: In the Cancer Prevention Study II Nutrition Cohort, continuous BMI, WtHR, and WC were all strongly correlated and categorical measures had fair to moderate agreement for men and women. Although BMI is a proxy for general adiposity, this study suggests it's generally a reliable, easy to measure way to ascertain body size.

Nutrition/Obesity

Gender differences in the Association Between Diagnosed Status of Metabolic Dysfunction-Associated Steatotic Liver Disease and Healthy Eating Index Wei-Ting Lin* Wei-Ting Lin Peng-sheng Ting Chiung-Kuei Huang Hui-Yi Lin David W. Seal Po-Hung Chen Chien-Hung Lee Tung-Sung Tseng

An increasing prevalence of metabolic dysfunction-associated steatotic liver disease (MASLD) was estimated particularly in overweight and obese adults (50.7%). Lifestyle and dietary factors have been related to the development of MASLD. This study aims to investigate gender differences in Healthy Eating Index (HEI) between people who were unaware of MASLD and people with diagnosed MASLD. Individuals reporting diagnosed MASLD and those who did not report a knowledge of liver disease but had a controlled attenuation parameter>302 and limited alcohol use were selected from the 2017-2020 National Health and Nutritional Examination Survey. The quality of the daily diet was reflected using HEI-2015. HEI components and total HEI scores were calculated from two-days 24-hour dietary recall interviews. All statistical analyses were performed under survey modules with an appropriate sampling weight. Both men and women with diagnosed MASLD had higher prevalence of comorbidities than those who with unaware of having MASLD (p's≤0.024). Women with diagnosed MASLD were more likely older and current smokers (p's≤0.023) compared to women with unaware of having MASLD. Higher dietary scores reflecting more healthy behavior for added sugars, total fruits, and whole fruits were found in women with diagnosed MASLD compared to women who were unaware of having MASLD (p's≤0.018). Women with diagnosed MASLD still had higher total HEI scores compared to women who were unaware of having MASLD, after adjusting for potential confounders (adj β=3.49, 95%=0.77-6.21). We did not find any significant differences in HEI components or total HEI scores between men with diagnosed MASLD and those who were unaware of having MASLD. Our findings emphasized women with diagnosed MASLD had a better quality of the daily diet than women who were unaware of having MASLD. However, we noted no significant difference in HEI-related factors between men who were unaware of having MASLD and those with diagnosed MASLD.

Occupational

Drivers of Annual Covid-19 Vaccine Uptake among NYC Transit Workers Michael Cziner*
Michael Cziner Daniel Hagen David Vlahov Alexis Merdjanoff Robyn Gershon

Background: Transit workers were essential workers throughout the COVID-19 pandemic and at elevated risk for infection. Updated COVID-19 vaccines provided annually may reduce the burden of disease in this workforce. Therefore, this study sought to examine attitudes of New York City (NYC) transit workers towards receiving annual COVID-19 vaccines.

Methods: A cross-sectional online survey of New York Metropolitan Transportation Authority workers was conducted between December 2023 and January 2024. Demographic and occupational characteristics, physical and mental health status, and attitudes towards pandemic working conditions were assessed. Logistic regression models were used to identify factors associated with intent to receive annual COVID-19 vaccines.

Results: Among n=1,362 respondents, 90% reported having received at least one dose of a COVID-19 vaccine and 27% indicated intent to get an annual COVID-19 vaccine. In models adjusted for demographic, occupational, health, and psychosocial characteristics, intent to receive an annual vaccine was positively associated with male (vs. female) gender (OR=1.65, 95%CI: 1.07,2.57) and Hispanic (vs. non-Hispanic) ethnicity (OR=3.07, 95%CI: 1.98,4.81), and negatively associated with Black/African American as compared to White race (OR=0.46, 95%CI: 0.30,0.73). Moreover, intent to get an annual vaccine was negatively associated with workers' impression that their employer was not ready for the next pandemic (OR=0.30, 95%CI: 0.19,0.46) and with a history of prior COVID-19 infection (OR=0.48, 95%CI: 0.29,0.77), and positively associated with having known someone who died from COVID-19 (OR=2.43, 95%CI: 1.57,3.80) and worrying about new infectious diseases (OR=9.03, 95%CI: 5.43,15.41).

Conclusion: Intent to get an annual COVID-19 vaccine appears to be low in NYC transit workers, especially among female and Black/African American workers. Understanding these drivers may help to improve future vaccination campaigns in this workforce.

Occupational

Workforce reductions may harm the health of those who remain at work Kevin Chen* Kevin Chen Ellen A. Eisen

Background: Survivors of workforce reductions may experience increased workplace demands coupled with reduced control, loss of social connections, survivor's guilt, strained relationships with employers, and greater perceived job insecurity. Here, we seek to estimate the association between experience of workforce reductions while employed and long-term risk of mortality due to preventable chronic diseases.

Methods: Using data from the UAW-GM autoworkers cohort (n = 36,121), we detected workforce reduction events over the years 1946-1985 by identifying months in which the percent reduction in the number of employees was greater than two standard deviations above the time-series prediction. Then, we estimated adjusted hazard ratios (HR) for mortality due to cardiovascular disease (CVD), cancer, and chronic liver disease in a Cox model, comparing levels of cumulative experience of workforce reduction.

Results: Over the follow-up period 1946-2015, we observed 6,711 deaths due to CVD, 4,286 deaths due to cancer, and 287 deaths due to chronic liver disease. The HRs for cancer and chronic liver disease mortality were monotonically increasing for increasing levels of cumulative experience of workforce reduction. Compared to no experience of workforce reduction, experiencing 1 to 2 reductions was associated with a 1.05 (1.03, 1.08) and 1.11 (0.75, 1.66) times greater hazard of cancer and liver disease mortality, respectively. The HRs associated with 7 or more reductions were 1.54 (1.00, 2.38) and 1.65 (1.16, 2.35) for cancer and liver disease mortality. The HRs for CVD mortality were null.

Conclusion: Workers who survived more workforce reduction events experienced a greater hazard of cancer and chronic liver disease mortality in the UAW-GM cohort. Since the number of workforce reduction events experienced depends on duration of employment, specialized methods to account for the healthy worker survivor effect may yield stronger positive associations, particularly for CVD.

Monthly percent reduction in number of employees in the UAW-GM autoworkers cohort and best-fitting ARIMA model
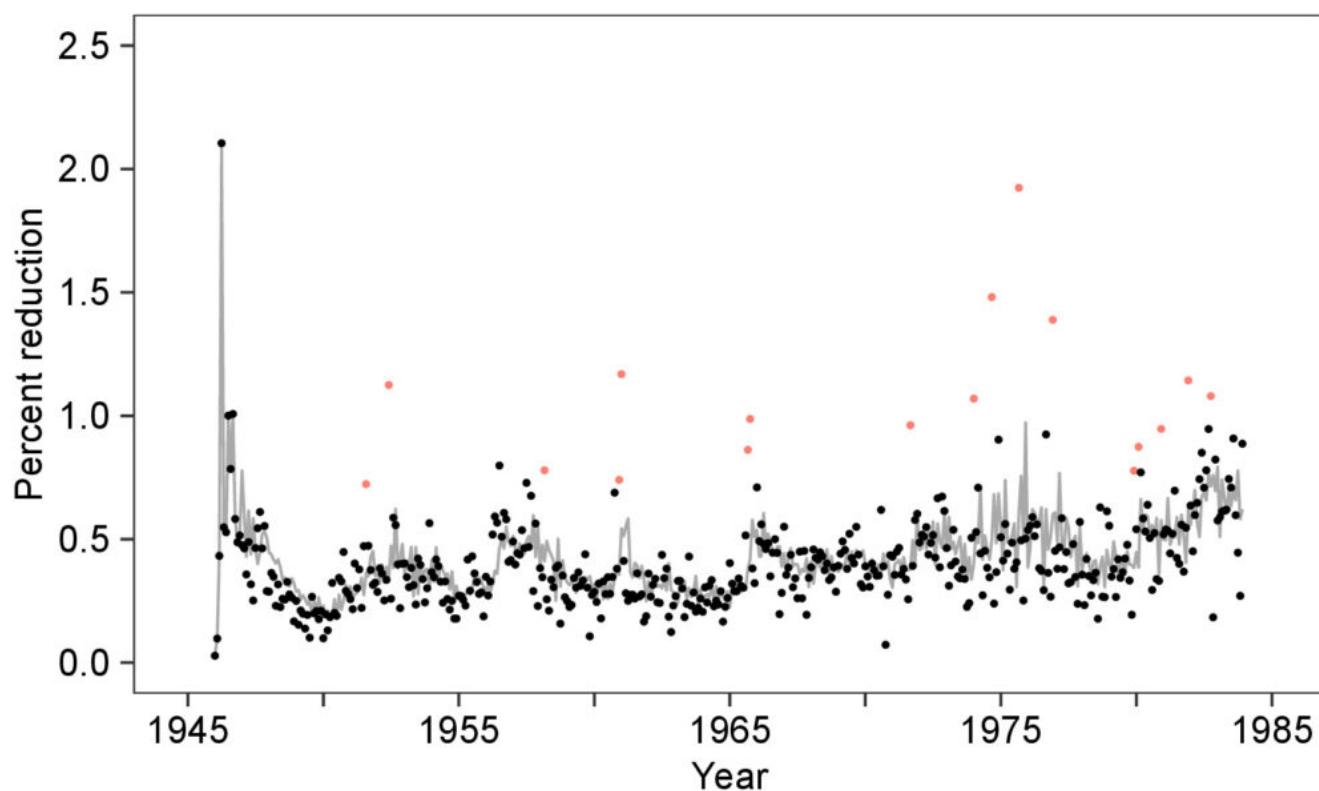
— Best-fitting ARIMA model

• Percent reduction within expected variation

• Percent reduction considered workforce reduction

Associations between U.S. high school student employment status during the COVID-19 pandemic and mental health outcomes, short sleep, and parental abuse: Analysis of Adolescent Behaviors and Experiences Survey (ABES) data. Taylor Shockey* Taylor Shockey Sharon Silver

Background: Work is a social determinant of health, and the COVID-19 pandemic affected the employment of many working Americans, including high school students. Employment status is linked to household economics, sleep, social networks, mental health, family relationships, and a person's overall daily life. This study sought to examine differences in mental health outcomes, hours of sleep per day, and parental abuse among U.S. high school students based on their employment status before and during the COVID-19 pandemic.

Methods: Adolescent Behaviors and Experiences Survey (ABES) data from January-June 2021 was analyzed to obtain weighted prevalences and adjusted prevalence ratios (aPRs) for select mental health outcomes (e.g., poor mental health during the past 30 days, poor mental health during the pandemic and persistent feelings of sadness or hopelessness), emotional abuse by a parent, and short sleep by among students who had or had not lost a job during the COVID-19 pandemic. Student age, sex, race/ethnicity, grade level, and sexual identity were evaluated as potential confounders.

Results: Among students reporting job loss during the COVID-19 pandemic, the unadjusted prevalences for persistent feelings of sadness or hopelessness (54.9%), poor mental health during the pandemic (48.7%), emotional abuse by a parent (67.9%) were all significantly elevated compared to the prevalences of students who had not lost jobs during the COVID-19 pandemic. The aPRs for these measures and short sleep also had statistically significant elevations.

Discussion: While the COVID-19 pandemic has been associated with negative health outcomes among adolescents, this is one of the first studies to examine associations between adolescent job loss during the pandemic and certain mental health outcomes, emotional abuse by a parent, and short sleep. These results highlight the importance of high school students' employment in maintaining mental health.

Occupational

Quantifying cumulative exposure to circadian disruption based on lifetime shift work information and biological sleep-wake timing in female nurses Linske de Bruijn* Linske de Bruijn Nina E. Berentzen Jelle J. Vlaanderen Roel C.H. Vermeulen Hans Kromhout Flora E. van Leeuwen Michael Schaapveld

Background: Shift work-induced circadian disruption (CD) may affect health. In epidemiological research, night shift work exposure and its frequency are mainly used as proxies for CD. However, night shift work may inadequately reflect CD as workers may also experience CD during other shift types if these shifts interfere with a worker's biological night. We aim to quantify individual cumulative CD based on past shift work and preferred sleep-wake timing in a cohort of nurses.
Methods: Data were derived from 59,947 Dutch female nurses who participated in the Nightingale Study (18-65 years (y) at baseline in 2011; mean [SD] age: 46.9y [11.0]). They retrospectively reported their job history since the start of their nursing career including start-stop years and shift-specific duration and frequency, allowing us to assess their cumulative exposure to shift work. In 2017, this information was updated in a second questionnaire (n=37,731, 63%) and additionally, sleep timing was collected (preferred sleep and wake time in a work-free period) and used to define biological night. To determine the individual cumulative exposure to CD, we quantified the overlap in hours (h) between shift work times and the biological night for 35,006 nurses.
Results: Regarding specific shift types, the median CD was 9.0 h (IQR 8.5-9.5) for night shifts, 2.5 h (2.3-3.3) for morning, and 1.0 h (0.5-1.5) for evening shifts (Figure). The median cumulative CD was 4,404 h (1,032-9,861) and ranged from 1,584 h in nurses with a work duration <10y to 8,285 h in nurses with a work duration ≥30y. Night shift work exposure (never/ever) and its frequency explained 13% and 33% of the variance in CD, respectively.
Conclusion: We assessed the cumulative shift work-related CD of nurses. CD is just partly correlated to classical measures of night shift work exposure as used in most epidemiological studies. This novel cumulative exposure metric may improve association studies on exposure to CD and health issues.

Distribution of circadian disruption per shift type
N = 35,006 nurses
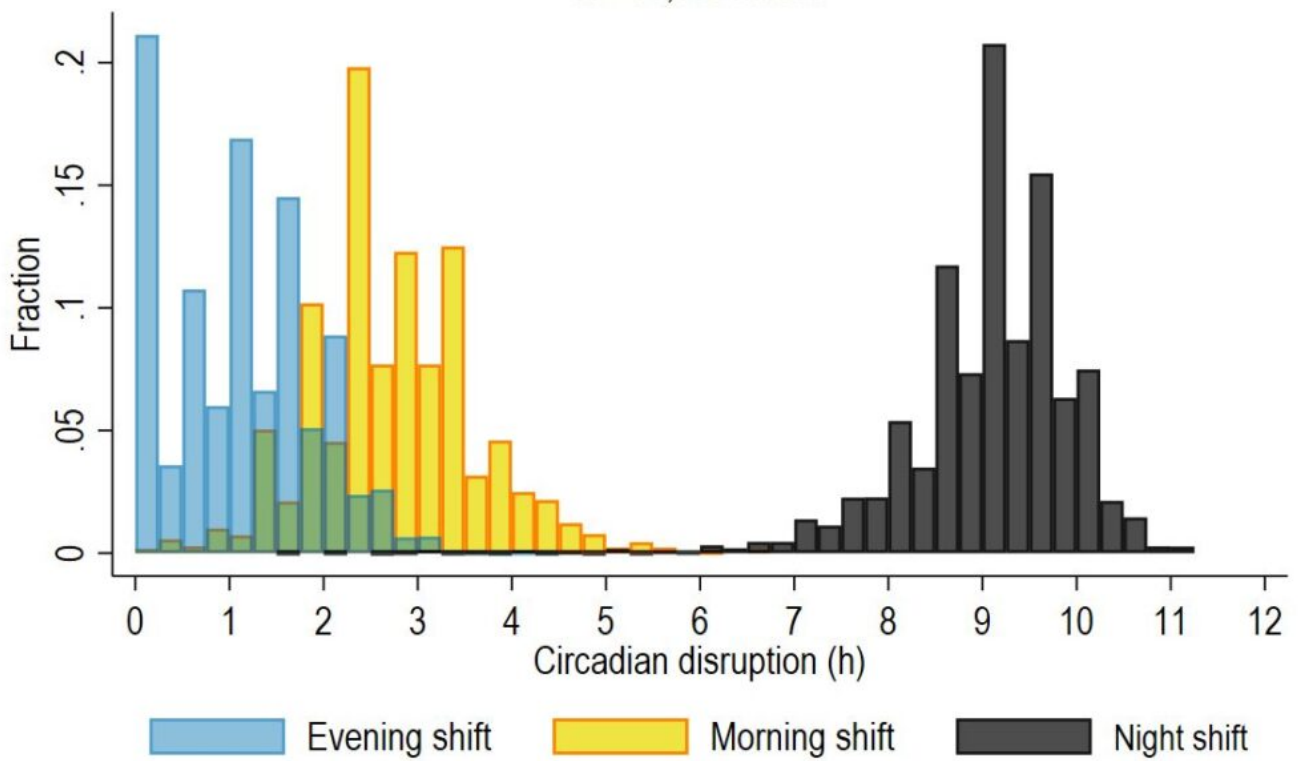
Evening shift: worked at least 1 h after 7:00 p.m. and shift ended no later than midnight
Morning shift: starts between 5:00 a.m. and 6:59 a.m.
Night shift: worked at least 1 h between midnight and 5:00 a.m.

Immigrant-Specific Policies and Programs and Maternal, Perinatal, and Paediatric Outcomes: A Scoping Review Rina Lall* Rina Lall Seungmi Yang

Background: Immigrants often face barriers in accessing healthcare and other essential services. These barriers during pregnancy and childhood may lead to adverse outcomes. Policies and support programs in receiving countries play a significant role in shaping the experiences of migrants and potentially affect outcomes among immigrant mothers and their infants. We sought to synthesize and appraise the current peer-reviewed literature on the impacts of immigration policies and programs to better understand the scope and benefits of specific policies and support programs on the health and development of immigrant mothers and their children.

Methods: Six databases (Scopus, Embase, Medline, Global Health Database, CINAHL, and the Public Health Database) were systematically searched using applicable keywords and subject headings for immigration, policy/program, and maternal/perinatal/paediatric outcomes. A total of 10,100 studies published in English from inception through October 2022 were identified, and 51 met our inclusion criteria.

Results: Overall, eligible studies examined periods ranging from 1980 – 2019. Paediatric outcomes were examined more (n = 37) than maternal or perinatal outcomes (n = 27), and 84% of studies focused on the immigrant receiving context specific to North America. Quasi-experimental methods were employed in 66% of studies. Commonly assessed paediatric outcomes included health insurance (38%), education (22%), and mental health (14%). Less restrictive policies (e.g., the Deferred Action for Childhood Arrivals) were associated with positive educational outcomes for recipients and their children. Restrictive policies that tightened eligibility for public health insurance programs, or increased immigration enforcement had negative impacts on the health insurance and healthcare access of immigrant children, but the magnitude of these effects varied. For maternal outcomes, 56% of studies reported birth outcomes and 30% addressed perinatal care. Restrictive policies reduced adequate prenatal care usage among migrant women.

Conclusion: Research on the impact of immigrant-specific policies and programs on maternal and child outcomes is limited in scope, focusing mainly on immigrant receiving countries in North America.

Latino children's physical fitness varies by place of birth and sex: Findings from New York City public school students 2006-2019 Emily M. D'Agostino* Emily D'Agostino Karen R. Flórez Caroline Nguyen Sophia Day Kevin Konty Kira Argenio Terry T. Huang Cody D. Neshteruk Brooke E. Wagner Hannah R. Thompson

Purpose: United States (US) minoritized and recent immigrant youth disproportionately experience health disparities in fitness, an established proxy of present and future health. Fitness differences by place of birth (POB) could exacerbate inequities in adulthood chronic disease development. This study examined fitness differences among Latino youth by POB and sex.

Methods: This cross-sectional study drew data from the NYC FITNESSGRAM (2006-2019) for public school Latino youth (grades 4&5) with objectively-measured fitness (n=376,466). Sex-/age-specific performance by POB was assessed using healthy fitness zones (HFZ) defined by The Cooper Institute as individual fitness sufficient for good overall health. Generalized estimating equations with a random effect for school were used to examine youth achievement of HFZ for aerobic capacity, muscular strength, and muscular endurance tests.

Results: The sample included 49% females, 25.6% English Language Learners, mean age=9.36±0.60 years with 20.8% overall prevalence of not achieving HFZ for all three tests. Models adjusted for sex, age, grade level, English-language learner, home language, school, neighborhood linguistic isolation, and neighborhood poverty showed that NYC-born students had a higher likelihood of not achieving all three HFZ (RR=1.12; 95%CI 1.08,1.15) versus US-born (non-NYC) students. Central America-born (RR=0.94; 95%CI 0.85,1.03) and Dominican-born (RR=0.92; 95%CI 0.86,0.99) students had the lowest likelihood of not achieving all three HFZ versus US-born (non-NYC) students. Sex-stratified models showed that male and female Dominican-born students had 0.86 (95%CI 0.79,0.95) and 0.97 (95%CI 0.89,1.05) the likelihood of not achieving all three HFZ, versus US-born (non-NYC) male and female students, respectively.

Conclusions: Fitness heterogeneity for Latino children highlights the need for tailored physical fitness programs and policies to reduce disparities, especially in large urban settings.

Obstetric Care Facility Closures and Healthcare Provider Experiences — Fall DocStyles Survey, United States, 2023 Jessica Meeker* Jessica Meeker Jerome Leonard Carrie Shapiro-Mendoza Elizabeth Clark Rebecca Hall Romeo Galang

Obstetric care facility closures (closures) in the US have exacerbated concerns about disparities in access to quality obstetric care, which is critical as maternal morbidity and mortality rates continue to rise. The purpose of this study is to report healthcare provider closures-related experiences. DocStyles, a web-based panel survey of a convenience sample of US primary healthcare providers US, was conducted October 6–25, 2023. Providers caring for pregnant women were asked about closures experiences, including those impeding transfer of high-risk patients to appropriate care, the importance and frequency of patient counseling on facility closures, and priority counseling-related topics. We calculated experience frequencies using R version 4.0.3. The sample of 1,371 respondents included family practitioners (35%), internists (30%), obstetrician-gynecologists (18%), and nurse practitioners/physician assistants (17%). Among respondents, 53% reported closures as a problem in connecting high-risk patients to a birth facility prepared to meet their health needs; 66% of rural and 52% of urban providers expressed this concern. A third of respondents (35%), reported if the birth facility where their patients typically deliver was closed or inaccessible, they would not have an alternative, or wouldn't have an alternative with the same level of care. Although 83% of providers reported the importance of talking with pregnant or postpartum patients about where to get emergency obstetric care in the case of closures, 54% had counseled zero, or very few of their patients. Among urban providers, 18% counseled all or almost all their patients, compared to 9% of rural providers. When asked which counseling topics should be included, providers reported knowing symptoms requiring emergency obstetric care (72%) and not waiting to seek care (66%) with the highest frequency. Provider experiences may inform efforts to ensure patients receive timely, quality obstetric care.

Determinants of short interpregnancy intervals Jennifer Dunne* Jennifer Dunne Gizachew Tessema Gavin Pereira

Introduction

Interpregnancy interval (IPI) is defined as the time between birth and commencement of the next pregnancy. Short IPI (<6-18 months) is a modifiable risk factor for adverse maternal, perinatal, and child health outcomes. Relatively little research has been undertaken to determine the factors that influence IPIs in high-income countries. This study investigated individual, relationship, community and societal factors that influenced IPIs in high-income countries.

Methods

A systematic search was undertaken in CINAHL Plus, Ovid/EMBASE, Ovid/MEDLINE, Ovid/PsycINFO, ProQuest, PubMed, Scopus, Web of Science, and Google Scholar for articles published in English from January 1st 1990 to October 17th 2023. Studies were included if they reported an effect estimate for at least one determinant of birth spacing. The socioecological model was used as a guiding framework to systematically examine multilevel risk and protective factors of IPIs.

Results

Of the 264 unique articles identified for full text review, 53 met the inclusion criteria for the final systematic review. Four levels of risk and protective factors related to short IPI were identified (individual, relationship, community, societal). The majority of the included studies reported influencing factors at the individual level (n=43), with maternal age, ethnicity, education, contraception use, and parity deemed risk factors. At the relationship level, peer influence and familial characteristics were risk factors of short IPIs. Access to health care services were a protective factor for short IPIs at the community level, with social insurance provision at the societal level the most influential factor on short IPIs.

Conclusion

Multi-dimensional factors influence short IPIs in high income countries. The outcomes of this study will inform prenatal and postpartum counselling programs, and the development of targeted educational programs, to improve optimum IPIs.

Postpartum Hemorrhage Trajectories in the United States Military Health System, 2013–2021 Sandra Maduforo* Sandra Maduforo Celeste J. Romano Clinton Hall Gia R. Gumbs Ava Marie S. Conlin

Background: A 2014 Military Health System (MHS) review identified higher rates of postpartum hemorrhage (PPH) at military vs civilian hospitals; by 2015, rates were reportedly similar. This work aimed to investigate trends in PPH in the MHS through 2021 and assess differences between military hospitals with distinct trajectories.

Methods: The Department of Defense Birth and Infant Health Research program was used to identify live born deliveries among US military families, 2013–2021. PPH was ascertained via diagnosis codes from delivery through 12 weeks postpartum. Annual rates of PPH were calculated by hospital type (military vs civilian) and for each military hospital. Military hospitals were then grouped by PPH rate trajectory: sustained high/increasing relative to other military hospitals (i.e., high), sustained low/decreasing (i.e., low), or variable. Risk factors were compared by trajectory.

Results: Among 643,065 identified deliveries, 45.5% occurred at a military hospital and 54.5% at a civilian hospital. Overall PPH rates at military hospitals declined from 2013-2015, falling below rates at civilian hospitals, but increased in subsequent years, exceeding pre-2015 rates at civilian and military hospitals. Compared to military hospitals with low (n=11) and variable (n=6) rate trajectories, those with high rate trajectories (n=14) had higher annual delivery counts (1206 high; 819 low; 958 variable), and deliveries were more likely to have several risk factors for PPH (e.g., preterm: 7.4% high; 4.8% low; 4.9% variable), but less likely to have others (e.g., anemia: 15.7% high; 18.9% low; 16.0% variable).

Conclusions: Despite an apparent decline in PPH at military hospitals from 2013-2015, rates rose from 2016–2021, with varying trajectories and associations with well-known risk factors. Findings suggest differences in measurement of PPH and warrant further assessment.

Annual rates of postpartum hemorrhage by hospital type, 2013–2021.

Perinatal & Pediatric
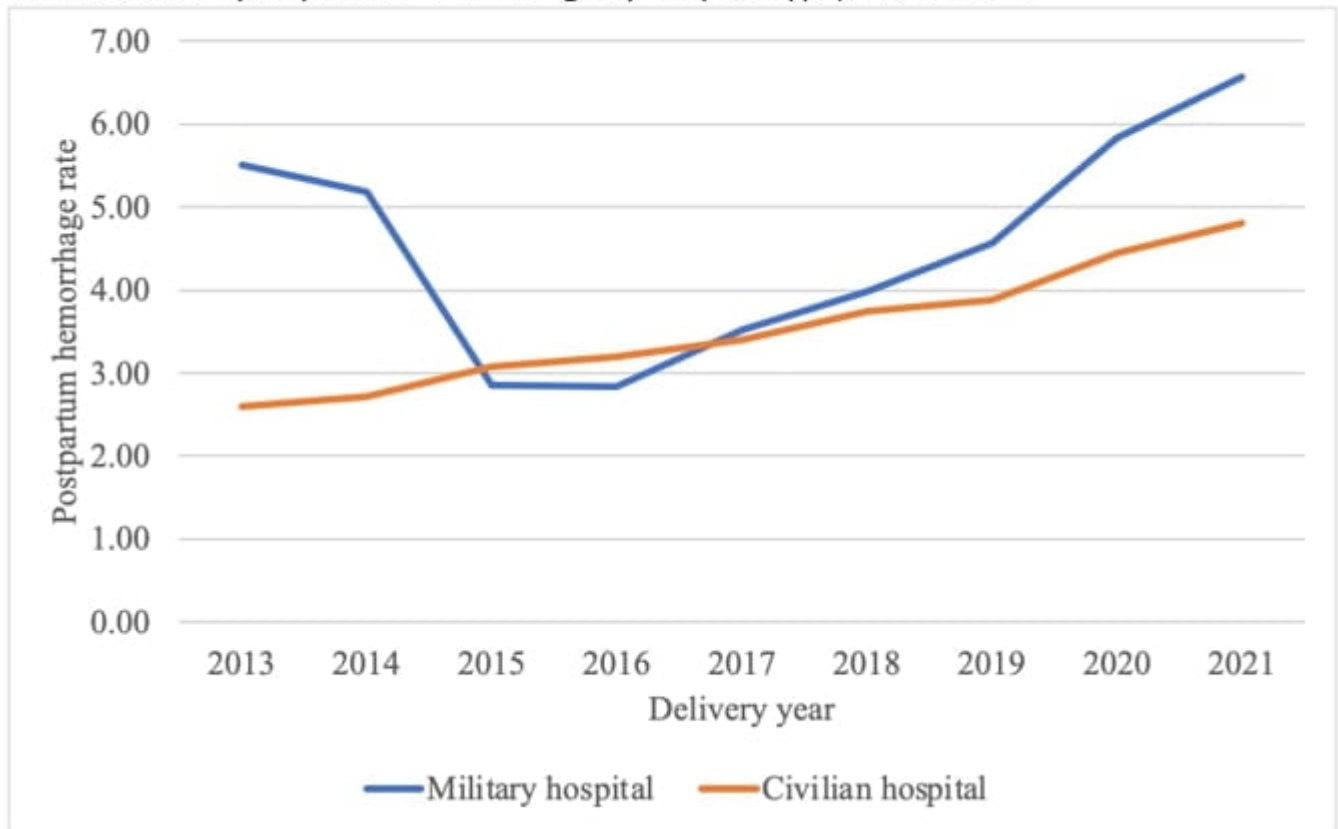
Maternal and paternal characteristics: associations with adverse birth outcomes in Chile 1992-2020 Estela Blanco* Estela Blanco Ana Karen Espinoza W. Conor Rork Paola Rubilar Raquel Jiménez

BACKGROUND AND AIM: Perinatal outcome research focuses almost exclusively on maternal characteristics. While a growing body of research indicates that paternal characteristics play a role as well, the literature is inconclusive due to limitations including poor sample sizing and data reliability. We evaluated maternal and paternal characteristics (age, education and employment status) and the relationship with preterm birth (birth <37 weeks' gestation), low birth weight (LBW, birth weight <2500 grams) and LWB at term (tLBW) using national data from Chile.

METHODS: Chilean birth records from 1992 – 2020 were used (n=7,084,698). We estimated whether paternal (<25, >40, compared to 25-40) and maternal age (<20, 20-35, >35), education (none, high school, greater than high school, compared to primary school), and employment status (employed versus not employed) related to preterm birth, low birth weight, and term low birth weight (tLBW), adjusting for year of birth.

RESULTS: Younger and older mothers (<20 and >35) and fathers (<25 and >40) had higher odds of having offspring with PTB, LBW, and tLBW, although the magnitude of the association was stronger for mothers (OR [95% CI] for PTB= 1.41 [95**%** CI 1.40-1.42] age >35 years compared to 20-35 versus 1.12 [95**%** CI 1.11-1.13] for men >40 compared to 25-40). Current employment among fathers was a protective factor for all perinatal outcomes (OR between 0.93-0.96) and the opposite was true for mothers, although the magnitude of the effect was modest (ORs between 1.01-1.03). For fathers, no education, compared to primary education, was a risk factor for PTB, tLBW, and LBW (1.12, 1.37, 1.21) and odds decreased as education increased from high school (OR=0.98, 95% CI 0.97-0.99) to greater than high school (OR=0.94, 95% CI 0.93-0.96). For women, no education was a risk factor for all perinatal outcomes and we observed no differential odds related to higher levels of education.

CONCLUSIONS: We found that both maternal and paternal characteristics (age, education and employment status) related to adverse birth outcomes. In general, the strength of association was stronger for maternal, compared to paternal, characteristics.

	PTB	tLBW	LBW
Paternal factors			
Age (ref=25-40)			
<25	1.01 (1.00-1.02)	1.15 (1.13-1.17)	1.09 (1.08-1.11)
>40	1.12 (1.11-1.13)	1.08 (1.05-1.10)	1.11 (1.10-1.13)
Education (ref=primary)			
None	1.12 (1.05-1.18)	1.37 (1.27-1.48)	1.21 (1.14-1.28)
High school	0.98 (0.97-0.99)	0.90 (0.88-0.92)	0.92 (0.91-0.93)
>High school	0.94 (0.93-0.96)	0.89 (0.86-0.91)	0.87 (0.86-0.89)
Employed	0.94 (0.93-0.95)	0.96 (0.94-0.98)	0.93 (0.92-0.94)
Maternal factors			
Age (ref=20-35)			
<20	1.19 (1.18-1.20)	1.23 (1.21-1.25)	1.23 (1.21-1.24)
>35	1.41 (1.40-1.42)	1.23 (1.21-1.25)	1.35 (1.34-1.36)
Education (ref=primary)			
None	1.10 (1.05-1.18)	1.56 (1.27-1.48)	1.25 (1.14-1.28)
High school	1.01 (0.99-1.02)	0.92 (0.90-0.94)	0.97 (0.96-0.98)
>High school	1.01 (1.00-1.03)	0.96 (0.94-0.99)	0.99 (0.98-1.01)
Employed	1.01 (1.00-1.01)	1.02 (1.01-1.04)	1.03 (1.02-1.04)

Perinatal & Pediatric

Development of a Pregnancy Cohort in Commercial Insurance Claims Data: Evaluation of Inpatient Versus Apparent Outpatient Deliveries Jacob C. Kahrs* Jacob C. Kahrs Katelin B. Nickel Michael Durkin Sascha Dublin Sarah Osmundson Dustin Stwalley Mollie E. Wood Elizabeth Suarez Anne M. Butler

In studies using insurance claims data for perinatal research, pregnancies are often identified by an observed pregnancy outcome (e.g. live or still birth). Some studies have stricter inclusion criteria for pregnancies with only outpatient delivery claims, with the rationale that outpatient claims may be less reliable.

In a US commercial insurance database (2006-2021), we identified potential pregnancies by the presence of delivery claims from a provider and/or facility. We classified deliveries as inpatient (claim date during inpatient admission) and apparent outpatient (no inpatient admission on claim date). We identified possible confirmatory evidence for each pregnancy including: (1) provider and facility delivery diagnosis and/or procedure code, (2) delivery diagnosis and delivery procedure code, (3) delivery revenue codes, (4) gestational age codes, (5) prenatal care codes, (6) linkage to infant claim, (7) infant birthdate within 1 month of the delivery date. We quantified the proportion of deliveries with confirmatory evidence by delivery setting. Among deliveries with ≥1 piece of confirmatory evidence, we compared characteristics of patients by delivery setting.

Overall, 4.9% of deliveries appeared to be outpatient. A larger proportion of apparent outpatient deliveries (5.7%) vs inpatient (0.1%) did not have confirmatory evidence. Confirmatory evidence (5) was most common (99.7% inpatient, 91.3% apparent outpatient). (4) was the least common evidence for inpatient deliveries (37.3%) and (1) was the least common for apparent outpatient deliveries (12.4%). Confirmed deliveries classified as inpatient occurred among patients who were older and more clinically complex, defined by more pregnancy complications, chronic diseases and prescription medication use.

The vast majority of inpatient and apparent outpatient deliveries had confirmatory evidence. Patient characteristics differed by delivery setting, which has implications for generalizing future study results.

Monitoring postpartum mood changes using a mobile phone-based app: MOMitorTM

Deepthi* Deepthi Varma Amie Goodin Xiaofei Chi Tony Wen Kay Roussos-Ross

Introduction: Unrecognized and untreated postpartum mood changes could lead to increased mortality and morbidity among mothers and newborns.

Objective: This poster presents the data on postpartum mood changes among women using MOMitorTM, a mobile phone-based application that utilizes ecological momentary assessment to continuously monitor women's moods, alerts triggered by the app based on their responses to mood assessments, and interventions provided.

Methods: Participants were women who were 18 years or older, delivered at a quaternary care university hospital, gave signed consent, could read and write English, were willing to download the app, and completed regular assessments from November 2021 to June 2022. Periodic mental health assessments using the Edinburgh Postpartum Depression Scale (EPDS) were done through the MOMitorTM app for 6 weeks. All were multiple choice questions and answered using their mobile phones' screens. An EPDS score with the threshold set as >11, indicates a need for further assessment/screening as potential PPD. Non-responsiveness or critical responses prompted a call from the nurse for further follow-up.

Results: Among the 244 women enrollees, 43.1% had Medicaid insurance, 20.9% had NICU admissions post-delivery, 18.4% were Blacks, 16.0% were Hispanics, and the mean age was 29.4 years (SD=5.7). 146 women completed 6 weeks of assessments. Women's mood did fluctuate during postpartum with the EPDS score being highest in the first two weeks postpartum followed by a decline in weeks 2-4 and increasing slightly in weeks 5 and 6. The app triggered 48 response-based alerts, initiating nurse contact, and 12 referrals (7 to clinic or wellness check, 4 to lactation) along with 1 hospitalization.

Conclusion: Daily monitoring of postpartum mood for the first 6 weeks is critical and could help in early diagnosis and intervention. The MOMitorTM app which utilizes EMA technology, is an effective tool for continuous monitoring of postpartum mood.

Exploring what drives the association between maternal depression prior to pregnancy and preterm birth Caitlin Meyer Krause* Caitlin Meyer Krause Keegan Krause Rebecca Campbell

Background: Preterm birth (PTB, birth at <37 weeks' gestation) is persistently high in US pregnancies, particularly among some minoritized populations, and causes infant mortality, morbidity, and long-term disability. Maternal prenatal depression increases the risk of PTB; whether pre-pregnancy depression influences PTB is unknown.

Objective: To examine the associations between maternal pre-pregnancy depression and PTB.

Methods: This study used 2016-2021 Region V (Illinois, Indiana, Michigan, Minnesota, Wisconsin) Pregnancy Risk Assessment Monitoring System data to assess PTB by pre-pregnancy depression status (n=24,048). Binary depression status was self-reported for the period three months before pregnancy. Prevalence ratios were estimated using survey-adjusted Poisson regression models adjusted for race/ethnicity, age, education, marital status, pregnancy intention, and parity. Effect modification by maternal race/ethnicity and by self-reported prenatal depression status was explored.

Results: PTB occurred in 8.7% of births; 15.4% reported pre-pregnancy depression; two-thirds of those with pre-pregnancy depression also reported prenatal depression. Compared to mothers with no pre-pregnancy depression, those with pre-pregnancy depression had 1.30 times the prevalence (95% CI: 1.15, 1.47) of PTB, adjusting for covariates, however, in stratified models the positive association persisted only in women who also reported prenatal depression. In models stratified by race/ethnicity, increased PTB risk with pre-pregnancy depression was apparent only for NH White mothers.

Discussion: Mothers reporting depression pre-pregnancy had a higher prevalence of PTB, but associations were observed only for those with depression that persisted during pregnancy and only among NH White mothers. Prospective studies using validated depression scales are needed to improve understanding of the contribution of maternal depression longitudinally to PTB risk and opportunities for intervention.

The Validity of Diagnostic Codes for Severe Maternal Morbidity from Electronic Medical Record Data Kelli Ryckman* Kelli Ryckman Eva Sileo Claire Carlson Stephanie Radke

Background: The rates of severe maternal morbidity (SMM) have been increasing in the United States. Use of electronic health record (EHR) data for research on and surveillance of SMM is important for identifying temporal trends and monitoring quality improvement initiatives. There has been an absence of literature evaluating the validity of the International Classification of Diseases, Tenth Revision (ICD-10) coding system in EHR data for accurately identifying cases of SMM.

Objective: To determine the validity of ICD-10 codes for non-transfusion related SMM.

Study Design: This retrospective cohort study using EHR data for deliveries occurring at a single midwestern tertiary care unit between July 1st 2016 and June 30th 2019. A total of 6,456 deliveries were evaluated for the presence of ICD-10 diagnostic codes for one or more of sixteen preselected clinical indicators of non-transfusion related SMM. Two trained primary reviewers reviewed the discharge summaries and clinical notes for the 226 deliveries identified as having an ICD-10 code for one or more clinical indicator for SMM. The percentage of correct codes for each of the 16 preselected clinical SMM indicators was calculated yielding a positive predictive value (PPV) and 99% confidence interval (CI).

Results: The overall number of correctly assigned ICD-10 codes was 149 out of 309 (PPV: 48.2%; 99% CI: 41.0%-55.5%). The most prevalent (>10 occurrences) clinical indicators of SMM with the lowest <40% PVV were acute renal failure, disseminated intravascular coagulation and puerperal cerebrovascular disorders. When removing these 3 clinical indicators the number of correctly assigned ICD-10 codes was 123 out of 176 (PPV: 70.3%, 99% CI: 60.8%-78.3%).

Conclusions: In general, care should be taken when using ICD-10 codes to classify cases of SMM, particularly for select conditions with low PPV's. This data can inform how to develop more nuanced and accurate ways for identifying cases of SMM in EHR data.

The association of various degree of hyperglycemia in pregnancy with future risk of diabetes among women with and without a diagnosis of gestational diabetes mellitus: a systematic review and meta-analysis Na Zeng* Na Zeng Wendy Wen Daniel J Corsi Mark Walker Daniel Krewski Steven Hawken Wenshan Li Taddele Kibret Zhong-Cheng Luo Ravi Retnakaran Shi Wu Wen

Introduction Recent studies have shown that the association between maternal hyperglycemia and future risk of diabetes had expanded from women with gestational diabetes (GDM) to those with hyperglycemia below the diagnostic thresholds for GDM. There is no published systematic review/meta-analysis summarizing whether and to what extent the association between maternal hyperglycemia and future risk of diabetes relates to the number of abnormal glucose values on the oral glucose tolerance test (OGTT) and the type of glucose challenge during pregnancy. This review was undertaken to fill this gap in the scientific literature.

Methods and analysis Comprehensive literature searches were performed in the following electronic databases: MEDLINE, EMBASE and CINAHL to retrieve relevant papers from inception to Jul 12, 2023. The Newcastle-Ottawa Scale (NOS) was used to assess their methodological quality. Meta analyses were conducted if the included studies were relatively homogeneous (tau-squared ($\tau2$) <0.48). Subgroup analyses and sensitivity analyses were implemented for the robustness of the study results.

Results Nineteen studies were identified in this review, which covered a total of 628,510 women with glucose measured during pregnancy. Twelve studies were included in the meta-analysis. All these studies were rated as good/high quality, with a score of seven and above. The pooled OR of risk of diabetes among those with one abnormal value on the OGTT and at least two abnormal values, compared to normal OGTT/normal glucose challenge test (GCT) were 4.26 [2.71, 6.69] and 11.47 [7.88, 16.70] respectively. The pooled OR for the comparison between abnormal GCT with normal OGTT to normal GCT was 2.39 [1.56, 2.42].

Conclusion Elevated maternal glucose level was associated with increased risk of future diabetes, regardless of whether abnormal glucose values meet the diagnostic criteria for GDM, although women with at least two abnormal OGTT values (the commonly accepted diagnostic criteria for GDM) had the highest risk of diabetes in the future.

Early-life living environment, parental mental health, gender differences and allergic diseases among children under-five years in the Greater Taipei Area Yohane Vincent Abero Phiri* Yohane Vincent Abero Phiri Yi-Hua Chen Ming-Lun Zou Chuen-Bin Jiang Ichtiarini Nurullita Santrif Chih-Da Wu Hsiao-Chun Huang Shih-Chun Candice Lung Ling-Chu Chien Yu-Chun Lo Fang-Yu Lee Hsing Jasmine Chao

Background:
Pediatric allergic diseases pose a significant global public health challenge, as the child's household and immediate environment, parental mental health, and gender differences all play a crucial role. We examined the association between various environmental characteristics and doctor diagnosed allergic diseases while exploring the role of parental mental health status and child gender differences.

Methods:
As part of the Longitudinal Examination Across Prenatal and Postnatal Health in Taiwan (LEAPP-HIT) study, we investigated children aged under five and their parents in the Greater Taipei Area. We collected data on the household environment, parental mental health, and the children's allergic disease medical history through standardized questionnaires. Additionally, we examined outdoor environmental factors such as air pollution, land use, and points of interest, and conducted indoor environmental sampling to assess levels of air pollutants, microbes, and allergens. Using logistic regression models, we analyzed the relationship between indoor/outdoor factors, parental mental health, gender differences, and allergic diseases in 136 children.

Results:
The purchase of new furniture (aOR=2.32, 95% CI [1.10-5.41]) and less frequent household cleaning (aOR=5.42, 95% CI [1.11-6.47]) were associated with allergic rhinitis and eczema in children, respectively. Children in households with carpets (aOR=12.42, 95% CI [1.36-18.10]), bedrooms having a moldy smell (aOR=2.51, 95% CI [1.29-4.82]), and beds with higher Der f 1 levels (aOR=1.69, 95% CI [1.10-2.91]) showed increased odds of allergic conjunctivitis. Additionally, ambient particulate matter with aerodynamic diameter ≤10 microns levels (aOR=1.11, 95% CI [1.00-1.23]), points of interest, and parental mental health significantly impacted the occurrence of allergic rhinitis, conjunctivitis, and eczema. We also observed gender differences, with males being more susceptible to allergic diseases than females.

Conclusion:
Our findings underscore the complexity of allergic disease development in children, emphasizing the need to consider the maintenance of a clean home environment, parental mental health, and the child's gender when offering medical advice to families with children affected by allergic diseases.

Abstract

Background:

Pediatric allergic diseases pose a significant global public health challenge, as the child's household and immediate environment, parental mental health, and gender differences all play a crucial role. We examined the association between various environmental characteristics and doctor diagnosed allergic diseases while exploring the role of parental mental health status and child gender differences.

Methods:

As part of the Longitudinal Examination Across Prenatal and Postnatal Health in Taiwan (LEAPP-HIT) study, we investigated children aged under five and their parents in the Greater Taipei Area. We collected data on household environment, parental mental health, and the children's allergic diseases medical history through standardized questionnaires. Additionally, we examined outdoor environmental factors such as air pollution, land use, and points of interest, and conducted indoor environmental sampling to assess levels of air pollutants, microbes, and allergens. Using logistic regression models, we analyzed the relationship between indoor/outdoor factors, parental mental health, gender differences, and allergic diseases in 136 children.

Results:

The purchase of new furniture (aOR=2.32, 95% CI [1.10-5.41]) and less frequent household cleaning (aOR=5.42, 95% CI [1.11-6.47]) were associated with allergic rhinitis and eczema in children, respectively. Children in households with carpets (aOR=12.42, 95% CI [1.36-18.10]), bedrooms having a moldy smell (aOR=2.51, 95% CI [1.29-4.82]), and beds with higher Der f 1 levels (aOR=1.69, 95% CI [1.10-2.91]) showed increased odds of allergic conjunctivitis. Additionally, ambient particulate matter with aerodynamic diameter ≤10 microns levels (aOR=1.11, 95% CI [1.00-1.23]), points of interest, and parental mental health significantly impacted the occurrence of allergic rhinitis, conjunctivitis, and eczema. We also observed gender differences, with males being more susceptible to allergic diseases than females.

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Keywords: Pediatric allergic diseases; Household environment; Gender differences; Allergen levels; Land use characteristics

Word count: 1998 characters with no spaces (not counting Keywords)

Can we use classification and regression trees to compare cesarean delivery rates across populations? Ruby Barnard-Mayers* Ruby Barnard-Mayers Martha Werler

Background: When researchers estimate the effect of delivery method on birth outcomes, cesarean deliveries (CDs) are often compared to a reference group of vaginal delivery. However, this reference group does not always satisfy the assumptions necessary to use vaginal delivery as a counterfactual to CD (e.g. cesarean sections due to breech births or twin gestation). The Robson Classification (or 10-group classification) is one of the most common systems used for the purpose of comparing cesarean section rates across populations (based on pregnancy characteristics) and is recommended by the WHO. However, there has not been much testing of the Robson Classification System for the purposes of epidemiologic analyses.

Objective: The purpose of this analysis is to test machine learning techniques by conducting classification and regression tree analysis (CART) and random forests to compare to the Robson classification system.

Method: Data for this analysis comes from the Pregnancy and Early Life Longitudinal (PELL) data system, comprising all birth certificate records in Massachusetts from 2011 to 2018. We used classification and regression trees (CART) and random forests to create groupings of individuals, using the same set of variables as used in the Robson classification system. We used the mean Gini decrease to calculate variable importance.

Results: Eight leaves (final groups) resulted from the CART analysis, two fewer than the Robson classification system. Trial of labor was the most important variable and preterm delivery was the least important. In the Robson classification system, the first branch for classification is plurality. Rates of CD varied across groups for each system. The highest contributor to CD rates were births with no trial of labor for the CART analysis and multiparous births to people with a prior CD for the Robson System.

Conclusion: The CART created different groups than the Robson system. These groupings may be better for causal analysis of CD.

Table 1a: CART Analysis Groups

Group	N (%)	Number of CD	CD Rate	CD Contribution
1	107638 (19.5%)	106781	0.992	62.4%
2	1567 (0.3%)	1149	0.733	0.7%
3	190767 (34.6%)	34281	0.18	20.0%
4	349 (0.1%)	286	0.819	0.2%
5	17768 (3.2%)	5675	0.319	3.3%
6	987 (0.2%)	578	0.586	0.3%
7	403 (0.1%)	132	0.328	0.1%
8	183351 (33.3%)	6841	0.0373	4.0%
UNDEFINED	48720 (8.8%)	15417	0.316	9.0%

Table 1b. Robson Classification System Groups

Group	N (%)	Number of CD	CD Rate	CD Contribution
1	138760 (25.2%)	20463	0.147	12.0%
2	62276 (11.3%)	27647	0.444	16.2%
3	139409 (25.3%)	3858	0.0277	2.3%
4	43059 (7.8%)	6356	0.148	3.7%
5	73356 (13.3%)	61269	0.835	35.8%
6	11511 (2.1%)	11122	0.966	6.5%
7	8923 (1.6%)	8401	0.941	4.9%
8	11255 (2%)	7943	0.706	4.6%
9	11945 (2.2%)	6699	0.561	3.9%
10	38398 (7%)	12562	0.327	7.3%
UNDEFINED	12658 (2.3%)	4820	0.381	2.8%

Perinatal & Pediatric

Prenatal characteristics and factors contributing to congenital syphilis: a descriptive analysis of cases reported to the Canadian Paediatric Surveillance Program between June 2021 and May 2023 Joanna Merckx* joanna merckx Geneviève Gravel Amandine Bemmo Kelly Baekyung Choi Jaskiran Sandhu Carsten Krueger Jared Bullard

Background: Congenital syphilis (CS) in Canada has surged in recent years, with incidence rates increasing from 2 to 32 confirmed cases per 100,000 livebirths from 2017 to 2022 (from 8 to 117 cases). Little is known about the prenatal characteristics and contributing factors to CS among the birthing parents (BP) of infants with in utero transmission of syphilis in Canada.

Methods: Paediatricians were invited through the Canadian Paediatric Surveillance Program to give an account of CS cases they attended to between June 2021 and May 2023. Data on cases meeting the study case definitions were collected voluntarily through a case-survey. We used descriptive statistics to examine prenatal health care access, diagnosis, and treatment as well as a subset of socio-economic and behavioral risk factors and determinants in BP.

Results: A total of 245 liveborn CS cases were reported from seven provinces and territories, including 71% from the prairies. The median age of BP was 27 years, 31% resided rurally. No prenatal care was reported in 25% (n=62) of BP, and only 25% (n=61) reported at least one visit per trimester. In a quarter (n=60) of the BP, no syphilis screening was performed during pregnancy. Prenatal treatment was not initiated among 20% (30/151) of the screened positives and was initiated <4 weeks pre-delivery in 35% (40/114). Syphilis coinfection with HIV and HCV were reported among 3% and 9% of BP, respectively. One out of six (18%) BP experienced housing insecurity or homelessness. Substance use prenatally was reported in 65% of the BP with use of stimulants and opioids in 60% and 31%, respectively.

Conclusion: In this country-wide picture, we identified substantial lack of access to care and care continuity in BP of liveborn diagnosed with CS. Public health action, such as community outreach to ensure prenatal care for and inclusion of all pregnant individuals, especially those with substance use, is pressing.

Maternal residential mobility between pregnancies: a California statewide sibling study

Giselle Bellia* Giselle Bellia Haoran Zhou Zeyan Liew

Introduction Geocoded residential address is often used in epidemiological research to indicate individual's social and environmental exposures from their living environment, but large-scale studies that characterize maternal residential mobility between pregnancies are sparse. Using a California statewide sibling study, we investigated the pattern of residential mobility between pregnancies and its association with several major social-demographic and perinatal factors.

Methods We geocoded maternal residential addresses extracted from the birth records of 919,013 sibling pairs from 2007-2015 in California. We described the moving patterns between pregnancies, and we utilized logistic regression to estimate the odd ratios for maternal moving according to demographic variables (age at delivery, education level, and race/ethnicity), pregnancy factors (pregnancy interval, pre-pregnancy obesity, smoking, and preeclampsia), and delivery/birth outcomes (mode of delivery, preterm delivery, and infant low birth weight) of the prior pregnancy. We also investigated predictors of maternal moving to a more disadvantaged neighborhood, indicated by a higher census-tract level social vulnerability index.

Results Overall, 52% of mothers moved between pregnancies. The median distance moved was 5.87 km. An additional year of the interpregnancy interval was associated with 33% higher odds of having moved between pregnancies, while having a college degree was associated with 60% lower odds. Mothers who were younger, reported smoking during pregnancy, and self-identified as non-Hispanic Black were associated with having moved to a more disadvantaged neighborhood between pregnancies.

Conclusions Maternal residential mobility between pregnancies was more common within certain demographic subgroups in California. Our findings have important implications for the understanding of potential carryover effects, time-varying confounding, and generalizability issues in sibling-matched analyses.

Maternal residential mobility between pregnancies: a California statewide sibling study

Giselle Bellia[a], Haoran Zhuo[ab], Zeyan Liew[ab]

[a] Yale Center for Perinatal, Pediatric and Environmental Epidemiology, Yale School of Public Health, New Haven, Connecticut
[b] Department of Environmental Health Sciences, Yale School of Public Health, New Haven, Connecticut

Abstract:

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Conclusions Maternal residential mobility between pregnancies was more common within certain demographic subgroups in California. Our findings have important implications for the understanding of potential carryover effects, time-varying confounding, and generalizability issues in sibling-matched analyses.

ASSOCIATION OF MATERNAL DIABETES WITH EPILEPSY IN CHILDREN: A POPULATION-BASED BIRTH COHORT STUDY.

Bénédicte Driollet* Bénédicte Driollet Emmalin Buajitti Asma Ahmed Jennifer Hutcheon Laura Rosella Seungmi Yang

Introduction. Maternal diabetes is the most common chronic disease of pregnancy and appears to be associated with neurodevelopmental disorders in the child, but the evidence is limited and quite heterogeneous, particularly concerning epilepsy. This study aims to examine the association between maternal diabetes and epilepsy in children.

Methods. We identified all in-hospital live births between 2002 and 2018 in Ontario, Canada (N= 2 105 186) and linked their health records to various administrative data, with a follow-up until March 2020. We estimated the crude and adjusted association between maternal diabetes— pre-gestational (type 1 and type 2 diabetes mellitus (T1DM and T2DM)) and gestational diabetes (GDM)—and epilepsy in children, using Cox proportional hazards models and examined the robustness of results using quantitative bias analyses.

Results. In our study population (51.3% male, mean gestational age 38.9 weeks (SD 1.8)), 160 648 (7%) children had mothers with diabetes (1.5% with PGDM and 6.1% with GDM) and 17 853 epilepsy cases were diagnosed (a median follow-up of 10.3 years). After adjusting for maternal socio-economic and clinical characteristics, children exposed to maternal diabetes had, at any time after birth, a modestly increased risk of epilepsy compared to those unexposed (aHR:1.20, 95%CI 1.13-1.27). Compared to children unexposed to maternal diabetes, the risk was higher for children exposed to T2DM (aHR:1.41, 95%CI 1.26-1.60) or exposed to T1DM (aHR:1.37, 95%CI 1.07-1.75) than those exposed to GDM (aHR:1.14, 95%CI 1.07-1.22).

Conclusion. In this population-based birth cohort study, maternal diabetes was associated with an increased risk of epilepsy in children, and this increased risk was more pronounced among mothers with pre-gestational diabetes. Monitoring and evaluation of the development of children exposed to maternal diabetes, especially pre-gestational, may be deemed necessary.

Does lifetime racial discrimination modify the impact of prenatal depression on risk of preterm birth among non-Hispanic Black, non-Hispanic White, and Hispanic women in the United States? Ashley Judge* Ashley Judge Kelli Ryckman Christina Ludema

Introduction: Experiences of racial discrimination are associated with increased risk of both depression and preterm birth; depression may also be associated with increased risk of preterm birth. We aimed to investigate the association between depression during the first and late second trimesters and preterm birth, and whether lifetime experience of racial discrimination modified this relationship.

Methods: We used prospective cohort data from the Nulliparous Pregnancy Outcomes Study: Monitoring Mothers-to-be which recruited between October 2010 and September 2013 from eight clinical, US sites. We fitted marginal structural log-binomial models with inverse probability weights to estimate risk ratios (RR) and 95% confidence intervals (CI) for the association between depressive symptoms in first and late second trimesters on the risk of preterm birth for non-Hispanic (NH) Black, NH White, and Hispanic women, separately. We further stratified our models by lifetime experience of racial discrimination measured in early second trimester. Missing data was accounted for using multiple imputation.

Results: Among an average of 1453 NH Black, 5697 NH White, and 1602 Hispanic women across four multiple imputed datasets, depressive symptoms in first trimester were associated with an increased risk of preterm birth only among NH Black women (RR: 1.52 (CI: 1.19, 1.95)). Among NH Black women, compared to if everyone had low depressive symptoms at both time points, having high depressive symptoms at both time points was associated with a 1.64 (1.05, 2.57) increased risk of preterm birth. In all models, the p-values for multiplicative and additive interaction between depressive symptoms at both time points were well above the specified 0.05 alpha level. With this cumulative measure of discrimination, there was a statistically significant difference between NH Black and NH White women in the high-high depressive symptoms, no discrimination group.

Conclusion: The association between prenatal depressive symptoms and preterm birth varied by race/ethnicity. Our findings suggest screening and intervention for depressive symptoms early in pregnancy may reduce the risk of preterm birth among NH Black women. Future studies with larger sample sizes may yield more insights into effect modification by racial discrimination.

Figure 1. Risk ratios and 95% confidence intervals for the association between first and third trimester depressive symptoms and risk of preterm birth by lifetime racial discrimination among non-Hispanic Black, non-Hispanic White, and Hispanic women
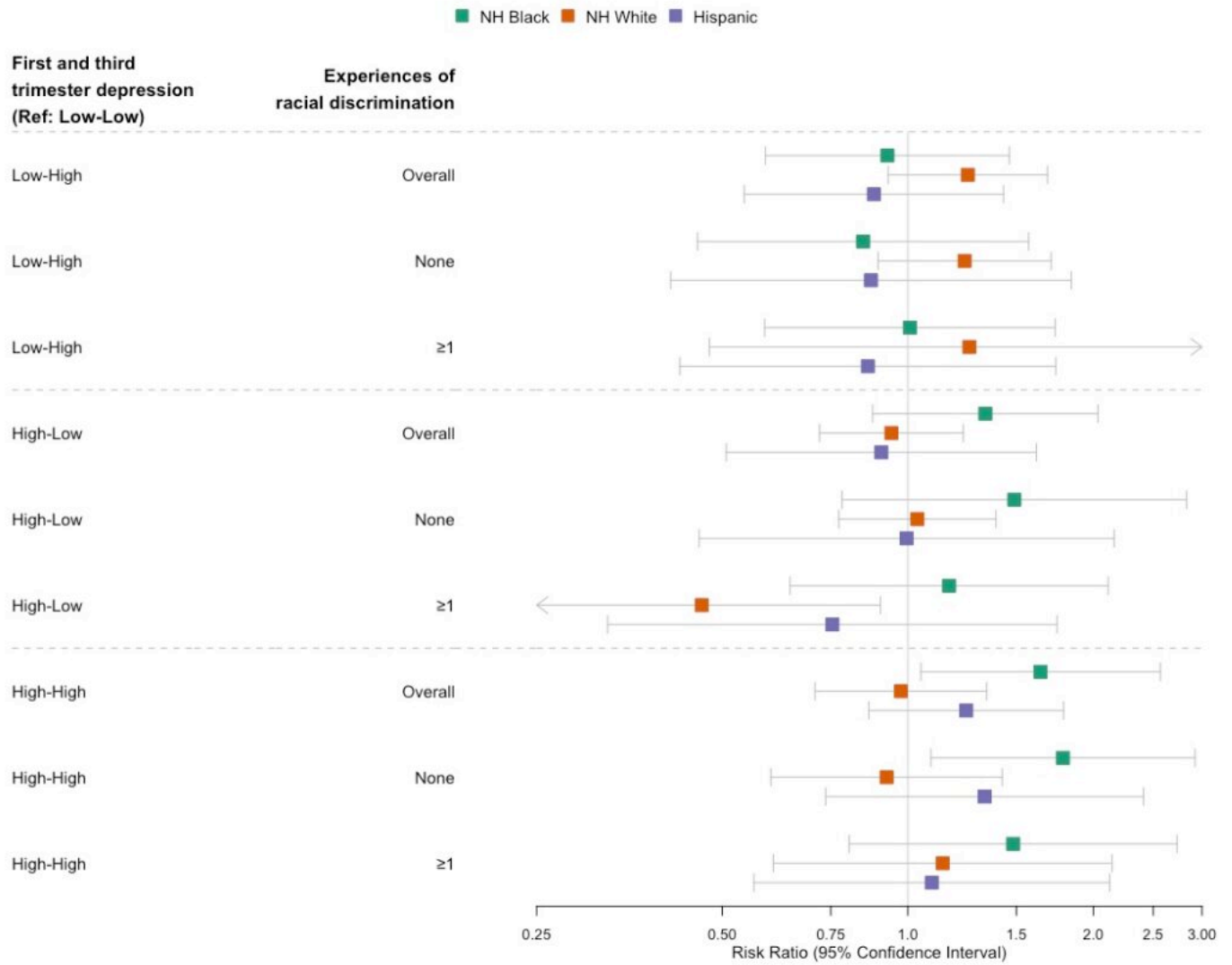
State patterns in maternal deaths due to disparity, 2018-2021 Lauren Rossen* Lauren Rossen Ashley Hirai Amy Branum Sarah Forrest
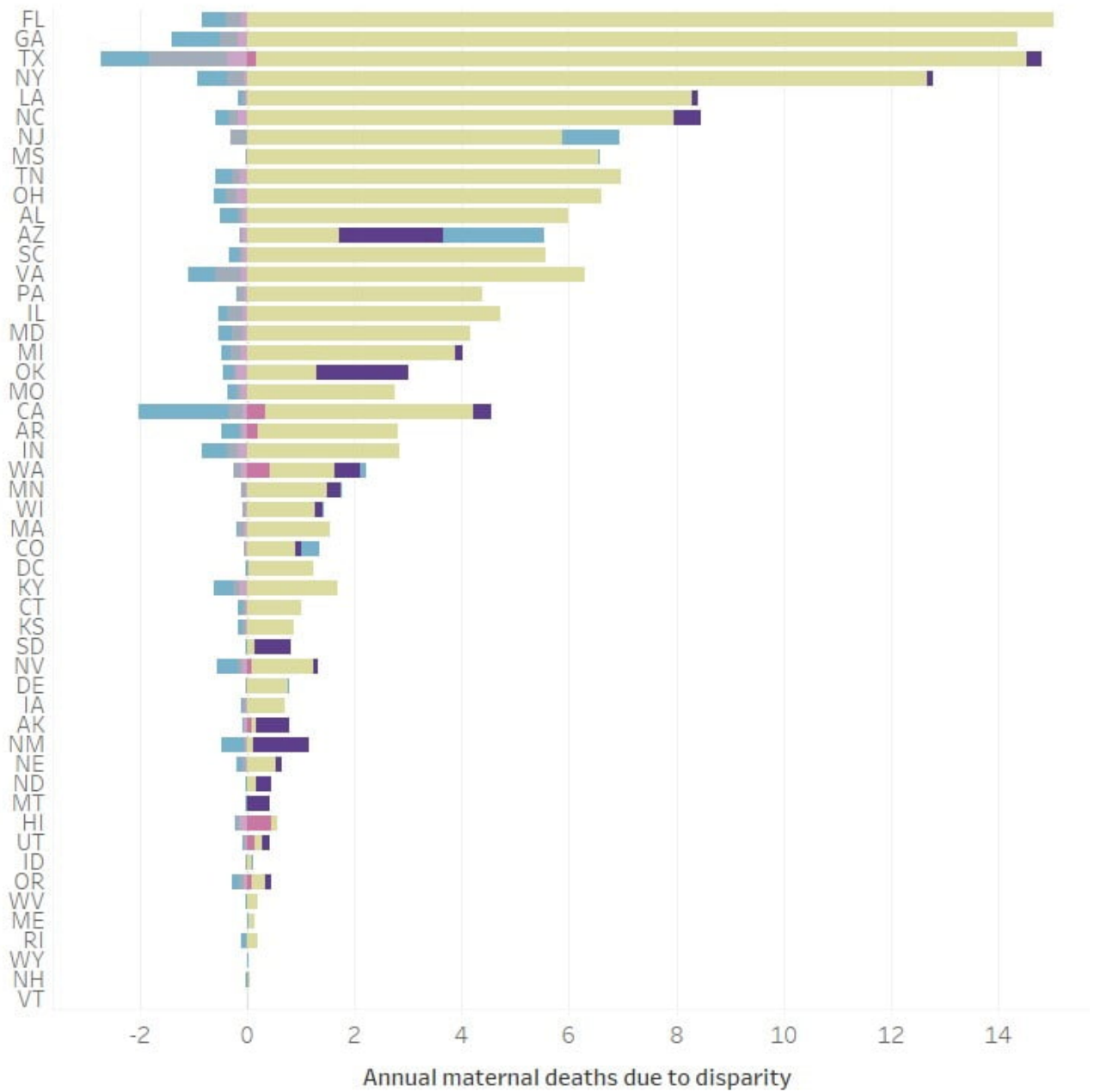
Maternal mortality is a major public health concern in the US. Given small numbers of events (generally <1000/year nationally), it is difficult to assess variation in maternal mortality and related disparities by state, as rates for many subgroups are unreliable. Spatial models can be used to produce more stable estimates for small geographic areas. A recent paper used spatiotemporal models to estimate state-level patterns in maternal mortality by race/ethnicity, but the focus was on trends over time from 1999-2019 and many single-year estimates were still unreliable.

Data on maternal deaths (while pregnant or within 42 days) and corresponding denominators (numbers of live births) were drawn from mortality and birth data from 2018-2021, tabulated by state of residence and race/ethnicity (Hispanic, and the following non-Hispanic [NH] groups: American Indian or Alaska Native [AIAN], Asian, Black, Native Hawaiian or Other Pacific Islander [NHOPI], and White). Log-binomial hierarchical Bayesian models with spatial random effects were used to estimate the number of maternal deaths per 100,000 live births by race/ethnicity, borrowing strength across states and racial/ethnic groups to produce more stable estimates of maternal mortality rates (MMRs). Deaths due to disparity were defined as the number of maternal deaths that could be avoided if all groups had the same rate as non-Hispanic White in each state.

The states with the largest annual number of maternal deaths due to disparities overall and for non-Hispanic Black women were Florida (15), Texas (14), Georgia (14), and New York (13). States with the highest percentages of maternal deaths due to disparity for NH Black women were New York, New Jersey, Colorado, and Mississippi (~66-71%). For NH AIAN women, Washington, Colorado, and Minnesota had the highest percentages.

More granular estimates of maternal mortality disparities at the state level could inform efforts to prevent maternal deaths and reduce inequities.

Figure. Annual Number of Deaths due to Disparity by State and Race/Ethnicity, 2018-2021

Association of polygenic score of birthweight-reducing maternal variants with fetal growth and the influence of parity: a study in two multi-ancestral pregnancy cohorts Prabhavi Wijesiriwardhana* Prabhavi Wijesiriwardhana Tesfa Dejenie Habtewold Guisong Wang Jessica L. Gleason Ronald Wapner Katherine L. Grantz Fasil Tekola-Ayele

Association of polygenic score of birthweight-reducing maternal variants with fetal growth and the influence of parity: a study in two multi-ancestral pregnancy cohorts

Prabhavi Wijesiriwardhana1, Tesfa Dejenie Habtewold1, Guisong Wang2, Jessica L. Gleason1, Ronald Wapner3, Katherine L. Grantz1, Fasil Tekola-Ayele1

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Background: Maternal genetic factors and reproductive history such as nulliparity have been associated with lower birthweight. However, it is unknown when the maternal genome begins to influence fetal growth and whether the effect varies by parity. This study aims to i) determine the gestational week in which maternal birthweight-reducing genetic variants influence fetal growth, and ii) assess whether the associations vary by parity.

Methods: Discovery analyses for weekly fetal growth measures (at 10-40 weeks gestation) were performed using a multi-ancestral cohort of pregnant women recruited through the NICHD Fetal Growth Studies-Singletons (n=1944; nulliparous n=885). Replication analyses for estimated fetal weight were performed using the nuMoM2b multi-ancestral cohort of nulliparous women (n=6058). Genetic risk score (GRS) was derived from 32 and 33 previously identified birthweight-reducing maternal variants, in the discover and replication cohorts, respectively. Parity was categorized as nulliparous and multiparous (i.e., ≥1 previous delivery ≥20 weeks' gestation). Associations of GRS with fetal growth measures were tested using linear regression adjusted for fetal sex and top 10 genetic principal components.

Results: GRS was significantly associated with lower fetal weight from gestational week 31 onwards (β at week 31=-8.59, 95%CI= -16.99, -0.19 grams), shorter humoral and femur lengths, and smaller head circumference beginning at 21, 29, and 31 weeks, respectively. Among nulliparas, all associations began earlier, and effect sizes strengthened (e.g., week 20 onwards in the discovery cohort, week 23 onwards in the replication cohort for fetal weight), but none was significant among multiparas.

Conclusions: Birthweight-reducing maternal genetic factors exhibited the earliest association with fetal skeletal bones followed by head circumference and overall weight. The pronounced association among nulliparas suggests a larger influence on physiological adaptations at first pregnancy and warrant further study.

Who do we leave out when we exclude discordant birth certificate records? Ruby Barnard-Mayers* Ruby Barnard-Mayers Martha Werler

Background: Many studies on maternal and child health use birth certificate data. However, this data is not always consistent, and individuals with discrepancies are often excluded from analyses, as their information can't be assumed to be reliable.

Objective: The purpose of this study is to understand who we exclude when we exclude discrepant records from birth certificate data.

Methods: Birth certificate data from the Pregnancy and Early Life Longitudinal (PELL) data system, which links birth certificate and hospital discharge records in Massachusetts from 2011 to 2018. For 4 conditions (pregnancy risk factor, delivery procedure, test or screening procedure, and labor and delivery complication) the birth certificate has a check box to indicate 'No." After each, the birth certificate has a list of specific conditions for checking off when present (

Results: Of the 552,806 births, 9,737 (1.8%) were discrepant. The most common discrepancy was for labor and delivery complications (67%), followed by tests and procedures (24%), parity (11%), pregnancy risk factors (6%), and finally delivery procedures (0.2%). Compared to birthing people with non-discrepant record, those with discrepant records were, on average, about one year older, were more likely to have private insurance (63.4% vs. 49.1%), were more likely to have a college degree (58.3% vs. 46.0%), were less likely to have a vaginal delivery (53.3% vs. 66.4%), and were less likely to have prenatal care (87.3% vs. 95.2%). Birthing people with discrepant records also appeared more likely to be non-Hispanic Black (18.4 vs. 9.9%) Distributions of BMI, parity, and country of birth were similar for the two groups.

Conclusion: Birthing people with discrepant birth certificate records differ from those without such discrepancies on socio-economic and reproductive indicators, raising the possibility of bias arising from their exclusion. Further research should focus on the potential impact excluding these people from analyses may have on results.

Table 1. Comparison of Birthing People with Discrepant and non-discrepant records

Variable	Discrepant Records	Non-Discrepant Records
Race		
API	906 (9.3%)	49,129 (9%)
Hispanic	1,847 (19%)	100,654 (18.5%)
NAA	46 (0.5%)	3,596 (0.7%)
NHB	1,792 (18.4%)	53,617 (9.9%)
NHW	5,058 (51.9%)	326,523 (60.1%)
Missing	88 (0.9%)	9,550 (1.8%)
Insurance Payer		
Free Care	154 (1.6%)	13,397 (2.5%)
Private	6,171 (63.4%)	266,718 (49.1%)
Public	3,293 (33.8%)	243,416 (44.8%)
Self-Pay	119 (1.2%)	18,803 (3.5%)
Missing	0 (0%)	735 (0.1%)
Age		
Mean (SD)	31.5 (5.77)	30.3 (5.67)
Median [Min, Max]	32 (15.0, 52.0)	31 [12.0, 80.0]
Missing	0 (0%)	4 (0%)
Education		
< HS	548 (5.6%)	52,808 (9.7%)
HS Degree	3,414 (35.1%)	227,666 (41.9%)
College+	5,675 (58.3%)	250,003 (46%)
Missing	100 (1%)	12,592 (2.3%)
BMI		
Mean (SD)	25.4 (5.87)	25.8 (5.99)
Median [Min, Max]	23.9 [11.0, 69.7]	24.4 [9.40, 93.9]
Missing	744 (0.076%)	33,805 (0.062%)
Marital Status		
Married	6,801 (69.8%)	355,878 (65.5%)
Not Married	2,936 (30.2%)	185,909 (34.2%)
Missing	0 (0%)	1,282 (0.2%)
Prenatal Care		
Any Prenatal	8,497 (87.3%)	517,138 (95.2%)
No Prenatal Care	34 (0.3%)	2,710 (0.5%)
Missing	1,206 (12.4%)	23,221 (4.3%)
Country of Birth (mother)		
Foreign	3,194 (32.8%)	161,132 (29.7%)
PR	166 (1.7%)	13,622 (2.5%)
US	6,374 (65.5%)	368,089 (67.8%)
Missing	3 (0%)	226 (0%)
Parity		
Mean (SD)	1.77 (1.06)	1.88 (1.11)
Median [Min, Max]	1 [1.00, 13.0]	2 [1.00, 22.0]
Missing	2 (0)	2,190 (0.004%)
Delivery Method		
Primary CS	1,905 (19.6%)	92,681 (17.1%)
Repeat CS	2,277 (23.4%)	75,196 (13.8%)
Vaginal	5,192 (53.3%)	360,615 (66.4%)
VBAC	363 (3.7%)	13,901 (2.6%)
Missing	0 (0%)	676 (0.1%)

Pharmacoepidemiology

Antiseizure medications use and the incidence of Parkinson's disease: A retrospective cohort study in Manitoba, Canada Laila Aboulatta* Laila Aboulatta Qier Tan Sherif Eltonsy

Introduction
Recent studies demonstrated and association between antiseizure medications (ASMs) and an increased risk of Parkinson's disease (PD). Our aim is to investigate the association between ASMs and incidence of PD.

Methods
Using the provincial administrative health databases in Manitoba, Canada, we conducted a population-based study including individuals aged >25 years from April 2008 to March 2022. We included all ASMs excluding clonazepam and safinamide, and examined individuals exposed to 1 ASM (monotherapy), >2 ASMs (polytherapy) and divided individuals into quartiles based on number of prescriptions issued. We examined the 7 most prescribed ASMs and defined PD diagnosis using ICD 9 and 10 codes. We used logistic regression models, adjusting for age, sex, and epilepsy to calculate ORs and 95% CI.

Results
During the study period, 63,286 individuals were exposed to ASMs and 883,667 were unexposed. Among the exposed group, 58.03% were female and 20.04% had epilepsy. We observed higher PD incidence among the exposed groups compared to the unexposed group. Excluding gabapentin, the odds of PD incidence significantly increased with any ASM use with adjusted OR of 1.34 (95%CI 1.11-1.62) and polytherapy (aOR=1.68,95% CI 1.31-2.15). Individuals in the fourth quartile, had higher odds of developing PD (aOR=2.44,95% CI 2.03-2.93) compared with individuals in quartile 1 (aOR=0.54, 95% CI 0.43-0.67). PD Incidence was significantly associated with the use of valproic acid (aOR=2.94,95% CI 2.42-3.58), levetiracetam (aOR=2.094,95% CI 1.602 -2.738), lamotrigine (aOR=1.91;95% CI 1.43-2.54), and gabapentin (aOR=1.48,95% CI 1.25-1.75).

Conclusion
Over the 15-year study period, we found an association between ASMs and PD incidence. Lamotrigine, levetiracetam, valproic acid and gabapentin were associated with increased risk of PD. Our findings provide insights into potential risks and future research are warranted to understand underlying mechanisms.

Pharmacoepidemiology

Sodium-Glucose Cotransporter 2 (SGLT2) Inhibitor Initiation and Pancreatic Cancer Prognosis Juhua Luo* Juhua Luo Fengge Wang Yu Du Michael Hendryx

INTRODUCTION: Emerging findings from laboratory studies indicate that sodium-glucose cotransporter 2 inhibitors (SGLT2i), a relatively new class of antidiabetic drugs, may offer therapeutic benefits in cancer treatment. Pancreatic cancer is a devastating disease with a 5-year survival rate of only around 12%. The aim of this study was to test the hypothesis that initiation of SGLT2i may improve pancreatic cancer prognosis.

METHODS: We conducted a study using the National Surveillance, Epidemiology, and End Results (SEER) and Medicare linked data in the United States to assess the impact of initiating SGLT2i on the survival of patients diagnosed with pancreatic cancer. The study included 6373 individuals aged 66 years or older, newly diagnosed with pancreatic cancer between 2014 and 2017, and with pre-existing type 2 diabetes. Participants were followed until the end of 2019. Data regarding the initiation of SGLT2i were obtained from the Medicare Part D file. Among the study sample, 309 (5%) used SGLT2i. Propensity score matching was used to control for potential confounding.

RESULTS: SGLT2i was marginally associated with lower mortality among patients with pancreatic cancer and type 2 diabetes (HR=0.85, 95% CI=0.71-1.01). The association was more pronounced with duration of drug use more than one year (HR=0.67, 95% CI=0.49-0.90). By using Dipeptidyl peptidase 4 inhibitors (DPP4i) as an active comparator in a sensitivity analysis, SGLT2i initiation was not significant overall but longer duration of SGLT2i use remained significant (HR=0.79, 95%CI=0.63-0.98).

CONCLUSION: Our large study utilizing SEER-Medicare linked data suggests that SGLT2i use is linked to improved overall survival among pancreatic cancer patients with pre-existing type 2 diabetes when compared to those not using SGLT2i or to those using DPP4i. Further research is needed to validate these findings and explore the potential mechanisms underlying this association.

Pharmacoepidemiology

Adherence Differences Between Infusible and Injectable Biologics Among Patients with Rheumatoid Arthritis During the COVID-19 National Emergency Jonathan P DeShazo*

Jonathan DeShazo Djeneba Audrey Djibo Erick Moyneur Cheryl Walraven-McMahill

Background: Patients must adhere to the therapeutic regimen to achieve the best clinical outcomes. COVID-19 presented numerous barriers to RA patients taking biologics, particularly those receiving infusions in a healthcare setting. Previous work has suggested a decrease in infusible biologic adherence for non-RA conditions, yet the effect on RA infusible therapy as well as non-infusible RA therapy (e.g., self-injection) are unknown.

Objective: To assess changes in adherence during the COVID-19 emergency among RA patients taking infusible and injectable biologics.

Methods: We conducted a retrospective, repeated, cross -sectional analysis of administrative claims for enrollees aged 18 years and above with an RA diagnosis and established on a biologic. We compared medication possession patio (MPR) and persistence among independent cohorts for 2019, 2020, and 2021 using a mixed model adjusting for age, race, and comorbidity. The analysis window was March 1 until discontinuation or December 31 of the cohort year. Persistence was calculated as days between March 1 and last dispense, plus last days' supply. MPR was calculated as days' supply dispensed divided by days in analysis window.

Results: Cohort 2019 (n=6,246), Cohort 2020(n=7,771), and Cohort 2021(n=7051) were comparable in biologics, sex, ethnicity, history of specific comorbidities, and combined comorbidity score.

2020 had significantly lower MPR compared to 2019 for most of the injection biologics(p<.001). This was followed by a significant increase in 2021 MPR(p<.001). MPR drops were not measured in either infusion-only biologic, but Rituximab persistence decreased in 2020(p<.001).

Conclusions: Adherence among RA patients taking most biologics declined in 2020, exhibited by lower MPR in some injectables and lower persistence in some infusions. This work suggests that COVID-19 impacted biologic adherence among RA patients in ways more complex than previously considered.
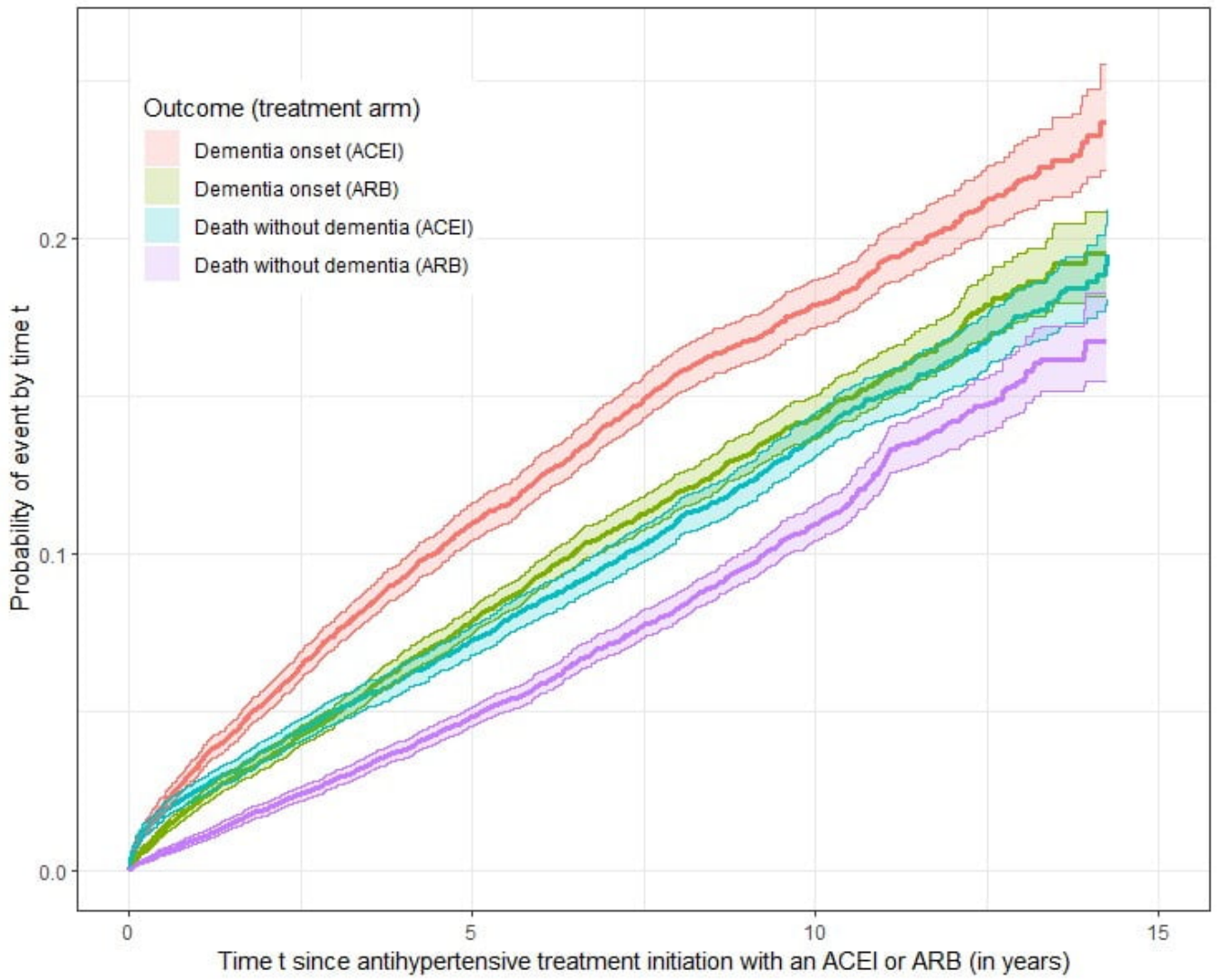
Persistence and MPR by Biologic During COVID-19
(Annually, March 1 - December 31 analysis window)

Pharmacoepidemiology
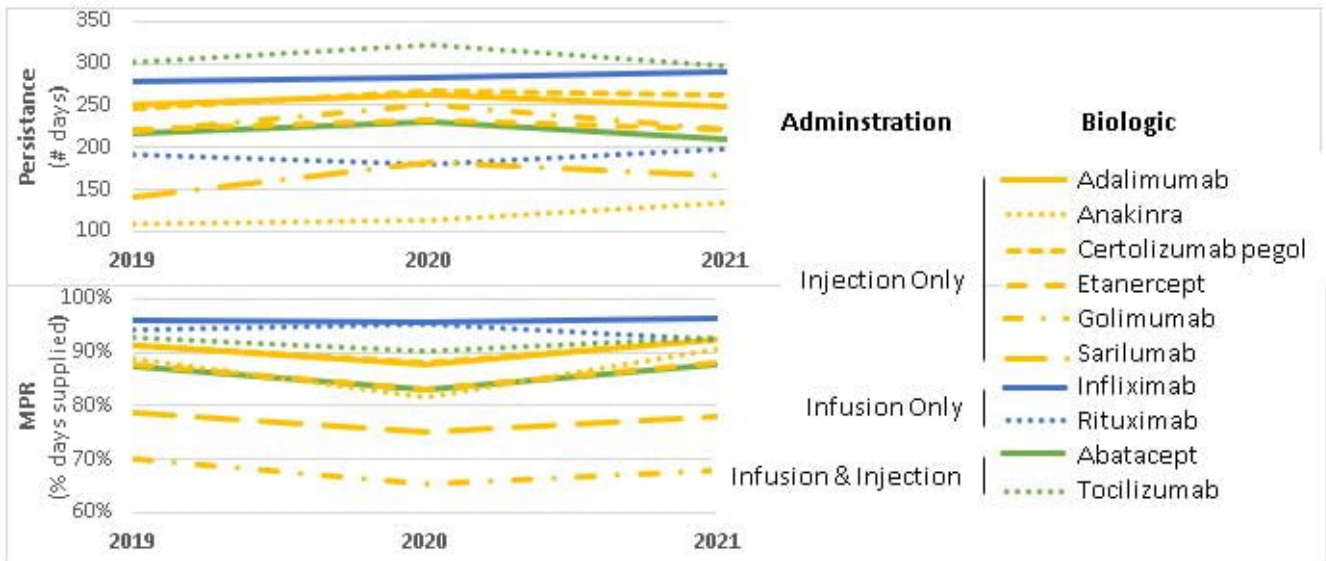
Antihypertensive target trial emulation for dementia prevention: combining US electronic health records with weighting strategies to inform drug repurposing alternatives Marie-Laure Charpignon* Marie-Laure Charpignon Bella Vakulenko-Lagun Colin Magdamo Bowen Su Sudeshna Das Anthony Philippakis Munther Dahleh Deborah Blacker Mark Albers

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 patients aged 50+, applying Inverse Propensity score of Treatment Weighting to balance the two treatment arms and accounting for competing risk of death. In a cause-specific Cox Proportional Hazards (PH) model, the hazard of dementia onset was lower in ARB vs ACEI initiators (HR=0.72 [95% CI: 0.68-0.77]). Findings were robust to outcome model structures (i.e., Cox PH vs nonparametric) and generalized to patients with no hypertension diagnosis at initiation. Our trial emulation suggests that ARB initiation may reduce the risk of dementia onset. Future work will evaluate differential effects by brain penetrance and the mediating role of blood pressure control in dementia prevention.

Outcome (treatment arm)
- Dementia onset (ACEI)
- Dementia onset (ARB)
- Death without dementia (ACEI)
- Death without dementia (ARB)

The Mediation Effect of Social Support on the Relationship Between Psychological Distress and Gratitude, Life Satisfaction, and Resilience following Hurricane Katrina Erin C. McCanlies* Erin C. McCanlies Monica Leppma Ja Kook Gu John M. Violanti

Background: Hurricane Katrina brought numerous challenges for police officers working in the New Orleans geographic area. This study evaluated potential protective factors that may mitigate symptoms of distress in police officers.

Methods: This cross-sectional study examined if social support mediates the relationship between the gratitude, resilience, and satisfaction with life and psychological distress in 111 police officers (30 females; 81 males) from the area impacted by Hurricane Katrina in Louisiana. The Interpersonal Support Evaluation List, Connor-Davidson Resilience scale, Satisfaction with Life Scale, and the Gratitude Questionnaire measured positive psychological factors. The Brief Symptom Inventory was used to measure psychological distress. Ordinary least square regression mediation analysis estimated direct and indirect effects between the study variables. Both unadjusted and adjusted models were estimated.

Results (Table 1): Higher gratitude was associated with higher social support, which was associated with a lower distress score. The total and direct effects were significant, but the indirect effect was not, indicating that gratitude has a direct effect on distress independent of social support. Higher resilience was positively associated with higher social support, which was negatively associated with distress. Both the direct and indirect effects were significant, indicating that resilience indirectly affects distress through social support. Lastly, satisfaction with life was positively associated with social support, which was negatively associated with distress. The direct and the indirect effects were significant, indicating that social support mediates the relationship between satisfaction with life and distress.

Conclusion: Social support mediates the relationship between both resilience and satisfaction with life to reduce psychological distress. Although social support did not mediate the relationship, gratitude was also associated with lower psychological distress. In general, these results indicate that targeting positive psychological factors including gratitude, resilience, and satisfaction with life may help mitigate symptoms of distress in police.

Table 1. Direct and indirect effects between satisfaction with life, resilience, gratitude and psychological distress mediated by social support

	Exposure (X)	Mediator (M)	Outcome (Y)		Unadjusted Model		
	Exposure (X)	Mediator (M)	Outcome (Y)		Total effect (= c)	Direct effect (= c')	Indirect effect (= ab)
					Coeff (95% CI)	Coeff (95% CI†)	Coeff (95% CI)
1	SWL	ISEL	log(BSI GSI)		-0.091 (-0.120, -0.062)*	-0.068 (-0.102, -0.035)*	-0.022 (-0.043, -0.008)*
2	Resilience	ISEL	log(BSI GSI)		-0.088 (-0.127, -0.049)*	-0.057 (-0.097, -0.016)*	-0.031 (-0.055, -0.013)*
3	Gratitude	ISEL	log(BSI GSI)		-0.082 (-0.113, -0.051)*	-0.051 (-0.091, -0.011)*	-0.031 (-0.062, -0.009)*
					Adjusted Model‡		
	Exposure (X)	Mediator (M)	Outcome (Y)		Total effect (= c)	Direct effect (= c')	Indirect effect (= ab)
					Coeff (95% CI)	Coeff (95% CI†)	Coeff (95% CI)
1	SWL	ISEL	log(BSI GSI)		-0.090 (-0.124, -0.055)*	-0.071 (-0.113, -0.030)*	-0.018 (-0.042, -0.001)*
2	Resilience	ISEL	log(BSI GSI)		-0.080 (-0.122, -0.037)*	-0.048 (-0.092, -0.005)*	-0.031 (-0.059, -0.013)*
3	Gratitude	ISEL	log(BSI GSI)		-0.076 (-0.109, -0.043)*	-0.055 (-0.100, -0.009)*	-0.022 (-0.051, 0.001)

† Bootstrapping 95% confidence interval

* The 95% confidence interval is significant.

‡ Adjusted age, alcohol consumption, and sick days increase since Katarina for model #1 and #3

  Adjusted age, race, and sick days increase since Katarina for model #2

Joint Effect of Maternal Smoking Patterns during Pregnancy and Pre-Pregnancy BMI on Infant Birth Outcomes Rachel E. Wacks* Rachel Wacks Christian P. Daniele Cassandra N. Spracklen

Background: The independent relationships between smoking during pregnancy or pre-pregnancy BMI (ppBMI) and increased risks for adverse maternal and fetal pregnancy outcomes are well understood. However, little is known about the potential interaction between patterns of smoking during pregnancy and ppBMI. As such, we aimed to evaluate the combined association between smoking patterns during pregnancy and ppBMI with risks for delivering an infant born small for gestational age (weight <10th % for gestational age; SGA), low or high birthweight (<2500g or >4000g; LBW or HBW), or preterm (<37 weeks; PTB).

Methods: Within the Iowa Health in Pregnancy Study (IHIPS), a population-based case-control study of PTB and SGA infants, 2,308 women completed a computer-assisted telephone interview in which they reported smoking during pregnancy (ever/never) during the index pregnancy. ppBMI and infant outcomes were obtained from prenatal and hospital delivery records. Multivariable logistic regression analyses were performed to assess the associations and potential interactions between ppBMI and smoking patterns during pregnancy on infant outcomes.

Results: Of 2,308 included IHIPS participants, there were 504 SGA (25.71%), 806 PTB (29.3%), 330 LBW (12.0%), and 121 HBW (4.4%) infants. Smoking during pregnancy was independently associated with LBW (OR: 1.79; 95% CI 1.45-2.09), SGA (OR: 1.57; 95% CI 1.22-2.01), and HBW (OR: 0.49; 95% CI 0.28-0.85). Having a ppBMI ≥30 was independently associated with PTB (OR: 1.45; 95% CI 1.16-1.81) and LBW (OR: 1.24; 95% CI 1.01-1.53), while having a ppBMI of 25.0-29.9 was a statistically significant predictor for HBW (OR: 1.78; 95% CI 1.16-2.71) and SGA (OR: 0.73; 95% CI 0.56-0.96).

Conclusions: We did not detect effect modification between smoking during pregnancy and ppBMI.

Reproductive

Reproductive Health Services at a Regional Health System Zoe Herrera* Zoe Herrera Erin Massey

Background

Samaritan Health Services (SHS), a 5 hospital system, provides care to patients living throughout 3 counties in Western Oregon. Since 2016, providers at SHS have anecdotally noted an increase in patients seeking long term contraception methods. Specifically, it has been noted that after the overturning of Roe vs Wade there was an increase in nulliparous young female patients seeking tubal ligations. This study aims to describe and compare utilization of reproductive health services over the last 10 years.

Methods

Patients who presented to a Samaritan facility for reproductive services between 01/01/2014 and 12/31/2023, will be included. Data will be extracted from electronic medical records. Data on vasectomies, tubal ligations, and long-term contraception methods (implants and intrauterine devices) will be collected. Encounter volume and patient demographics will be compared over the study period.

Results

Results pending, data collection ended December 31st, 2023. The distribution of services over the study period will be explored using a time series analysis. Patient demographics will be compared using descriptive statistics. A sub-analysis is planned to identify changes pre and post the overruling of Roe vs Wade.

Conclusions

Data will be used to identify changes in patient demographics and encounter volume for reproductive services following significant legislative change. Findings may help to provide evidence-based justification for increased funding for reproductive services.

Reproductive

Preconception folic-acid containing supplement use and associated factors in the Birth Defects Study To Evaluate Pregnancy exposureS (BD-STEPS) Anne Marie Darling* Anne Marie Darling Eirini Nestoridi Rashida Smith-Webb Wendy Nembhard Jenil Patel Bailey Wallace Shannon Evans Suzan Carmichael Gary Shaw Mahsa Yazdy

Background: Preconception folic acid supplementation has been recommended to prevent neural tube defects for the past 30 years, but there is suboptimal adherence to this recommendation. We sought to determine the prevalence of preconception folic acid-containing supplement use and associated factors in a population-based sample. **Methods:** This study included 1,371 BD-STEPS participants who gave birth to liveborn infants without birth defects between 2014-2019. Participants completed computer-assisted telephone interviews pertaining to their demographics, lifestyle, and health. Modified Poisson regression models were used to evaluate associations between these factors and folic acid-containing supplement use. Eight multivariable models were constructed based on confounders identified through directed acyclic graphs and implemented in the following sequence: pre-birth factors, education, geographic factors, pregnancy history, socioeconomic factors, pregnancy intention, lifestyle factors, and health status. Each model included all variables from the preceding models. **Results:** Only fifty percent of participants reported preconception folic acid-containing supplement use. Participants aged 25 years and younger were less likely to report supplement use compared to those aged 25-34 (RR 0.47, (95% CI 0.37, 0.60)). Participants planning to become pregnant were twice as likely to report supplement use (RR 2.11, (95% CI 1.77, 2.51)) compared to those who were not. Those who had health insurance (RR 1.49 (95% CI 1.09, 2.03)) and those with partners who had completed college (RR 1.48, (95% CI 1.00, 2.19)) were also more likely to report supplement use compared to those who did not. None of the other assessed variables showed an association. **Conclusions:** Adherence to folic-acid supplement recommendations continues to fall short of targets. Patterns of use are similar to those identified previously.

Current breastfeeding and blood lead concentrations in U.S. premenopausal individuals: Results from NHANES 2003-2012 Kristen Upson* Mandy S. Hall Arianna V.E. Foster Nicole M. Talge Renee Heffron Robert O. Wright Julio Landero Michael Yin Flavia Matovu Quaker E. Harmon Kenneth Mugwanya Andrew Mujugira Chenxi Li Kristen Upson

To meet infant nutritional needs, calcium is mobilized from maternal skeleton during lactation. We hypothesized that greater bone remodeling with breastfeeding also increases mobilization of toxic metal lead (Pb) stored in bone to blood. We conducted a cross-sectional analysis using National Health and Nutrition Examination Survey (NHANES) 2003-2012 data. The study population comprised premenopausal individuals ages 20-42 with an intact uterus, ≥1 ovary, and blood Pb data (unweighted n=4,209). Accounting for the complex survey sampling, we used multivariable linear regression to estimate the percent difference in blood Pb levels and 95%CI by current breastfeeding status; we adjusted for age, education, smoking, alcohol use, NHANES year, 25-hydroxyvitamin D, calcium intake, energy intake, current hormonal contraceptive use, and pregnancy status. Those currently breastfeeding had a higher geometric mean Pb concentration (0.88 µg/dl, 95%CI: 0.80, 0.97) compared to others (0.77 µg/dl, 95%CI: 0.75, 0.78). Current breastfeeding was associated with 20% higher blood Pb levels (95%CI: 9%, 33%). We explored the underlying mechanism using NHANES 1999-2002 data that had bone turnover marker data (bone alkaline phosphatase (BAP) and N-terminal telopeptides (NTX)). We observed 46% higher BAP (95%CI: 32, 61) and 50% higher NTX (95%CI: 17, 91) with current breastfeeding. Among those not currently breastfeeding, those with higher BAP levels (third vs. first tertile) had 19% higher blood Pb levels (95%CI: 6, 33); those with higher NTX levels (third vs. first tertile) had 13% higher blood Pb levels (95% CI:-2, 31). We yielded similar results among those who had given birth in the past year. These data suggest increased blood Pb levels with current breastfeeding from greater bone turnover and skeletal mobilization of Pb. Given the health benefits of breastfeeding, replication of our findings and investigation into factors that mitigate skeletal mobilization of Pb are warranted.

Reproductive

Subjective sleep health and menstrual cycle characteristics in a North American prospective cohort study Chad M. Coleman* Chad M. Coleman Traci N. Bethea Tanran R. Wang Andrea S. Kuriyama Julia C. Bond Wendy Kuohung Yael I. Nillni Lauren A. Wise Amelia K. Wesselink

Introduction: Menstrual cycle disturbances affect up to 30% of reproductive-aged individuals. Few studies have examined the effect of sleep on menstrual cycle characteristics.

Methods: We estimated the associations of subjective sleep duration and quality with menstrual cycle characteristics in Pregnancy Study Online, a web-based North American preconception cohort study (2013-2023). Eligible participants were aged 21-45 years, assigned female sex at birth, and not using contraception or fertility treatment. On the baseline questionnaire, participants reported sleep duration (hours/day) in the past month. Beginning in October 2020, we assessed sleep quality in the past month via the Pittsburgh Sleep Quality Index (PSQI). On a follow-up questionnaire completed 8 weeks after baseline, participants reported menstrual cycle characteristics, including regularity, cycle length, bleed length, flow volume, intermenstrual bleeding, and menstrual pain. We used log-binomial regression models to estimate prevalence ratios (PRs) and 95% CIs adjusting for socio-demographic, behavioral, and reproductive factors.

Results: Short (<6 hours/day) and long (≥9 hours/day) sleep durations were associated with increased prevalence of prolonged bleed length (≥7 days; PRs vs. 7-<9 hours/day=2.10 [CI: 0.99-4.45] and 1.64 [CI: 0.89-2.99], respectively) and intermenstrual bleeding (PRs=1.59 [CI: 1.01-2.51] and 1.50 [CI: 1.05-2.14], respectively). Relative to good sleep quality (PSQI ≤5), poor sleep quality (PSQI >5) was associated with prolonged bleed length (PR=1.44 [CI: 0.93-2.23]), intermenstrual bleeding (PR=1.13 [CI: 0.88-1.45]), and severe menstrual pain (PR=1.29 [CI: 1.09-1.53]). Sleep duration and quality were not appreciably associated with other menstrual characteristics.

Conclusions: Sleep duration and quality were associated with menstrual cycle disturbances in this cohort. As sleep is a modifiable health behavior, this work may inform interventions to improve gynecologic health.

Depression is purple, but unmet need for treatment is red Catherine Ettman* Catherine Ettman Ross Hatton Brian Castrucci Sandro Galea

As depression becomes more visible in the public conversation, it has also become bound in national divides, with suggestions that depression is more likely among persons who affiliate with one political party. We sought to assess 1) whether depression is associated with political party affiliation and 2) the use of mental health care by political affiliation. Using a nationally representative sample of U.S. adults (N=2,325) surveyed in March-April 2023, we assessed the relation between political party and 1) positive screen for depression (PHQ-9>9) or anxiety (GAD-7>9), and 2) self-reported use of a mental health care provider in the past 12 months. We used logistic regression models and adjusted for social and economic characteristics to test for differences by political party in the predicted probability of a positive PHQ or GAD screen and reporting not having seen a mental health provider in the past 12 months. Adjusted models controlled for: sex, race and ethnicity, age, education, household income, home ownership, parent status, marital status, and metropolitan status). The weighted prevalence of depression was 19.2% among Republicans and 24.2% among Democrats, but these differences were not statistically significant (p=0.07). In adjusted models controlling for sociodemographic factors, the adjusted prevalence of depression was 21.2% among Republicans and 25.3% among Democrats (p=0.152). However, in both unadjusted and adjusted models, Republicans were significantly more likely (88.3% in unadjusted and 86.8% in adjusted) to report not having seen a mental health provider in the past 12 months relative to Democrats (76.2% in unadjusted models <0.01 and 76.6% in adjusted models, p <.01). Results were consistent for symptoms of anxiety. Poor mental health is common across Democrats and Republicans; however, use of mental health care is lower among Republicans than Democrats. Lower use of mental health care may be due to stigma (demand) or lack of access to health care (supply). Mental health and access to mental health care may be bipartisan public health topics to pursue during the 2024 election and in coming years. Mental health could be a national priority that unites the U.S. population in increasingly divided times.

Figure 1. Adjusted Odds Ratios for Positive PHQ and GAD Screens by Political Party
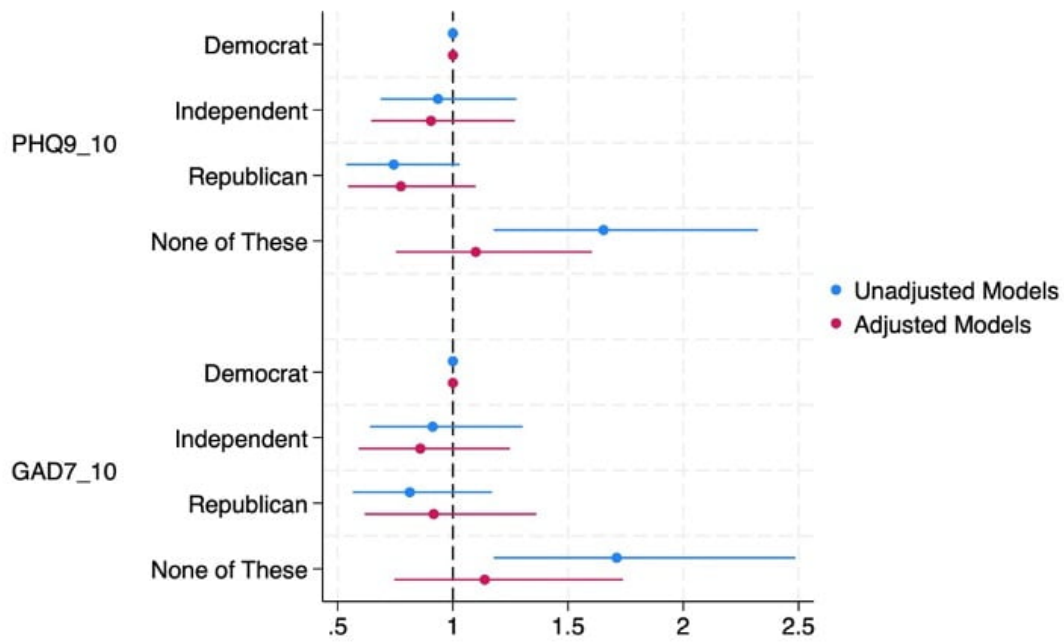
Desirable properties of public health communication tools on ambient air quality from muti-pollutants for better interpretation Hwashin H. Shin* Hwashin Shin Hwashin H. Shin Patrick Brown Guowen Huang

Background: Adverse health effects of ambient air pollutants (AP) have been reported worldwide, and public health communication tools were introduced to mitigate AP-related health risks. The Air Quality Health Index (AQHI) considers AP-related health risks, whereas the Air Quality Index (AQI) considers air pollutant concentrations. Existing communication tools may be insensitive to unpredicted high AP concentrations (e.g., wildfires), and interpretations of the index levels are unclear.

Methods: To convert air quality of multiple pollutants to a simple metric, we consider three components of the metric: reference risk, levels (or scales), and between-level differences. The public communication metric should be: 1) determined by relative health risk attributable to real-time air quality; 2) based on relevant reference risk; 3) accounted for general population and vulnerable subpopulations; and 4) transparent and interpretable. The WHO global air quality guidelines offer thresholds and limits for key APs that pose public health risks, which can serve public health communication metrics as an international reference risk, not varying over country.

Results: Taking the WHO global air quality guidelines as the reference risk, we propose (N+1)-point levels (1 to N and N+), which can be determined based on linear or non-linear concentration-response function (CRF). Using Canadian data of 47 census divisions (60% of population), we demonstrate an example based on a linear CRF, where: N=10, reference risk N=5, and between-level difference indicates ±1.5% increases/decrease in relative risk. Overall this metric is responsive to Canadian wildfire events in the past years and interpretation of the level becomes clearer compared to the WHO guidelines.

Conclusions: If the three components (reference risk, levels and between-level differences) are used internationally, the public health communication tools would become more transparent and interpretable based on global standards.

Disparities in Colorectal Cancer Screening Among U.S. Immigrants: The Impact of Time in the U.S. and Socioeconomic Factors Khezia Kawaya-Tshola* Khezia Kawaya-Tshola Christian Okitondo

This study explored the factors influencing Colorectal Cancer (CRC) screening among U.S. immigrants, particularly examining the impact of duration of residency in the U.S., socioeconomic factors, and healthcare access. Despite the known effectiveness of CRC screening in reducing mortality, there is a notable disparity in screening rates between U.S. immigrants and native-born Americans.

Data from the National Health Interview Survey spanning 2010-2018 was utilized. The study focused on a sample of 6,537 immigrants aged 50-75, stratified into two distinct groups based on their time in the U.S.: 833 immigrants with less than 15 years in the country, and 5,704 with 15 years or more. The assessment of CRC screening adherence was conducted using sample weight-adjusted multivariable logistic regression, enabling the calculation of adjusted odds ratios (AORs) with 95% confidence intervals (CIs).

The overall CRC screening rate among U.S. immigrants was 50.6%, varying significantly based on time in the U.S. Those in the U.S. for less than 15 years had a rate of 31.5% compared to 53.2% for those with 15 or more years ($p<.001$). Additionally, the likelihood of undergoing screening was significantly higher among immigrants with 15 or more years in the U.S. (AOR 1.57; 95% CI 1.25-1.98; $p<.001$). Health insurance emerged as a critical factor, with insured individuals demonstrating more than double the likelihood of screening compared to uninsured counterparts (AOR 2.12; 95% CI 1.66-2.73; $p<.001$). The presence of a regular healthcare provider was also significantly associated with increased screening likelihood (AOR 2.91; 95% CI 2.23-3.79; $p<.001$).

This study highlights the need for policy efforts to improve healthcare system adaptation among U.S. immigrants, particularly those newly arrived. It emphasizes the crucial role of health insurance and access in enhancing CRC screening rates, underscoring the importance of addressing healthcare disparities in immigrant populations.

Historical state compulsory schooling laws and pandemic-era mortality: A quasi-experimental study Whitney Wells* Whitney Wells Yea-Hung Chen Marie-Laure Charpignon Ah-Reum Lee Ruijia Chen Andrew C. Stokes Jacqueline Torres M. Maria Glymour

Low educational attainment is linked to increased COVID-19 mortality, but it remains unclear whether this link is causal or due to confounding factors, e.g. childhood SES. To address this question, we evaluated if older adults' risk of COVID-19 mortality was associated with historical state-level compulsory schooling laws (CSLs) when they were school-aged. We also evaluated if the impact was unique to COVID-19 or applied to all-cause mortality, before and during the pandemic.

US death certificate data Mar 2019-Dec 2021 were used to define mortality outcomes for people born pre-1964. 2019 American Community Survey data was used to determine the population at risk, representing 78.7 million born pre-1964. We linked individuals to CSLs based on state and year of birth. We estimated intention-to-treat effects of CSLs on mortality using logistic regressions controlling for state-of-birth fixed effects, birth year, sex, race, ethnicity, and state-level factors.

We identified a dose-response relationship between CSLs and mortality. In the first year of the pandemic, people mandated to receive 8 vs 9 (reference) years of education had higher odds of COVID-19 mortality (OR: 1.15; 95% CI: 1.10, 1.19), while those mandated to receive 10 vs 9 (reference) years of education had lower odds of COVID-19 mortality (OR: 0.96; 95% CI: 0.94, 0.98). The association of CSLs with COVID-19 mortality was similar in pandemic years 1 and 2; for all-cause mortality in pandemic years 1 and 2; and for all-cause mortality in the year prior to the pandemic. Results were robust to alternative model specifications.

These findings support a causal benefit of education for reduced mortality during the COVID-19 pandemic. State investments in children's education may have reduced pandemic-era mortality decades later. Our research has implications beyond the pandemic context, as our results suggest the observed relationship mirrors a pre-existing relationship between CSLs and all-cause mortality.

Figure 1. Effect of CSLs on COVID-19 mortality and all-cause mortality, Mar 2019-Dec 2021

COVID-19 mortality

All-cause mortality
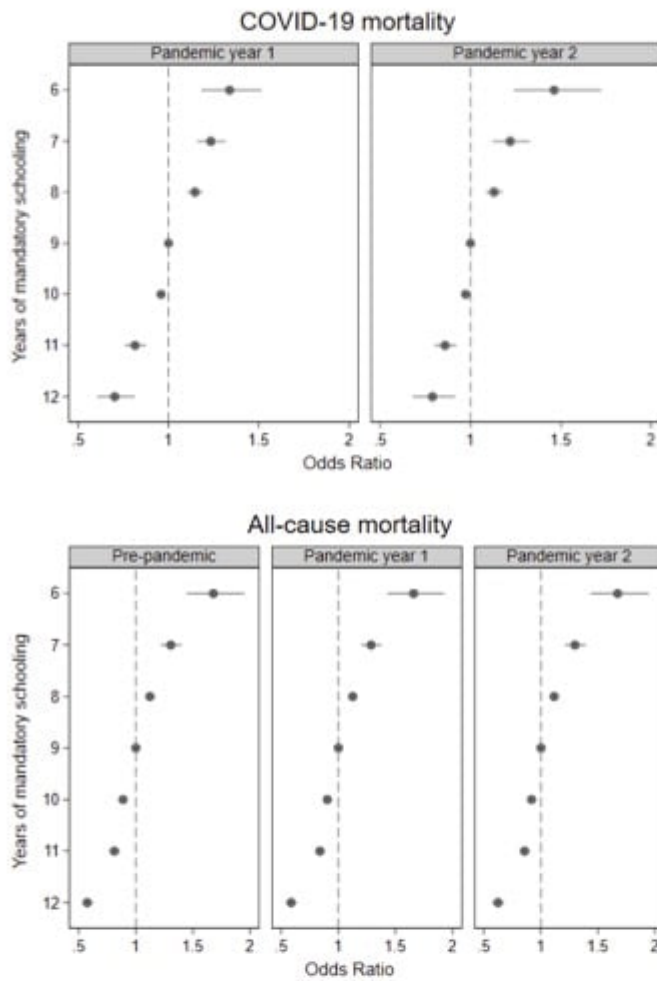
Source: Population from ACS PUMS 1% 2019 and decedents from March 2019 - December 2021 US death certificates, born before 1964. Years are defined as pre-pandemic: Mar 2019-Feb 2020, pandemic year 1: Mar 2020-Feb 2021, pandemic year 2: Mar 2021-Dec 2021. Weighted N=85.1M. Abbreviations: Million (M). American Community Survey (ACS). Public Use Microdata Sample (PUMS). Compulsory Schooling Law (CSL).
Group sizes by years of mandatory schooling are as follows: 6: 0.05%, 7: 0.25%, 8: 11.9%, 9: 67.4%, 10: 11.1%, 11: 3.5%, 12: 5.7%.

1

Social

Adverse Childhood Experiences and Utilization of Preventive Healthcare among Children in Rural Communities in the United States (NHIS 2022) Mary Labuhn* Mary Labuhn Andrew Williams

Background. Children residing in rural communities have increased risk for Adverse Childhood Experiences (ACEs), and children in rural communities are less likely to receive preventive healthcare. Additionally, the associations between ACEs and health behaviors may be sex specific. Given rural-urban disparities in chronic health conditions, examination of drivers of these disparities is needed.

Methods. Data for children between the ages of 9 and 17 (weighted n=3,949,102) were collected from the 2022 National Health Interview Survey. Sample included those identified as residing in "nonmetropolitan" areas according to the 2013 NCHS Urban-Rural Classification. Physician visit in the past 12 months (yes/no) and dental visit in the past 12 months (yes/no) were self-reported. Participants self-reported (yes/no) to 8 ACEs (high ACEs ≥ 1). Logistic regression estimated odds ratios and 95% confidence intervals for associations between ACEs and doctor visit and dental visit, adjusted for demographic and healthcare factors.

Results. Children with ≥ 1 ACE were 28% less likely (OR=0.71,95%CI:0.78,0.79) to visit a doctor and 48% less likely (OR=0.52,95%CI0.51,0.52) to visit a dentist, compared to children with 0 ACEs. Further, boys had decreased odds (OR=0.23,95%CI0.23,0.23) while girls had increased odds (OR=1.23,95%CI:1.22,1.25) of visiting a doctor within 1 year. Both boys (OR=0.22,95%CI:0.22,0.23) and girls (OR=0.87,95%CI 0.86,0.88) had decreased odds of visiting a dentist.

Discussion. For children living in rural communities, those with ≥ 1 ACE were less likely to have a recent doctor or dentist visit. We observed sex differences, such that boys with ≥ 1 ACE were significantly less likely to have had a recent doctor or dentist visit than girls with ≥ 1 ACE. A higher prevalence of particular ACES, such as "lacking basic needs" among boys may explain the observed differences by sex. Further research is warranted to best inform prevention efforts in rural communities.

Social

Food and housing instability drive low sexual relationship power with heterosexual intimate partners among women sex workers in Vancouver, Canada: Findings from 12 years of longitudinal cohort data Kaylee Ramage* Kaylee Ramage Kate Shannon Andrea Krüsi Charlie Zhou Ran Hu Shira Goldenberg

Background: Unequal power dynamics within intimate partner relationships have been associated with intimate partner violence (IPV) and adverse impacts on physical and mental health; however, limited research has examined sexual power dynamics within sex workers' intimate partner relationships. Using Pulerwitz' Sexual Relationship Power Scale (SRPS), we examined the relationship between socio-economic factors and sexual relationship power scores among women sex workers (SWs) with heterosexual intimate partners in Metro Vancouver, Canada.

Methods: Using data from a prospective, community-based cohort study of SWs (2010–2022), we separately estimated the independent associations between socio-economic factors (i.e., food, housing, and income security) and SRPS scores. We conducted complete case bivariate and multivariable ordinal regression using generalized estimating equation modelling.

Results: Of 722 SWs who had ≥1 men-identified intimate partner during the study period and answered the SRPS, 60.25% reported high SRPS scores in their relationship(s). In bivariable and multivariable analyses, food insecurity (aOR: 0.66, 95%CI:0.51-0.85) and lack of stable housing (aOR: 0.62, 95%CI:0.48-0.80) were independently linked to lower SRPS scores, indicating lower power within their relationships. Compared to those who solicited sex work on the street or in public, SWs who primarily solicited indoors or online were significantly more likely to report high SRPS scores (aOR: 1.72).

Conclusion: Food and housing instability are directly linked to low sexual relationship power among SWs within heterosexual partnerships. Amidst growing food security and housing crises, these data suggest that lack of access to secure housing and food place criminalized and low-income women at risk of unintended pregnancies, sexual coercion and violence and STIs/HIV. Policy reform to ensure access to basic human rights remain critical to promote SWs' agency and control in sexual relationships.

Table X. Socio-structural exposures associated with odds of high sexual relationship power within women sex workers' intimate relationships with their men-identified partners in Vancouver, BC, 2010 – 2022: Unadjusted and adjusted odds ratios (ORs), 95% confidence intervals (95% Cis) and p-values from bivariate and multivariable ordinal regression using generalized estimating equations.

Socio-Structural Exposures	Unadjusted	Adjusted*
	OR (95% CI)	OR (95% CI)
Income Insecurity		
Having been cut off or denied income assistance[†]	0.84 (0.53 – 1.31)	
Most often relying on others for money[†]	0.99 (0.79 – 1.23)	
Financially supports child(ren)[†]	**1.50 (1.10 – 2.04)**	
Food Insecurity		
Food insecurity[†]	**0.51 (0.40 - 0.64)**	**0.66 (0.51 – 0.85)**
Having exchanged sex directly for food[†]	**0.62 (0.41 – 0.93)**	0.81 (0.51 – 1.30)
Housing Insecurity		
Any unstable housing[†]	**0.51 (0.41 – 0.65)**	**0.62 (0.48 – 0.80)**
Been homeless or living on the street[†]	**0.64 (0.51 – 0.80)**	**0.74 (0.58 – 0.96)**
Having been evicted or forced to move[†]	0.60 (0.33 – 1.09)	0.74 (0.37 – 1.48)
Sex Work Environment		
Solicitation environment[†]		
Street or public	**Reference**	**Reference**
Indoor	**2.64 (1.96 – 3.54)**	**1.72 (1.15 – 2.56)**
No sex work	**2.00 (1.47 – 2.74)**	**1.74 (1.26 – 2.41)**
Service environment[†]		
Outdoor or public space	**Reference**	**Reference**
Informal indoor	**1.71 (1.30 – 2.24)**	**1.62 (1.23 – 2.13)**
Formal indoor	**3.05 (2.19 – 4.23)**	**1.89 (1.16 – 3.09)**
No sex work	**2.07 (1.50 – 2.87)**	**1.77 (1.26 – 2.50)**

Note. OR = odds ratio; 95% CI = 95% confidence intervals, IPV = intimate partner violence
[†]In the last 6 months
*Adjusted models controlled for Childhood Trauma Score, race/ethnicity, age, education, sexual and gender identity, and number of years involved in sex work

The Association Between Area-Level Gun Violence and Child and Adolescent General Health Status Across the United States, 2020 – 2022 Nandita Somayaji* Nandita Somayaji Emily Knapp Marie L. Churchill Cassandra Crifasi Judy L. Aschner Theresa M. Bastain Traci A. Bekelman Courtney Blackwell Patricia A. Brennan Carrie V. Breton Carlos A. Camargo, Jr. Nicholas Cragoe Lisa Croen Amy J. Elliott Assiamira Ferrara Jody M. Ganiban Rima Habre Theresa Herrera Alison E. Hipwell Kelly A. Hirko Zoe Baysdorfer Kaplan Margaret R. Karagas Barry M. Lester Leslie D. Leve Kristen Lyall Cindy T. McEvoy Kimberly S. McKee Richard K. Miller Hooman Mirzakhani Jenae Neiderhiser Thomas G. O'Connor Mike O'Shea Amy Padula Christina A. Porucznik Annemarie Stroustrup Aruna Chandran

The impact of gun violence on youth health in the United States is a vital public health issue. With gun violence data limitations and research policy restrictions, gaps remain in characterizing the population health burden. This study explores the association between area-level gun violence and general health status of youth nationwide leveraging individual-level data from the Environmental influences on Child Health Outcomes (ECHO) study. 12,902 youth aged 0-18 and parents reported general health status with the most recent reporting used for the study. Gun violence incidents, defined as any death or injury caused by a gun, were extracted from the publicly available Gun Violence Archive by county between 2020 and 2022. Counts of county-level gun violence incidents were categorized into tertiles: high (≥ 232), medium (27 – 231), and low (≤ 26). A generalized estimating equation logistic model with robust variance was used to estimate the association between binary general health status (good/fair/poor vs. excellent/very good) and county-level gun violence incidents adjusting for imputed individual and county-level sociodemographic covariates. In low gun violence counties, most participants identified as White (81%), followed by other races (12%) and Black (7.5%). Contrastingly, in counties with high gun violence, 42% reported White race, 37% Black, and 21% Other races. Odds of reporting excellent/very good general health was 35% higher in counties with low gun violence compared to those with high gun violence (OR = 1.35, 95% CI: 1.08, 1.70). Additionally, there were higher odds of reporting excellent/very good general health status in low compared to medium gun violence counties (OR = 1.22; 95% CI: 1.04, 1.43). Findings reiterate that higher levels of gun violence associate with poorer general health status in youth, even when adjusting for socioeconomic indicators. This data linkage will allow further research on the impact of gun violence across the life course.

Social

Expansion of 4-year colleges in the United States associated with lower later-life blood pressure with similar relationships at all quantiles of blood pressure Amanda Irish* Amanda Irish M. Maria Glymour Fei Jiang Anusha Vable

Introduction: More schooling predicts lower mean blood pressure in later life, however impacts along the entire blood pressure distribution are unclear. Increases in education may have differential impacts for people who would otherwise have high versus low blood pressure; for example, educational benefits in the high-risk right tail of the blood pressure distribution could disproportionately reduce stroke and heart attack risk compared to benefits at the mean or low-risk left tail. We evaluate the effect of the increase in 2- and 4- year colleges from the 1940s to the 1980s on the systolic blood pressure distribution, and test for differential relationships in race-by-gender subgroups.

Methods: Using Health and Retirement Study data (N = 6,145), we estimated the association of the number of 2- and 4-year colleges per county per year, standardized to the number of 18- to 22-year-olds from 1940 to 1982, with measured systolic blood pressure. We used linear regression to evaluate mean effects and conditional quantile regression to evaluate distributional effects, and adjusted for individual- and state-level covariates. Interaction terms evaluated differential associations by the combination of race (Black vs White) and gender (male vs female).

Results: In pooled analysis, the number of 2-year colleges in the county was not associated with the mean or any quantile of systolic blood pressure. However, the number of the 4-year colleges in the county was associated with lower mean systolic blood pressure (b= -0.1 mmHg (95% CI: -0.19, -0.015), which was consistent across its distribution: there was no evidence of differential impact. We also did not find meaningful differences in the effect of education across race-by-gender subgroups.

Conclusion: Geographic accessibility to 4-year colleges was associated with lower systolic blood pressure, with little distributional or subgroup variation.

Figure. Linear and conditional quantile regression estimates for the association between the number 4-year colleges per 100,000 18 - 22-year-olds in the respondent's county and systolic blood pressure, in race-by-gender subgroups
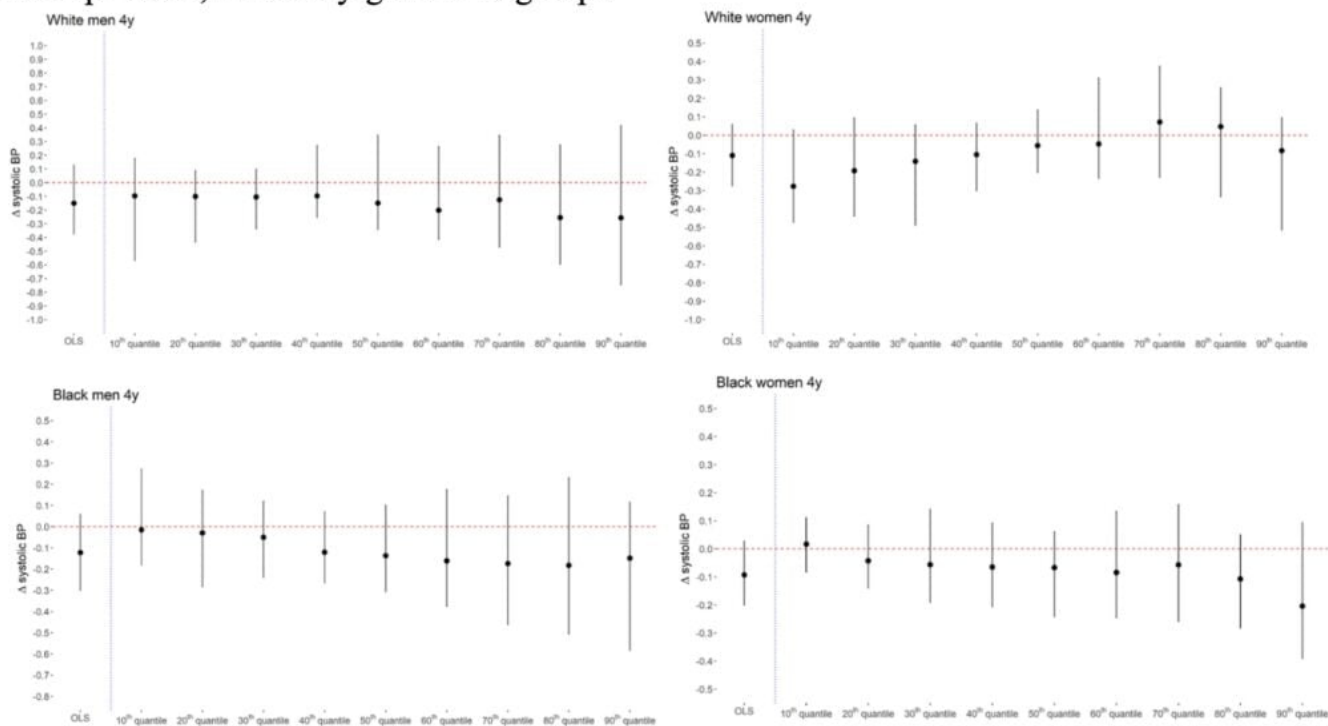
Learning from the Unexpected: Drivers of Life Expectancy in Urban Areas of the United States Jeanette Stingone* Jeanette Stingone Teshawna Badu

Background: Neighborhood is a strong predictor of life expectancy. Prediction methods are often used to classify spatial areas by life expectancy and target public health intervention in efforts to reduce disparities. But, can we learn from areas where models don't perform well and improve public health intervention? In previous work, researchers in Brazil used machine learning methods and traditional sociodemographic factors to predict life expectancy and then analyzed modifiable health characteristics of the municipalities whose observed life expectancies deviation from the prediction.

Methods: We replicate the Brazilian approach in urban areas in the United States using random forest to predict life expectancy at birth using twenty-six variables that represent social and structural drivers of health. Standard pipelines including data partitioning and cross-validation were applied. We then compared modifiable, health-related characteristics of the under and overachievers (i.e., census tracts that have a 10% worse or better outcome than predicted), calculating the median difference in values between the two groups. Data come from the U.S. Small-area Life Expectancy Estimates Project, the US Census American Community Survey and the CDC 500 Cities Project.

Results: Initial results from New York City found 43% of variability in life expectancy at the census tract level was explained solely by sociodemographic predictors. Overachieving neighborhoods reported greater leisure time for physical activity, sleeping at least 7 hours a day, health insurance coverage and lower rates of smoking. In contrast, there were no differences in prevalence of routine medical checkups and mammography, while underachieving neighborhoods had higher rates of cervical cancer screening.

Discussion: Exploring areas that deviate from prediction may generate hypotheses for future research. The performance of the prediction model is a key limitation. Results from national data are forthcoming.

Assessing the Measurement Properties of Neighborhood Environment Scales in Rural Alabama Mahasin S. Mujahid* Khin Oo Juan Cabrera Stephanie T. Broyles Tené T. Lewis Viola Vaccarino Apurv Soni Vasan Ramachandran Mahasin S. Mujahid

Despite robust evidence that neighborhood environments influence disease risk, most studies have employed neighborhood measures in urban settings. To assess the validity of neighborhood scales in rural settings, we examined the psychometric and ecometric properties of survey-based measures of physical and social environments in rural neighborhoods (i.e., census tracts) in Alabama. Data were obtained from the Risk Underlying Rural Areas Longitudinal (RURAL) Study, a cohort study designed to investigate the heart and lung health of rural dwelling adults aged 25-64 years of age in four southeastern states (Alabama, Mississippi, Louisiana, and Kentucky). A preliminary Alabama subsample collected in 2021-2022 includes 657 residents across 22 census tracts, with a mean of 30 participants per tract (SD = 19). The mean age was 48.7 (SD=10.9), 73.1% were assigned female sex at birth, 74.6% self-identified as Black, and 31.4% held a high school diploma or GED. Using a mHealth app, we collected six dimensions of neighborhood environments: aesthetic quality, walkability, access to healthy foods, safety, social cohesion, and activities with neighbors. Cronbach's alpha was calculated to assess the internal consistency across scale items within these six dimensions. Intraclass correlation coefficients (ICCs) and neighborhood reliability were calculated to assess the ecometric properties of these scales. Cronbach's alpha coefficients indicated good internal consistency ranging from 0.74 to 0.88. Neighborhood reliabilities indicated good reliability, ranging from 0.75 (activities with neighbors) to 0.89 (safety). However, ICCs were lower, ranging from 0.08 (activities with neighbors) to 0.20 (safety), possibly due to the larger square mileage of rural areas compared to urban areas and the lower population densities. Overall, these measures have good psychometric and ecometric properties and will be investigated in relation to rural health outcomes in future studies.

Social

Education and Midlife Cognitive Functioning: Evidence from the High School and Beyond Cohort John Robert Warren* John Warren Chandra Muller Eric Grodsky

INTRODUCTION: Education is associated with cognitive functioning and risk of Alzheimer's Disease and related dementias (ADRD). However, researchers rarely consider anything about education other than highest degree completion. Do schools' social and academic contexts and students' other (non-attainment) schooling outcomes independently predict cognitive outcomes? If so, this opens the possibility of manipulating educational policies and practices to improve long term cognitive well-being. METHODS: This study included a nationally representative sample of 12,530 Americans followed prospectively from high school through age ~60 as part of the High School and Beyond cohort study. OLS regression models estimated associations between various aspects of education – including schools' social and academic contexts; students' grades, test scores, and course taking; and degree attainment – and multiple dimensions of cognition, before and after adjustment for confounders. RESULTS: Educational attainment predicts cognitive functioning at age ~60. However, the social and academic contexts of schools and other measures of students' educational performance predict cognition at least as well—even after adjusting for attainment. DISCUSSION: Education is more than just how far in school people go, and degree attainment is not the only – or perhaps even the primary – thing about education that has long run consequences for cognitive functioning and ADRD risk. Advancing our understanding of how and why education shapes cognitive functioning and ADRD risk requires analyses of data with nuanced information about schools, schooling, and student performance.

Reductions in household poverty and neighborhood moves: a randomized trial of cash transfers to low-income newborn U.S. families Tim Bruckner* Tim Bruckner Abhery Das THeresa Osypuk Katherine Magnuson

Child poverty is pervasive, spatially patterned, and harmful to child development and life chances. Because of racial segregation and structural racism in the housing market, Black and Hispanic children are much more likely to experience both child and neighborhood poverty. The evidence of how to change poverty or neighborhood poverty, however, suffers from bias including reverse causation and strong confounding. This study examines the Baby's First Years (BFY) randomized trial of unconditional cash transfers to 1,000 low-income families with newborn infants in year 2018, within four US cities. We test whether the BFY treatment, of receiving \$333/month (vs. \$20/month) for three years, causes families to make opportunity moves to better quality neighborhoods. We use Intent to Treat linear regression models for this test. Secondarily, we explore whether the mother's health at baseline modifies any effect of the BFY cash transfer on neighborhood opportunity. We find that the BFY treatment precedes a slight (but not statistically detectable) increase in neighborhood opportunity across time, but this increase is lower than that of the control group (p=0.76). On the other hand, we find effect modification by maternal baseline health. For mothers with poor self-rated health at baseline, the BFY cash transfer caused improvements in cumulative neighborhood opportunity, compared to the control group (coef: 11.34, SE=5.66, p=.04). Our results provide rigorous evidence of heterogeneous treatment effects of the cash transfer. An unconditional cash transfer promotes opportunity moves, but only among mothers with poor health at baseline. Explanations for this heterogeneity require subsequent investigation.

State policy climate and mental distress among working-age US adults during the COVID-19 pandemic: A longitudinal study Ariel Beccia* Ariel Beccia Dougie Zubizarreta Chloe Gao Madina Agénor Jamie Hart Jonggyu Baek S. Bryn Austin

Pandemic mitigation policies (eg, lockdowns) have been linked to adverse mental health outcomes and exacerbated inequities during early waves of COVID-19, yet whether concomitantly implemented economic relief policies (eg, income support) alleviated such harms is unknown. We examined overall and group-specific associations between the US state pandemic policy climate and mental distress among working-age adults in April 2020.

Data came from the COVID-19 Sub-Study of the Nurses' Health Studies 2/3 and Growing Up Today Study (N=34,843 participants <65 years). Using 2 state-level policy indices (pandemic mitigation, economic relief) from the Oxford COVID-19 Government Response Tracker, we estimated longitudinal associations between participants' past-month exposure to state policy climate (weak mitigation/weak relief, weak mitigation/strong relief, strong mitigation/weak relief, strong mitigation/strong relief) and subsequent depression (PHQ-2 score >3) via logistic models with state fixed-effects and demographic controls. Secondary models explored effect heterogeneity by gender, sexuality, and race.

The prevalence of depression varied across state policy climates, with the highest prevalence observed among participants living in strong mitigation/weak relief states (20.5%). Economic relief policies buffered against the adverse impacts that pandemic mitigation policies had on depression, such that participants in strong mitigation/strong relief states had reduced odds of depression compared to those in strong mitigation/weak relief states (OR:0.70;95%CI:0.53,0.91). Relative to their non-marginalized counterparts, marginalized groups benefited more from living in states with strong economic relief policies and some (eg, Black and LGB people) experienced attenuated inequities in strong mitigation/strong relief states.

Economic relief policies may have safeguarded against the mental health consequences of necessary pandemic mitigation measures for US adults in April 2020.

State pandemic policy climate in April 2020
Data source: Oxford COVID-19 Government Response Tracker

- Strong mitigation policies, strong economic relief policies
- Strong mitigation policies, weak economic relief policies
- Weak mitigation policies, strong economic relief policies
- Weak mitigation policies, weak economic relief policies
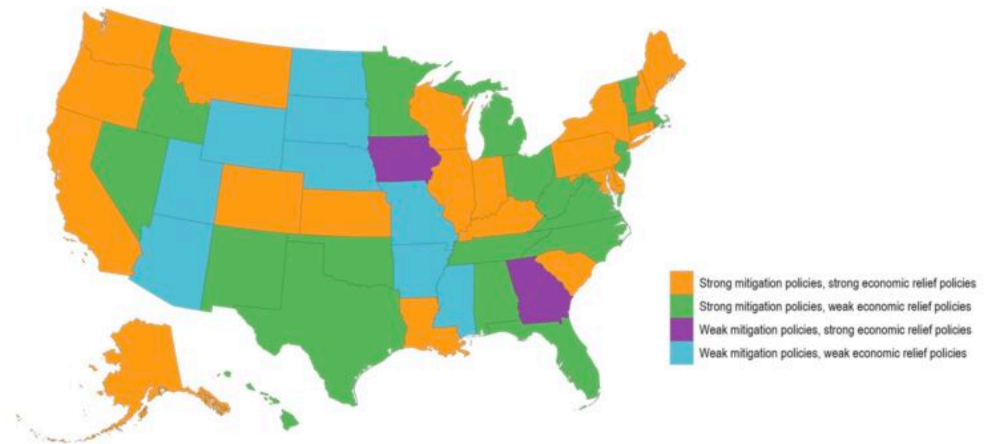
Figure. State pandemic policy climate in April 2020. States were categorized using two policy indices – a pandemic mitigation index (which includes indicators for stay-at-home orders, school and business closures, etc.) and an economic relief index (which includes indicators for income support, debt relief, etc.) – from the Oxford COVID-19 Government Response Tracker. Each index is a weighted, averaged, and scaled composite of its component indicators and ranges from 0 to 100; based on prior studies, we defined states as having "strong" pandemic mitigation or economic relief policies if they had a score of 70 or greater in a given month.

Staggered interventions with no control groups Brice Batomen* Brice Batomen Tarik Benmarhnia

The limitations of the two-way fixed effects for the impact evaluation of interventions occurring at different times for each group, 'staggered interventions' have been highlighted in the last decade in the econometric literature and, more recently, in epidemiological research. Although many alternative strategies (staggered difference-in-differences, generalized synthetic control method, etc..) have been proposed, the focus has predominantly been on scenarios where one or more control groups are available. However, control groups are often unavailable, due to limitations in the available data or because all units have received the intervention. In such context, interrupted time series (ITS) designs can be applied. The extent to which common model specifications for ITS analyses are limited in the case of staggered interventions remains an underexplored area in the methodological literature. In this work, we aim to demonstrate that standard ITS model specifications typically yield biased results for staggered interventions, and we propose alternative model specifications inspired by recent developments in the difference-in-differences literature to propose adapted analytical strategies.

Study Design

Validation of a 24-hour timing grid to assess weekday and weekend sleep in the Cancer Prevention Study-3 Charlie Zhong* Charlie Zhong Matthew Masters Sidney M Donzella Alpa V Patel Marjorie McCullough

Sleep misalignment (difference in weekday vs weekend sleep patterns) is increasingly being implicated in higher risk of mortality and morbidity. Several prospective cohorts have assessed sleep in their populations, but typically assess overall sleep or utilize clinic-based instruments (e.g., Pittsburgh Sleep Quality Index). To better understand sleep misalignment, we validated a 24-hour grid-based sleep assessment tool. In 2015, participants of the American Cancer Society Cancer Prevention Study-3 (CPS-3) indicated on a grid consisting of one-hour blocks, when they were eating or sleeping, encompassing all 24-hours of the weekday and weekend. A subset of 170 participants were also enrolled in the Activity Validation SubStudy (AVSS), a validation study of activity patterns and provided a Daysimeter – a device designed to capture light exposure during the day and sleep at night. We utilized the method of triads to calculate validity coefficients (VCs) and bootstrapped 95% CI for sleep duration between the grid, device, and sleep diaries; and correlation coefficient (Kendall's Tau) for chronotype between grid and questionnaire. Among 134 participants with data for at least 3 weekdays and 1 weekend, average weekday sleep duration was longer on the grid (459 minutes) than for device or diary (409 and 405 min, respectively). Similar patterns were seen for the weekends (517 min grid, 441 min device, 433 min diary). Weekday grid sleep duration exhibited good validity with a VC of 0.68 (95% CI 0.54, 0.79) compared to weekend (VC 0.55, 95% CI 0.39, 0.69). On average, midpoints (clock time between going to sleep and waking) from the grid were 15.3 min later than diary on weekdays, and 10.7 min later on weekends. The correlation coefficient for chronotype was 0.52. The grid over-estimated sleep duration compared to device and sleep diary due to the coarser nature of the hour-long grids, but still provided a succinct and valid method to assess weekday and weekend sleep patterns.

Substance Use

Differences in Prevalence of Current Cigarette and E-Cigarette Use Among Monoracial, Biracial, and Multiracial Asians Ayesha Azeem* Ayesha Azeem Kelvin Choi

Background: Previous studies showed that multi-racial individuals have high prevalence of tobacco use, while Asian individuals have low prevalence. However, how tobacco use varies across monoracial, biracial, and multiracial Asian adults remain unclear. We investigate differences in current cigarette and e-cigarette use among monoracial, biracial, and multiracial Asians living in the US.

Methods: Data from the 2003-2019 Tobacco Use Supplement to Current Population Survey were used to assess Asian identity and current (i.e., every-day or some-day) cigarette (n=32,298) and e-cigarette (n=13,292; assessed since 2010) use. Monoracial identity was defined as Asian only, biracial as Asian and another race/ethnicity, and multiracial as Asian and at least 2 other races/ethnicity. We used weighted multivariate logistic regressions adjusted for demographics to assess the associations.

Results: Current cigarette and e-cigarette use was more prevalent among biracial (15.4%, 2.8% respectively) and multiracial (17.4%, 3.6% respectively) Asians than monoracial Asians (8.3%, 1.0% respectively) (Chi-square test p<0.01). Adjusting for age and sex, biracial (AORcigarette=1.79, AORe-cigarette=2.47) and multiracial (AORcigarette=2.00, AORe-cigarette=3.55) Asians were more likely than monoracial Asians to use both products. Further adjusting for education, income, and citizen did not nullify the association between Asian identities and current cigarette use (F-test p<0.01), but the association between these identities and current e-cigarette use (F-test p=0.21).

Conclusion: Biracial and multiracial Asians use both cigarettes and e-cigarettes at a higher rate compared to monoracial Asians. These prevalence rates are higher than those of the general US population. Further research needs to investigate the life context promoting initiation and barriers to cessation to create effective interventions to reduce tobacco product use among biracial and multiracial Asian adults.

Substance Use

Prevalence and harms associated with injecting in public spaces: a systematic review and meta-analysis Mehrdad Khezri* Mehrdad Khezri Sarah Kimball Courtney McKnight Saba Rouhani Danielle Ompad Don Des Jarlais

Background: Although it is essential to understand the current risk environments encountered by people who inject drugs to develop harm reduction services, a review that quantitatively synthesizes evidence on public injecting is lacking. We aimed to summarize evidence on the prevalence and harms associated with public injecting globally.

Methods: We searched Medline, Embase, PsycINFO, CINAHL, Scopus, Global Health, and Web of Science until March 11, 2023. We pooled data from included studies using random-effects meta-analyses. The timeframe for recent was defined as current or within the last year. The risk of bias was assessed using the Joanna Briggs Institute's critical appraisal tool.

Results: Of 3114 records, 58 studies were included. The pooled prevalence of recent public injecting was 50.05% (95%CI 45.19-54.90, I2=99.1%, number of studies [n]=44). Public injecting was associated with recent non-fatal overdose (OR 2.22, 95%CI 1.81-2.72, I2=30.6%, n=13), needle/syringe sharing (OR 2.70, 95%CI 2.08-3.51, I2=66.4%, n=15), arrest/incarceration (OR 2.14, 95%CI 1.83-2.50, I2=47.2%, n=9), sex work (OR 2.26, 95%CI 0.97-5.28, I2=85.3%, n=5), unstable housing/homelessness (OR 4.45, 95%CI 3.32-5.96, I2=88.3%, n=15), and higher willingness to use supervised injection facilities (OR 2.66, 95%CI 1.86-3.80, I2=87.4%, n=8). We also found the association between public injecting and HIV (n=3), HCV (n=2), skin and soft tissue infections (n=4), and mental health outcomes (n=3).

Conclusions: Public injecting is prevalent and associated with experiencing a multitude of adverse outcomes, underscoring the need to increase access to safe injection spaces. Findings support developing interventions to minimize harms of public injecting, including addressing structural risks tied to encounters with law enforcement and expanding naloxone programs and overdose prevention centers. Housing interventions could serve as an effective upstream strategy to reduce public injecting and its harms.

Substance Use

Adulterants in Unregulated Opioids and Associations with Specific Adverse Events Samuel Tobias* Samuel Tobias Jennifer Angelucci Evan Wood Jane A. Buxton Lianping Ti

In recent years, the unregulated drug supply in North America has become permeated by novel adulterants (e.g., fentanyl analogues, benzodiazepines, xylazine) with limited information about their specific health effects. While fentanyl has been shown to be associated with overdose mortality and other non-fatal health outcomes, adverse events (AE) associated with novel adulterants remain largely unknown.

Drug checking samples were anonymously analyzed using combination Fourier-transform infrared spectroscopy and immunoassay strips at community harm reduction sites in British Columbia (BC) by trained technicians. Self-reported AE (e.g., non-fatal overdose, blackouts, prolonged sedation) were recorded from individuals who checked samples post-consumption. We restricted to samples reported by service users to be opioids. aPR and 95% CI of AE among common adulterants were calculated using generalized linear models with a Poisson and log link, adjusted for the presence of common adulterants and city.

Between Feb 2022 and Sep 2023, 9,999 eligible opioid samples were analyzed at community drug checking sites in BC. Of these, 42.4% were checked post-consumption by the participant. AE were noted by individuals in 17.1% of post-consumption checks. After adjustment, the presence of benzodiazepines in post-consumption opioid samples was positively associated with an increased likelihood of an AE (aPR = 1.86, 95%CI: 1.54–2.23). When restricted to specific events, benzodiazepines were associated with increased likelihood of overdose (aPR = 2.19, 95%CI: 1.67–2.88) and blackouts or prolonged sedation (aPR = 3.03, 95%CI: 2.04–4.49).

Prevalence of non-fatal AE associated with unregulated opioid use has been largely undescribed. This research reports specific AE associated with different adulterants in the unregulated opioid supply and the likely impact of benzodiazepines. With this information, precise public health interventions and services can target specific drug using populations.

Substance Use

Exploring linkages between injecting-related interpersonal dynamics and high-risk injecting behaviors in dyads of people who inject drugs Neia Prata Menezes* Neia Prata Menezes Maia Scarpetta Julie Bruneau Kimberly Page Torsten Neilands Meghan D. Morris

Injecting behaviors can occur in the context of injecting partnerships, yet the role of injecting dynamics on individual behaviors is not well understood. We conducted secondary analyses of baseline hepatitis C virus (HCV) serology and behavioral survey data to assess linkages between interpersonal factors and behaviors in injecting dyads of people who inject drugs (PWID) (San Francisco, USA and Montreal, Canada, 2017). A 54-item Injecting-Related Interpersonal Relationship Dynamics Scale (IRDS) measured interpersonal factors (injecting-related cooperation, intimacy, risk perception, power imbalance, and trust; α=0.92-0.68). Using Actor-Partner Interdependence Models, we estimated actor and partner effects of individual IRDS scores on equipment and needle sharing. Dyads were indistinguishable. Mixed effect models accounted for a cross-classified data structure with random intercepts for site, actor, and partner. We assumed a Poisson distribution to estimate relative risks (RR) and 95% confidence intervals (95%CI). Among 180 PWID (136 dyads), median age was 30, 74% were male, 21% were non-white, and 49% had HCV infection. Overall, 68% and 18% reported equipment and needle sharing, respectively. Actor's risk perception (RR=0.89, 95%CI: 0.85-0.92) and partner's cooperation (RR=1.10, 95%CI: 1.09-1.12) were associated with actor's equipment sharing. Actor's (RR=0.81, 95%CI: 0.80-0.83) and partner's (RR=0.93, 95%CI:0.91-0.95) power were negatively linked to actor's equipment sharing. Actor's (RR=1.07, 95%CI: 1.03-1.10) and partner's (RR=1.20, 95%CI: 1.16-1.24) trust were positively associated with actor's equipment sharing. We observed similar findings for needle sharing. Injecting-related cooperation and trust may facilitate equipment/needle sharing in injecting dyads; risk and power may have opposite effects, while intimacy had no effect. Accounting for injecting dyad dynamics may better inform individual-level strategies for HCV treatment or harm reduction engagement.

Multivariable APIM models[*] assessing actor and partner effects of Injecting-Related Interpersonal Relationship Dynamic (IRDS) factors (injecting-related cooperation, intimacy, risk perception, power imbalance, trust) on sharing of injecting equipment and needles among 136 injecting dyad pairs (N = 180 people who inject drugs across San Francisco, USA and Montreal, Canada, 2017)

Ancillary Equipment Sharing

Injecting Needle Sharing

● Actor effect   ● Partner effect
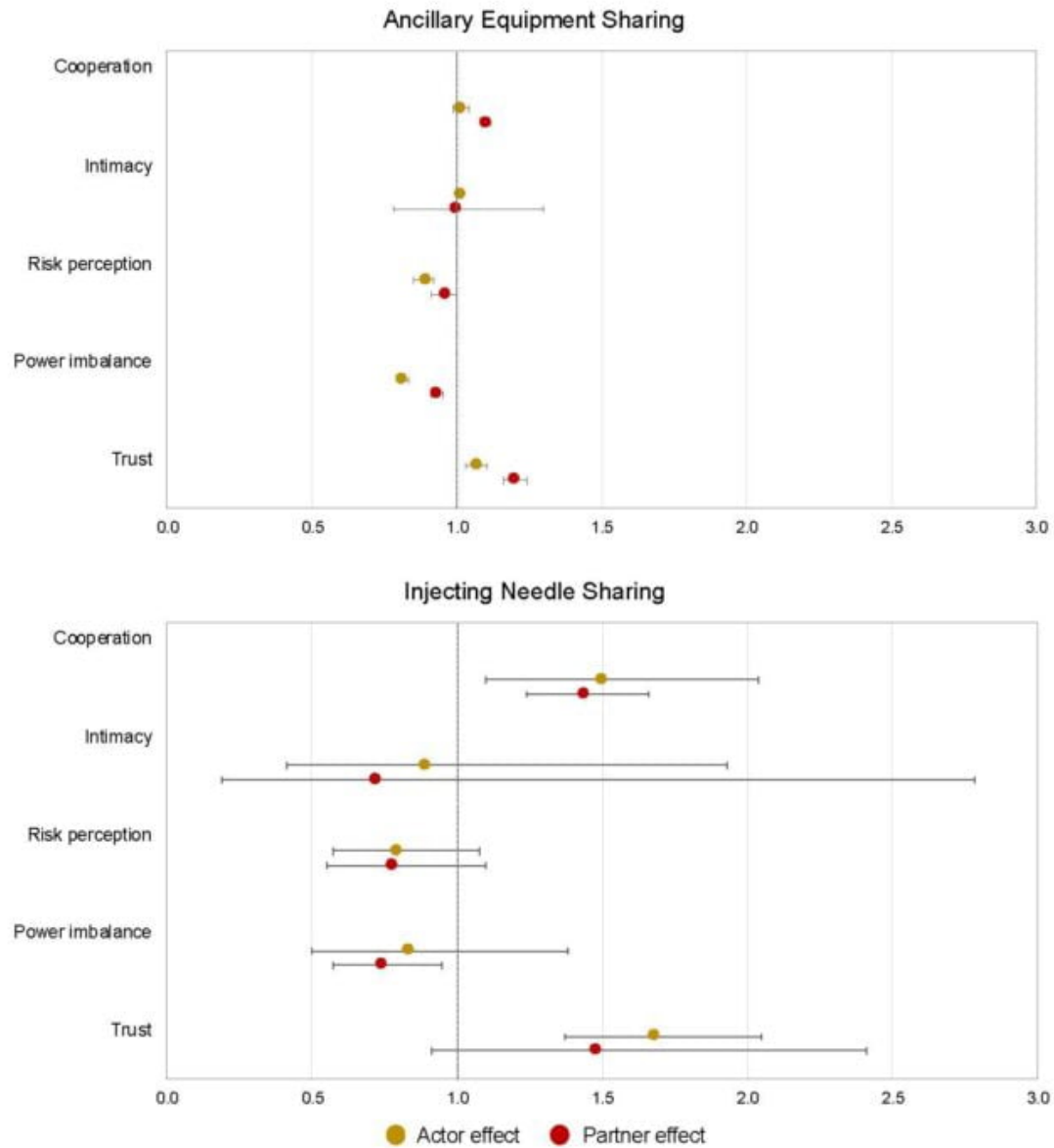
* All models adjust for actor age, gender, primary drug injected, disclosed HCV status, number of other injecting partners in past the month, years injecting with partner, and if in sexual relationship with partner. *Example interpretation*: For each one unit increase in actor's injecting-related cooperation, we observed a 50% increase in the likelihood of the actor engaging in needle sharing behaviors (RR=1.50, 95%CI: 1.10-2.04). For each one unit increase in partner's injecting-related cooperation, we observed a 44% increase in actor's needle sharing behaviors (RR=1.44, 95%CI: 1.24-1.66).

Substance Use

Effect of partial nicotine reduction on young e-cigarette users in the US: a cross-over clinical trial Tarana Ferdous* Tarana Ferdous

Background: The advent of salt-based, high-nicotine e-cigarettes has contributed to their epidemic use among young people in the US, necessitating the need for policies to address the addictiveness of these products. Therefore, using an experimental clinical design, this study evaluates the effect of partial nicotine reduction (NR) on e-cigarette users' puffing behaviors.

Methods: In this repeated-measure within-subject clinical cross-over study, 50 current high nicotine concentration e-cigarette users aged 21-35 attended two e-cigarette use sessions with the same brand (JUUL/NJOY) of 3% (28-35 mg/ml) and 5% (58-59 mg/ml) nicotine concentration in random order up to 60 minutes ad libitum, preceded by 12-hour nicotine abstinence. Puffing topography was recorded during each session to measure smoking time, puff time, average puff duration, average flow rate, average inter-puff interval, number of puffs, total inhaled volume, average puff volume, and maximum puff volume. Blood samples were collected before and after each session, and plasma nicotine levels were assessed retrospectively using gas chromatography-mass spectrometry.

Results: The median topography parameters were significantly higher during the e-cigarette use sessions with 3% nicotine concentration compared to the sessions with 5% nicotine concentration (i.e., puffing time: 1.33 min vs. 1.21 min, p = 0.021; average puff duration: 2.57 sec vs. 2.44 sec, p=0.017; total inhaled volume: 1990 ml vs. 1490 ml, p = 0.045), indicating the presence of compensatory puffing behavior for partial NR. The median nicotine boost observed in the 5% nicotine condition (6.35 ng/ml) was significantly higher than in the 3% condition (4.10 ng/ml, p = 0.012).
Conclusion: Using a sensitive within-subject design, this study provides clear evidence of compensatory puffing on e-cigarette use when partial NR is employed with the potential to add to toxicants' exposure.

Substance Use

Social determinants of blunt use among youth in the US: National Youth Tobacco Survey 2022 Rime Jebai* Rime Jebai Sarah D. Kowitt Jennifer Cornacchione Ross

The use of blunts (hollowed-out cigars filled with marijuana) has become popular among youth. Research on psychological distress and other determinants of blunt use is scant. This study examined social determinants of blunt use among a nationally representative sample of US youth.

Data were from middle and high school students who participated in the 2022 cross-sectional National Youth Tobacco Survey (n=28,291). Psychological distress was classified into none, mild, moderate, and severe based on the four-item Patient Health Questionnaire (PHQ-4) for depression and anxiety. Youth who reported using a blunt at least once in their lifetime were classified as ever blunt users. To estimate the association between psychological distress, race, sexual orientation, and ever blunt use, weighted logistic regression was performed adjusted for sex, age, school type, and past 30 days use of tobacco products.

Overall, 8% of youth reported ever blunt use and nearly 13% reported severe psychological distress. In addition, 16% of youth reported being lesbian, gay, or bisexual (LGB), and 12% were non-Hispanic Black. Compared to youth without psychological distress, those with mild [OR=1.54, 95% CI (1.15,2.06)], moderate [1.73, (1.29,2.31)], and severe [2.29, (1.74,3.01)] distress were more likely to report ever blunt use. Compared to non-Hispanic White youth, non-Hispanic Black [2.07, (1.54,2.79)] and Hispanic [1.48, (1.16,1.89)] youth were more likely to report ever blunt use. The odds of ever blunt use were higher among youth identifying as LGB [1.47, (1.29,1.82)] compared to straight/heterosexual. The odds of ever blunt use were also higher among polytobacco users (>2 tobacco products) vs. single use (only one tobacco product) [2.50, (1.51,4.12)] and among cigar smokers [3.29, (1.71,6.34)].

Youth who reported being LGB, Black, or Hispanic and those with psychological distress were more likely to report ever blunt use. Findings underscore the importance of tobacco and substance use control efforts designed to reach minority communities and those with psychological distress.

Effect of the survey mode on drug use reports: results of a mixed method for data collection during the COVID-19 pandemic in Chile

Nicolas Rodriguez* Nicolas Rodriguez Jose Miguel Cabezas Mariel Mateo Pinones Francisco Cumsille Esteban Pizarro

Background: The COVID-19 pandemic presented unprecedented challenges to data collection worldwide, prompting the need for innovative solutions to ensure the continuity of surveys. This study tested the survey mode effect on drug use reports during the COVID-19 pandemic in Chile. **Methods:** We use data from the National Study of Drugs in the General Population in Chile, a nationally representative cross-sectional survey implemented since 1994. In 2020, along with the traditional CAPI (Computer-Assisted Personal Interviewing) mode, the CATI mode (Computer-Assisted Telephone Interviewing) was used if sanitary conditions did not allow face-to-face application. At the national level, 89% of the interviews were conducted face-to-face (CAPI) and 11% by telephone. Propensity Score Weights were used to balance respondent characteristics in comparing face-to-face and telephone respondents. **Results:** Results indicate that telephone respondents were more likely to report marijuana, alcohol, and cigarette smoking than in-person respondents. The survey mode effect was not significant in the lifetime report but was significant in the past year and past 30 days. In the past year, their 95% confidence intervals (CI) did not include the value of one for reporting intervals of the smoking cigarettes (OR = 1.52; 95% CI= 1.20–1.92), alcohol (OR = 1.31; 95% CI= 1.07–1.60), and marihuana (OR = 1.64; 95% CI= 1.10–2.45). In the past 30 days, confidence intervals did not include one for smoking cigarettes (OR = 1.53; 95% CI= 1.19–1.96), alcohol (OR = 1.28; 95% CI= 1.00–1.64), and marihuana (OR = 2.16; 95% CI= 1.28–3.65). We found consistent results using other matching techniques. **Conclusions:** Future research is needed to evaluate the mixed-mode surveys and their potential effect on the trend and data quality in household-based drug survey administration.

Substance Use

Trends in births diagnosed with Neonatal Abstinence Syndrome during the COVID-19 pandemic in the US- A time-series analysis. Alaxandria Crawford* Alaxandria Crawford Courtney Lynch Parvati Singh

Following the onset of the COVID-19 pandemic, data suggest a rise in drug use and overdose mortality in the US. Concurrently, birth rates decreased substantially following the pandemic, with a marked decline in hospital births, in particular. Given the countervailing patterns of drug use (increase) and live births (decline) following the onset of the pandemic, we examined whether infants diagnosed with Neonatal Abstinence Syndrome (NAS) changed during the pandemic. NAS represents a class of conditions observed in neonates exhibiting drug withdrawal symptoms following *in utero* exposure. We used nationally representative monthly data from the National Inpatient Sample Database (2016 to 2020, 60 months) and tested whether the monthly counts of two outcomes- (1) infants with NAS and (2) pregnant individuals diagnosed with drug use – changed during March to December 2020 (binary exposure indicating COVID-19 pandemic), relative to pre-pandemic period, nationally, as well as across 9 US Census Divisions. We identified diagnoses of NAS and drug use during pregnancy using ICD 10 codes (148,015 NAS births and 3,497,780 pregnant individuals diagnosed with drug use over study period). We used AutoRegressive Integrated Moving Average (ARIMA) time-series analyses to remove seasonality, trends, and autocorrelation in the monthly counts of our outcome series and controlled for monthly volume of total births. Results from ARIMA analyses of national data indicate 151 fewer infants diagnosed with NAS and about 4,300 fewer pregnant individuals diagnosed with drug use in the 10-month span of March-December 2020, relative to prior time period. This decline concentrates in Mid-Atlantic, East North Central, South Atlantic and East South Central US Census Divisions. Our findings provide the first national evidence of decline in the diagnosis of NAS during the COVID-19 pandemic in the US and suggest that drug use among pregnant individuals may have declined following the pandemic onset.

Substance Use
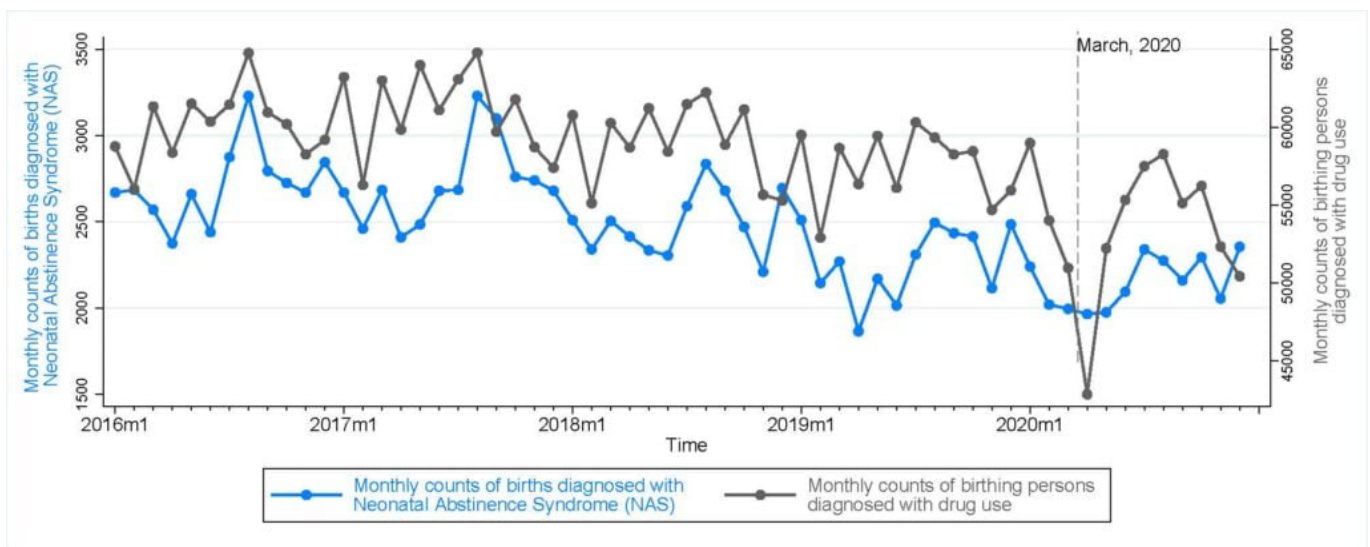
**Sexual orientation disparities in perinatal tobacco use** Sarah McKetta* Sarah McKetta Brittany Charlton

Introduction. Sexual minority women—SMW, i.e., those with same-sex partners, attractions, or lesbian/bisexual sexual orientation identities—have twice the risk of cigarette smoking as their heterosexual peers. During pregnancy, SMW are 50% more likely to smoke cigarettes than heterosexual women, with bisexual women having the highest risks. The prenatal period is a critical time not only for fetal development but also as an opportunity for healthcare engagement and to encourage women to start healthy habits, like smoking cessation, that may persist long after the pregnancy. However, very few studies have examined tobacco use across the perinatal period, i.e., from conception to the postpartum.

Methods. Using data from Nurses' Health Study 3, we investigate sexual orientation disparities in cigarette smoking at various timepoints: study baseline, prior to conception, during pregnancy, and in the postpartum. Participants' sexual orientation was categorized as completely heterosexual; heterosexual with same-sex attractions/behaviors or prior identity; bisexual; mostly heterosexual; lesbian/gay. We used log-binomial general estimating equations controlling for age, marriage status, and education, and multiple imputation for missing data.

Results. Relative to heterosexual participants, SMW reported more tobacco use at study baseline (risk ratio [RR]: 1.98 [1.35–2.89]), prior to conception (RR: 1.70 [1.27–2.29]), and in the postpartum (RR: 2.36 [1.35–4.13]), but not during pregnancy (RR: 1.67 [1.00–2.79]). Bisexual women had the highest risk both at baseline (RR: 2.55 [1.23–5.29]) and prior to conception (RR: 1.91 [1.09–3.36]), but lesbian women had the highest risk at postpartum (Figure 1; RR: 5.76 [1.88–17.60]).

Conclusion. Compared to heterosexual women, SMW were more likely to use tobacco before and after pregnancy, suggesting the need for clinicians to tailor perinatal anti-smoking efforts to this population.

Figure 1: Disparities in smoking by sexual orientation across the perinatal period

Substance Use
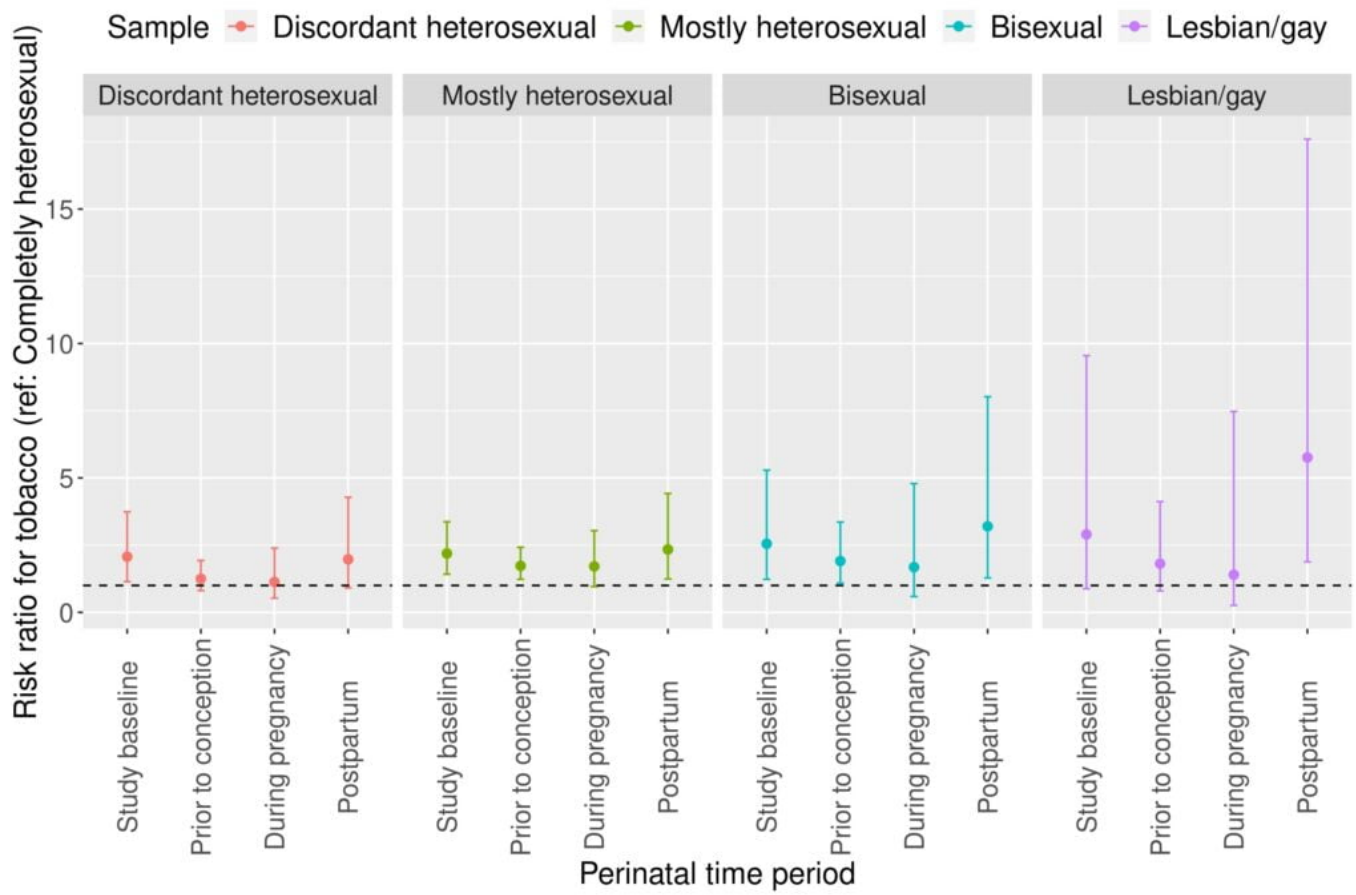
Impact of the adoption of smoke-free policies in Indonesia on tobacco use: A difference-in-differences approach Sarah Windle* Sarah Windle Wahyu Septiono Arijit Nandi

Background: More than two-thirds of individuals who currently smoke reside in low- and middle-income countries (LMICs). While the effectiveness of policy-based interventions to reduce smoking has been established in high-income countries, the optimal adoption of these policies in LMICs is unclear.

Methods: Using longitudinal cohort data from the Indonesia Family Life Survey (IFLS), we estimated the effect of provincial and district-level adoption of smoke-free policies (SFPs) on tobacco use among adults, using a difference-in-differences design. This approach compared trends in tobacco use from 1997-2014 among IFLS respondents (n=20,529 in 1997; n=36,391 in 2014) living in areas which did versus did not adopt SFPs.

Results: Current tobacco use across survey waves ranged from 59.4 to 64.1% among men and 2.6 to 5.9% among women. Cigarette smoking comprised the vast majority of tobacco use among men, and about half of current tobacco use among women. Nine provinces (33.3%) and 94 districts (n=30.4%) included in the IFLS adopted SFPs from 2005-2014. Provincial SFPs decreased current tobacco use by 2.2 percentage points (cluster-robust 95% CI: -4.4, -0.0) after controlling for district-level SFPs; bans on tobacco advertising and promotion; age; urbanicity; education; and sex. The effect was similar among men (RD: -2.3; CI: -4.7, 0.0), and very imprecise among women (RD: 3.0; CI: -5.3, 11.3). The adoption of district-level SFPs did not have a substantial impact on current tobacco use overall (RD: 0.9; CI: -1.0, 2.8), for men (RD: 0.7; CI: -1.1, 2.6), or for women (RD: 1.7; CI: -10.1, 13.5), after controlling for provincial SFPs and other covariates (as above).

Conclusions: Given the strongly negative health effects of tobacco, even small population-level reductions in tobacco use have important societal impacts. While provincial SFPs reduced tobacco use, more research is needed to determine why district-level SFPs did not have an impact on tobacco use in Indonesia.

Development of a national index of county-level access to opioid use disorder care and its performance using 2018 Medicaid administrative claims data Jannat Saini* Jannat Saini Helen Powell Ester Villalonga-Olives Nishant Shah Susan dosReis Danya Qato

Introduction: Factors informing access to opioid use disorder (OUD) treatment in the US are multifaceted, yet are often examined singularly as if independent from one another. A composite index of access to OUD care is valuable to quantify OUD resource environment. Medicaid, the largest payer for OUD treatment, is central to addressing the OUD crisis. Therefore, establishing such an index with linkages to Medicaid claims data provides a more holistic view of the OUD population. This study aims to generate a novel county-level OUD Resource Index (OUDRI).

Methods: To ensure OUDRI content validity, we established a conceptual framework with expert feedback to generate index domains representing OUD resource environment. We used publicly-available data (American Community Survey, Census, etc.) to measure characteristics under each domain. We used principal components analysis (PCA) to generate OUDRI. We derived a cohort of beneficiaries with OUD in 2018 from a national sample of Medicaid administrative claims database representing 3 million beneficiaries with OUD (2010-2018). We linked OUDRI to each beneficiary using state-county FIPS codes for a cross-sectional study. Binomial logistic regressions evaluated the relationship between medication for OUD (MOUD) utilization and OUDRI (tertiles; ranked from 1-3, representing lowest to highest potential access to OUD care) to assess construct (convergent) validity.

Results: The OUDRI, constructed from the first PCA component, comprises information from 22 variables representing all theoretical domains. The index was linked to a final sample of 1,237,812 beneficiaries representing 3,003 counties. In multivariate analysis (adjusted for 3 variables excluded from PCA due to low correlation), OUDRI tertiles 1 (33.3% of overall sample) and 2 (33.5%) had lower odds of MOUD utilization (OR: 0.65; 95% CI: [0.65, 0.66] and 0.89; [0.88, 0.90], respectively) compared to those in OUDRI tertile 3 (33.3%).

Conclusions: The OUDRI summarized multiple theoretical domains of OUD resource environment in each county and encompasses characteristics often unmeasured in observational studies of OUD. Likelihood of MOUD utilization was higher in the highest OUDRI tertile compared to the lowest, suggesting construct validity of OUDRI which can be leveraged by other researchers.

The role of depression on the association between preventative cancer screening and use of marijuana: results from a national level study S. Cristina Oancea* S. Cristina Oancea Cassidy Johnson

Introduction: This study investigates if cancer screening influences marijuana use in US adults. Understanding this association is vital for healthcare decision-making and public health policy, since currently 50% of US states have ratified legislation to allow recreational marijuana use.

Methods: Testing the association between a history of screening for cancer (HSC) and use of marijuana was performed on the combined data from the 2016, 2018, 2020, and 2022 version of the Behavioral Risk Factors Surveillance System (BRFSS) study. This association was investigated using weighted and adjusted logistic regression models on multiple sex- and age-based groups chosen according to cancer screening recommendations. Individuals previously diagnosed with cancer and pregnant women were excluded from the study. Confounders were selected based on previous literature and included in the analyses after a thorough evaluation via directed acyclic graphs (DAG). The effect modifying role of depression was tested.

Results: Compared to their counterparts with a HSC, the weighted and adjusted odds (WAO) of using marijuana among individuals without a HSC were significantly greater in: depressed married 1.71 (95%CI:1.14, 2.56) and separated, divorced and widowed 1.43 (95%CI:1.06, 1.92) women when screening for cervical cancer; depressed women 2.31 (95%CI:1.32, 4.05) when screening for breast cancer; and depressed males 2.08 (95%CI:1.40, 3.08) when screening for prostate cancer . No notable association was detected between colorectal HSC and use of marijuana in either males or females.

Conclusion: When compared to individuals with a HSC, their counterparts with no HSC have significantly greater odds of using marijuana, especially if they are depressed. Regarding the use of marijuana, particularly among depressed individuals, focused interventions are needed, and personal health behaviors such as screening for cancer should be encouraged.

Examining the illicit use of prescription painkillers among Canadian university students

Sanewal Singh* Sanewal Singh Samantha Meyer

Background and Aims

Individuals between the ages of 18-25 years old are among the highest illicit prescription painkiller users, which coincides with university students. The aim of this research is to examine the predictors and characteristics of illicit prescription painkiller use among Canadian university students.

Design, Setting, and Participants

This study consists of a secondary analysis of data from the American College Health Association, National College Health Assessment Survey II Canadian university edition. In addition to descriptive statistics, a binary logistic regression was conducted.

Findings

Of the 54,895 valid survey responses, 3221 were prevalent users of prescription painkillers without a prescription from a healthcare professional in the last 12 months. Factors such as being West Asian (Exp(B) = 2.167, p<0.001, CI = 1.690-2.779) or Black (Exp(B) = 1.309, p<0.01, CI = 1.081-1.565), having lower cumulative grade point average of a C (Exp(B) = 1.311, p<.001, CI = 1.160-1.482) or lower, and more frequently using cigarettes and cocaine in the last 30 days, on average, increased the odds of illicit painkiller use. Students who smoked 10-19 days over the span of the last 30 days were (Exp(B) = 1.690, p<.001, CI = 1.261-2.266) on average more likely to illicitly use prescription painkillers. Conversely, factors such as being White (Exp(B) = .786, p<.001, CI = .692-.893) and a second-year undergraduate student (Exp(B) = .851, p<.001, CI = .761-.951) or higher decreased the odds of illicit prescription painkiller use, on average.

Conclusions

This study identifies various predictors, characteristics, and risk factors for Canadian university students that may use prescription painkillers without the prescription from a healthcare professional. These findings provide valuable insights for policymakers and university student health care systems support at-risk students.

Neighborhood Disadvantage and Vaccine Preventable Diseases in Dogs Christopher Pierson*
Christopher Pierson Kendra Ratnapradipa Elizabeth VanWormer Christopher Wichman Edward
Peters

A One Health model suggests that a dog's neighborhood has a similar impact on its health as in humans. In humans, increasing neighborhood disadvantage (ND) has been associated with negative impacts on health outcomes; however, the impact of ND on companion animal health is understudied.

The American Animal Hospital Association (AAHA) recommends companion dogs be vaccinated for distemper, adenovirus, parvovirus, parainfluenza, and rabies, as well as Leptospira, Lyme disease, Bordetella, and canine influenza depending on the dog's risk. This analysis assesses the impact of ND on the development of vaccine-preventable diseases in dogs, with the exception of distemper, parvovirus, and rabies, which had no cases during the study period.

The Dog Aging Project (DAP) is a longitudinal cohort of dogs across the United States. Although enrollment in the DAP is ongoing, this analysis was limited to the 2021 DAP dataset consisting of 15,720 dogs with information on disease status and their neighborhood, at both baseline and one annual follow-up.

This study used mixed-effects longitudinal logistic regression to examine the association between ND and common canine infectious diseases. Each disease was modeled individually. Cases were defined as dogs who developed the disease between baseline and follow-up, and non-cases were all other dogs in the cohort who did not develop that disease, independent of their diagnosis with another diseases.

Dogs in more disadvantaged neighborhoods had lower odds of developing kennel cough during the study period (OR: 0.65, 95% CI: 0.46, 0.90) after adjustment for the number of days at daycare per month and vaccination status. No other diseases were associated with ND (p-value> 0.05).

This observed inverse relationship between neighborhood disadvantage and kennel cough could inform veterinarians when prioritizing vaccinations with owners. This relationship may result from improvements to the neighborhood that increase dog contact, such as dog parks.

Women's Health

Oral contraceptives and uterine fibroid development in a prospective ultrasound study of Black and African American women Christine Langton* Christine Langton Donna Baird Quaker Harmon

Uterine fibroids are highly prevalent benign tumors of the uterine muscle. Fibroids are the leading indication for hysterectomy, and Black and African American women are disproportionally burdened. Fibroids are dependent on estrogen and progesterone and oral contraceptives (OCs) manipulate these hormone levels. Studies examining the relationship between OCs and fibroids have had mixed results, and none utilized ultrasounds to prospectively assess fibroid incidence and growth.

We evaluated the association between OCs and fibroid development among 1,610 self-identified Black/African American women aged 23-35 years in the Study of Environment, Lifestyle & Fibroids. A standardized ultrasound examination was conducted at 4 clinic visits over 5 years to detect fibroids ≥0.5 cm in diameter. OC use was assessed at each visit and age at first use was reported at enrollment and derived thereafter. We used Cox regression to estimate hazard ratios (HRs) and 95% CIs for the association between OCs (time-varying current use and age at first use) and incident fibroids. Fibroid growth was defined as change in log-volume per 18 months for fibroids matched at successive visits. Incidence and growth models were adjusted for time-varying demographic and reproductive factors.

Of 1,232 fibroid-free participants at enrollment, 122 (10%) were current OC users, 79 (6%) first used OCs before age 15 years, and 295 (24%) developed incident fibroids over the study. Current OC use was not associated with risk of incident fibroids compared to no current use (aHR=1.15; 95% CI: 0.79, 1.69), yet was associated with a 13.7% reduction in fibroid growth (95% CI: -24.2%, -1.7%). Risk of incident fibroids was decreased for those who began using OCs before age 15 (aHR=0.53; 95% CI: 0.30, 0.94), but average fibroid growth differed little by age at first use.

Results from this ultrasound-based, prospective fibroid study add important data to understanding the complex relationship between OC use and fibroids.

Women's Health

Health system barriers and facilitators to accessing non-barrier contraceptives among women sex workers in Vancouver, Canada: Findings from a longitudinal cohort study (2010-2023)

Emma Stirling-Cameron* Emma Stirling-Cameron Andrea Krüsi Esteban Valencia Kaylee Ramage Shira Goldenberg

Background: Despite purportedly universal health care access in Canada, sex workers (SWs) experience suboptimal access to care, particularly in relation to sexual and reproductive health. Given limited data regarding health system factors influencing access to non-barrier contraception among SWs, we aimed to assess the association between health system factors (health insurance coverage, access to family physicians) and difficulty accessing non-barrier contraceptives (i.e., hormonal, long-acting, and emergency contraceptives, excluding condoms) in a prospective cohort of SWs in Vancouver, Canada.

 Methods: Baseline and semi-annual questionnaire data were from an open community-based cohort of women SWs, 2014-2023. Analysis was restricted to people of reproductive age who had never experienced hysterectomy or tubal ligation. Bivariate and multivariable logistic regression with generalized estimating equations (GEE) modelled the association between health system factors and experiencing difficulty accessing non-barrier contraceptives in the past 6 months. Multivariable models adjusted for a-prior confounders.

Results: Among 496 SWs over an 8-year study period, 29% reported difficulties accessing non-barrier contraceptives at least once, 60% lacked health insurance coverage at least once, and 16% never saw a family physician. In multivariable analysis, SWs who lacked health insurance coverage faced higher odds of experiencing difficulties accessing non-barrier contraceptives (AOR:1.7,95%CI:1.3-2.3). Participants who saw a family physician in the last six months faced reduced odds (AOR:0.8,95%CI:0.6-1.1) of experiencing difficulties accessing non-barrier contraceptives.

Conclusion: SWs face gaps in access to non-barrier contraceptives, which was enhanced among those with limited access to health coverage and primary care. Scale-up of confidential sexual and reproductive health services is needed, alongside structural interventions to decriminalize and destigmatize sex work.

Women's Health

A conceptual model for understanding how caste-based discrimination may underlie disparities of medical sterilization of Scheduled Caste/Scheduled Tribe women in India
Sage Smith* Sage Smith Parvati Singh

Historically, the caste system has formed the foundation of hierarchical discrimination in India. One of the groups most impacted by caste-based discrimination comprise women from the Scheduled Castes and Scheduled Tribes (SC/ST), which form the lowest ranked castes in the caste system. Women from these groups are viewed as "ritually polluted," and face discrimination in the economic, political, educational, and health sectors in India. We present a conceptual framework that links caste-based discrimination to coercive reproductive suppression through female surgical sterilization among SC/ST women in India. Introduced during The Emergency by Indira Gandhi's government in the 1970s, female surgical sterilization has been used aggressively to control India's population crisis. Because SC/ST women are devalued in Indian society, their fertility remains highly stigmatized and continues to be viewed as the driving force behind the population crisis. It is thus plausible that SC/ST women experience coercive sterilization at higher rates relative to upper caste women in India. Consequently, SC/ST women may also exhibit higher rates of sterilization regret relative to women from the higher castes. This group also faces unique barriers in access and utilization of health care services. We propose a conceptual model that links caste based discrimination, healthcare access, government policies and coercive sterilization among SC/ST women in India. Our conceptual framework may aid research and policy towards identification and reduction of adverse reproductive health outcomes in vulnerable groups.
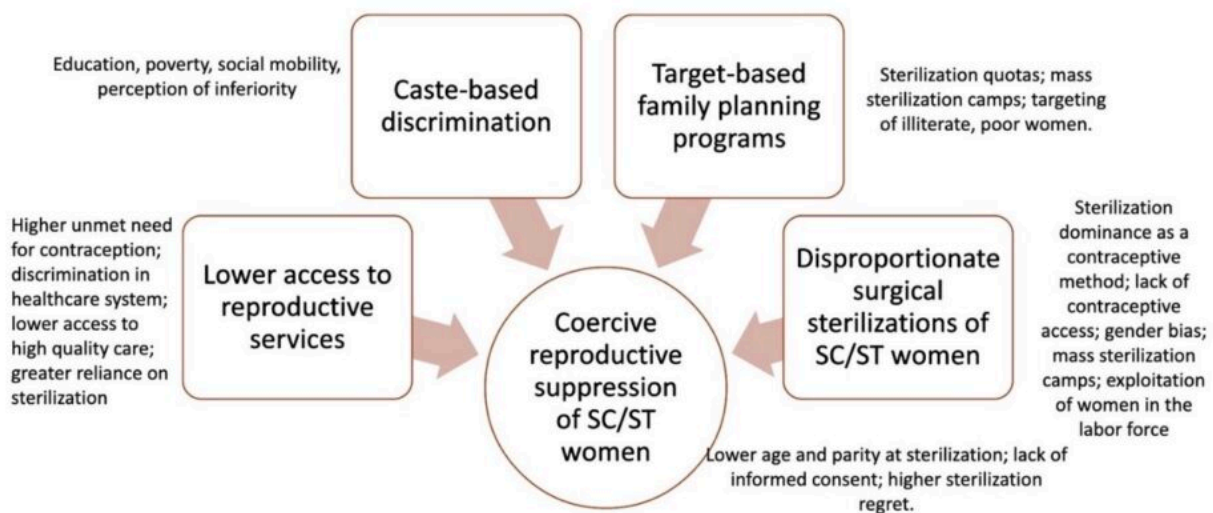
LATEBREAKER

Women's Health

Association of Prenatal Smoking and Low Birth Weight: A Comprehensive Analysis of Colorado PRAMS Data Sunghyun* Sunghyun Chung

Introduction
Prenatal smoking is a significant public health concern due to its association with adverse infant outcomes such as low birth weight (LBW), which increases the risk of mortality and morbidity. Understanding the epidemiology of prenatal smoking and its impact on infant outcomes is crucial for designing effective interventions. This study aims to investigate the prevalence of prenatal smoking and its association with LBW infants in Colorado, as well as to identify social and economic disparities in smoking cessation during pregnancy.

Methods
Data between 2019-2021 from the Pregnancy Risk Assessment Monitoring System (PRAMS) in Colorado were analyzed (n=1,147). Descriptive statistics and prevalence ratios were calculated to assess the prevalence of prenatal smoking and its association with LBW infants, as well as social and economic disparities in smoking cessation during pregnancy.

Results
Prenatal smoking prevalence varied across demographic groups, with higher rates observed among Black/Non-Hispanic women (25.9%). The lower the income, especially those who are beneath the poverty level (27.5%), the higher the smoking prevalence over the past 3 months. Prenatal smoking was associated with a higher risk of LBW, with infants exposed to smoking in the last trimester having an 80% increased risk of LBW compared to unexposed infants.

Discussion/Conclusion
Addressing social and economic disparities in smoking cessation during pregnancy is essential for improving maternal and infant health. This study highlights the need for comprehensive public health efforts and interventions to support smoking cessation during pregnancy and ultimately improve birth outcomes, especially among those in the high-risk populations identified in this study.

LATEBREAKER

Women's Health

The Impact of Pre-Pregnancy Obesity on the Relationship between COVID-19 Infection and Preeclampsia and Eclampsia in South Carolina (2020-2022) Sarah E. Simpson* Sarah E. Simpson Angela Malek Chun-Che Wen Brian Neelon Dulaney A. Wilson Julio Mateus John Pearce Kalyan Chundru Erin Wilkie Jeffery E. Korte Hermes Florez Kelly J. Hunt

Introduction: COVID-19 has been associated with adverse maternal birth outcomes with some studies reporting an increased risk of preeclampsia (PE) and eclampsia (E). Moreover, while obesity has been associated with increased risk of severe COVID-19, it is unclear whether obesity modifies the association between COVID-19 and risk of PE and E during pregnancy. Therefore, we aim to assess the impact of pre-pregnancy obesity on the association between COVID-19 and PE/E in South Carolina from 2020-2022.

Methods: SC vital records and hospitalization/ED visit data were linked for women with liveborn singleton births to define PE and E; COVID-19 infection data was also linked. Adjusted logistic regression models assessed the interaction of COVID-19 infection by trimester and obesity in relationship to development of PE/E.

Results: In our cohort of pregnancies in South Carolina from 2020 through 2022, the prevalence of COVID-19 was 6.7% prior to pregnancy, 6.0% during the 1St/2nd trimester and 3.6% during the 3rd trimester with 83.6% of pregnancies unexposed to COVID-19. The prevalence of PE/E was 9.2%. Among the non-Obese, relative to those without a history of COVID-19, having COVID-19 pre-pregnancy (OR:1.21,95% CI=1.09 -1.34), during the 1st/2nd trimester (OR:1.24,95% CI:1.11-1.37) and during the 3rd trimester (OR:1.21, 95% CI: 1.06-1.39) was associated with an increased odds of PE/E. Among the obese, having COVID-19 pre-pregnancy (OR:1.09,95% CI: 0.99-1.20), during the 1st or 2nd trimester (OR:1.03,95% CI: 0.92-1.14) and the during 3rd trimester (OR:1.00, 95% CI:0.87-1.14) was not associated with a PE/E.

Conclusion: In non-obese women a history of COVID-19 prior to pregnancy and during pregnancy was associated with PE/E. In contrast, in obese women neither a history of COVID-19 prior to or during pregnancy was associated with increased risk of PE/E. Our results highlight the importance of preventive strategies (e.g. weight management and vaccines) for this population.

Table. Odd Ratios (ORs) for Preeclampsia or Eclampsia ([PE or E]) by COVID-19 infection status stratified by pre-pregnancy obesity.

	PE or E OR (95% CI) Model 1[b]
COVID-19 infection (Non-obese pre-pregnancy)*	
No history of COVID-19	**REF**
Prior to pregnancy	**1.21 (1.09-1.34)**
First and/or second trimester	**1.24 (1.11-1.37)**
Third trimester	**1.21 (1.06-1.39)**
COVID-19 infection (Obese pre-pregnancy)*	
No history of COVID-19	**REF**
Prior to pregnancy	1.09 (0.99-1.20)
First and/or second trimester	1.03 (0.92-1.14)
Third trimester	1.00 (0.87-1.14)
Socio-Demographic Factors	
Maternal age at delivery	**1.02 (1.02-1.02)**
Delivery quarter time	1.01 (1.00-1.01)
Medicaid	**1.17 (1.12-1.23)**
Race/ethnicity	
Non-Hispanic White	**REF**
Non-Hispanic Black	**1.17 (1.12-1.22)**
Hispanic	**0.88 (0.81-0.95)**
Other	0.92 (0.83-1.01)
Education level[a]	
<High school	**1.20 (1.12-1.29)**
High school graduate/GED	**1.14 (1.07-1.20)**
Some college	**1.15 (1.09-1.22)**
≥College graduate	**REF**
Rural residence (vs. urban)	0.97(0.93-1.01)
Lifestyle and Clinical Factors	
Tobacco use during or pre-pregnancy[a]	0.96 (0.89-1.03)
Firstborn[a]	**1.98 (1.90-2.07)**
Previous preterm delivery	**1.59 (1.48-1.71)**
Pre-pregnancy hypertension	**4.03 (3.86-4.22)**
Pre-pregnancy diabetes	**1.69 (1.55-1.85)**

[a] Missing values: education, 573; tobacco use during or pre-pregnancy, 55; firstborn,155

[b] Interaction of COVID-19 infection and pre-pregnancy obesity on PE or E for socio-demographic, lifestyle and clinical factors (**Bolded** indicates significance).

* P-value for the interaction between COVID-19 infection status and pre-pregnancy obesity for PE or E was 0.03 (unadjusted).
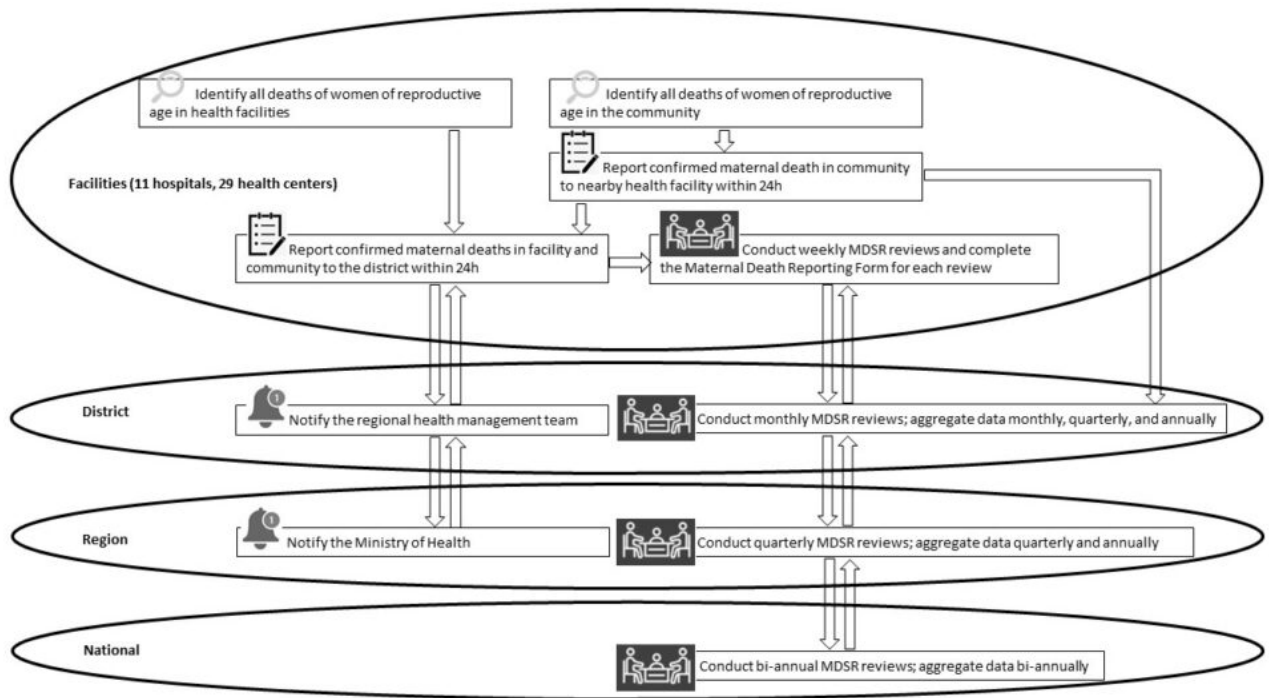
Women's Health

Evaluation of the Maternal Death Surveillance and Response (MDSR) System in the Kigoma Region, Tanzania
Sifang Kathy Zhao* Sifang Kathy Zhao Carly Malburg Carrie Shapiro-Mendoza Florina Serbanescu

Background: In 2020, about 287,000 women died worldwide during or after pregnancy and childbirth. Most of these deaths occurred in low-income countries and are preventable. To reduce maternal mortality, many countries use Maternal Death Surveillance and Response (MDSR). Since 2015, Tanzania has used MDSR for monitoring deaths, reviewing causes, and implementing interventions. Kigoma, the Tanzanian region with the greatest need for improved maternal services, has not evaluated their MDSR.

Methods: Leveraging an ongoing collaborative evaluation with the Tanzania Ministry of Health, we visited all 11 hospitals and 29 health centers that provided maternity care in Kigoma during May 2023. We interviewed facility staff using a standardized questionnaire to assess how the 2019 Tanzania MDSR Guidelines were being implemented (Figure). We compared facility activities to national guidelines and assessed the regional MDSR system using the US Centers for Disease Control and Prevention guidelines for evaluating surveillance systems, specifically the attributes of acceptability (actual engagement in MDSR activities) and timeliness (reviews conducted within 7 days of death required by the national guidelines).

Results: All hospitals (100%) and most health centers (93%) had an MDSR coordinator, a review committee, and a formal system for reviewing maternal deaths. Only 36% of hospitals and 28% of health centers documented and reviewed community-occurring deaths. Reviews within 7 days of death were held in 73% of all hospitals and 66% of all health centers. Others held reviews monthly (27% of hospitals; 3% of health centers) or quarterly (24% of health centers).

Conclusion: In Kigoma, acceptability of MDSR is high in hospitals and health centers. However, about 1 in 4 committees did not hold reviews within 7 days, and most committees did not review community deaths. Improving timeliness and community reporting processes may strengthen MDSR and help reduce preventable maternal deaths.

Figure. Summary of Maternal Death Surveillance and Response (MDSR) guidelines, Tanzania, 2019.
Abbreviations: h, hours; MDSR, Maternal Death Surveillance and Response.

Women's Health

Healthy People 2030: Examining Progress and Disparities in Women's and Girls' Health
Leda Gurley* Leda Gurley LaJeana Hawkins

Healthy People is a national initiative to promote health and reduce disease through the setting and tracking of objectives and targets. The fifth and current iteration of the initiative, Healthy People 2030 (HP2030) includes an overarching goal to eliminate health disparities and achieve health equity. Of the 359 HP2030 core objectives, 251 have data on women and girls, and 22 solely track women's and girls' health. This analysis examines the progress made toward national targets and assesses disparities for five HP2030 objectives related to the reproductive health and well-being of women and girls.

Progress toward the targets was measured using the percentage of targeted change that was achieved. Disparities were assessed within specified demographic characteristics (race/ethnicity, age, education, and geographic location) and quantified using the highest rate (Rmax), lowest rate (Rmin), and maximal rate ratio (MRR).

Assessment of progress toward national targets shows that two of the five HP2030 objectives have little or no detectable change (cervical cancer screening among females 21-65 years; sexually active females 16-24 years screened for chlamydia), two are getting worse (pregnant women receiving early and adequate prenatal care; maternal deaths), and one is improving (emergency department visits for pelvic inflammatory disease). Evaluation of disparities of objectives with demographic data shows that disparities exist. For example, White, non-Hispanic pregnant women had the highest rate (80.5%) of receiving early and adequate prenatal care among racial/ethnic groups, 70% higher than Native Hawaiian or Other Pacific Islander, non-Hispanic pregnant women who had the lowest rate (47.2%).

Our assessment of progress and disparities shows that progress toward meeting national targets is mixed and that disparities exist. Continuing efforts are needed to address disparities in women's and girls' health, and tracking progress may help guide prevention efforts.

Women's Health

Preexisting Anemia Prevalence and Association with Severe Maternal Morbidity Indicators During Inpatient Hospitalization Deliveries from 2016-2022 Ashley Finke* Ashley Finke Alley Masocco

Maternal anemia has been reportedly associated with an increased risk of maternal morbidity. Anemia disproportionately affects American Indian, Black, and other minoritized patients, significantly amplifying severe maternal morbidity (SMM) disparities.

This study aims to determine the prevalence of in-hospital anemia among delivering patients with specific SMM indicators, assess the prevalence of hospital-acquired (HA), preexisting-acquired (PA), and inherited (IA) anemia among demographics, and examine the association of non-HA among delivering mothers with specific SMM outcomes.

This retrospective cohort study was conducted using data from the PINC AI™ Healthcare Database, 2016-2022. All measures were defined using ICD-10-CM diagnosis or procedure codes**.** Descriptive analysis was performed to assess the prevalence of anemia, SMM and patient demographics. Multivariable logistic regression models were utilized to examine the associations between PA with each SMM indicator. Models were adjusted to account for potential confounding patient, hospital, and COVID-19 effects. Exposure variable p-values were adjusted using the false discover rate to account for the multiplicity impact of multiple comparisons.

Among the 6,306,303 unique hospital deliveries, the highest rates of any anemia occurred among patients aged 10-19 (26%), Medicare/Medicaid payors (24%,23%), and American Indian and Black patients (25%,30%) in comparison to White reference patients (16%). The prevalence of anemia per 1,000 discharges: PA 127, IA 11, and HA 63. PA is associated with 11 SMMs and IA is associated with 3 SMMs. PA and IA both had statistically significant increased odds ($p<0.05$) of air and thrombotic embolism (OR:1.8,1.7). PA had a statistically significant increased odds of eclampsia and sepsis (OR:1.2,2.1).

This study contributes to critical insights into the impact of maternal anemia (including among preexisting anemia subtypes) among individual SMMs and demographic attributes.

Preexisting Anemia Significant Associations with SMM Indicators