Aging

Prevalences of United States Preventive Services Task Force-recommended cancer screenings in older adults with Medicare Advantage versus traditional Medicare Elyse Miller* Elyse Miller Allison Musty Emilie D Duchesneau Anna Kuzma Til Stürmer Amresh Hanchate Dae Hyun Kim Jennifer L Lund

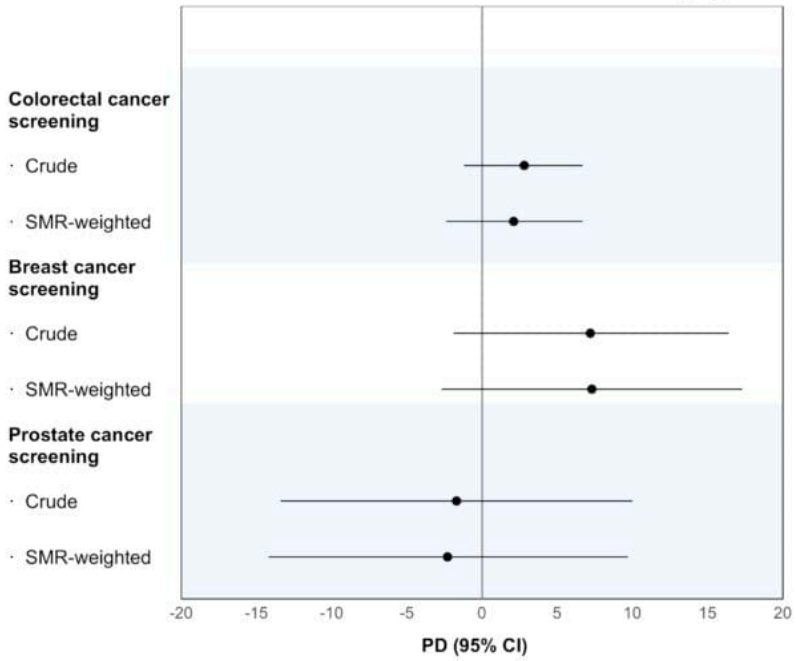
Background: Medicare Fee for Service (FFS) claims are an established resource for epidemiologic research while the utility of Medicare Advantage (MA) data, only made available for research in 2019, remains largely unexamined. To address this, we compared standardized prevalences of cancer screenings in MA encounter vs FFS claims data.

Methods: We used Medicare enrollment, claims, and encounter data linked with the National Health and Aging Trends Study (NHATS), a nationally-representative cohort of Medicare beneficiaries >65 years. Round 7 (2017) NHATS interview participants with continuous enrollment in Medicare for 365 days ('pre-index period') before the interview were included. We identified cancer screenings using ICD-10 diagnosis codes and defined participants with >1 code during the pre-index period as 'screened'. To account for differences in the beneficiary populations, we standardized FFS beneficiaries to MA beneficiaries by age, gender, race, ethnicity, rurality, education, frailty, dementia, comorbidities, smoking, sensory impairment, falls, and hospitalizations measured in NHATS. We estimated the prevalence difference (PD) and 95% confidence interval (CI) for colorectal cancer screening, breast cancer screening (among women), and prostate cancer screening (among men) in MA vs FFS data.

Results: Of the 4,804 beneficiaries in our cohort (median age 74 years, 56% female), 40% had MA and 60% had FFS plans. MA beneficiaries were more likely to be Black, Hispanic, have less than a high school degree, and reside in a metropolitan area. Comparing MA to FFS data, standardized prevalence differences were 2.1% (95% CI -2.4–6.7%) for colorectal cancer screening, 7.3% (95% CI -2.7–17.3%) for breast cancer screening, and -2.3% (95% CI -14.2–9.7%) for prostate cancer screening. Crude estimates were similar.

Conclusions: Cancer screening prevalences were comparable between MA and FFS, supporting the use of MA encounter data for epidemiologic research among older adults.

Figure 1. SMR-weighted differences in prevalence of cancer screenings between Medicare Advantage and Fee-for-Service beneficiaries in the Round 7 National Health and Aging Trends Study (2017).



	MA (%)	FFS (%)	PD (95% CI)
Colorectal cancer screening			
· Crude	20.6	17.8	2.8 (-1.2, 6.7)
· SMR-weighted	20.6	18.5	2.1 (-2.4, 6.7)
Breast cancer screening			
· Crude	62.4	55.2	7.2 (-1.9, 16.4)
· SMR-weighted	62.4	55.1	7.3 (-2.7, 17.3)
Prostate cancer screening			
· Crude	31.9	33.6	-1.7 (-13.4, 10.0)
· SMR-weighted	31.9	34.2	-2.3 (-14.2, 9.7)

Abbreviations: SMR=standardized mortality ratio; FFS=Fee-for-Service; MA=Medicare Advantage; PD=prevalence difference; CI=confidence interval.

Screening

Transporting the effects of lung cancer screening from the National Lung Cancer Screening Trial to a US target population screened within the past year Xiaomeng Chen* Xiaomeng Chen Louise M. Henderson Gauri Bhatkhande I-Hsuan Su Bria Carmichael Michael G. Hudgens M. Patricia Rivera Daniel S. Reuland Til Stürmer Jennifer L. Lund

Background: The National Lung Screening Trial (NLST) showed that low-dose computed tomography (LDCT) versus chest radiography (CXR) reduces lung cancer mortality. However, the broader population eligible for and undergoing lung cancer screening differs from trial participants; these differences, along with others, may impact real-world population effectiveness. We aimed to estimate the effects of screening with LDCT versus CXR on lung cancer mortality, had the NLST been conducted in a target population undergoing screening in 2024.

Methods: We used individual-level data from the NLST and 2024 Behavioral Risk Factor Surveillance System (BRFSS). BRFSS respondents meeting NLST eligibility criteria and reporting lung cancer screening in the past year were included. We applied inverse odds weights for trial participation, combined with BRFSS survey weights, and Poisson regression to estimate the average effects of LDCT versus CXR on lung cancer mortality in the screened population (i.e., average treatment effect in the treated). We estimated 95% confidence intervals (CIs) using a robust variance estimator.

Results: This analysis included 53,452 NLST participants and 4,259 BRFSS respondents (weighted n=1,683,411) recently screened with LDCT. Compared with the NLST, the target population was older, more racially and ethnically diverse, and had more comorbidities. In the unweighted NLST population, the overall lung cancer mortality rate was 280 deaths per 100,000 person-years (PYs); the incidence rate ratio (IRR) comparing LDCT versus CXR on lung cancer mortality was 0.80 (95% CI 0.69-0.92). In the weighted NLST population, the lung cancer mortality rate was 453 deaths per 100,000 PYs; the IRR of lung cancer mortality for LDCT versus CXR was 0.88 (95% CI 0.69-1.13).

Conclusion: Compared to the unweighted NLST population, the weighted NLST population had substantially higher lung cancer mortality rates but a slightly attenuated relative mortality benefit of LDCT versus CXR.

Screening

Real-World Adherence to Annual Lung Cancer Screening with Low-Dose CT Accounting for Competing Risks Gauri Bhatkhande* Gauri Bhatkhande Louise M. Henderson I-Hsuan Su Til Stürmer M. Patricia Rivera Michael G. Hudgens Daniel S. Reuland Virginia Pate Xiaomeng Chen Bria Carmichael Jessie K. Edwards Jennifer L. Lund

Background:

Annual lung cancer screening (LCS) with low-dose computed tomography (LDCT) reduces lung cancer mortality among high-risk individuals, but the effectiveness of this intervention depends upon adherence to annual screening. We quantified and described real-world adherence to annual LCS with LDCT among Medicare beneficiaries.

Methods:

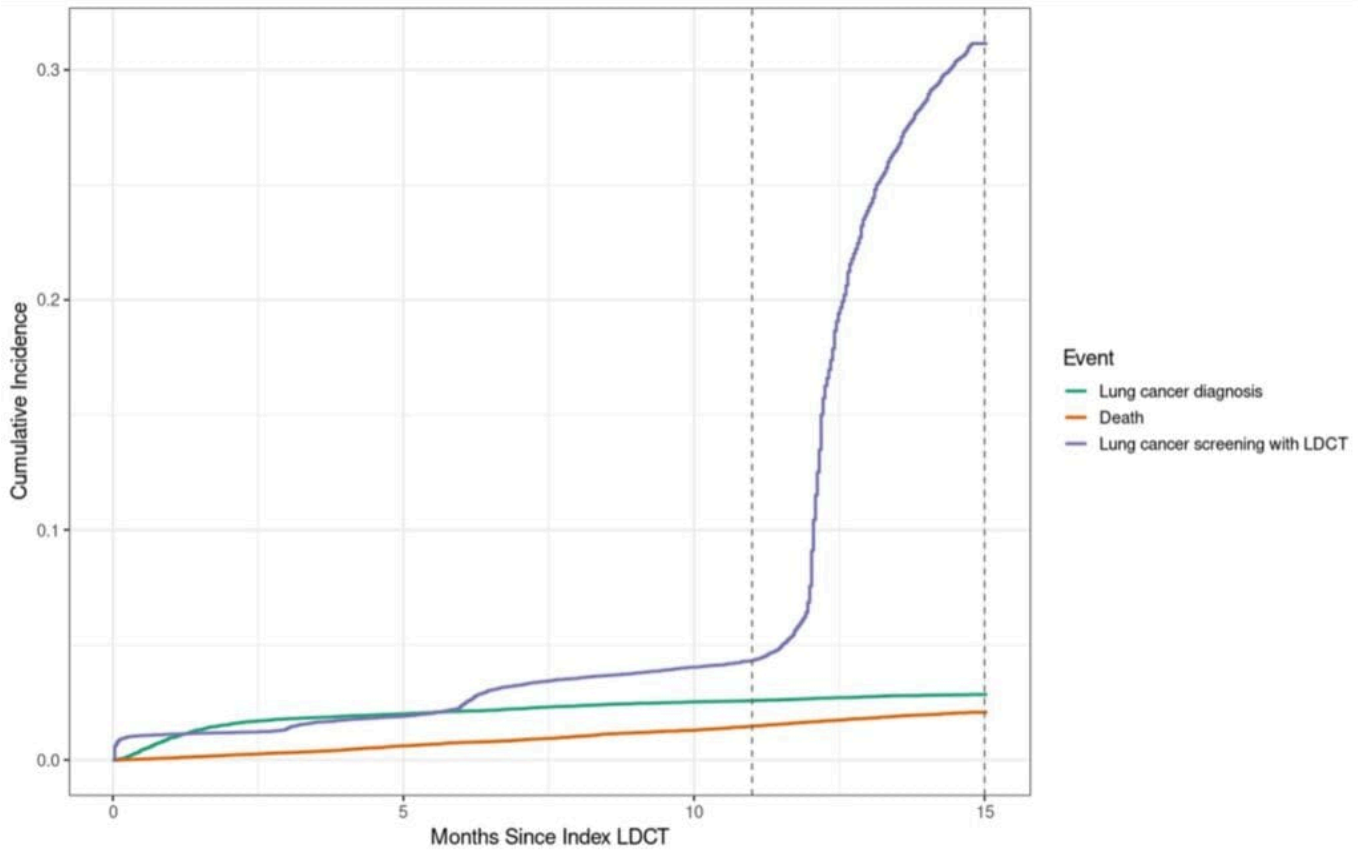
We conducted a retrospective cohort study of individuals, aged ≥66 years, who received a first LCS with LDCT between 2015 and 2019, and had no prior history of lung cancer, using Medicare fee-for-service claims. Annual adherence was defined as receipt of a subsequent LDCT screening within 11 to 15 months of the first screen. We estimated cumulative incidence functions (CIFs) using Aalen-Johansen estimator, treating lung cancer diagnosis and death as competing events. CIFs were estimated overall and stratified by age, sex, race and ethnicity, comorbidity index, and frailty index. We reported the cumulative incidence from 11 to 15 months, as this represents a reasonable window for determining adherence to annual LCS. We estimated 95% confidence intervals using non-parametric bootstraps with 500 replicates.

Results:

Among 54,978 patients with an initial LDCT claim, the cumulative incidence of subsequent LCS was 4.3% (95% CI: 4.1-4.5%) at 11 months, and 31.1% (95% CI: 30.7-31.6%) at 15 months, with an annual adherence of 26.8% (95% CI: 26.3-27.3%) between 11 and 15 months. Adherence to LCS was higher among those who were younger, white, less frail, and had lower comorbidity burden. The cumulative incidences of lung cancer and death were 2.1% (95% CI: 2.0-2.2%) and 2.9% (95% CI: 2.7-3.0%), respectively.

Conclusions:

Real-world adherence to annual lung cancer screening with LDCT remains suboptimal among Medicare beneficiaries, with fewer than one-third completing subsequent screening within 15 months. These findings highlight a gap in screening implementation that may limit its effectiveness at the individual and population-levels.


0.3
0.2
0.1
0.0
Cumulative Incidence
0
5
10
15
Months Since Index LDCT
Event
Lung cancer diagnosis
Death
Lung cancer screening with LDCT

Occupational

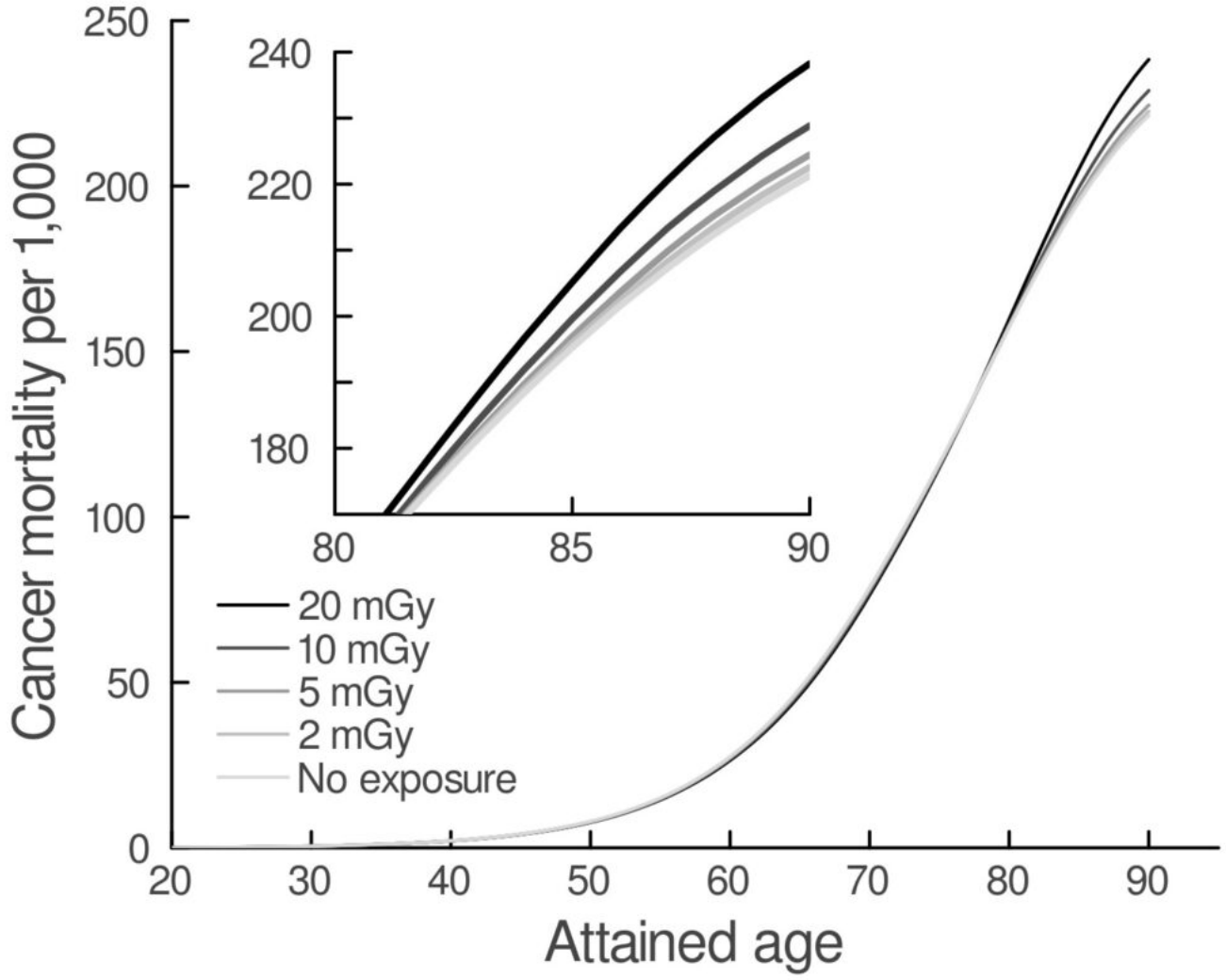
Ionizing Radiation and Cancer Mortality in the INWORKS pooled cohort: Assessing Healthy Worker Survivor Bias Alexander P. Keil* Alexander Keil Kaitlin Kelly-Reif Stephen Bertke Robert D. Daniels Isabelle Thierry-Chef Monika Moissonnier Ausrele Kesminiene Mary K. Schubauer-Berigan Clemence Baudin Dominique Laurier Richard Haylock David B. Richardson

Ionizing radiation is an established carcinogen. Occupational cohort studies have provided statistically precise estimates of associations between protracted, low dose exposure to ionizing radiation and various health effects. However, uncertainty about whether these statistical estimates of association accurately represent the causal effects of exposure remains due, in part, to potential for healthy worker survivor bias.

Using data from the International Nuclear Workers Study, 1944-2005 (a pooled cohort mortality study of 308,297 radiation-monitored workers employed in France, United Kingdom, and United States) we assessed whether conditions of healthy worker survivor bias are present. Given evidence of potential for this bias, we used g-computation to address healthy worker survivor bias and estimate impacts of hypothetical radiation exposure scenarios on subsequent cancer mortality.

Remaining employed was associated with lower cancer mortality than leaving employment, a key condition of healthy worker survivor bias. We estimate that if all workers had been exposed to 5, 10, or 20 mGy per year while employed approximately 3.2 (90% CI: -1.9, 8.8), 7.6 (90% CI: 0.8, 15), or 17 (90% CI: 6.5, 26) excess cancer deaths per 1,000 workers would be observed by age 90 years as compared to what would have been observed if all workers had been exposed to 0 mGy per year while employed (Figure).

Results suggest that healthy worker survivor bias is present and that standard regression methods may underestimate radiation dose-cancer mortality associations. Our estimates from a population of workers, most of whom were occupationally exposed to low doses of radiation at low dose rates, strengthens understanding of cancer risks associated with protracted low dose exposure to ionizing radiation.


Cancer mortality per 1,000
250
200
150
100
50
0
20
30
40
50
60
70
80
90
Attained age
240
220
200
180
80
85
90
20 mGy
10 mGy
5 mGy
2 mGy
No exposure

Cancer

Survival Patterns in Early-Onset Colorectal Cancer Among Rural Residents in the USA

Ransome Eke* Ransome Eke Joedrecka Brown Speights Shermeeka Hogans-Mathews Ericka Horne Shannon Smekle

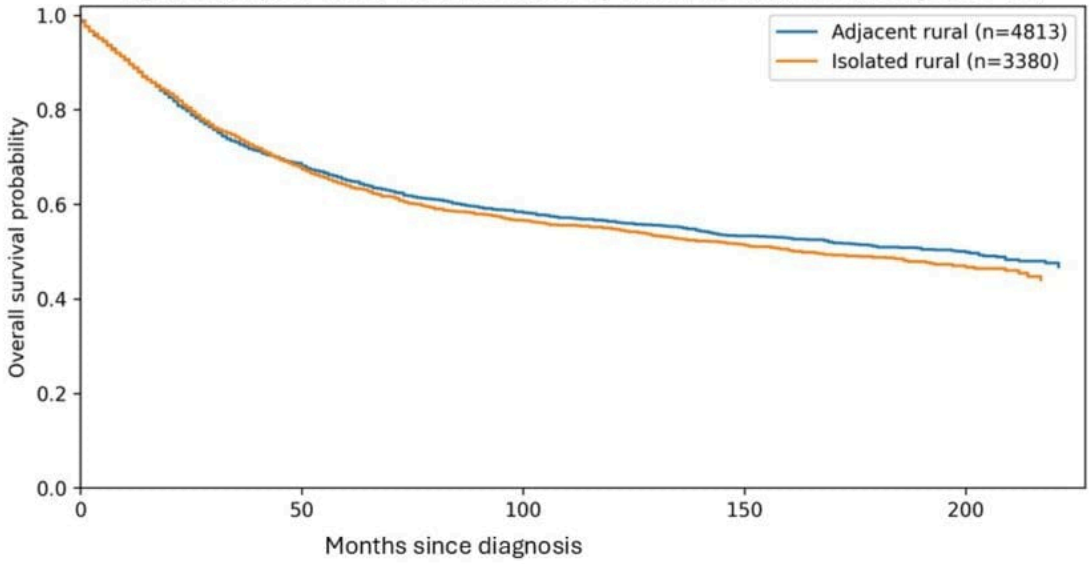
Background: Early-onset colorectal cancer (EOCRC), defined as diagnosis before age 50 years, is increasing in the United States. Rural populations face structural barriers to timely diagnosis and cancer care, yet survival patterns among rural adults with EOCRC remain incompletely characterized. We examined overall survival and within-rural heterogeneity among adults with EOCRC in the USA.

Methods: We conducted a population-based cohort study using Surveillance, Epidemiology, and End Results (SEER) data from 2013–2022. Adults aged 20–49 years with a first primary colorectal cancer residing in nonmetropolitan counties at diagnosis were included. Rural isolation was defined by adjacency to metropolitan areas. Overall survival was the primary outcome. Unadjusted survival differences were assessed descriptively, and a multivariable Cox proportional hazards model estimated the adjusted association between rural isolation and mortality.

Results:
The analytic cohort included 8,193 rural EOCRC patients; 46.0% were female. Forty-one percent (n=3,380) resided in nonmetropolitan counties not adjacent to metropolitan areas. Median overall survival was 66 months. Survival was lower among isolated rural residents compared with metro-adjacent rural residents (median 62 vs 69 months), with higher all-cause mortality (44.7% vs 41.6%; χ^2 p=0.04). In adjusted Cox models controlling for sex, race/ethnicity, tumor site, and year of diagnosis, isolated rural residence was associated with a modest but not statistically significant increase in mortality risk (HR=1.06; 95% CI: 0.97–1.17; p=0.21).

Conclusions: Rural adults with EOCRC in the USA experience substantial mortality, with worse unadjusted survival among those living in more geographically isolated communities. Findings underscore the importance of examining within-rural structural and healthcare access factors, including stage at diagnosis and treatment patterns, to better understand and address EOCRC survival disparities.

Figure 1. Kaplan–Meier Overall Survival by Rural Isolation (EOCRC, ages 20–49)



Cancer

Patient Experience and Provider Symptom Review During Survivorship Care Among Black and White Survivors in the Carolina Endometrial Cancer Study Mu Jin* Mu Jin Marc Peterson Taylor Ellington Brittney Gedeon Victoria Bae-Jump Andrew Olshan Hazel Nichols

Background: Endometrial cancer (EC) is the most common gynecologic cancer in the United States. National Comprehensive Cancer Network (NCCN) survivorship guidelines recommend evaluation of 9 symptom domains: cardiac toxicity; mental health (anxiety, depression, trauma, and distress); fatigue; lymphedema; hormone-related symptoms; pain; sexual function; sleep disorders; and healthy lifestyle components (weight, diet, and physical activity). We investigated variation by race in patient-reported symptoms and whether symptoms were discussed with medical providers.

Methods: We analyzed data from 555 EC survivors enrolled in the ongoing Carolina Endometrial Cancer Study. We estimated the association between race and patient-reported symptoms (and symptom discussions) using multivariable Poisson regression models to calculate prevalence ratios (PR) and 95% confidence intervals (CI) adjusted for age at survey, tumor stage, and treatment received.

Results: The cohort included 202 Black and 353 White survivors (mean age at survey=63, mean time since diagnosis=1.8 years). Majority of survivors reported weight/diet concerns (80%), sleep disorders (63%), and pain (55%). All symptom domains had higher prevalence among Black survivors compared to White, with the largest differences seen for hormone-related symptoms (50% vs. 17%), lymphedema (43% vs. 28%) and pain (61% vs. 51%). In multivariable models, Black survivors were 41% more likely to report lymphedema (CI: 1.10, 1.81) and 43% more likely to report hormone-related symptoms (CI: 1.15, 1.77) compared to White survivors. Provider discussions were statistically different only for fatigue. Black survivors who reported fatigue were 14% less likely to discuss their symptoms with a provider than White survivors (79% vs. 93%, PR=0.86; 0.75-0.99).

Conclusion: Widespread implementation of NCCN survivorship guidelines may help reduce racial disparities in long-term EC survivorship outcomes.

Behavior

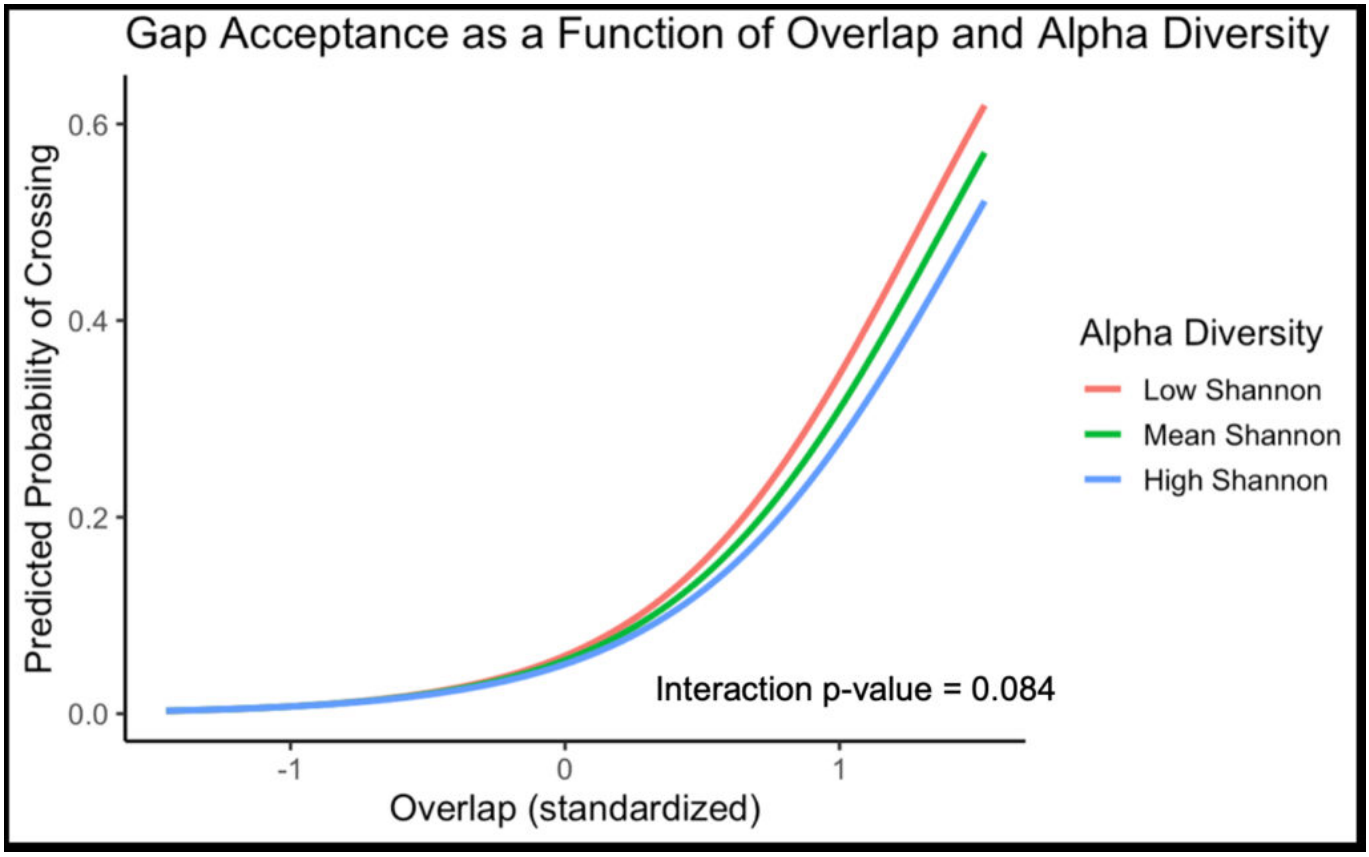
Using Virtual Environments to Study Gut Microbiome-Linked Decision Making During Road Crossing in Older Adults Kshitij Sachdev* Kshitij Sachdev Ella Mucciolo Hammad Ahmad Joeseph Eggers Natalie Denburg Shoshannah Eggers Elizabeth O'Neal

Background: Older adults experience disproportionately high rates of pedestrian injury and mortality, in part due to age-related declines in Executive Function (EF) that impair safe road-crossing decisions. The Gut Microbiome (GM) regulates brain function via the gut-brain axis, including through microbial metabolites such as Short-Chain Fatty Acids (SCFAs). However, the role of the GM in decision making remains largely unexplored.

Methods: Participants (n = 102), aged 60-87, completed cognitive testing, a virtual reality (VR) road-crossing task, and provided stool samples. GM composition was characterized using 16s sequencing to derive alpha and beta diversity metrics. Stool SCFAs (acetate, butyrate, propionate) were quantified using mass spectrometry. EF was assessed using the NIH Cognitive Toolbox and Trail Making Test, a behavioral measure of EF. In the VR task, participants crossed two lanes of opposing traffic 20 times, with repeated crossing opportunities defined by temporal overlap between near- and far- lane traffic gaps. VR Crossings were modeled using logistic mixed-effects regression with participant random intercepts, including traffic structure, microbiome features, and their interaction as predictors, adjusting for age, gender, and education. Associations between GM, SCFAs, and EF were evaluated using linear regression and PERMANOVA.

Results: Higher butyrate levels were associated with faster performance on Trail Making Test Part A ($\beta = -0.0259$, $p = 0.048$). Beta diversity (Bray-Curtis) was associated with NIH Toolbox measures of EF ($R2 = 6.12\%$, $p = 0.048$), Inhibitory Control ($R2 = 6.13\%$, $p = 0.053$), and Processing Speed ($R2 = 6.11\%$, $p = 0.057$). In the VR task, gap acceptance was strongly driven by near-far lane overlap. Alpha diversity modestly modified this relationship ($p = 0.084$), such that individuals with lower microbial diversity showed a steeper increase in crossing probability as overlap increased, indicating reliance on larger gaps.

Conclusion: These findings suggest lower microbial diversity amplifies conservative gap-selection strategies during road crossing. Together, these results support the gut microbiome as a modifiable target for improving cognitive mechanisms underlying pedestrian safety and decision making in aging populations.


Gap Acceptance as a Function of Overlap and Alpha Diversity
Predicted Probability of Crossing
0.6
0.4
0.2
0.0
-1
0
1
Overlap (standardized)
Interaction p-value = 0.084
Alpha Diversity
Low Shannon
Mean Shannon
High Shannon

Neurology

Sleep Health in Late Life and APOE4-associated Risk for Neuropathologic Lesions at Death: the Honolulu-Asia Aging Study Tianyi Huang* Tianyi Huang Susan Redline Lenore Launer Lon White

Introduction: Apolipoprotein E ε4 (ApoE4) drives lipid dysregulation and neurotoxic protein accumulation, contributing to brain lesions. Population-based evidence is limited on whether sleep health mitigates APOE4-associated neuropathologic risk.

Methods: In the Honolulu-Asia Aging Study, 533 Japanese-American men completed ≥2 sleep assessments across four exams (1991–2000) and participated in the autopsy substudy, with APOE4 genotyping available. We created a cumulative average sleep health score (SHS; range 0–5) from repeated questionnaires, assigning 1 point for each favorable sleep factor: sleep duration of 6–8 hrs, no insomnia symptoms, no loud snoring, no daytime sleepiness, and moderate napping (>0 but <60 min). Using multivariable logistic regression, we examined associations between APOE4 and neuropathologic outcomes, including vascular lesions (microinfarcts, lacunar infarcts), Alzheimer's-related pathology (neuritic plaques [NPs], neurofibrillary tangles (NFTs), Braak stage), Lewy bodies (LBs), and generalized brain atrophy, overall and stratified by SHS categories.

Results: Mean (SD) baseline age was 77.4 (4.3) years; the interval between the last sleep assessment and death was 4.7 (3.3) years; 21.4% were APOE4 carriers. After adjustment for baseline age, age at death, education, and cognitive scores, APOE4 carriers had higher odds of microinfarcts, NPs, NFTs, Braak stage V/VI, and LBs, with no associations for lacunar infarcts or brain atrophy. Associations were stronger among participants with poorer sleep health. For example, the OR (95% CI) between APOE4 and NFTs was 4.55 (1.44, 14.38), 2.37 (1.27, 4.41), and 1.33 (0.54, 3.29) in poor, fair, and good sleep health groups, respectively. Further adjustment for behavioral and cardiovascular factors yielded similar results.

Conclusions: Better sleep health may attenuate APOE4-associated risk for multiple brain lesions, suggesting sleep as a potentially modifiable factor relevant to genetic vulnerability.

Aging

Association between prenatal PM2.5 exposure and telomere length among school-age children Hsin-Yi Huang* Hsin-Yi Huang Wen-Chi Pan Chih-Da Wu Ju Chang-Chien Shih-Ling Wang Hui-Ju Tsai Tsung-Chieh Yao

Background: Telomere length is a marker of biological aging that reflects cumulative oxidative stress and inflammation. While prenatal PM2.5 exposure has been associated with telomere length at birth, its influence on telomere length during childhood remains uncertain and unstudied. This study evaluated the association between prenatal PM2.5 exposure and telomere length in school-age children to provide insights into environmental influences on molecular longevity.

Methods: We recruited 1,278 singleton children (mean age: 6.4 years; 43.7% of girls) from the LIGHTS cohort in Taiwan. Telomere length was measured by quantitative real-time PCR at the age of 5-8 years. Prenatal PM2.5 exposure was estimated using hybrid kriging-land use regression models with XGBoost algorithm. A distributed lag non-linear model (DLNM) was applied to evaluate the association between weekly prenatal PM2.5 exposures and childhood telomere length, allowing identification of sensitive exposure windows.

Results: A 10-μg/m3 increment in prenatal PM2.5 exposure during the entire pregnancy was associated with 5.3% (95% CI, -10.3% to -0.2%) shorter telomere length in childhood. DLNM models identified late gestation (28–30 weeks) as a critical window for inverse associations. In stratified analyses, the inverse association between prenatal PM2.5 exposure and childhood telomere length remained statistically significant and more robust within specific strata, including girls, children exposed to environmental tobacco smoke (ETS), and those exclusively breastfeeding for less than 3 months.

Conclusion: This cohort study suggests an association between prenatal PM2.5 exposure and shorter telomere length in school-age children, particularly among girls, those exposed to ETS, and those who were not breastfed.

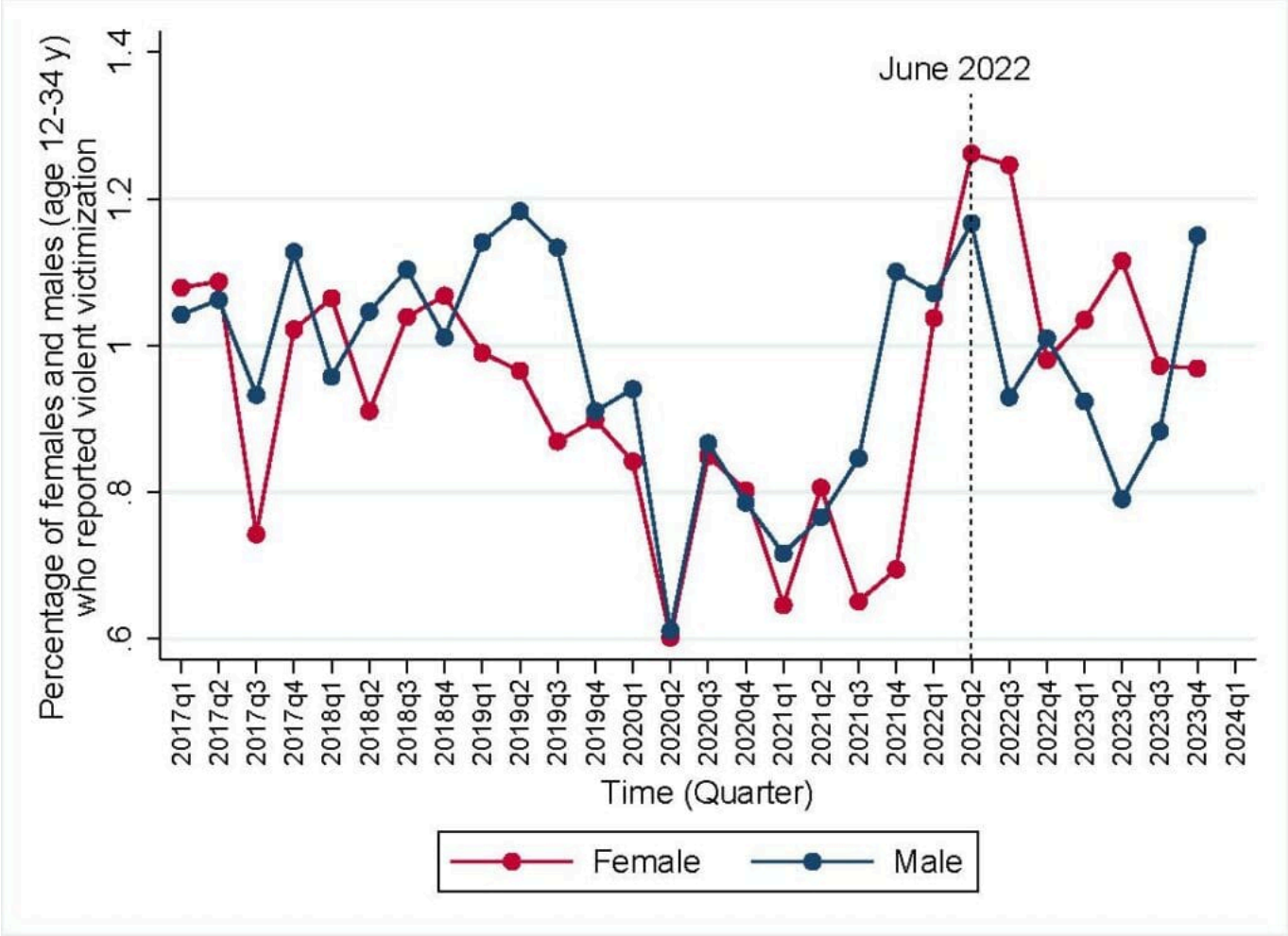
Women’s Health

Impact of the Dobbs Decision on Violent Victimization Among Young Women and Girls in the United States: Evidence from NCVRS (2017–2023) Parvati Singh* Parvati Singh

The 2022 Dobbs v. Jackson Women’s Health Organization decision reshaped reproductive rights in the United States and raised concerns about downstream effects on women’s safety. Structural violence theory suggests that policies restricting bodily autonomy create conditions that elevate vulnerability to harm by reducing agency and reinforcing power imbalances. Reproductive coercion theory further explains how limitations on reproductive choice can intensify control dynamics within intimate relationships, increasing risk for violence. Prior research indicates that younger women and those from lower-resource groups may experience disproportionate impacts of Dobbs through diminished autonomy, which may compound existing vulnerabilities.

We analyzed data from the National Crime Victimization Survey (NCVRS) from 2017–2023 (N = 611,578; weighted population ≈ 699 million) using a difference-in-differences design. The treated group included females aged 12–34 years (comparison group being similarly aged males), and the treatment period began in June 2022 (1 for June 2022 onward, 0 prior). The outcome measured violent victimization as a binary indicator. Logistic regression models adjusted for race, continuous age, region, rurality, employment, marital status, and year, month fixed effects with survey weights.

Results indicate that after Dobbs, younger reproductive-aged females (<34 years) faced a 19% higher likelihood of violent victimization compared to pre-Dobbs and relative to males (OR = 1.194, $p < 0.05$). Effects appeared strongest among non-White females with less than high school education (OR = 1.44, p 35 y) and for higher of exposure to property crime post Dobbs in younger females. These results suggest that reductions in bodily autonomy may amplify violence risks among younger females and underscore the need for policy responses that integrate reproductive health protections with violence prevention strategies.


June 2022
Percentage of females and males (age 12-34 y) who reported violent victimization
.6
.8
1
1.2
1.4
2017q1
2017q2
2017q3
2017q4
2018q1
2018q2
2018q3
2018q4
2019q1
2019q2
2019q3
2019q4
2020q1
2020q2
2020q3
2020q4
2021q1
2021q2
2021q3
2021q4
2022q1
2022q2
2022q3
2022q4
2023q1
2023q2
2023q3
2023q4
2024q1
Time (Quarter)
Female
Male

Social

Running Out of Time? The Health Costs of Being Time Poor Laura Chen* Laura Chen

Introduction: Theories of scarcity and chronic stress suggest that time poverty – a lack of discretionary time outside of work and other responsibilities – may harm health and compound the effects of material deprivation, but these effects are not well studied. Using causal methods and longitudinal data (2017–2023) from the Panel Study of Income Dynamics, we estimate the effects of time poverty – alone and in combination with income poverty – on cardiometabolic and mental health.

Methods: The analytic sample included n=14,900 adult respondents free of cardiovascular disease in 2017. At each wave, respondents were classified as time poor, income poor, both, or neither based on household income and total weekly hours in paid work, housework, childcare, and personal care. Stabilized inverse probability of treatment weights were constructed from sociodemographic characteristics and time–varying data on employment, earnings, functional status, and household composition. We fit marginal structural models to estimate the effects of persistent time and/or income poverty on odds of CVD, hypertension, obesity, depression, and emotional/psychiatric problems.

Results: Time poverty alone had little effect on most outcomes but increased the odds of emotional/psychiatric problems (OR 1.41, 1.04–1.81) relative to those who were neither time nor income poor. Income poverty in the absence of time poverty was associated with higher odds of CVD (OR 1.90, 1.15–3.15) and depression (OR 2.77, 1.77–4.33), and modestly higher odds of obesity (OR 1.32, 0.95–1.82). Being both time and income poor was associated with 1.59 times the odds of emotional/psychiatric problems (95% CI 1.12–2.63), and more than doubled the odds of obesity (OR 2.10, 1.43–3.10) and depression (OR 2.61, 1.45–4.68).

Discussion: These findings underscore time as an important, but understudied resource for health. When both time and money are scarce, the combined strain may be particularly harmful to health.

Outcome	Neither	Income poor only	Time poor only	Both time and income poor
CVD	1.00 (ref)	**1.90 * (1.15, 3.15)**	0.52. (0.26, 1.02)	0.96 (0.52, 1.78)
Hypertension	1.00 (ref)	1.06 (0.76, 1.50)	0.77 (0.58, 1.01)	1.11 (0.70, 1.75)
Obesity (BMI ≥ 30)	1.00 (ref)	1.32 . (0.95, 1.82)	1.01 (0.80, 1.27)	**2.10 *** (1.43, 3.10)**
Depression (K6 score ≥13)	1.00 (ref)	**2.77 *** (1.77, 4.33)**	1.33 (0.83, 2.14)	**2.61 ** (1.45, 4.68)**
Emotional or psychiatric problems	1.00 (ref)	0.92 (0.64, 1.31)	**1.41 * (1.08, 1.84)**	**1.59 * (1.12, 2.63)**

Note: . p<0.01, *p<0.05, ** p<0.01, *** p<0.001

Reproductive

Endometriosis Typology and Infertility Rachel Myrer* Rachel Myrer Bin Yang Joseph Stanford Christy Porucznik Leslie V. Farland Anna Z. Pollack C. Matthew Peterson Karen Schliep

Background: Endometriosis affects approximately 11% of women of reproductive age and is a significant cause of female factor infertility. Current classification systems inadequately predict infertility diagnoses, highlighting the need for improved classification approaches. **Objective:** The main objective is to evaluate the relationship between endometriosis subtypes and infertility risk using a large population-based cohort. **Methods:** We used a retrospective cohort from the Utah Population Database (1996–2020) including 461,684 women, with 79,600 diagnosed with endometriosis. Endometriosis subtypes were classified as superficial endometriosis (SE), ovarian endometriomas (OE), deep infiltrating endometriosis (DE), and other endometriosis. The primary analysis used Cox proportional hazards models to assess the hazard ratio of infertility diagnosis across endometriosis subtypes. **Results:** Women with endometriosis had a significantly higher risk of infertility compared to women without endometriosis (adjusted Hazard Ratio [aHR] 6.07, 95% CI 5.77-6.40). Infertility risk differed by endometriosis subtype, with the highest risk among those with deep infiltrating disease and/or ovarian endometriomas (aHR 9.01; 95% CI: 8.45–9.60), followed by other endometriosis (aHR 5.35; 95% CI: 4.94–5.79) and superficial endometriosis (aHR 4.36; 95% CI: 4.04–4.71). **Conclusion:** Endometriosis subtypes demonstrate different infertility risks, with deep infiltrating and ovarian endometriomas associated with the highest risk. These findings suggest the importance of considering endometriosis typology in clinical practice and research, potentially offering a more nuanced approach to patient care and fertility management.

Women’s Health

Control group matters: Differences in population vs. surgical controls for endometriosis research Amy Shafrir* Amy Shafrir Mary DePari Ashley Laliberte Kurtis Garbutt Allison F. Vitonis Naoko Sasamoto Katy Vincent Krina T. Zondervan Kathryn L. Terry Stacey A. Missmer

Many of the controls included in endometriosis case-control studies are surgically-disconfirmed for endometriosis, who present with various indications for surgery (fibroids/infertility/pelvic pain). Factors/biomarkers associated with endometriosis and pain symptoms may also be associated with these indications. We compared 754 population-based and 282 surgically-disconfirmed controls aged >18 years from two studies. Participants completed surveys on demographics, pain, menstrual, and reproductive factors. We used logistic regression to compare these factors between control groups and between endometriosis cases and controls by control type, adjusting for age, study site, and hormone use. Surgical controls were older (22% vs 6% >40 years), had less current hormone use (24% vs 55%) and more prescription pain medication use (29% vs 6%), compared to population-based controls. Surgical controls were more likely to present with severe dysmenorrhea and general pelvic pain compared to population-based controls (OR:3.89; 95%CI:2.19-6.91 and OR:4.86; 95%CI: 2.24-9.87, respectively). In case-control analyses, the association between endometriosis and severe dysmenorrhea was stronger when compared to population-based (OR:19.4; 95%CI:13.4-28.1), as opposed to surgical (OR:2.20; 95%CI:1.39-3.50), controls. Similar differences by control type were observed for general pelvic pain and dyspareunia. There was also a decreased odds of endometriosis with increasing age at menarche when cases were compared to population-based controls (OR=0.91; 95%CI:0.85-0.98), but not surgical (OR=1.05; 95%CI:0.94-1.17) controls. Control populations differ on several characteristics and pain symptoms. Carefully considering the sampling frame endometriosis cases arose from, and using multiple control group types that are well characterized should aid interpretation of results.

Cancer

Endometriosis and ovarian cancer risk by histotype: a pooled analysis from the Ovarian Cancer Cohort Consortium Holly Harris* Holly Harris Kara Cushing-Haugen Naoko Sasamoto Kathryn Terry Leslie Farland

Background: Endometriosis is a common inflammatory condition that is characterized by the presence of endometrial-like tissue outside the uterine cavity. People with endometriosis have approximately a two to three-fold increased risk of endometrioid and clear cell ovarian cancer. However, the associations with other histotypes are less certain given the potential for detection bias as well as small sample sizes.

Methods: Our objective was to examine the association between endometriosis and invasive epithelial ovarian cancer risk in 10 prospective cohorts in the Ovarian Cancer Cohort Consortium (n=725,122 total participants). Endometriosis was self-reported in most of the studies. We used pooled logistic regression with time divided into two-year intervals. This approach estimates beta coefficients interpreted as log ORs that are analogous to cause-specific HRs.

Results: 7.1% of participants reported an endometriosis diagnosis. During follow-up 4,327 incident ovarian cancer cases were diagnosed, with 380 cases among those with endometriosis and 3,947 cases among those without. We observe a 64% higher risk of ovarian cancer (95% CI=1.47-1.82) in those with endometriosis compared to those without endometriosis. We observed a higher risk of all major ovarian cancer histotypes among those with endometriosis with ORs (95% CI) of 1.23 (1.05-1.45) for high-grade serous, 2.09 (1.30-3.35) for mucinous, 2.24 (1.65-3.03) for endometrioid, 3.02 (1.63-5.57) for low-grade serous, and 4.21 (3.00-5.89) for clear cell.

Conclusions: This prospective consortium analysis is one of the largest to demonstrate associations with high grade serous and mucinous ovarian cancer histotypes as well as endometrioid, clear cell, and low-grade serous. Given the distinctive cell of origins proposed for distinct ovarian cancer histotypes, this may indicate that pathways linking endometriosis to ovarian cancer may differ across histotypes.

Cardiovascular

Heterogeneity in the Association Between Endometriosis and Early-Onset Cardiovascular Disease by Systemic Inflammation: NHANES 1999–2006 Chidinma Oli* Chidinma Oli

Background: Endometriosis is a chronic inflammatory condition associated with increased cardiovascular disease (CVD) risk, yet the role of systemic inflammation in shaping this association remains poorly understood. We examined whether systemic inflammation modifies the association between endometriosis and early-onset CVD among U.S. women.

Methods: We analyzed data from 5,309 women aged 20–54 years in the National Health and Nutrition Examination Survey (1999–2006). Endometriosis and early-onset cardiovascular disease (i.e., CVD before age 55) were based on self-reported physician diagnoses. Early-onset CVD included congestive heart failure, coronary heart disease, angina, myocardial infarction, or stroke. Systemic inflammation was characterized using high-sensitivity C-reactive protein [hs-CRP; low (<1 mg/L), moderate (1–3 mg/L) and high (>3mg/L)] and the systemic immune-inflammation index (SII; tertiles). Survey-weighted logistic regression was used to assess heterogeneity across inflammation levels, with stabilized inverse probability of treatment weighting (IPTW) to adjust for confounding.

Results: Among 5,309 women, 356 (7.06%) reported an endometriosis diagnosis and 152 (3.02%) early-onset CVD. After IPTW adjustment for age, body mass index, smoking, education, age at menarche, physical activity and race/ethnicity, endometriosis was associated with higher odds of early-onset CVD among women with high hs-CRP (prevalence odds ratio [POR] = 2.37, 95% CI: 1.50–3.74), but not among those with low or moderate hs-CRP levels (p-interaction= 0.24). Across SII strata, the strongest association was observed among women in the medium SII tertile (POR = 3.09, 95% CI: 1.55–6.16), with no associations in the low or high tertiles (p-interaction = 0.16).

Conclusion: The association between endometriosis and early-onset CVD showed heterogeneity across levels of systemic inflammation, with stronger associations observed at higher hs-CRP and intermediate SII levels.

Women’s Health

Reframing Polycystic Ovary Syndrome as a Lifelong Disease Beyond Reproductive Endocrinology: Implications Across the Female Lifespan Anoosha Keshav* Anoosha Keshav

Polycystic ovary syndrome (PCOS) is among the most common endocrine disorders worldwide, yet it continues to be primarily defined and managed as a reproductive condition centered on menstrual irregularity and infertility, limiting recognition of its broader and long-term health consequences. Increasing evidence indicates that PCOS is a chronic, multisystem condition with clinical and public health implications that extend across the female lifespan. This narrative review synthesizes epidemiologic and clinical evidence from adolescence through postmenopause to examine how PCOS-related risk evolves over time. The literature demonstrates that PCOS often emerges during adolescence, when early metabolic and psychological features may be overlooked or attributed to normal pubertal development, resulting in delayed diagnosis and missed preventive opportunities. During the reproductive years, clinical management frequently remains fertility-focused despite consistent associations with adverse pregnancy outcomes and early cardiometabolic dysfunction. With advancing age, reproductive manifestations may diminish; however, underlying metabolic risk persists or progresses, with insulin resistance, metabolic syndrome, type 2 diabetes, and cardiovascular disease commonly extending into midlife and later adulthood. Prolonged exposure to unopposed estrogen further increases lifetime risk of endometrial hyperplasia and endometrial cancer, underscoring the relevance of PCOS beyond reproductive endocrinology. Across all life stages, gaps in longitudinal follow-up and surveillance contribute to preventable morbidity. Collectively, these findings support reframing PCOS as a lifelong condition and highlight the importance of a life-course approach to improve early recognition, continuity of care, and prevention of chronic disease in women with PCOS.

Diabetes

Patterns of Body Mass Index Trajectories and Incident Diabetes Across Adulthood: a 24-year U.S. cohort study Jane Obi* Jane Obi Daniel McCarthy Solveig Argeseanu Cunningham Karen Siegel Mary Beth Weber

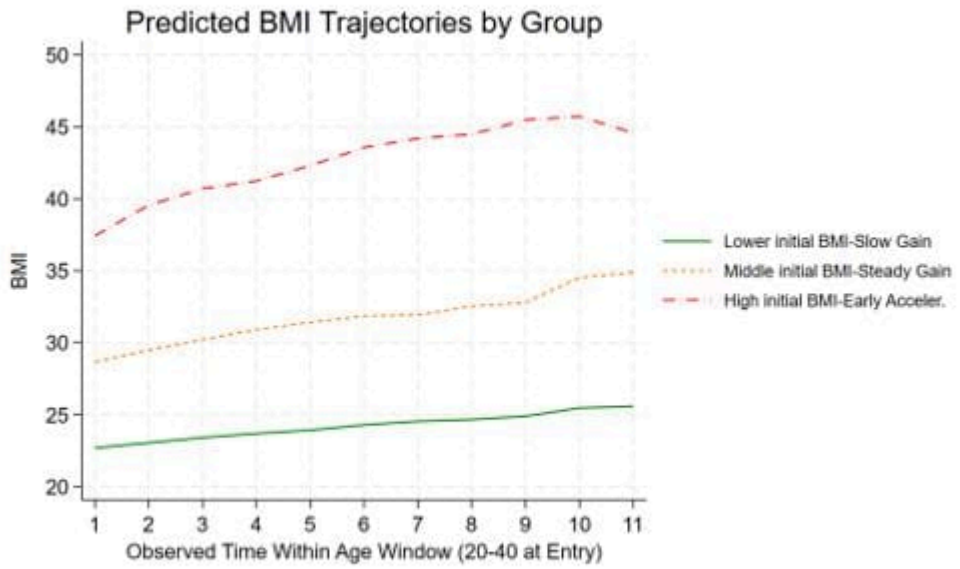
Background: Excess body weight is a major risk factor for type 2 diabetes, yet most epidemiologic studies rely on single-time body mass index (BMI) measures that obscure how weight changes unfold across adulthood. Trajectory-based approaches may better capture the timing and pattern of weight gain relevant to metabolic risk.

Methods: We analyzed longitudinal anthropometric data from 18,527 U.S. adults in the Panel Study of Income Dynamics (1999-2023). BMI trajectories were identified separately for early adulthood (ages 20-39) and mid-adulthood (ages 40-59) using group-based trajectory modeling among participants with at least three observations per window and no diabetes at baseline. Diabetes-free survival was estimated using age-scale Cox proportional hazards models with delayed entry, adjusting for sex, race and ethnicity, education, marital status, income, and baseline BMI. Sensitivity analyses assessed robustness to age-period-cohort (APC) parameterizations.

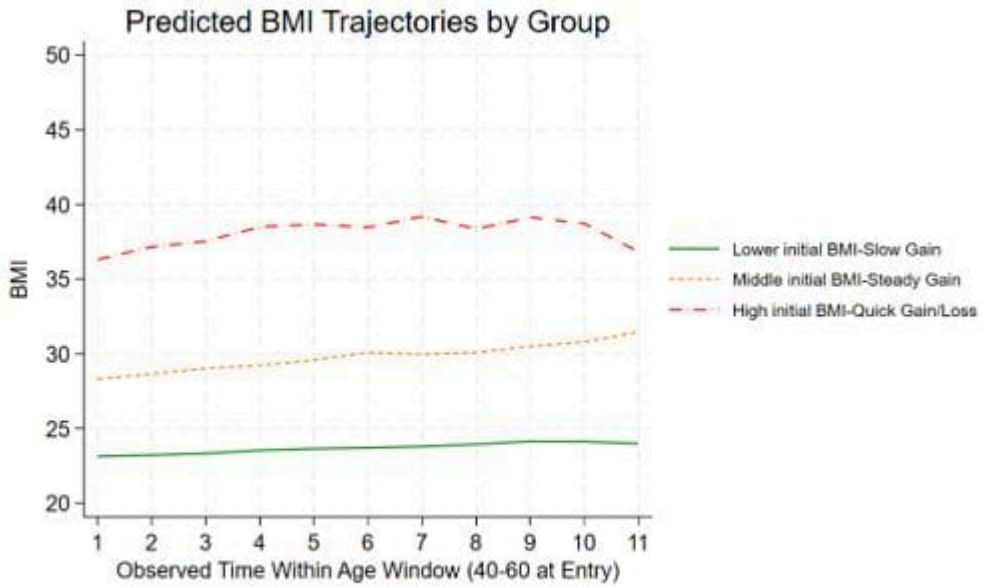
Results: Three trajectory groups were identified in each age window. In early adulthood, compared with a low-stable trajectory, diabetes hazards were 2.45-fold higher for a moderate-increasing trajectory (95% CI: 1.83-3.29) and 3.10-fold higher for a high-accelerating trajectory (95% CI: 2.11-4.57). In contract, in mid-adulthood, corresponding associations were weaker in magnitude, though still elevated (1.56 [95% CI: 1.23-1.99] and 2.19 [95% CI: 1.61-2.97], respectively). Findings were robust across APC sensitivity analyses.

Conclusions: BMI trajectories reveal substantial heterogeneity in diabetes risk that is not captured by static BMI classification alone. The magnitude of risk associated with adverse trajectories is greatest when high-risk patterns emerge in early adulthood, underscoring timing as a critical dimension of adiposity-related risk. These results support life-course approaches to diabetes prevention that incorporate longitudinal weight history to identify high-risk individuals earlier.

Early Adulthood BMI Trajectory Group Distributions



Middle Adulthood BMI Trajectory Group Distributions



Summary: Severe obesity emerged predominantly in earlier adulthood, before age 40. No trajectory group in the 40-60 window exceeded BMI 40, suggesting earlier-life emergence of extreme adiposity.

Health Services/Policy

The Impact of NY Paid Family Leave on Postpartum A1C after Gestational Diabetes: A controlled interrupted time series analysis Natalie Boychuk* Natalie A. Boychuk Jennifer A. Hutcheon Teresa M. Janevic

Paid family leave (PFL) is linked with improved infant health, breastfeeding, and postpartum healthcare use, but potential benefits for postpartum physical health are underexplored. Hemoglobin A1C may signal future cardiometabolic risk and is mandatorily reported in New York City (NYC), providing a marker of postpartum health. We examined the impact of New York PFL on A1C 4-12 months postpartum in privately insured women with gestational diabetes using a controlled interrupted time series of linked NYC birth, hospital discharge, and A1C registry data, 2014-2019 (n=3,371). Deliveries were classified as pre- (January 2014-December 2018) or post- (January 2018-March 2019) PFL. We estimated policy effects in women who were employed during pregnancy, with women who were unemployed as a control series. We used log binomial, linear, and quantile segmented regression to assess level/slope changes in 1) risk of prediabetic postpartum A1C (≥5.7%), 2) A1C z-score, and 3) median A1C, adjusting for race, education, parity, and nativity. Almost 80% (78.5%) of women were employed. Median A1C was 5.5 (IQR: 0.5). When A1C was binarized, no immediate post- vs. pre-PFL differences or sustained changes by employment were present (post vs. pre, treatment vs. controls, adjusted risk ratio (aRR): 1.00, 95% CI: 0.85, 1.17), post-PFL slope treatment vs. controls aRR: 1.00, 95% CI: 0.96, 1.05). In models of A1C z-score, we found an adjusted post vs. pre difference between treatment and control groups of -1.01 standard deviations (95% CI: -1.96, -0.07); however, a positive post-policy difference in slope by treatment was present (β: 0.28, 95% CI: 0.03, 0.52). In quantile regression, we similarly found an immediate -0.09 percentage point reduction in median A1C post- vs. pre-PFL in treatment vs. controls (95% CI: -0.25, 0.02) but no sustained changes by employment. Results suggest that PFL may have improved postpartum A1C among privately insured women immediately after policy implementation.

Women’s Health

Premenstrual syndrome and incident type 2 diabetes in a prospective study Aparna Tiwari* Aparna Tiwari Donghao Lu Yihui Yang Jamie Hartmann-Boyce Cassandra N. Spracklen Susan Sturgeon Elizabeth Bertone-Johnson

Type 2 diabetes (T2D) prevalence is rising among women in the US. Women bear more severe consequences from T2D than men, making it a major public health concern. Premenstrual syndrome (PMS) is a reproductive disorder with heterogeneous physical and emotional symptoms occurring during the luteal phase of the menstrual cycle. Common physiological mechanisms appear to contribute to both PMS and T2D, including dysfunction of the stress response, renin-angiotensin-aldosterone system, and immune systems, which suggests that PMS may be an early marker of an elevated risk for developing T2D. We tested this hypothesis using prospective data from women enrolled in the Nurses’ Health Study II PMS Substudy who were 25-42 years of age at baseline. Participants included 1,257 women meeting validated criteria for incident moderate-to-severe PMS during follow-up (1991-2005) and 2,463 age-matched comparison women without PMS, assessed using a validated questionnaire based on the Calendar of Premenstrual Experiences. Women self-reported incident T2D diagnosed after PMS assessment until 2021, with diagnoses further confirmed using a supplemental questionnaire and standard criteria. Over 20-30 years of follow-up, 105 women with PMS and 140 without PMS reported T2D. Adjusting for age, race, childhood trauma, and time-varying covariates, including body mass index, smoking, physical activity, and alternative healthy eating index, women with PMS had a modest, non-significant higher risk of T2D (HR=1.18; 95% CI, 0.87, 1.60). Risk was significantly higher for T2D diagnosed at younger ages; PMS was associated with a 59% higher risk of T2D diagnosed before age 54, the median age at diagnosis in the cohort (HR=1.59; 95% CI, 1.04-2.41; p-for-interaction= 0.07). Our findings suggest that PMS may be a novel indicator of T2D risk in women, particularly for younger-onset T2D. This association should be assessed in other population-based prospective studies.

Health Disparities

Combining Target Trial Emulation with Causal Decomposition to Estimate Intervention Effects on Health Disparities Chloe R. Bennett* Chloe Bennett Louisa Smith

Researchers often ask how much health disparities could be reduced under more equitable conditions, but “equity” can be operationalized in many different ways, each representing distinct interventions. Causal decomposition analysis provides principled guidance for distinguishing which covariates represent inequitable barriers (constituting the disparity) versus legitimate sources of variation (appropriate for standardization) and allows researchers to estimate disparity reduction under hypothetical equitable scenarios. Target trial emulation provides a framework for defining such an intervention by requiring explicit definition of a protocol—including eligibility criteria, treatment assignment mechanisms, time zero, and follow-up periods—thereby transforming abstract equity goals into concrete, evaluable interventions. Using continuous glucose monitor (CGM) access and racial disparities in diabetes outcomes as an example, different equity framings lead to fundamentally different target trial designs. Equity as universal access would result in examining outcomes if all patients across racial groups received CGMs. Equity as equalized access rates would examine outcomes if the disadvantaged group’s CGM access matched the advantaged group’s existing rate. Equity as need-based allocation would provide CGMs to anyone exceeding clinical thresholds (e.g., A1C > 8%), eliminating socioeconomic barriers to clinically-indicated care. Each scenario requires different target trial specifications and yields different disparity reduction estimates. By combining causal decomposition with target trial emulation, researchers can systematically evaluate multiple operationalizations of equity, identifying which specific, implementable interventions would most effectively reduce disparities while maintaining rigorous causal identification.

Diabetes

Cash transfers and cumulative incidence of diabetes and elevated glucose in South Africa: Evidence from the HAALSA Indepth cohort Maria Klein* Maria Klein Evan Jordan Corey Kalbaugh Indrakshi Roy Molly Rosenberg

INTRODUCTION: Lower household income is associated with earlier onset of diabetes. It follows that household income supports such as cash transfer programs could reduce diabetes risk. Cash transfer programs are effective at improving child and maternal health outcomes through increased food security and health services utilization. The same pathways could also improve diabetes-associated outcomes, but cash transfer impact specific to diabetes is not well studied. Thus, the objective of this study was to determine the association between cash transfer access and cumulative incidence of diabetes and elevated glucose.

METHODS: We used a population-based sample of 5059 people aged 40+ from Health and Aging in Africa: Longitudinal Studies in South Africa (HAALSA Indepth). Our exposure was cumulative household cash transfer (HCT) available to HAALSA Indepth participants between 2000 and their Wave 1 interview (2014/2015). Our outcomes were the cumulative incidences of self-reported and biomarker-indicated 1) diabetes and 2) elevated glucose between Waves 1 and 3 (2021/22). We assessed the relationship between continuous HCT and outcomes with log-binomial and modified Poisson models. Models were fit with inverse probability weights to account for attrition, mortality, and refusal of point of care measurement. We specified unadjusted models and models adjusted for age and sex.

RESULTS: Between Waves 1 and 3, cumulative incidences of diabetes and elevated glucose were 16.8% and 37.4%, respectively. Each R10,000 increase in cumulative HCT was associated with reduced cumulative incidence of diabetes [aCIR (95% CI): 0.96 (0.94, 0.98); p=<0.001] and elevated glucose [aCIR (95% CI): 0.97 (0.96, 0.99); p=0.001].

DISCUSSION: Our findings suggest that greater household cash transfer access is associated with reduced risk of diabetes and elevated glucose. To our knowledge, this is the first study on cash transfer income and diabetes risk in sub-Saharan Africa.

Environment/Climate Change

Wildfire Smoke Exposure Increases Risk for Gestational Hypertension Samantha Piekos*
Samantha Piekos Qi Wei Michael Strasser Jennifer Hadlock

Wildfire smoke exposure is a growing environmental threat, yet its effects on pregnancy remain poorly characterized. In a retrospective cohort study, we examined associations between wildfire smoke exposure and pregnancy complications among 287,612 singleton deliveries (2015–2020) across five western US states (CA, ID, MT, OR, and WA) through partnership with Providence St. Joseph Health. Daily wildfire-attributable $PM_{2.5}$ exposure was estimated using the Childs et al. (2020) model mapped to residential census tracts. Smoke exposure was common (n=194,918; 67.8% of pregnancies). There was higher exposure among rural residents, middle socioeconomic and second-lowest area deprivation quintiles, younger individuals, those conceiving in the first half of the year, and non-Hispanic, Native American, Pacific Islander, or White populations (all $p<0.0001$ except Pacific Islander, $p<0.05$).

The primary outcomes were gestational hypertension, preeclampsia, and preterm birth. We identified 21 confounders using outcome-specific directed acyclic graphs and key predictors from an XGBoost model of smoke exposure (PR-AUC = 0.998), and we adjusted for these using propensity score matching. We identified gestational week susceptibility windows by comparing exposure levels between cases and controls. There was an increased risk of gestational hypertension during two periods: gestational weeks 3-7 (aOR=1.09, 95% CI: 1.03–1.15, $p<0.01$) and weeks 22-25 (aOR=1.07, 95% CI: 1.01–1.13, $p<0.05$). There was no difference in rates of preeclampsia or preterm birth in people exposed to smoke during these periods of pregnancy.

Smoke exposure during the early first or late second trimester increases the risk of gestational hypertension. Understanding this temporal vulnerability is essential for developing targeted public health interventions and mitigation strategies to protect pregnant people in wildfire-prone regions.

Environment/Climate Change

Associations of maternal PFAS exposure with birthweight and placental weight in a New York City-based birth cohort Eleanor Medley* Eleanor Medley Amy Padula Maya Deyssenroth Linda G. Kahn Whitney Cowell

Exposure to per- and polyfluoroalkyl substances (PFAS) has been previously associated with lower birthweight, but less is known about how PFAS may impact the placenta. We investigated associations of maternal PFAS exposure with birthweight, placental weight, and their relation in the New York University Children's Health and Environment Study. We measured concentrations of 13 PFAS in prenatal serum collected between 2017-2020 (n=500). Analyses included 7 PFAS detected in >50% of samples: 5 long-chain compounds (PFOS, PFOA, PFDA, PFNA, PFUnDA), and 2 shorter-chain replacements (PFHxS, PFBS). Subsets of 498 and 247 participants with available birthweight and placental weight data, respectively, constituted the analytic samples. We computed birthweight-for-gestational age z-scores with INTERGROWTH-21st, and the residuals of birthweight regressed on placental weight and gestational age (eBW) to estimate placental efficiency. We modeled associations of individual PFAS with birthweight z-scores (BWGA), placental weight, and eBW using linear regression adjusted for maternal age, race/ethnicity, parity, BMI, insurance status, and child sex. We estimated joint effects of the PFAS mixture on BWGA and placental weight using Bayesian Kernel Machine Regression (BKMR). In single-pollutant models, PFHxS was associated with lower BWGA (β -0.11 SD [-0.23, 0.00]), and PFUnDA and PFOA were associated with higher placental weight (β PFUnDA 14 g [1, 27], β PFOA 13 g [-6, 33]). PFHxS was associated with lower eBW, indicating lower placental efficiency. In BKMR analyses, long- and short-chain PFAS had similar posterior inclusion probabilities. Exposure-response functions resembled linear regression models. The overall effect of the PFAS mixture was associated with higher placental weight. These results suggest that maternal PFAS exposure may affect placental and fetal growth, supporting future investigation into potential impacts on placental structure and function.

Environment/Climate Change

Associations between gestational exposure to extreme heat events and early life blood pressure in North Carolina Sam J. Neally* Sam J. Neally Celeste Butts-Jackson Thomas J. Luben Jaime C. Slaughter-Acey Michael Emch Marie S. O'Neill Cathrine Hoyo Chantel L. Martin

Background: Extended periods of high temperatures are associated with adverse cardiovascular health outcomes. Little is known on the relationship between gestational heat exposure and offspring cardiovascular health.

Aim: We examined associations of extreme heat events (EHE) during pregnancy with offspring early-life elevated blood pressure (BP).

Methods: The Newborn Epigenetics STudy (NEST, 2005-2011) is a birth cohort of 2,681 gestational parent-child pairs recruited from prenatal visits at obstetrics care facilities in Durham County, NC. We analyzed data from 1,067 participants with at least one BP measurement from 3 to 9 years and complete information on geographic residence and covariates. EHE were defined as mean daily apparent temperature ≥95th percentile for ≥2 consecutive days or ≥90th percentile for ≥3 consecutive days during each trimester of pregnancy within census block group of residence, with percentiles relative to NC temperatures from 2004-2012. Continuous systolic and diastolic BP from medical abstracts were converted to age-, sex-, and height-standardized national percentiles. Elevated BP was defined as ≥90th percentile.

Longitudinal logistic mixed effects regression models estimated OR and 95%CI for having at least one EHE during each trimester and elevated BP, adjusting for season of conception and gestational parent age, race, marital status, and education. Analyses were performed for the full sample, among term births (n=913), and among children whose gestational parent did not report hypertensive disorder during pregnancy (n=888).

Results: Prevalences of elevated BP ranged from 17-26% from ages 3 to 9 years. Imprecise associations were observed in the full sample. Among term births, having at least one compared to no EHE in the second trimester was associated with greater odds of elevated BP (OR:2.12, 95%CI=1.17-3.82).

Conclusions: Extreme heat experiences during certain periods of pregnancy may contribute to lifecourse cardiovascular outcomes.

Environment/Climate Change

Longitudinal patterns and predictors of urinary organophosphate ester metabolite concentrations from gestation through childhood in the MIREC Cohort Yohane Vincent Abero Phiri* Yohane Vincent Abero Phiri Aimin Chen Jillian Ashley-Martin Tye E. Arbuckle Joseph M. Braun Sheniz Moonie Youssef Oulhote William Fraser Melissa Legrand Michael M. Borghese John Krzeczkowski Maria Velez Bruce Lanphear Katherine Morrison Mandy Fisher Mark R. Palmet Maryse Bouchard Ann M. Vuong

Background: Organophosphate esters (OPEs) are ubiquitous flame-retardant replacements, yet longitudinal exposure patterns remain unclear; thus, we aimed to identify the determinants of early-life OPE exposure trajectories.

Methods: Urinary OPE metabolites were quantified in the Maternal-Infant Research on Environmental Chemicals (MIREC) cohort characterizing longitudinal exposure patterns. We measured concentrations of bis(2-chloroethyl) phosphate (BCEP), bis(1-chloro-2-propyl) phosphate (BCIPP), bis(1,3-dichloro-2-propyl) phosphate (BDCIPP), di-n-butyl phosphate (DNBP), and diphenyl phosphate (DPHP) at 6-13 and 16-21 weeks of gestation and at ages 2-5 and 7-9 years, adjusting for specific gravity. Temporal variability was assessed using random-intercept linear mixed-effects models with intraclass correlation coefficients (ICCs). We also used Spearman correlations to evaluate cross-time and cross-metabolite associations, latent class growth analysis (LCGA) to identify longitudinal exposure trajectories, and logistic regression to identify predictors of high-exposure trajectories.

Results: Urinary OPE levels were 1.8-14 times higher in childhood than during gestation, with prenatal reproducibility strongest for BCEP, BCIPP, and BDCIPP (ICCs: 0.63-0.70), moderate for DPHP (0.45-0.51), and low for DNBP (0.21-0.25), whereas childhood and prenatal-childhood ICCs were uniformly low (0.02-0.19). LCGA identified two distinct patterns per metabolite including a reference trajectory increasing from low concentrations and either a high-stable or early-peak prenatal trajectory. Predictors of the elevated trajectory included older maternal age, higher parity, smoking, female child sex, and lower household income.

Conclusion: Distinct trajectories and predictors revealed longitudinal variability and weak prenatal-childhood correlations in OPE exposures, highlighting the value of MIREC’s repeated childhood measurements for capturing dynamic exposure patterns.

Environment/Climate Change

Children Sleep Patterns under Road Traffic Noise Exposure: Evidence from a Taiwanese Birth Cohort Yi-Di, Wang* Yi-Di Wang Xin-Chun Peng Hsin-Yi Huang Siang-Chen Chen Tsung-Chieh Yao Wen-Chi Pan

Background:

Environmental noise is one of the major environmental risks affecting human health and contributing to sleep disturbance. Insufficient sleep is associated with adverse cardiovascular, psychological, cognitive, and immune outcomes. However, evidence on noise exposure and sleep among children is limited, despite children being in a critical developmental period. Therefore, investigating the association between environmental noise and children's sleep is warranted.

Objective:

This study aimed to investigate the association between environmental noise exposure and sleep problems among adolescents in the LIGHTS birth cohort.

Methods:

We recruited 1,513 children from the LIGHTS cohort at baseline (2010-2011) in the northern Taiwan, and conducted a follow-up in 2024-2025. Sleep quality was assessed using the Pittsburgh Sleep Quality Index (PSQI) in the follow-up period. Environmental noise in 2025 was estimated using low-cost noise sensors and modelled by machine-learning algorithms. We applied linear regression models to evaluate associations between noise exposure and PSQI scores, adjusting for potential confounders.

Result:

A total of 117 children (out of 421 participants) has poor sleep quality in the follow-up period. We found nighttime noise exposure (Lnight) was positively associated with insufficient sleep (OR= 1.09 per 1dBA increment; 95% CI= 1.01 to 1.18). We found that boys are more vulnerable to night-time noise exposure (OR= 1.21 per 1 dBA, 95% CI= 1.06 to 1.41) compared to those in girls. Findings were still robust after further adjusting for parental socioeconomical status factors.

Conclusion:

Our findings indicates that nighttime environmental noise is associated with poor sleep quality in children. These results underscore the importance of focusing on nighttime noise exposure in environmental health research and suggest that noise mitigation strategies targeting nighttime periods may contribute to improved sleep health among children.

Environment/Climate Change

Tree Canopy Surrounding Schools and Standardized Test Scores in a Large Urban School District Mozhgan Naji* Mozhgan Naji Kirsten M.M. Beyer Laleh Jamshidi Michael D Laiosa Chibuzor Abasilim Amy E Kalkbrenner

Green space near schools may support academic performance through stress reduction, attention restoration, thermal comfort/air quality, and opportunities for physical activity and social interaction. Tree canopy is a specific and actionable component of green space, with existing epidemiologic evidence limited to one study reporting positive, and two reporting null associations. Given limited evidence from large, racially and economically diverse U.S. urban school districts, we studied Milwaukee Public Schools (MPS), with students from lower-income and historically marginalized racial and ethnic groups. We linked tree canopy, using the 2023 National Land Cover Database within circular buffers around school locations, with English Language Arts (ELA) and Math scores from the Wisconsin Forward Exam, for 25,709 MPS students, grades 3–8, in 2023–2024. We modeled tree canopy in quartile categories because it exhibited better fit than continuous coding and allowed flexible modeling. Multilevel linear regression models with a random intercept for school adjusted for student demographics, mobility, and child residential neighborhood socioeconomic and segregation measures. Unadjusted associations suggested positive impacts but attenuated after adjustment. For the 100m buffer, comparing the top quartile of tree canopy (9 to 20% coverage) to the bottom (0-4%) adjusted results were: ELA: β = -7.6 (95% CI: -14.9, -0.3; mean score = 1,566), and Math: β = -4.1 (95% CI: -12.0, 3.8; mean score = 1,556). Results were similar for buffers of 50, 300, and 500 m, with no clear dose-response or buffer-specific pattern. Overall, school-based tree canopy showed largely null associations with test scores, suggesting it may not benefit academic outcomes in urban settings, but limited exposure contrast or measurement limitations may also explain these findings. Future work will incorporate broader green space measures and home exposures, to inform equitable, place-based interventions.

Women’s Health

Association between pregnancy loss and risk of subsequent drug overdose Tosin Oyetunji*
Tosin Oyetunji Sidra Goldman-Mellor

Pregnancy-associated overdose morbidity and mortality have risen, yet the incidence of nonfatal overdose after pregnancy loss and whether the risk differs by prior overdose history compared with live delivery remains unclear. Using longitudinally linked California hospital discharge and emergency department (ED) data (2016–2021), we created cohorts of individuals with an index live delivery (N = 1,659,293) or pregnancy loss (N = 171,170). We compared these cohorts’ risks of an ED visit for nonfatal drug overdose within 365 days after the index pregnancy outcome; we also examined whether a prior overdose modified the association between pregnancy outcome and subsequent overdose. We used generalized linear models to estimate adjusted odds ratios with 95% confidence intervals (CIs) for pregnancy loss versus live delivery; moderation analyses included an interaction term with prior overdose history. Models controlled for age, insurance type, residence, prior pregnancy outcome, and comorbid alcohol, drug, psychotic, mood, and anxiety disorders. Within 365 days after index visit, 2,731 individuals (0.15%) experienced a nonfatal overdose ED visit (0.12% after live delivery vs. 0.44% after pregnancy loss). Pregnancy loss was associated with significantly higher odds of overdose compared with live delivery (aOR = 2.57; 95% CI: 2.35, 2.81). Prior overdose strongly predicted subsequent overdose (aOR = 2.93; 95% CI: 2.17, 3.95), but there was no evidence that the association between pregnancy outcome and overdose differed by prior overdose history (aOR for interaction term = 0.90; 95% CI: 0.59, 1.39). These findings suggest that pregnancy loss is associated with substantially higher nonfatal overdose morbidity than live delivery, without evidence of differential risk among individuals with a history of overdose. Targeted screening, treatment, and support services following pregnancy loss may help mitigate overdose risk. Future research should examine longer-term overdose trajectories beyond the first postpartum year.

Reproductive

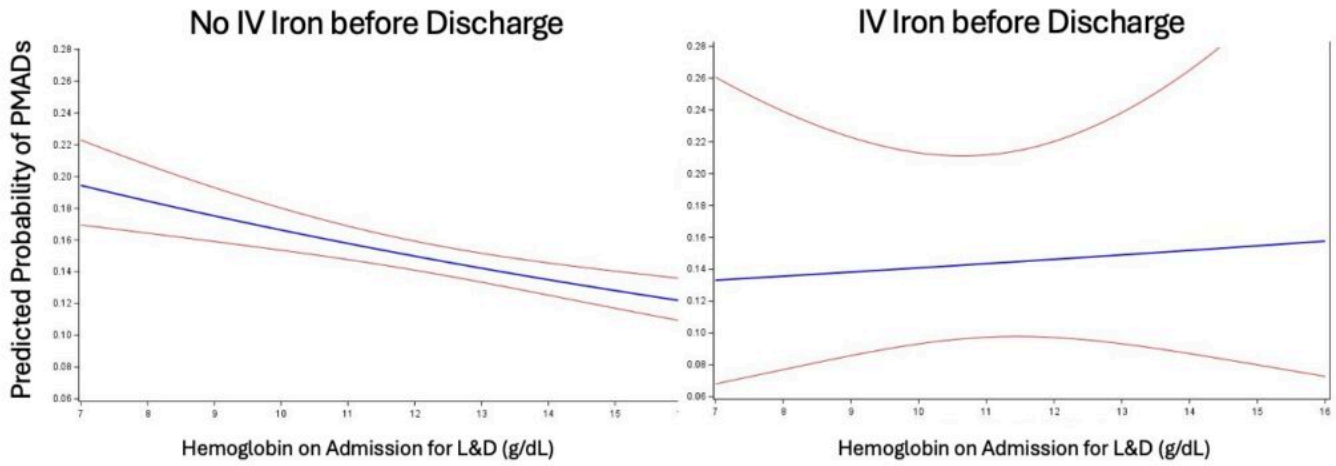
Anemia on Admission for Childbirth and Perinatal Mood and Anxiety Disorders –Modification by Intravenous Iron Katharine E. Bruce* Katharine E. Bruce Kimiko Van Wickle Alison M. Stuebe Stephanie M. Engel

Background: Perinatal anemia is common and may increase risk of Perinatal Mood and Anxiety Disorders (PMADs). Prior association studies have been mixed, and none have examined the role of IV iron in modifying this association.

Methods: This retrospective cohort study evaluated the relationship between hemoglobin (Hb) on admission for childbirth and PMADs within 3 months postpartum using medical records data from UNC Health System. Participants gave birth at ³20 weeks gestation from April 1, 2016 to June 12, 2024. Hb, collected from complete blood count labs, was categorized as severe (<9mg/dL), moderate (9-<11 mg/dL), or none (≥11mg/dL). Patients were considered to have PMAD symptoms if they screened positive on the Edinburgh Postnatal Depression Scale (cutoff: 10), Patient Health Questionnaire 9 (cutoff: 5), and/or General Anxiety Disorder 7 (cutoff: 5). Generalized Estimated Equations calculated risk ratios, adjusting for age, race/ethnicity, insurance, parity, multifetal gestation, comorbidities, and Area Deprivation Index of home address.

Results: Among 26,186 participants, 24% met criteria for 3rd trimester anemia, 3% received IV iron before discharge, and 16% had PMADs. Compared to those without anemia, those with severe anemia had 1.24 times the risk of PMADs (95% Confidence Interval (CI): 1.02-1.52), and those with moderate anemia had 1.10 times the risk of PMADs (CI: 1.03-1.17). The relationship between anemia and PMADs persisted in those who did not receive IV iron (Severe: relative risk (RR): 1.21, CI: 0.97-1.52; Moderate: RR: 1.08, CI: 1.01-1.16), but there was less evidence of an association in those who did (Severe: RR: 1.05, CI: 0.60-1.87; Moderate: RR: 1.14, CI: 0.77-1.70).

Conclusion: Anemia on admission for childbirth was associated with an increased risk of PMADs. The stronger relationship between anemia and PMADs among those who did not receive IV iron compared to those who did suggests that treating anemia before discharge may mitigate this risk.



Reproductive

Pregnancy and contraception service utilization among transmasculine and nonbinary patients attending a sexual health clinic Ruby Lucas* Ruby Lucas Christine M. Khosropour Stephen E. Hawes Avery Everhart Molly R. Altman Genya Shimkin Anna Berzkalns Timothy W. Menza Chase Cannon Diana M. Tordoff

Introduction: While historically sexual health clinics have focused on HIV/STI services for transgender populations, transmasculine and nonbinary individuals assigned-female-at-birth (AFAB) have pregnancy and contraceptive needs.

Methods: We used electronic health record and computer-assisted self-interview data from transgender/nonbinary patients AFAB attending a municipal sexual health clinic in Seattle from January 2019 to December 2024. We compared differences in pregnancy and contraception service utilization by gender identity and testosterone use. Among patients capable of pregnancy, we assessed correlates of contraception use and desire for a pregnancy test at the visit-level using Poisson regression with robust standard errors clustered by patient ID. Adjusted models included age, gender identity, sexual orientation, race, ethnicity, insurance status, and gender of sexual partners.

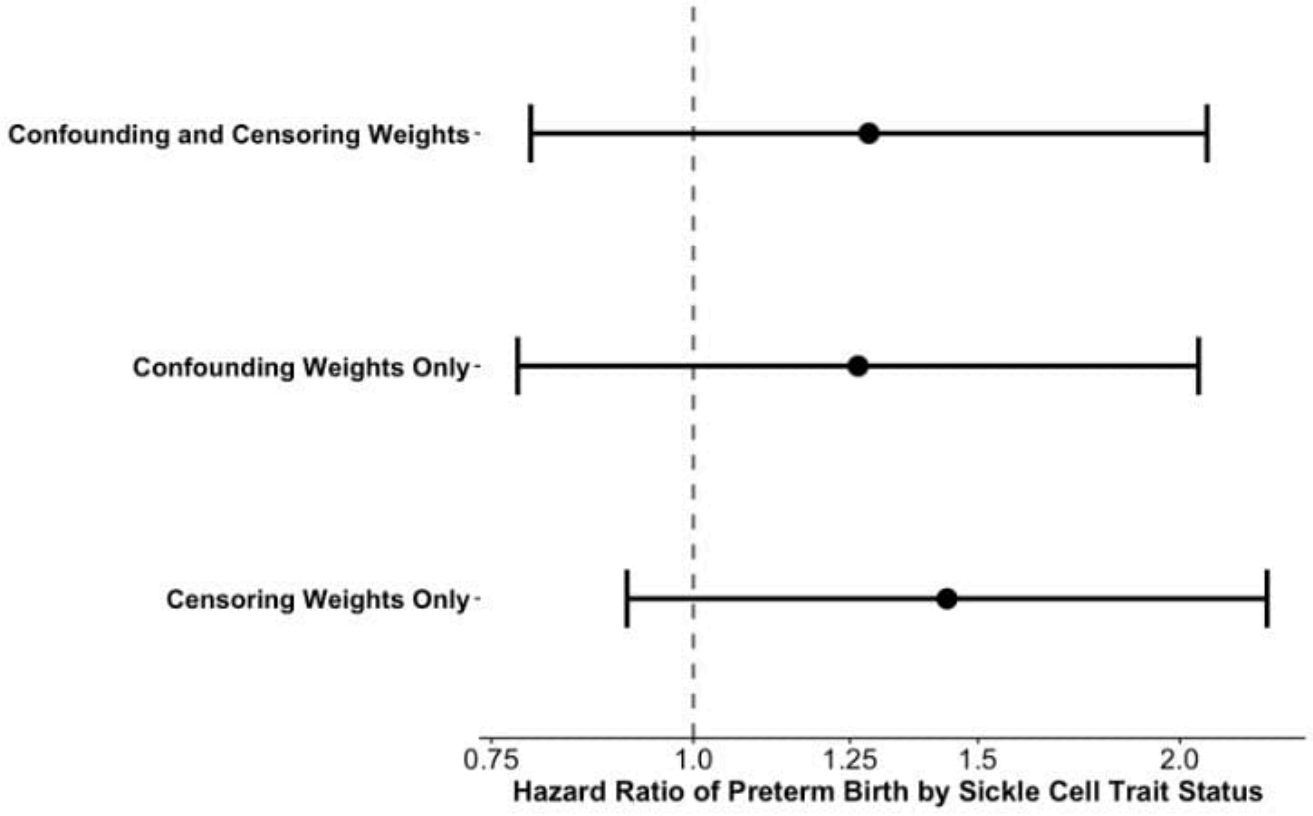
Results: Of 369 unique trans/nonbinary patients, 36% (n=106/302) reported testosterone use at their last visit. Half of the 550 patient-visits reported birth control use (54%), with most being long-acting reversible contraceptive methods (42%), followed by non-long-acting (7%), and barrier only (5%). Overall, 20% desired a pregnancy test, 2% thought they may be pregnant, and <1% were actively attempting conception. In unadjusted models, testosterone use was associated with contraception use (prevalence ratio [PR]=1.25, 95% CI: 1.08-1.40). In adjusted models, testosterone use was positively associated with desire for pregnancy test (aPR=2.38, 95% CI: 1.38-4.13), while male (aPR=0.29, 95% CI: 0.09-0.93) and transgender man (aPR=0.31, 95% CI: 0.15, 0.62) gender identities were inversely associated. Male gender identity was inversely associated with contraceptive use (aPR=0.39, 95% CI: 0.22-0.71).

Conclusion: Our findings suggest that public sexual health clinics can play an important role in providing trans-inclusive pregnancy planning and preventative care.

Reproductive

The association between sickle cell trait, a prevalent genetic condition, and the risk of preterm birth in a pregnancy cohort Kimi Van Wickle* Kimi Van Wickle Samuel Wilson, MD, MSCD Nigel Key, MB, ChB, FRCP Lauren Kucirka, MD, PhD Mollie Wood, PhD, MPH Julie Daniels, PhD, MPH Stephanie Engel, PhD

Associations between preterm birth and sickle cell trait (SCT) have been reported, yet few studies account for selection into SCT prenatal screening and competing risk of fetal loss. SCT is prevalent among individuals with African ancestry (7–10%), making rigorous evaluation of its role in preterm birth important for population attributable risk. We evaluated the association between SCT and preterm birth in a pregnancy cohort derived from electronic health records of over 32,000 pregnancies in Black/African American women receiving care at the University of North Carolina Healthcare system. Analyses included 2,080 pregnancies with laboratory-confirmed SCT status (positive or negative) from 2014–2024. Gestational age and pregnancy outcome algorithms were used to construct discrete pregnancy episodes followed over time. Pregnancies with conception dates occurring >19 weeks before data collection began or >43 weeks before data collection ended were excluded. Preterm birth was defined as delivery at ≥22 and <37 completed weeks' gestation. Cox proportional hazards models with inverse probability of censor weights accounted for censoring and the competing risk of fetal loss. Risks were estimated using the Aalen–Johansen estimator. Inverse probability of treatment weights adjusted for SES, maternal age, prenatal care, BMI, and prenatal screening recommendation at year of conception. In analyses accounting for censoring or competing risks due to fetal loss, but not selection into SCT prenatal screening and confounding, SCT had a modest association with higher risk of preterm birth (hazard ratio [HR] = 1.45; 95% CI: 0.90, 2.27), which was attenuated after applying inverse probability of treatment weights to control for (HR = 1.26; 95% CI: 0.78, 2.05). These findings highlight the importance of accounting for selection into prenatal screening and confounding when evaluating genetic risk factors for adverse pregnancy outcomes in pregnancy cohorts.


Confounding and Censoring Weights
Confounding Weights Only
Censoring Weights Only
0.75
1.0
1.25
1.5
2.0
Hazard Ratio of Preterm Birth by Sickle Cell Trait Status

Reproductive

A Target Trial Emulation Assessing the Effects of Prenatal Cannabis Exposure on Menarche Onset in Pre-Adolescents in the Adolescent Brain and Cognitive Development Study Adaeze Anamege* Adaeze Anamege Catalina Lopez-Quintero Deepthi Varma

Background: Prenatal cannabis exposure (PCE) has been linked to adverse physiological and behavioral outcomes in children. However, its influence on developmental milestones that mark the onset of reproductive capacity in early adolescence, such as menarche, remains poorly understood. This study estimated the effect of PCE on time to menarche among pre-adolescent girls.

Methods: Using a target trial emulation framework, we analyzed data from the prospective Adolescent Brain and Cognitive Development study. The analytic sample included 4,861 biological mother–child dyads, of whom 296 reported PCE and 4,565 did not report PCE. Stabilized inverse probability of treatment and censoring weights were applied to approximate randomization and account for loss to follow-up. The outcome was time to menarche. A piecewise exponential hazards model was used to estimate the effect of PCE during two time intervals: 0–120 months (early menarche) and >120 months (normal timing). SAS 9.4 was used for all analyses.

Results: In weighted models that did not account for clustering, PCE was associated with a 60% higher hazard of reaching menarche at or before 120 months (HR = 1.60; 95% CI: 1.29–1.99) compared with the no PCE group. After accounting for shared genetic environment among twins and triplets, the hazard ratio remained the same while precision significantly improved (HR = 1.60; 95% CI: 1.54-1.67).

Conclusions: PCE was associated with an increased hazard of early menarche. These findings suggest that prenatal substance exposures may play a meaningful role in shaping reproductive development in offspring and highlight the need to better understand the underlying biological pathways linking early-life cannabis exposure to accelerated pubertal timing. Future studies should explore potential biological mediators and further disentangle prenatal effects from broader familial and developmental factors influencing menarcheal timing.

Reproductive

Long-term exposure to ambient air pollution concentrations and fecundability among U.S. Black women Sydney Carolan* Sydney Carolan Yvette C. Cozier Mary D. Willis Jacqueline Hicks Junenette L. Peters Stephanie T. Grady Jean Costello Wendy Kuohung Julie R. Palmer Lauren A. Wise Amelia K. Wesselink

Previous research shows associations between air pollution and infertility. However, few studies have included large numbers of Black women, despite documented inequitable exposures to air pollution in the United States. Using data from the Black Women's Health Study, a prospective cohort study of 59,000 U.S. Black women, we examined the association of long-term exposure to ambient air pollution with fecundability, the per-cycle probability of conception. Participants enrolled in 1995 and are followed by biennial questionnaires. In 2011, participants were asked about time-to pregnancy for planned pregnancies that resulted in a birth and unsuccessful pregnancy attempts. Our analysis included 2,199 pregnancy attempts from 1,716 participants during 1995-2011. We used annual average ambient concentrations of particulate matter ≤2.5 µm (PM2.5), nitrogen dioxide (NO2), and ozone (O3) estimated using spatiotemporal models and linked to geocoded participant addresses. We fit proportional probabilities regression models with generalized estimating equations to estimate fecundability ratios (FR) and 95% confidence intervals for each pollutant adjusting for age, calendar year, geographic region, educational attainment, neighborhood SES, and co-pollutants. We fit adjusted generalized additive models (GAM) with smooth terms to assess joint effects and non-linear associations between pairs of pollutants. Residential concentrations of NO2 and O3 were associated with decreased fecundability: FRs for a 5-ppb increase in exposure were 0.93 [95% CI: 0.88-1.00] and 0.92 [95% CI 0.85-1.00], respectively. In contrast, PM2.5 exposure was associated with greater fecundability (FR=1.26 per 5-µg/m3 increase, 95% CI: 1.09-1.46). GAM results indicated little evidence of non-linear associations or interactions between pollutants. Our findings add to the body of evidence for federal air quality standards aimed at mitigating the impact of air pollution on adverse reproductive health outcomes.

Health Disparities

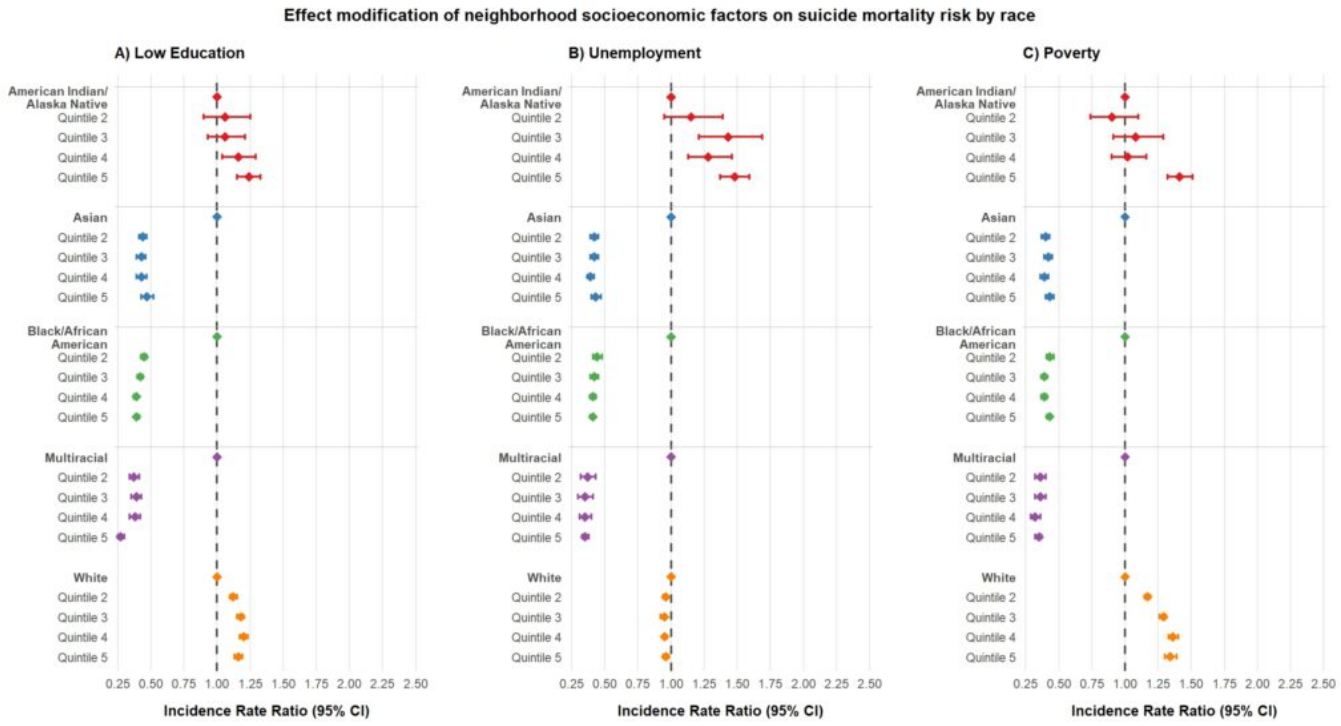
Racial disparities in suicide mortality in the United States: examining the mediating role of neighborhood socioeconomic conditions in a nationwide study, 2011-2021 Alua Yeskendir* Alua Yeskendir James Kirkbride Jennifer Dykxhoorn Justin C. Yang Kate M. Lewis Benson S. Ku

Suicide is a major public health problem in the United States, exacerbated by substantial racial disparities, with rates increasing 37% between 2000 and 2022. Neighborhood socioeconomic conditions are a plausible pathway through which these disparities may arise, yet their mediating role remains unclear at the national level. We used data from the National Violent Death Reporting System covering 49 states and the District of Columbia (2011–2021; 267,349 suicide deaths) to examine racial differences in suicide mortality and to quantify mediation by neighborhood socioeconomic conditions.

We calculated age-adjusted suicide rates, estimated race-specific associations between neighborhood socioeconomic deprivation and suicide using negative binomial regression, and applied exploratory causal mediation analysis using the g-formula to decompose racial disparities into direct and indirect effects through neighborhood-level poverty, unemployment, and low education.

American Indian/Alaska Native populations had the highest suicide rates (22.1 per 100,000, 95% CI 21.4–22.8), followed by White populations (18.6 per 100,000, 95% CI 18.5–18.7), who accounted for 88% of all deaths, while Asian, Black/African American, and Multiracial populations had lower rates (6.4–7.9 per 100,000). Suicide rates were 1.17–1.34 times higher (95% CI 1.14–1.37) in the most versus least deprived neighborhoods for education and poverty, with dose-response relationships present among American Indian/Alaska Native and White populations but not other groups. Despite these gradients, neighborhood socioeconomic factors mediated less than 9% of racial disparities in suicide.

These findings suggest that racial disparities in suicide mortality largely operate through pathways beyond neighborhood socioeconomic conditions, underscoring the need to investigate alternative social and structural mechanisms shaping suicide risk.


Effect modification of neighborhood socioeconomic factors on suicide mortality risk by race
A) Low Education
B) Unemployment
C) Poverty
American Indian/ Alaska Native
Asian
Black/African American
Multiracial
White
Quintile 2
Quintile 3
Quintile 4
Quintile 5
0.25 0.50 0.75 1.00 1.25 1.50 1.75 2.00 2.25 2.50
Incidence Rate Ratio (95% CI)
Models adjusted for age, sex, year, and other SES factors. Q1 = least disadvantaged (reference). Race × SES interactions: Education LR χ² = 447.41; Unemployment LR χ² = 330.74; Poverty LR χ² = 329.29, all p < 0.001.

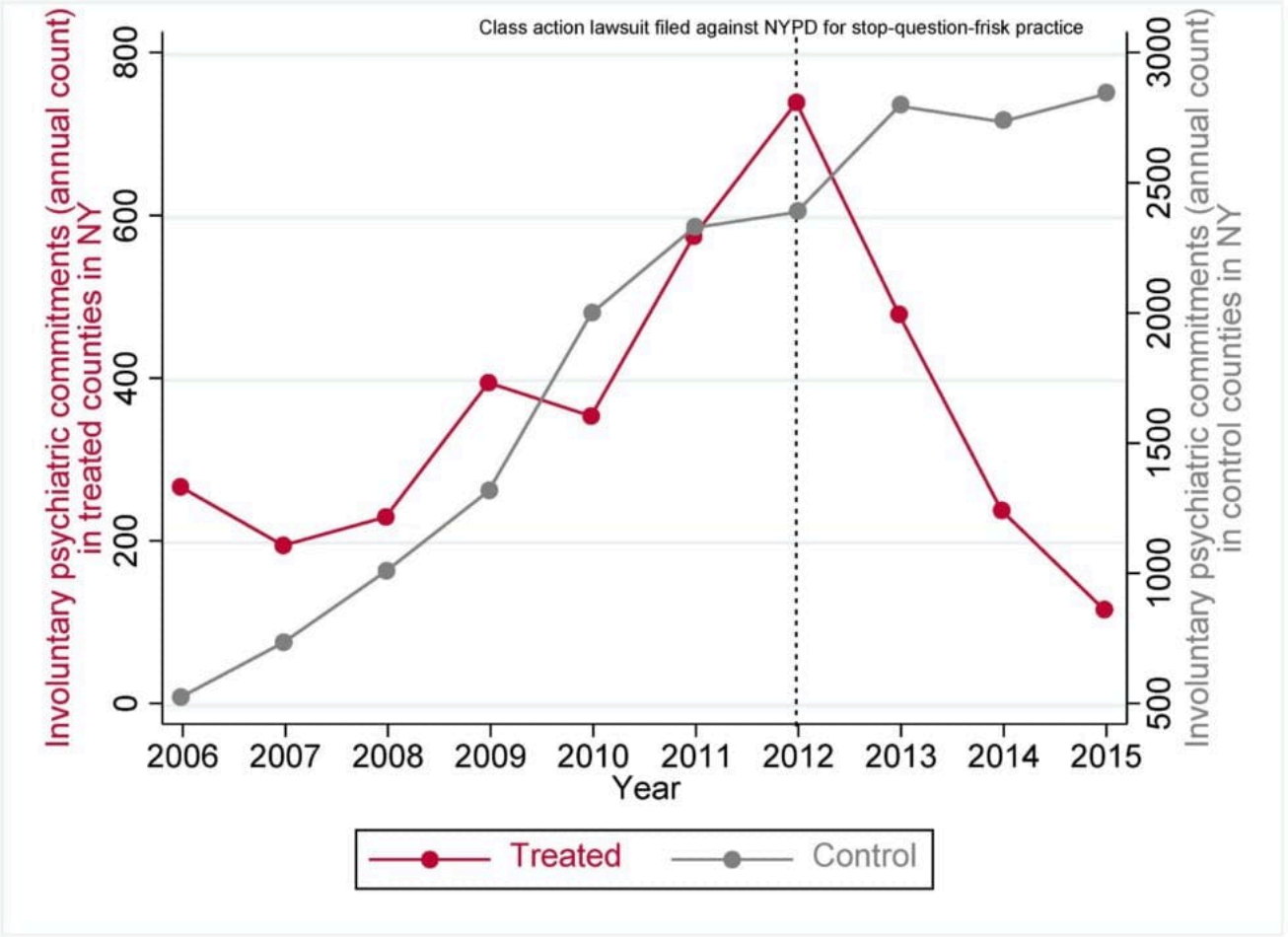
Mental Health

Involuntary psychiatric commitments following decline in police stop-question-frisk practice in New York City: A natural experiment Parvati Singh* Parvati Singh

Involuntary psychiatric commitments, often initiated through law enforcement or court orders, are significantly more prevalent among Black populations, occurring at five times the rate of other groups. Structural factors, including disproportionately higher surveillance by law enforcement and racial bias in healthcare, may contribute to these disparities. However, whether reductions in police hyper-surveillance (police stops, frisks, searches) can mitigate racial disparities in psychiatric commitments remains unexplored. We leverage a natural experiment to examine the effects of sharp decline in police stops on involuntary psychiatric commitments in New York City. We analyze the impact of the 2012 federal class-action lawsuit against the New York Police Department's stop-question-frisk policy, a practice disproportionately targeting Black individuals. Following the lawsuit, stop-and-frisk encounters declined rapidly, providing an opportunity to assess potential shifts in involuntary commitment trends through a quasi-experimental approach.

Using data from the Healthcare Cost and Utilization Project's State Inpatient Database, we conducted panel interrupted time series analyses to evaluate changes in annual involuntary psychiatric commitments across New York State from 2006 to 2015. The five boroughs of New York City-Bronx, Brooklyn, Manhattan, Queens, and Staten Island-were classified as treated regions, while all other counties in the state served as controls. We designated 2012 as the intervention year and adjusted for key covariates, including autocorrelation, demographic factors (age, sex, race), unemployment rate, and fixed effects for county and year. Results indicate a significant decline in involuntary psychiatric commitments in New York City relative to the rest of the state post-2012 (coefficient = -0.55, $p < 0.001$). However, stratified analyses reveal that this decline does not concentrate among Black individuals but rather affects Black and all other groups similarly. These findings suggest that while reductions in police hyper-surveillance may correspond with overall declines in involuntary commitments in a population, they alone may not be sufficient to address racial disparities.

Figure 2. Trends in involuntary psychiatric commitments in treated and control counties in New York State, 2006 to 2015



Social

Highway displacement and mortality: impacts of the “Tucson Limited Access Highway” Rae Anne Martinez* Rae Anne Martinez Andrew Fenelon David Van Riper

In the post WWII era, the US increasingly invested in highways as an essential piece of infrastructure. Often, these highways were built through cities, leading to displacement of residents whose homes were demolished and potentially disrupting social and material resources needed for health. Here, we examine the construction of the “Tucson Limited Access Highway” in AZ to conduct an individual-level investigation of the relationship between displacement and mortality (age at death), as well as to investigate the change in neighborhood quality following displacement. Using full count 1940 census and other historical sources, we identified individuals displaced by highway construction and created a propensity score-matched comparison population. For PS-matching, logistic regression was used to estimate the odds of displacement based on Hispanic surname, race, education, age, nativity, individual income/wages, and home ownership. Matches were made using the nearest neighbor method without replacement until a sample of 3:1 (unexposed:exposed) was generated (N=1960). We then used extant linkage files from the IPUMS Multigenerational Longitudinal Panel to link individuals from the full-count 1940 census to the Social Security Administration Numident file. However, individuals who are Hispanic, immigrant, and women (key characteristics of our study population) are less likely to have been linked between data sources. Thus, we developed a standardized, two-step process for collecting mortality data for those not linked, leveraging publicly available death certificates and gravesite/cemetery data. At present, we have completed 95% of the mortality data collection. Once done, we will conduct descriptive analysis to assess differences in demographic characteristics between groups and use linear regression to estimate age at death by displacement status. For displaced individuals, we will also descriptively examine change in neighborhood characteristics and distance of move.

Table. Characteristics of displaced residents compared to non-displaced Tucson residents and the PS-Matched population.

	Displaced (N= 490)		Rest of Tucson (N = 36374)		PS-Matched (N = 1470)	
	N	%	N	%	N	%
Sex						
Female	249	50.8	18749	51.5	760	51.7
Male	241	49.2	17625	48.5	710	48.3
Race						
AI/AN	35	7.1	333	0.9	57	3.9
Asian	0	0.0	341	0.9	0	0.0
Black	12	2.4	1032	2.8	30	2.0
White	443	90.4	34668	95.3	94.1	100.0
Hispanic last name						
Hispanic last name	431	88.0	36374	32.6	1291	87.8
Non-Hispanic last name	59	12.0	24516	67.4	179	12.2
US Citizen	409	83.5	33535	92.2	1265	86.1
Home Ownership						
Homeowner	323	65.9	16002	42.2	952	64.8
Renter	167	34.1	20372	57.8	518	35.2
Highest grade completed						
No schooling	122	24.9	4131	11.4	334	22.7
Nursery - grade 4	165	33.7	4731	13.0	538	36.6
Grades 5-8	152	31.0	9659	26.6	455	31.0
Grades 9-11	35	7.1	5388	14.8	96	6.5
Grade 12	8	1.6	5196	14.3	22	1.7
1+ years of college	8	1.6	5788	15.9	25	1.5
Missing	0	0	1481	4.1	0	0
Age (years), Mean (Sd)	22.6	(17.8)	30.51	(19.35)	22.1	(17.0)

"Displaced residents" (N=490) and "Rest of Tucson" (N = 36,3374) sums to total population of Tucson in 1940.

Health Disparities

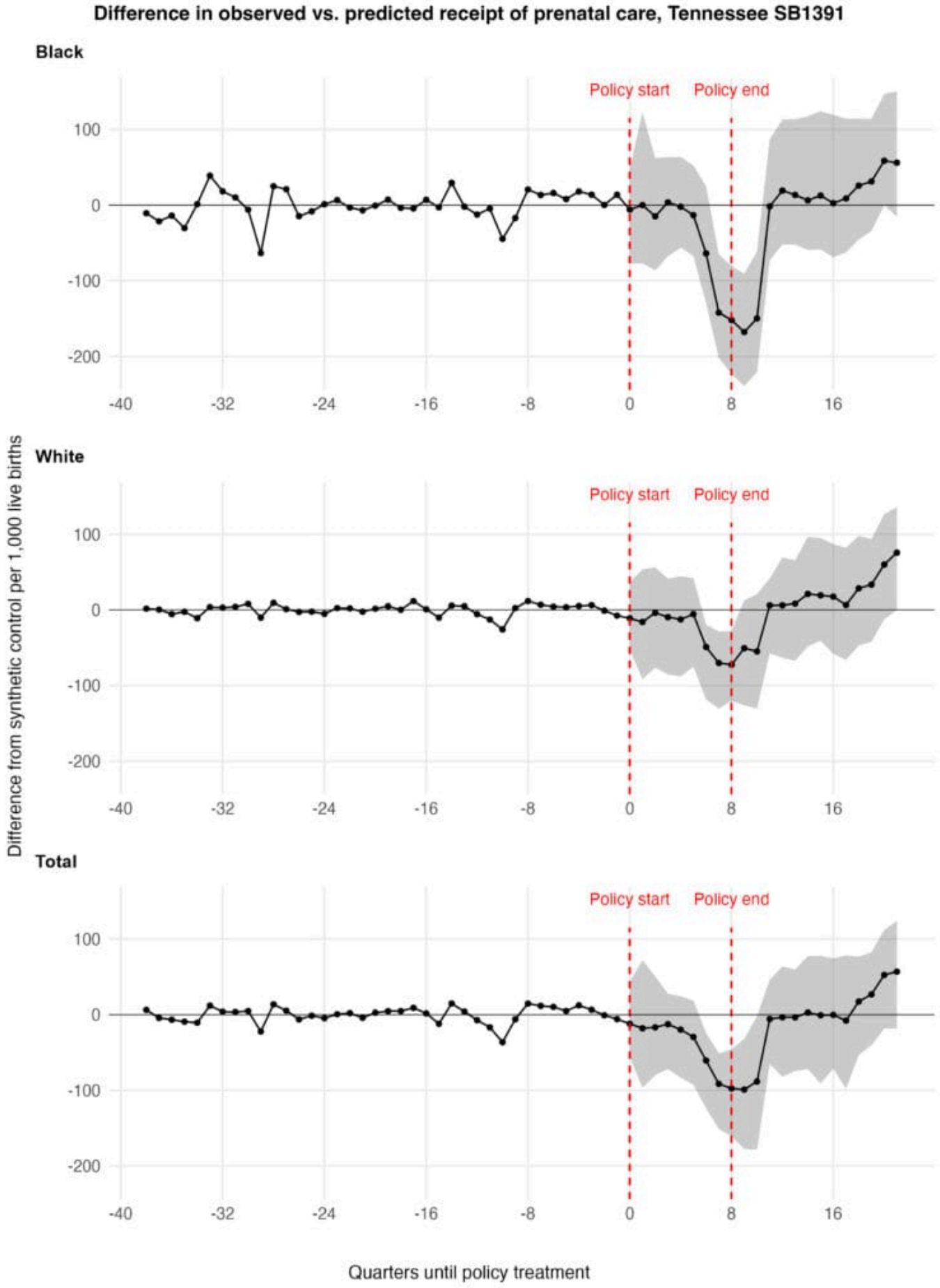
Defining policy exposures when differential enforcement occurs: a case study using Tennessee's prenatal substance use law Simone Wien* Simone Wien Elizabeth D. Wagner Timothy L. Lash Whitney S. Rice Stephen W. Patrick Melvin Livingston Hannah L.F. Cooper Michael R. Kramer

The consistency assumption for causal inference of policies depends on uniform policy implementation across social groups. This assumption is frequently violated and can result in misleading policy estimates. In the setting of differential enforcement, non-stratified estimates can mask harmful or beneficial policy effects within sub-populations due to aggregation. We use Tennessee's (TN) 2014 law criminalizing prenatal substance use (SB1391) as a case study: while disproportionate prosecution of Black women and women in Northeast TN was documented, studies reported only statewide estimates.

We estimated SB1391's effect on preterm birth, entry to prenatal care, and in-hospital delivery using vital records from 2005-2020. We estimated the stratified race/ethnicity average treatment effect on the treated (ATT) using augmented synthetic controls (comparing TN to a synthetic control) and interrupted time series for regional analyses (comparing Northeast TN to the rest of the state). Sensitivity analyses examined robustness to missing prenatal care data in TN during policy implementation. Regional analyses are ongoing.

Statewide estimates obscured racial differences in decreased prenatal care. In the law's last quarter, Black women experienced greater decreases (ATT -151 per 1,000 births, 95% CI -223, -81), than the total population (ATT -98, 95% CI -161, -46) and White women (ATT -72, 95% CI -130, -31). Prenatal care returned to predicted levels for all groups once the law ended. Northeast TN had a modest decrease of in-hospital deliveries (differential slope change -0.95 per 1,000 pregnancies per quarter, 95% CI -1.90, -0.01) and preterm births (- 0.33, 95% CI -1.90, -0.01). Black prenatal care estimates remained robust assuming 50% of missing cases received care, while White and total estimates were robust at 25%.

Stratified estimates support evidence of differential implementation of SB1391. Analytical plans for social policy estimation should consider stratification.


Difference in observed vs. predicted receipt of prenatal care, Tennessee SB1391
Black
White
Total
Policy start
Policy end
100
0
-100
-200
-40
-32
-24
-16
-8
0
8
16
Difference from synthetic control per 1,000 live births
Quarters until policy treatment

Health Disparities

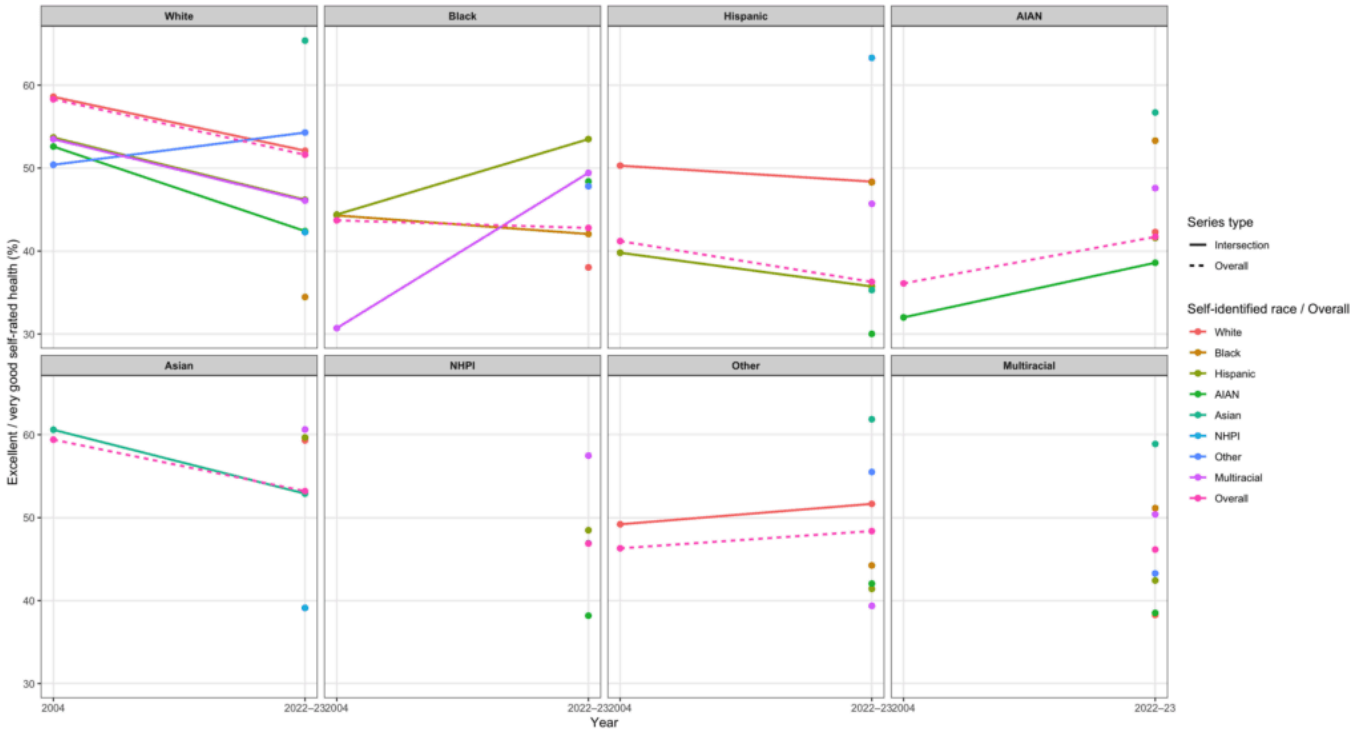
Shifts in relationships between socially-assigned and self-identified race with self-rated health, BRFSS 2022-2023 Tracy* Tracy Lam-Hine David Rehkopf

Background: Socially-assigned race (the race one is perceived by others to be) may relate to self-rated health (SRH) differently than self-identified race. Jones et al. 2008 used data from the 8 states using the first Reactions to Race (R2R) module fielded in the 2004 Behavioral Risk Factor Surveillance System, finding strong protective effects of social assignment as White race, particularly among Multiracial adults. We aimed to assess how the influence of socially-assigned and self-identified race on SRH has evolved in more recent data.

Methods: We used data from the 35 states administering the R2R module in 2022-2023. Replicating the prior analysis, we estimated design-weighted prevalence of excellent or very good SRH using predictive marginal standardization from a logistic regression adjusting for age, education, and questionnaire language, and stratified results across combinations of self-identified and socially assigned race. In a sensitivity, we restricted analysis to the same states from the prior study.

Results: Among 391,318 adults with complete data, mean EVGH was 48.5% (95% CI: 48.1-48.9). Marginal SRH was highest among people perceived as Asian and lowest among people perceived as Hispanic, a pattern that held across several self-identified race strata. Among people perceived as Black, SRH increased dramatically for self-identified Multiracial or Hispanic adults, but not for self-identified Black adults. Differences in SRH by socially-assigned race among Multiracial adults were not more pronounced than for other groups. Similar patterns emerged in the sensitivity, suggesting that observed shifts did not solely result from differences in sampling.

Discussion: Our results indicate that the relationship between socially-assigned race and SRH has shifted in the last 20 years, potentially reflecting changes in the process of racialization. Socially-assigned race and health have a time-dependent and contextual relationship which should periodically be revisited.


White
Black
Hispanic
AIAN
Asian
NHPI
Other
Multiracial
Excellent / very good self-rated health (%)
60
50
40
30
2004
2022–23
Year
Series type
Intersection
Overall
Self-identified race / Overall
White
Black
Hispanic
AIAN
Asian
NHPI
Other
Multiracial
Overall

Social

Detection of Loneliness and Social Connectedness from Passive Sensor Data Using Machine Learning Afzalbek Fayzullaev* Afzalbek Fayzullaev Jingxuan Wang Andrew Philips Dylan Tran Yulin Yang M. Maria Glymour Peter James Ruijia Chen

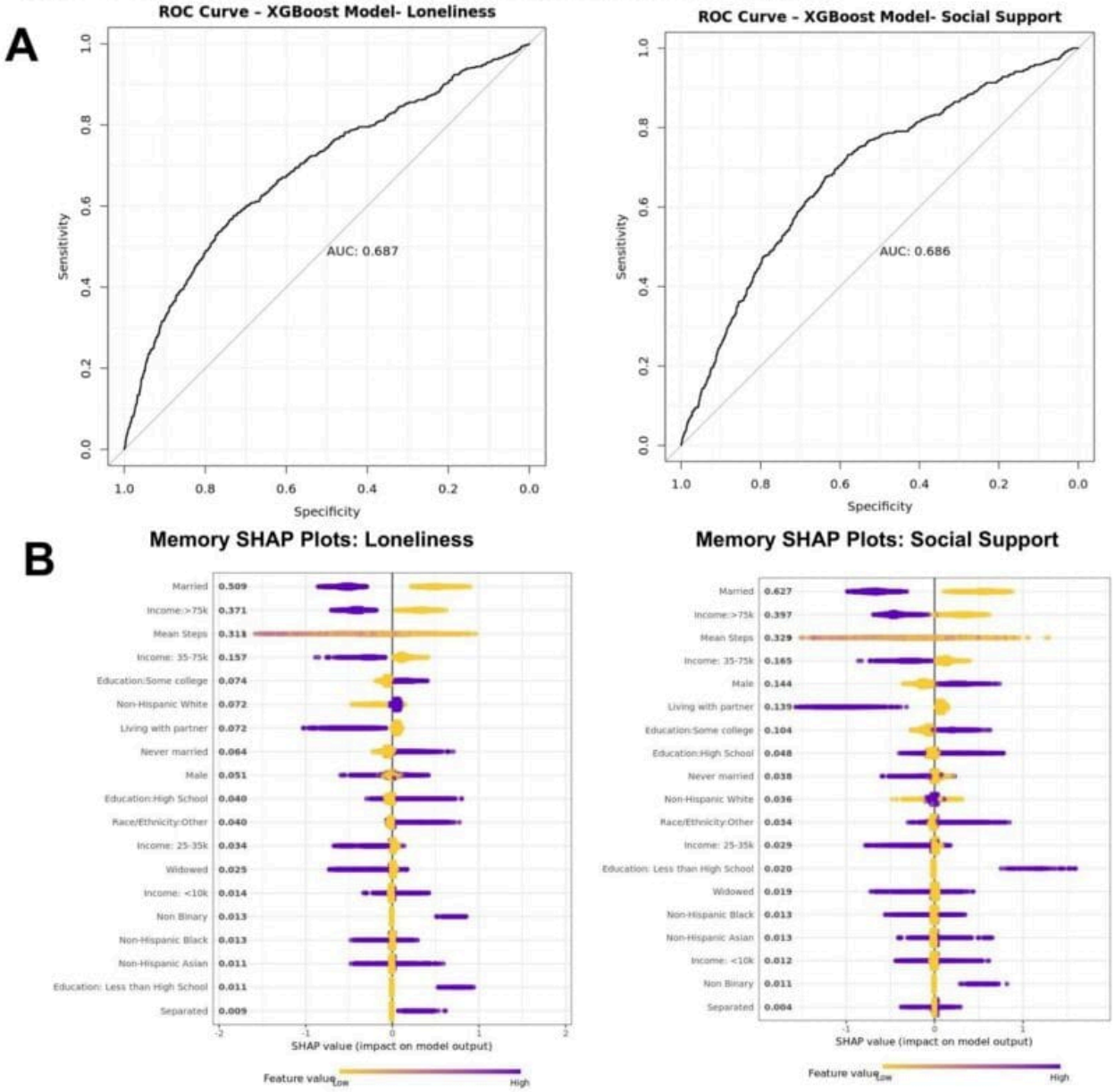
Passive sensor data from wearable devices collect information on everyday life and behavioral patterns, making them a promising tool for detecting loneliness and social connectedness. This study evaluated the feasibility of using Fitbit data to identify loneliness and low social support.

Data were from 17,127 respondents to the Social Determinants of Health (SDOH) Survey from the All of Us Research Program who were aged ≥ 18 years old with valid Fitbit data (defined as at least 10 hours of wear time and 100-45,000 daily steps per day, collected during the 7 days preceding SDOH survey administration). The sample was randomly split into training (80%) and test (20%) sets. Loneliness was measured using the UCLA 8-Item Loneliness Scale (range: 8-32); participants with a score ≥ 21 were classified as lonely. Lack of social support was calculated using the RAND Social Support Survey Instrument (range: 8-40); participants with a score ≥ 26 were classified as lacking social support. Extreme gradient boosting (XGBoost) models predicted loneliness and lack of social support using mean step count, age, gender, race and ethnicity, income, education, and marital status. Model performance was evaluated in the test set using sensitivity, specificity, and SHAP values for variable importance.

The average age was 53.9 years (SD=15.0); 70.3% were female and 78.5 % were non-Hispanic White. The XGBoost model for loneliness achieved sensitivity of 0.58 and specificity of 0.71, whereas the models for predicting social support achieved a sensitivity of 0.59 and specificity of 0.70. According to the SHAP values, mean step count was the most influential predictor after marriage and income.

In one of the largest Fitbit-based studies to date, models using mean daily step counts showed modest performance in predicting loneliness and social connectedness. Future work will evaluate alternative algorithms, address class imbalance, and extend the observation window.

Fig. 1: Receiver operating characteristic (ROC) curves and feature importance plots of classification models for loneliness and social support



A *ROC curves for loneliness and social support*
B *Feature importance according to SHapley Additive exPlanations (SHAP) plots for loneliness and social support. SHAP values represent the impact of that variable on the model output. Each point represents an individual participant and its horizontal reflects the effect of that feature. The dot color corresponds to the feature value, ranging from low to high*

Injuries/Violence

Predicting Fatal and Non-Fatal Suicide Attempts Among Privately Insured Residents of North Carolina Using Machine Learning Matthew Turnure* Matthew Turnure Lina Montoya Brian Pence Naoko Fulcher Bradley Gaynes Tim Carey Shabbar Ranapurwala

Statement of purpose: Suicide is a major public health problem. In North Carolina, age-adjusted suicide mortality rates increased by 31% from 1999 to 2022. While decades of research have identified many risk factors for suicide attempt, interventions in the healthcare settings can be strengthened by identifying high-risk individuals using risk prediction algorithms and linking them to appropriate care. We predicted the risk of suicide attempt in the next month in a privately insured population in North Carolina using machine learning.

Methods: We conducted a nested case-control study of covered people aged 12 and older. Administrative claims data were linked to North Carolina death certificate records for 2006 to 2020. Cases (n=5,276) were all fatal and non-fatal suicide attempts, and controls (n=226,310) were identified using an incidence-density risk-set sampling approach. We used super learning, an ensemble machine-learning approach that formed a weighted average of several algorithms to achieve the best possible predictions given our performance metric of interest, negative log likelihood. To estimate population-based risks, we used inverse probability of sampling weights. Model covariates included diagnoses, procedures, and prescriptions known to be associated with suicide.

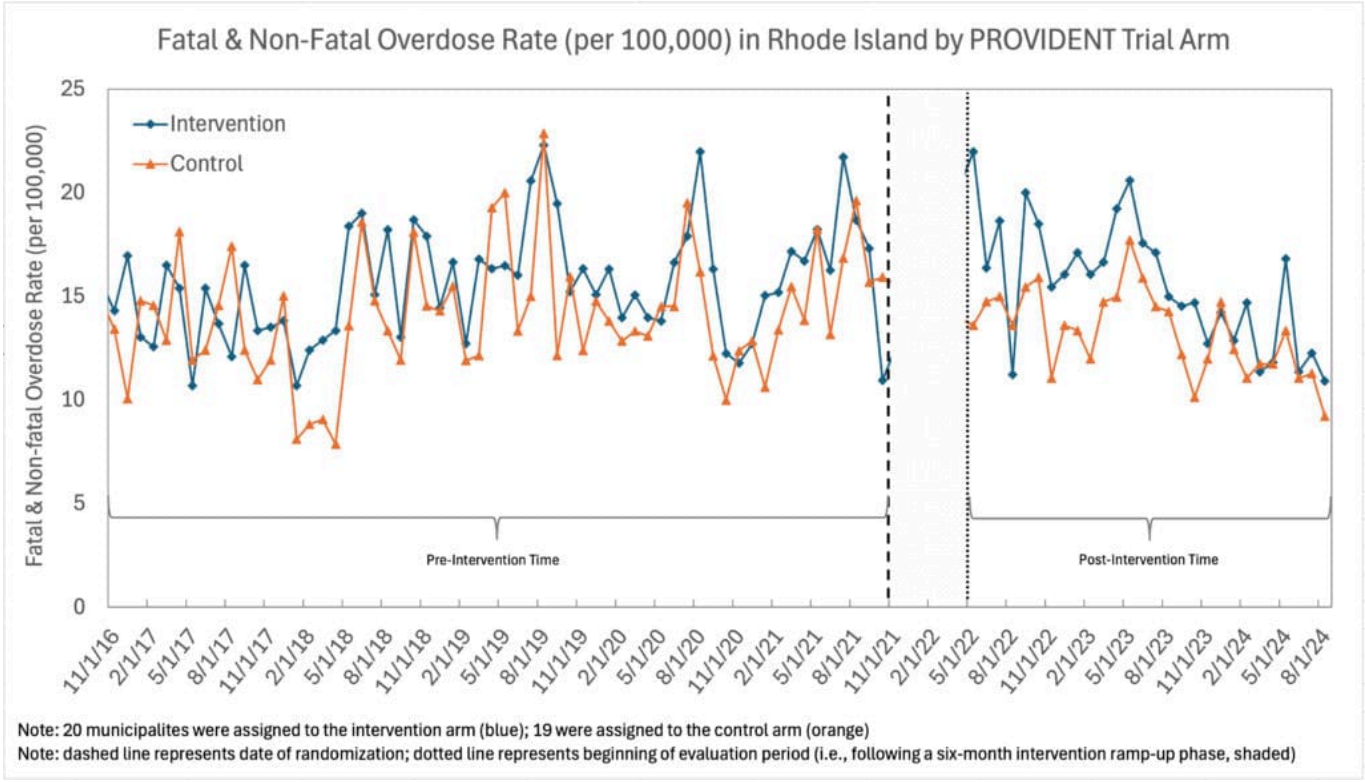
Results: In predicting the 1-month risk of suicide attempt, the super learner improved on the best single algorithm by 27%. At 95% specificity, the model had 20.6% sensitivity and 8.8% positive predictive value.

Significance: Although the super learner ensemble model was substantially better at predicting suicide attempt than individual algorithms, risk categorization thresholds that achieved high specificity resulted in low sensitivity. This suggests that future models could benefit from tailoring to subpopulations by age, rurality, and other demographics, and based on suicide subtypes with firearm or intimate partner violence involvement.

Substance Use

A Machine Learning-Based Forecasting Tool to Predict Future Overdose Deaths: Results of the PROVIDENT Randomized Community Intervention Trial Yu Li* Brandon Marshall Yu Li Claire Pratty Maxwell Krieger Jesse Yedinak Gray William Goedel Benjamin Hallowell Daniell Neill Bennett Allen Jennifer Ahern Magdalena Cerdá

Overdoses are an ongoing public health problem, necessitating timely, proactive responses directed towards communities at highest risk. We developed, validated, and disseminated a machine learning-based forecasting tool that predicts future overdose deaths at the neighborhood level in Rhode Island. We then conducted a randomized, population-based, community intervention trial to determine whether municipalities randomized to receive predictions about which neighborhoods are most at risk of future overdose would experience greater reductions in overdoses compared to municipalities receiving traditional surveillance data. To evaluate the effect of the intervention on the primary endpoint, municipal-level fatal and non-fatal overdose rates, we used a generalized linear mixed effects model, including fixed effects for pre-/post-time, trial arm, their interaction, and municipal-level covariates. Randomization occurred in November 2021; the analysis included 2 years of post-intervention data (see figure). We randomized 20 and 19 municipalities to the intervention and standard-of-care, respectively; neighborhood characteristics and historical overdose rates were balanced. Over the study period, 36 service providers registered to use the PROVIDENT decision tool and to view the neighborhood forecasts in the treatment arm, logging in 562 times; however, engagement declined over time. We observed no effect of the intervention on the study endpoint (adjusted incidence rate ratio=1.06, bootstrapped 95%CI: 0.96-1.20, p=0.358). Results were robust to sensitivity analyses under different model specifications. While machine learning-based approaches can successfully predict neighborhoods at highest risk of overdose, dissemination of these forecasts to policymakers and community leaders had no significant effect on overall overdose burden. Future research is needed to improve integration of predictive analytic approaches into statewide governance and service provider networks.



Note: 20 municipalites were assigned to the intervention arm (blue); 19 were assigned to the control arm (orange)
Note: dashed line represents date of randomization; dotted line represents beginning of evaluation period (i.e., following a six-month intervention ramp-up phase, shaded)

Cardiovascular

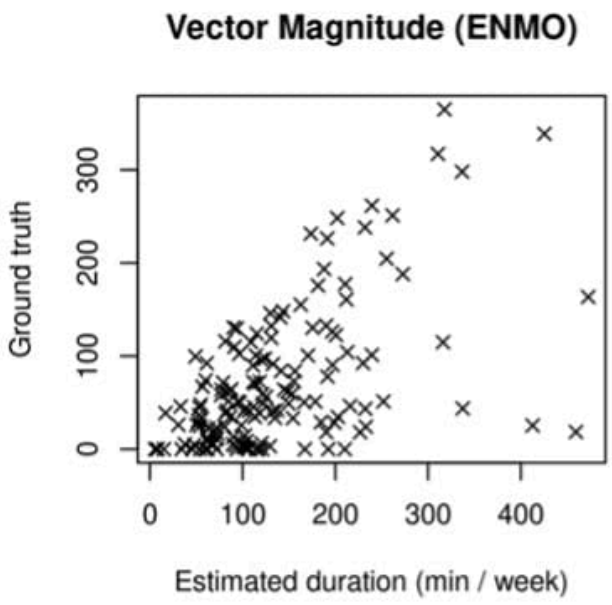
Association Between Urban Greenness and Machine Learned Physical Activity Measures: A Cross-Sectional Study Using UK Biobank Hiroshi Mamiya* Yacine Lapointe Hiroshi Mamiya Emily Hum

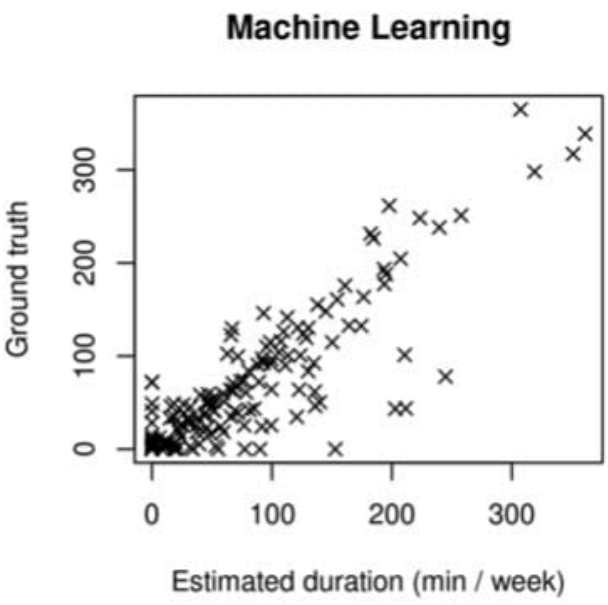
Background: Physical activity is a major preventable risk factor for chronic disease and mental health disorders. Residential proximity to urban greenness has been shown to positively influence physical activity. However, most studies have relied on self-reported measures of physical activity, which are prone to bias. Wearable devices can provide more objective measures of activity duration and intensity using accelerometry signals. This study compared associations between urban greenness and physical activity using self-reported measures and three accelerometer-derived methods, including a novel Machine learning–based approach.

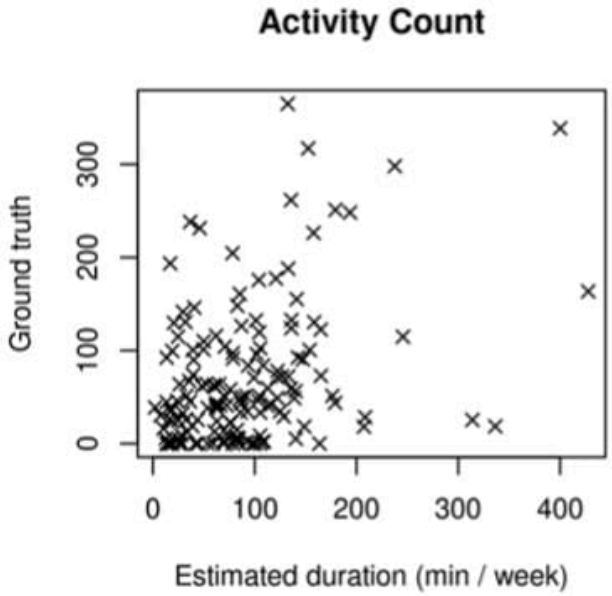
Methods: We analyzed UK Biobank accelerometer data from 81,582 urban participants aged 40–69 years, collected in 2013. Exposure to urban greenness was measured using the Normalized Difference Vegetation Index within a 300 m residential buffer. Participants' mean weekly duration of light physical activity was derived from self-reports and 7-day wrist-worn accelerometers. Three accelerometer-based metrics were generated: Vector magnitude, Activity counts, and a Machine learning–based measure. Linear mixed models accounting for within-city clustering were adjusted for diet, transportation, socioeconomic characteristics, and neighbourhood environmental factors, and stratified by household income.

Results: The Machine learning-based measure demonstrated the strongest agreement with gold-standard measures and the strongest positive association with greenness (Fig. 1), particularly among low-income households. Accelerometer-derived metrics showed curvilinear relationships, whereas self-reported physical activity showed weaker and inconsistent associations.

Conclusions: These findings support evidence that urban greenness promotes higher physical activity. Machine learning-based accelerometer processing yielded stronger and more consistent associations than traditional methods, highlighting its value for physical activity research.


Vector Magnitude (ENMO)
Ground truth
0
100
200
300
0
100
200
300
400
Estimated duration (min / week)

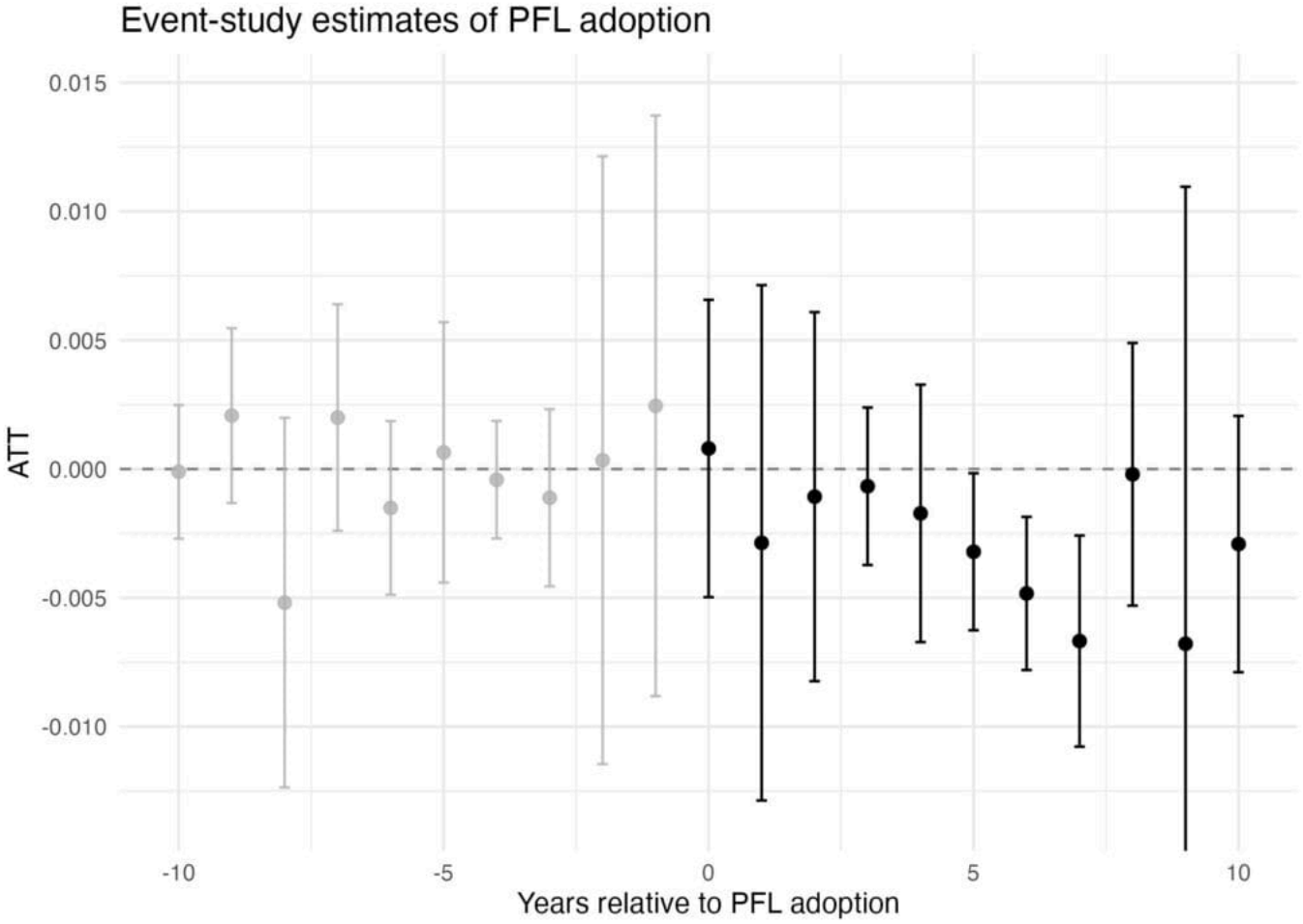

Machine Learning
Ground truth
0
100
200
300
0
100
200
300
Estimated duration (min / week)


Activity Count
Ground truth
0
100
200
300
0
100
200
300
400
Estimated duration (min / week)

Injuries/Violence

Paid Family and Medical Leave and Physical Abuse During Pregnancy: Evidence from a Multi-State Quasi-Experimental Analysis Krista Neumann* Krista Neumann Katherine deCourcy Ann E. Richey Heather D. Hill Avanti Adhia

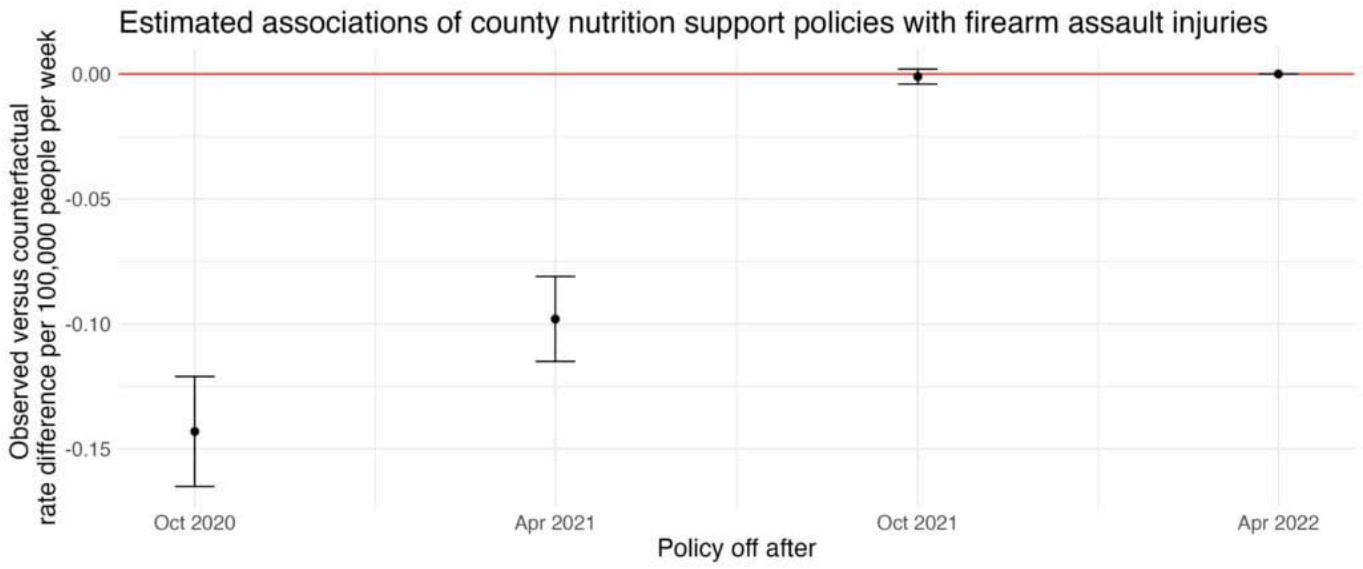
Abuse during pregnancy is associated with serious maternal and infant health consequences. Structural economic policies may influence risk of abuse by reducing financial stress and relationship conflict. Paid family leave (PFL), although typically used postpartum, may affect prenatal experiences by shaping economic security and household dynamics around childbirth. Evidence, though, on whether state PFL adoption is associated with abuse during pregnancy is limited. We used data from the Pregnancy Risk Assessment Monitoring System (PRAMS), a population-based survey of postpartum individuals, from 2000–2022 and restricted to respondents with valid information on physical abuse during pregnancy. The outcome was a binary indicator of self-reported physical abuse by a husband or partner during pregnancy. The exposure was state adoption of a PFL policy, defined as the first year benefits became available. We estimated the association between PFL adoption and abuse during pregnancy using a staggered difference-in-differences design that compared states with PFL policies to those that had not yet adopted PFL. Event-study estimates were used to assess pre-policy trends and post-adoption dynamics. Standard errors were clustered at the state level. Between 2009 and 2021, six states participating in PRAMS adopted PFL. Overall, 2.3% of respondents reported physical abuse during pregnancy. Event-study estimates showed no evidence of differential pre-policy trends. In the 1–3 years following adoption, PFL was associated with a 0.15 percentage-point decrease in abuse during pregnancy (95% CI: −1.14, 0.83). Larger reductions were observed in years 4–7 post-adoption (0.41 percentage-point decrease; 95% CI: −0.94, 0.12). These findings contribute to limited empirical evidence on structural policy interventions for reducing abuse during pregnancy and suggest PFL policies may have benefits for abuse prevention during pregnancy, especially as programs become more established.


Event-study estimates of PFL adoption
0.015
0.010
0.005
0.000
-0.005
-0.010
ATT
-10
-5
0
5
10
Years relative to PFL adoption

Injuries/Violence

Impacts of county-level housing, nutrition, and utilities support policies on rates of community firearm violence Rafael Charris* Rafael Charris Ellicott Matthay Matthew Magdalena Iván Brita Sidra Rita Sharon Ryan

Insecurity in housing, nutrition, utilities, and income are recognized correlates of community firearm violence, yet little research has assessed whether public policies that support access to these basic needs help prevent community firearm violence. During the COVID-19 pandemic, several counties enacted policies to mitigate the economic consequences of the pandemic by offering different types of economic supports. We estimated the impact of these policies on firearm assault injuries across 31 California counties from January 2020 to December 2022. We analyzed weekly county-level population-representative data policies from the US COVID-19 County Policy Database, firearm assault injuries from statewide emergency department and inpatient hospitalization discharge records, and confounding variables from multiple public sources. Using longitudinal targeted minimum loss-based estimation with standard errors clustered at the county level and adjusted for time-varying confounders, we compared changes in firearm assault injury rates associated with each type of policy as-observed versus the rates had all counties prematurely stopped the given policy on a specified date. Across the 4,836 county-weeks of observation, the average weekly firearm assault injury rate was 0.18 per 100,000 people. Nutrition support policies were associated with lower rates of firearm assault injuries (RD per 100,000 [RD], -0.143; 95% CI, -0.099, -0.187), as were paid sick leave policies (RD, -0.079; 95% CI, -0.099, -0.059), but only for certain pandemic periods (through April 2021 and after October 2021, respectively). Housing protections, unemployment supports, other income supports, or utilities payment supports were not associated with firearm assault injuries. Associations varied by racial/ethnic group, gender, and age group. This study adds to a small but growing literature on the effectiveness of economic support policies in reducing community firearm violence.



Injuries/Violence

Racial differences in the association of physical disability and healthcare access with firearm violence at the neighborhood level in Chicago, 2011-2023 Bennett Allen* Bennett Allen Cale Basaraba Madison Offstein Spruha Joshi Jacquelyn Jacobs

Background: Firearm violence remains a public health crisis in the United States, disproportionately affecting racially minoritized and historically disinvested neighborhoods. The relationship between neighborhood-level disability prevalence and healthcare access with firearm violence risk remains poorly understood.

Methods: We conducted an ecological, spatiotemporal analysis of 77 community areas in Chicago from 2011 to 2023. Using Bayesian negative binomial models adjusted for neighborhood economic and demographic covariates, we estimated associations between community-level disability prevalence and healthcare underservice—defined as proportion of land designated as a Medically Underserved Area (MUA)—with annual rates of nonfatal firearm victimizations and firearm homicides. Models were adjusted for income, poverty, and racial/ethnic composition and stratified by neighborhood racial/ethnic plurality.

Results: A 5–percentage point increase in disability prevalence was associated with a 10% higher rate of firearm victimization (95% credible interval [CrI], 3%–18%) and an 11% higher rate of firearm homicide (95% CrI, 2%–22%). A 5–percentage point increase in MUA coverage was associated with a 4% increase in firearm victimization (95% CrI, 2%–6%) and 3% increase in firearm homicide (95% CrI, 2%–5%). In stratified models, disability was most strongly associated with firearm violence in plurality non-Hispanic Black neighborhoods. Associations between MUA coverage and firearm violence were largest in plurality non-Hispanic white and Hispanic neighborhoods.

Conclusions: Neighborhood-level disability and healthcare underservice are significantly associated with firearm violence in Chicago, with differences by racial/ethnic composition. Findings illustrate how disability intersects with racialized social and geographic structures and underscore the need to integrate disability and healthcare access into public health violence prevention frameworks.

Injuries/Violence

Racial and ethnic disparities in community violence and its association with maternal and infant health in California Emily Liu* Emily Liu Shelley Jung Rachel Morello-Frosch Jennifer Ahern

Structural racism may shape exposure and susceptibility to community violence (CV), contributing to racialized disparities in perinatal health. Few studies have evaluated whether exposure to, and health impacts of, CV vary by race and ethnicity.

We analyzed over 4 million singleton live births in California (2007–2018) using linked hospital discharge, birth, and death records. CV was measured at the ZIP code level and binarized as high (≥50th percentile) versus lower levels. We used targeted maximum likelihood estimation for race-stratified risk differences (per 1000) with perinatal outcomes. The analysis was restricted to ZIP codes with overlapping propensity scores for high community violence.

Exposure to high CV was most common among Black (79.0%), Hispanic (74.1%), American Indian/Alaska Native (73.6%), Native Hawaiian/Pacific Islander (NHPI; 67.7%), and Multiracial (57.3%) pregnant people, compared with White (45.0%) and Asian (36.6%) pregnant people. NHPI pregnant people had among the highest prevalence of gestational diabetes (GDM; 14.3%), hypertensive disorders of pregnancy (HDP; 12.9%), preeclampsia (PE; 6.0%), and preterm birth (PTB; 10.0%), and experienced large risk increases associated with high CV, including GDM (RD 11.11 [95% CI 11.04–11.17]), HDP (RD 24.54 [95% CI 24.48–24.60]), PE (RD 12.25 [95% CI 12.21–12.30]), and PTB (RD 7.15 [95% CI 7.09–7.22]). Black pregnant people had the highest prevalence of HDP (14.6%), PE (6.2%), and PTB (11.0%), with substantial violence-associated risk increases, including HDP (RD 19.35 [95% CI 19.34–19.35]), PE (RD 6.63 [95% CI 6.62–6.63]), and PTB (RD 5.39 [95% CI 5.39–5.40]).

Large racial and ethnic differences in both exposure and susceptibility to CV were observed. NHPI and Black pregnant people appear particularly vulnerable to violence exposure and violence-related perinatal risks, underscoring CV as a potential contributor to persistent health disparities.

Injuries/Violence

Suicide and overdose mortality among victims and defendants in felony domestic violence criminal cases Warren Szewczyk* Warren Szewczyk Spencer Hensley David Martin Alastair Matheson

Domestic violence (DV), death by suicide, and death by overdose are major public health concerns in the United States. While existing studies have documented associations of DV with both suicide and overdose, most studies utilize nonfatal outcomes and lifetime DV exposure. In this population-based case-control study, we aimed to estimate the association of both suicide death and overdose death with involvement in a DV case, either as a victim or defendant, referred for felony charges in the year prior to death. All deaths in King County, Washington, USA or deaths occurring elsewhere among King County residents from 2016–2022 were included (N=113,388). Felony DV referral records from 2016–2021 were sourced from the King County Prosecuting Attorney's Office and included both victims and alleged perpetrators of DV. All people with DV referral records had at least one year of observation after referral. Suicide deaths (n=2,246) and overdose deaths (n=3,588) were separately matched to deaths of all other causes based on age, gender, year of death, and calendar year quarter of death. Conditional logistic regression was used to estimate associations of case status with DV referral in the year prior to death. Suicide cases had nearly 4 times greater odds of being a defendant in a DV referral within the year prior to death than matched controls (OR=3.68, 95% CI: 2.33–5.81, $p<0.01$). No association was found for suicide and being a victim in a felony DV case (OR=0.74, 95% CI: 0.18–3.02, $p=0.42$). Overdose cases had greater odds of both being a defendant (OR=2.47, 95% CI: 1.67–3.66, $p<0.01$) and being a victim (OR=4.36, 95% CI: 2.76–6.87, $p<0.01$) in the year prior to death. These findings highlight a need for a public health approach to implementing evidence-based suicide and overdose prevention efforts among people involved in DV cases. Future research could examine mediating links between DV and both suicide and overdose and evaluate the efficacy of prevention strategies.

Injuries/Violence

Racial Disparities in In-Hospital Mortality Following Firearm Injury in a Level I Trauma Center Hiwot Weldemariam* Hiwot Weldemariam Heather Barnett Ali Rowhani-Rahbar

Background: Firearm injury is a leading cause of morbidity and mortality in the United States. While racial differences in firearm injury incidence are well documented, little is known about disparities in in-hospital mortality and injury characteristics. **Methods**: We conducted a retrospective cohort study of patients presenting with firearm-related injuries to a Level I trauma center between January 1, 2004, and December 31, 2024 (n = 6,551), using our institution's trauma registry. The primary outcome was in-hospital mortality. Race was the primary exposure (Black or African American, White, and Other). We used logistic regression, adjusting for calendar year, injury severity, age, sex, injury intent, and insurance type. Injury severity was classified using the Injury Severity Score (ISS): minor (1–8), moderate (9–15), severe (16–24), and very severe (≥25). Effect modification by injury severity was assessed using race × ISS interaction terms. **Results:** In adjusted main-effects models, White patients had lower odds of in-hospital mortality compared with Black patients (OR = 0.65; 95% CI: 0.48–0.87). The race × injury severity interaction was statistically significant (p = 0.0025), indicating that racial differences in mortality varied by injury severity. Among patients with severe injuries, Black patients experienced substantially higher odds of mortality compared with White patients (OR = 4.54; 95% CI: 2.06–10.00). There were no statistically significant racial differences in mortality among patients with minor, moderate, or very severe injuries. **Conclusions:** Racial disparities in in-hospital mortality following firearm injury vary by injury severity. Among patients with severe but potentially survivable injuries, Black patients experience markedly higher mortality compared with White patients, even within the same Level I trauma center. These findings highlight the importance of severity-specific analyses when evaluating racial inequities in trauma outcomes and suggest that disparities in clinical processes or access to timely, high-quality trauma care may be most consequential in the severe injury range.

Environment/Climate Change

In Utero Exposure to Organophosphate Esters and Anxiety and Depressive Symptoms in Early Adolescence Michaela Olabisi* Michaela Olabisi Jagadeesh Puvvula Yingying Xu Kim M. Cecil Antonia M. Calafat Maria Ospina Ann M. Vuong Joseph M. Braun Bruce P. Lanphear Jeffrey R. Strawn Kimberly Yolton Aimin Chen

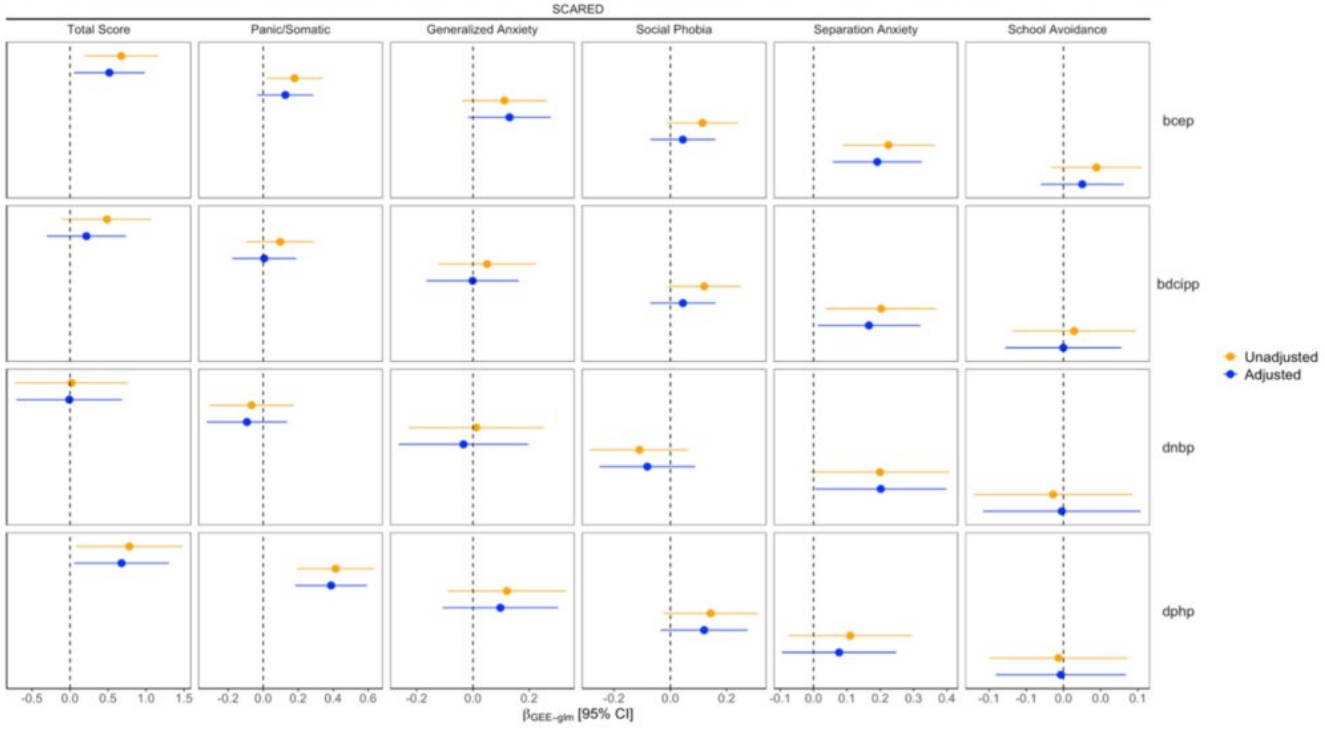
Anxiety and depression often emerge during adolescence, a period of vulnerability to mood disorders. In utero exposure to organophosphate esters (OPEs), widely used flame retardants and plasticizers, may alter behavior. However, their role in adolescent mental health is unclear.

Using data from 249 mother–child pairs in the Health Outcomes and Measures of the Environment Study (2003–2006), associations between in utero OPEs and anxiety and depressive symptoms at age 12 years were examined. Maternal urinary concentrations of four OPE metabolites, including bis(2-chloroethyl) phosphate (BCEP), bis(1,3-dichloro-2-propyl) phosphate (BDCIPP), di-n-butyl phosphate (DNBP), and diphenyl phosphate (DPHP), were measured at 16 and 26 weeks' gestation and delivery, standardized for specific gravity, and log2 transformed. Anxiety and depressive symptoms were assessed at 12 years with the Screen for Child Anxiety Related Emotional Disorders and the Children's Depression Inventory-II, and associations with repeated OPEs across gestation were estimated using multiple informant models with covariate adjustment. As secondary analyses, generalized linear models evaluated individual exposure windows, and modified Poisson models evaluated dichotomized outcomes.

Higher prenatal OPE concentrations were associated with increased anxiety, but not depressive symptoms. Each doubling in BCEP was associated with higher separation anxiety (β = 0.5, 95% CI: 0.05–0.98) and total anxiety (β = 0.19, 95% CI: 0.06–0.3). In addition, BDCIPP and DNBP were associated with increased separation anxiety and DPHP with higher panic/somatic and total anxiety. In secondary analyses, associations were stronger in females, with higher OPEs associated with a modest increase in risk of having clinically significant anxiety (RRs = 1.03–1.08).

These results suggest that in utero OPE exposure in this cohort was a risk factor for anxiety, particularly separation anxiety and panic/somatic symptoms, in early adolescence.

Figure 1: Associations Between In Utero OPE Exposure and Anxiety Symptom Scores at Age 12 Years



Environment/Climate Change

Prenatal and postnatal exposure to ambient temperature and risk of ASD/ADHD among Medicaid recipients Stefania Papatheodorou* Stefania Papatheodorou Matthew Shupler Xinye Qiu Krista Huybrechts Sonia Hernandez Diaz Hayon Michelle Choi Michael Leung Yaguang Wei Joel Schwartz Marc Weisskopf Antonella Zanobetti Wanyu Huang

Abstract

Background:
Epidemiologic evidence linking ambient temperature exposure to the risk of autism spectrum disorder (ASD) and attention-deficit/hyperactivity disorder (ADHD) remains limited, particularly among low-income populations who may be disproportionately vulnerable to environmental stressors.

Methods:
We constructed a population-based mother–child cohort using the Medicaid Analytic eXtract (MAX) from 2001–2014. ASD and ADHD diagnoses were identified using ICD-9/10 codes. Ambient temperature was assigned at the ZIP-code level at the last menstrual period and at birth. Cox proportional hazards models were used to estimate associations between average prenatal and postnatal temperature exposure and risk of ASD and ADHD. Distributed lag non-linear models characterized exposure windows across pregnancy (0–37 weeks) and early childhood (0–3 years). Models adjusted for maternal and child demographics, behavioral risk factors, ambient $PM_{2.5}$, season of conception, and area-level socioeconomic status. Effect modification by child sex was evaluated.

Results:
Among 1,548,303 births, a 1 °C increase in average prenatal temperature was associated with a modestly higher risk of ASD (hazard ratio [HR] = 1.02; 95% CI: 1.00–1.03) and a lower risk of ADHD (HR = 0.96; 95% CI: 0.95–1.00) over the cumulative prenatal lag. Postnatal exposure to heatwaves was associated with increased risk of ASD (HR = 1.08; 95% CI: 1.02–1.15) and ADHD (HR = 1.02; 95% CI: 1.00–1.10) across early childhood. No evidence of effect modification by child sex was observed.

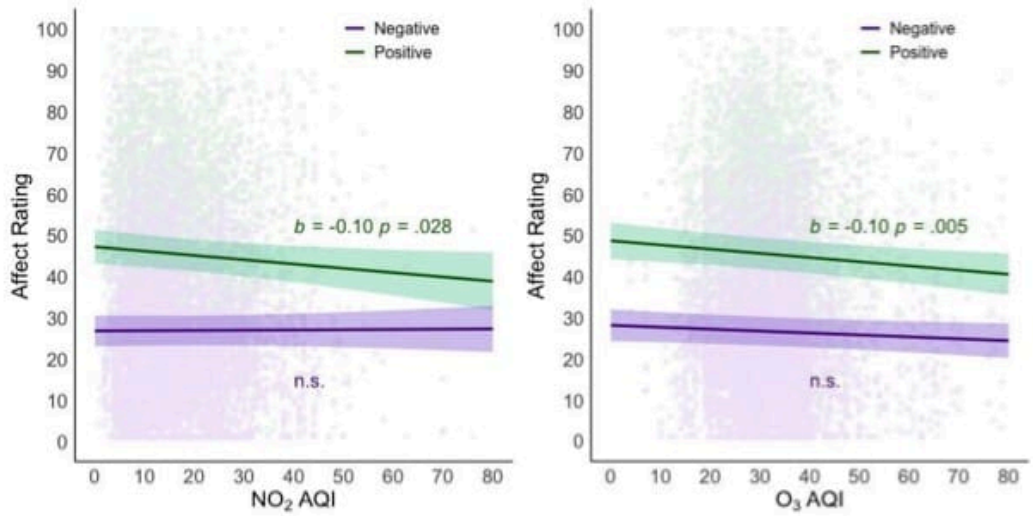
Conclusions:
Prenatal and early-life temperature exposures were associated with increased risk of ASD among low-income children in the United States, underscoring the potential neurodevelopmental implications of weather-related exposures in socioeconomically vulnerable populations.

Environment/Climate Change

The effects of daily air pollution on affect in adolescents: An ecological momentary assessment study Sarah Rocha* Sarah Rocha Chase Antonacci Jessica P. Uy Ian H. Gotlib

Air pollution is a global environmental threat and growing evidence suggests that it is particularly harmful to adolescents' mental health. To date, however, we know little about how air pollution affects daily emotional functioning. In this study using ecological momentary assessment, we assessed daily levels of air quality across a 14-day period in 158 adolescents (59% female, MAge=16.1 years) in the San Francisco Bay Area. Adolescents reported on their levels of positive and negative affect, or emotion, and their experiences of stress three times/day, resulting in 4,113 observations. We examined associations of daily levels of four major air pollutants (carbon monoxide [CO], nitrogen dioxide [NO2], ozone [O3], and particulate matter < 2.5μm [PM2.5]) with adolescents' same- and next-day ratings of their affect levels, the lability (i.e., variability) of their affect, and their affective reactivity to stressors. We found that on days with higher levels of NO2 and O3, adolescents reported lower levels of positive affect (NO2: b=-0.10, p=.028; O3: b=-0.10, p=.005). Positive affect was more labile on days with higher O3 (b=0.84, p<.001), CO (b=3.23, p<.001), and PM2.5 levels (b=0.42, p<.001), with effects extending into the following day (O3: b=0.53, p=.006; CO: b=2.40, p=.003; PM2.5: b=0.19, p=.027). Negative affect was also more labile on days with higher levels of CO and PM2.5 (CO: b=1.20, p=.022; PM2.5: b=0.22, p<.001). Finally, adolescents reported stronger negative affect after experiencing stress on days with higher levels of CO (b=0.69, p=.007) and PM2.5 (b=0.11, p<.001) and on the following day (CO: b=0.64, p=.01; PM2.5: b=0.10, p=.001). These findings indicate that multiple air pollutants are associated with poorer daily emotional functioning in adolescents, including damped positive affect and greater affective lability and reactivity to stress. Future research should elucidate underlying mechanistic pathways and long-term implications for mental health.

Figure 2. Daily levels of NO_2 and O_3 and same-day levels of positive and negative affect



Note: Green dots reflect adolescents' observed positive affect ratings while purple dots reflect negative affect ratings. Regression lines denote the associations of daily levels of NO_2 (left plot) and O_3 (right plot) with positive and negative affect from linear mixed effect models. Coefficients are adjusted for age, sex, ethnicity, SES, and daily maximum temperature. AQI levels of 0–50 are considered satisfactory/good and AQI levels of 51–100 are considered moderate air quality. AQI = Air Quality Index; NO_2 = nitrogen dioxide; O_3 = ozone

Environment/Climate Change

Rapid Surveillance of the Mental Health Impact of the 2025 Los Angeles Wildfires among Adolescents Alyssa F. Harlow* Alyssa Harlow Daniel W. Soto Jennifer B. Unger Ryan C. Lee Jessica L. Barrington-Trimis

Background: In January 2025, the greater Los Angeles (LA) area experienced the largest and most destructive wildfire disaster in the region's history that destroyed thriving communities and exposed individuals to numerous toxins from burned building materials. Natural disasters such as the LA wildfires require adaptability and quick response in epidemiology to conduct real-time rapid surveillance of public health crises.

Methods: Immediately after the January 2025 wildfires, our team integrated a module into two existing prospective cohort studies of Southern California adolescents to assess stressors experienced as a result of the wildfires and association with mental health symptoms. Among 10th and 12th graders in Southern California (n=2839), we examined associations of wildfire-related stressors with depression and anxiety symptoms 3 months after the fires, adjusting for sociodemographic factors and mental health symptoms 3 months before the fires.

Results: Due to the wildfires, 35.8% of adolescents were worried about the health of family members, nearly one-quarter feared for their personal safety (23.1%), personal health (22.3%), and/or felt anxious, stressed or depressed (21.9%), and 10.4% had a family or loved one who lost their home. Several wildfire-related stressors (e.g., life changes, loss of possessions, family and friend impacts) were associated with 1.5-2.0 times greater odds of anxiety and depressive symptoms post-fires.

Conclusions: A substantial proportion of Southern California adolescents experienced direct or indirect stressors from the 2025 LA wildfires. These stressors were associated with worse mental health 3 months later. As wildfires increase, public health professionals should be aware of the growing need for mental health support services for adolescents exposed to wildfires. This work demonstrates the utility of leveraging existing research infrastructure to inform and monitor evolving public health environments and emergencies.

Mental Health

Longitudinal associations between environmental mixtures and depressive symptoms in older adults: the Reasons for Geographical and Racial Differences in Stroke (REGARDS) study Jeroen van Baar* Jeroen van Baar Yingyan Wu Jaimie Gradus Maria Glymour Yorghos Tripodis Koichiro Shiba Peter James Jennifer Weuve Kevin Lane Marcia Pescador Jimenez

Depressive symptoms are common in older age, but their environmental determinants are poorly understood. We assessed the relationship between multiple environmental exposures and depressive symptoms in 21,949 Black and white older Americans in the longitudinal Reasons for Geographic and Racial Differences in Stroke (REGARDS) study (mean age = 64.3 ± 8.9 (s.d.) yrs at baseline, 2003-2007). We linked data on air pollution (PM2.5, NO2, O3), anthropogenic noise, neighborhood socioeconomic status (nSES), and neighborhood segregation (Income index of concentration at the extremes [ICE], Race ICE, Race-Income ICE) to subjects' time-varying addresses (2005-2016). Depressive symptoms were measured 1-5 times per subject using the 4-item Center for Epidemiologic Studies Depression scale (CESD4; 2008-2016). We first analyzed each exposure independently, regressing CESD4 onto the cumulative mean exposure since baseline in zero-inflated Poisson models adjusted for antidepressant use, demographics, and individual SES. NO2 (IRR = 1.02 per one-quartile increase, 95% CI = [1.00–1.04]) and anthropogenic noise (IRR = 1.02 [1.00–1.04]) predicted more depressive symptoms; nSES (IRR = 0.97 [0.95–0.99]) and the three ICEs (IRRs between 0.95 [0.93–0.97] and 0.96 [0.94–0.97]) predicted fewer symptoms. We then modeled the mixture of all cumulative exposures using quantile g-computation, adjusting for the same covariates. Greater mixture exposure predicted more depressive symptoms (IRR = 1.08 [1.05–1.10] per quartile increase in all exposures at the same time). The strongest mixture contributors were income ICE (weight = -0.54) and NO2 (weight = 0.51). In stratified analyses, Race ICE and Race-Income ICE contributed to more depressive symptoms in Black participants but fewer in white participants. These findings suggest that multiple exposures jointly contribute to depressive symptom risk in later life and motivate further research on potential racial differences in environmental risk factors.

Aging

The effect of hearing aid use on incidence of dementia among older adults Matas Griskaitis*
Matas Griskaitis Jordan Weiss Lorna Thorpe

An estimated 22.2% of the U.S. population has hearing loss, which is associated with cognitive decline and increased dementia risk. Prior studies suggest that hearing aid (HA) use may reduce cognitive decline, and target trial emulation analyses have proposed a protective causal effect on dementia incidence. However, effect estimates may be biased due to model misspecification. To address this, we used the causal roadmap and applied a doubly robust targeted maximum likelihood estimation (TMLE) approach combined with a SuperLearner package to estimate the causal effect of HA use on 2-year dementia incidence among hearing-impaired adults aged ≥65 years.

We used data from the nationally representative National Health and Aging Trends Study, restricting to Medicare beneficiaries aged ≥65 years with objectively measured hearing impairment at wave 11 and no dementia at baseline. Baseline self-reported HA use was compared with non-use after adjustment for baseline confounders. TMLE with SuperLearner was used to estimate marginal risk differences, accounting for censoring. Among 2,148 participants (555 HA users and 1,593 non-users), the 2-year risk difference for incident dementia was − 1.2% (95% CI: -5.3% – 2.9%, p = 0.565). Age-stratified analyses showed no statistically significant effects. A sensitivity analysis using an alternative hearing impairment threshold yielded similar null results.

In this representative sample of older adults, HA use was not associated with a statistically significant reduction in dementia incidence within two years. Longer follow-up and repeated exposure assessment may be required to better evaluate the potential preventive role of hearing aid use on dementia risk.

Causal Inference

Associations of genetic risk for Alzheimer’s disease with late-life social connectedness in Health Retirement Study: Evaluating reverse causation Azuna Sawada* Azuna Sawada M. Maria Glymour Jacqueline Torres Scott C. Zimmerman Koichiro Shiba

While social connectedness is often associated with Alzheimer’s disease (AD), such associations may reflect reverse causation, where preclinical AD symptoms change social engagement. Associations between AD genetic risk scores (AD-GRS) and social connectedness would likely reflect such reverse causation because AD-GRS predict AD but should not cause social disconnection. Thus, we examined at what age AD-GRS predicts social connectedness outcomes to identify when reverse causation emerges. We analyzed Health and Retirement Study participants aged ≥50 with genetic data and at least one wave of data on social connectedness between 2006 and 2022 (n=15,574 with 41,826 person-wave observations). AD-GRS was categorized into quintiles. Social connectedness outcomes included continuous scores for social participation (range: 18-126; mean±SD: 80.39±0.09), loneliness (8-56; 19.86±0.04), perceived neighborhood social cohesion (3-28; 8.38±0.02), and positive (8-43; 19.1±0.03) and negative (2-48; 22.4±0.07) social support. We fit mixed-effects linear regression models stratified by age group (50s, 60s, 70s, ≥80 years), adjusting for sex, race/ethnicity, and 10 genetic ancestry principal components. Those at the highest genetic AD risk (Q5) showed reduced social participation across all age groups compared to the lowest genetic risk group (Q1): 50s (β=−1.75, 95% CI: −2.64, −0.86); 60s (β=−2.33, 95% CI: −3.02, −1.63); 70s (β=−2.06, 95% CI: −2.76, −1.37); ≥80 (β=−2.68, 95% CI: −3.52, −1.84). Q5 was also associated with higher loneliness among those in their 60s (β=0.66, 95% CI: 0.25, 1.07) and with lower perceived social cohesion among those in their 60s (β=-0.51, 95% CI: -0.75, -0.27) and 70s (β=-0.26, 95% CI: -0.51, -0.01). We found no evidence of association for social support. Reverse causation may affect observational studies of social connectedness and AD, with concerns for social participation emerging as early as age 50-59.

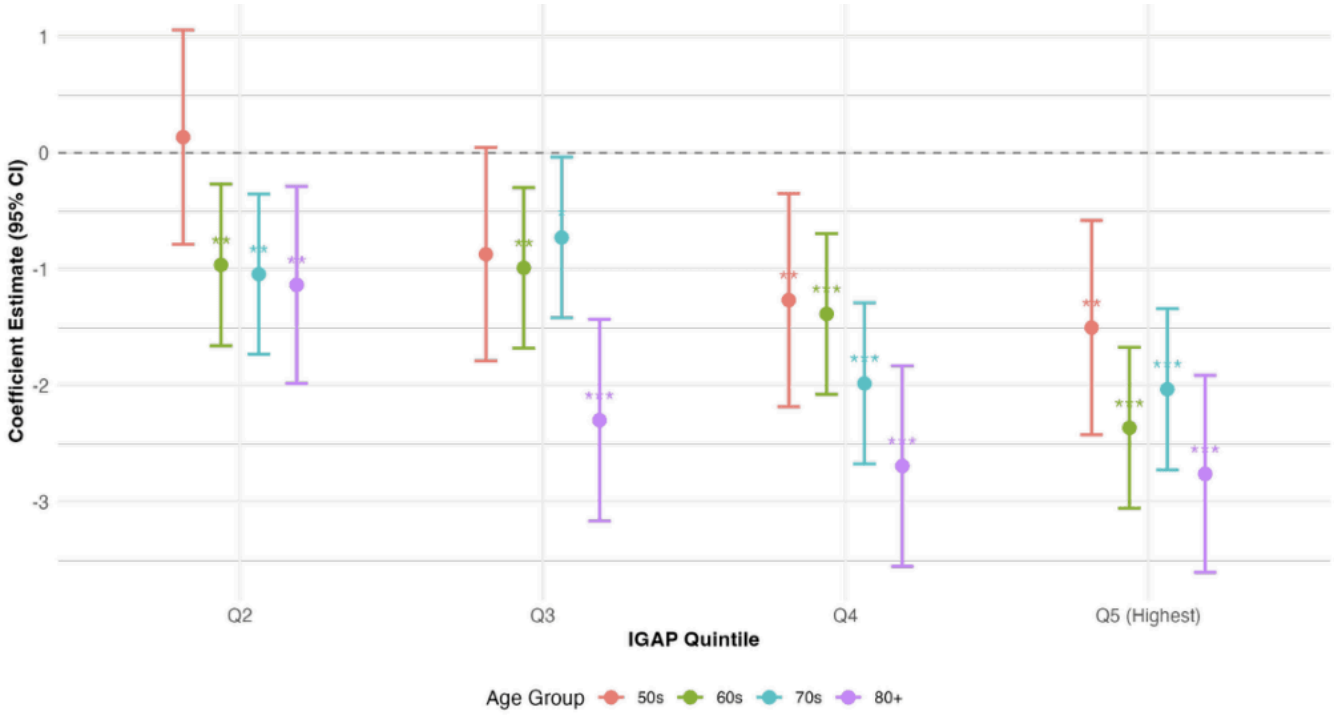


Figure 1: Association between AD-GRS quintiles (reference = lowest quintile Q1) and social participation score stratified by age groups.

Methods/Statistics

The impact of vision center establishment on patient visits and cataract surgical volume: a multi-country staggered adoption difference-in-differences analysis Brittany Peterson*
Brittany Peterson Lauren Jesudason Carolyn Brandt Angela Cheng Kieran O'Brien

Visual impairment impacts millions globally, with a disproportionate burden in low- and middle-income countries (LMICs). Vision centers (VCs) have been established to expand access to eye care for individuals living in remote communities, yet rigorous evidence on their impact is limited. Evaluating such interventions is complicated by staggered implementation across hospitals. We used staggered difference-in-differences methods to estimate the impact of VC establishment on patient visits and cataract surgical volume across eye hospitals in 10 LMICs.

We analyzed hospital-level quarterly data from 41 hospitals between January 2020 and April 2024. As a benchmark, we estimated two-way fixed effects models and used the Goodman–Bacon decomposition to assess potential bias arising from staggered adoption. Our primary analysis employed the Callaway and Sant'Anna (C&S) group-time difference-in-differences estimator, which is robust to staggered adoption and treatment effect heterogeneity. Parallel trends were assessed, and comparisons were restricted to pre-treatment periods that did not exhibit differential trends. We additionally examined heterogeneity by geographic region.

Using the C&S estimator, VC establishment was associated with a modest, non-significant increase in average number of cataract surgeries per quarter (ATT=31.9; 95% CI -32.4, 96.2; p=0.31) and a significant increase in average number of patients per quarter (ATT=723.1; 95% CI 272.2, 1,173.5; p=0.029). Region-stratified analyses suggested larger effects in hospitals located in India and South/Central America.

In this staggered adoption setting, VC establishment was associated with increased patient volume. Results suggested a potential effect on cataract surgical volume as well, although the same size was not large enough to detect this. These findings underscore the importance of applying modern difference-in-differences methods when evaluating health system interventions implemented at different times.

Aging

Alzheimer's Disease and Related Dementia's State Policies and Mortality in the United States from 2008-2020: A Descriptive Study Nicola Churchill* Nicola Churchill Roch A Nianogo

Alzheimer's disease and related dementias (ADRD) are the sixth leading cause of death among people aged 65+ in 2022 and are currently the leading cause of disability and morbidity in older adults. In 2025, an estimated 7.2 million Americans aged 65 years and older were living with Alzheimer's disease (AD), with prevalence projected to rise. Wedescribe 1) the trends in the adoption of Alzheimer's Disease and Related Dementia (ADRD) policies that were implemented in the U.S. from 2008-2020, as well as 2) the trends in ADRD mortality during 1999-2022. We presented mortality data for the age-adjusted rate of ADRD mortality per 100,000 people in 1999-2022 from the Centers for Disease Control and Prevention Wide-ranging Online Data for Epidemiologic Research (CDC WONDER). We also collected policy data from state websites from 2008-2020. Policies were implemented for all 50 states, starting in 2008 and ending in 2020. ADRD mortality steadily rose during 1999 to 2022 period. The first states to implement ADRD in 2008 were Iowa and Kentucky. The greatest number of states—10 in total—implemented policies in 2013. South Dakota, Wyoming, Ohio, and Kansas were the last states to implement policies in 2018-2020. Our study suggests that all the states in the United States implemented a policy to reduce ADRD cases and burden. The contents of these state ADRD policies varied from state to state. Although ADRD policies were implemented, there was still a rise in mortality. This can be partially due to increases in life expectancies because age is one of the greatest risk factors for ADRD. Another for reason the consistent increase in ADRD mortality is the persistent disparities that remain due to the unaddressed social determinants of health. Finally, recognition of ADRD in patients and increasing awareness can increase ADRD mortality by detecting previously undiagnosed cases.

Methods/Statistics

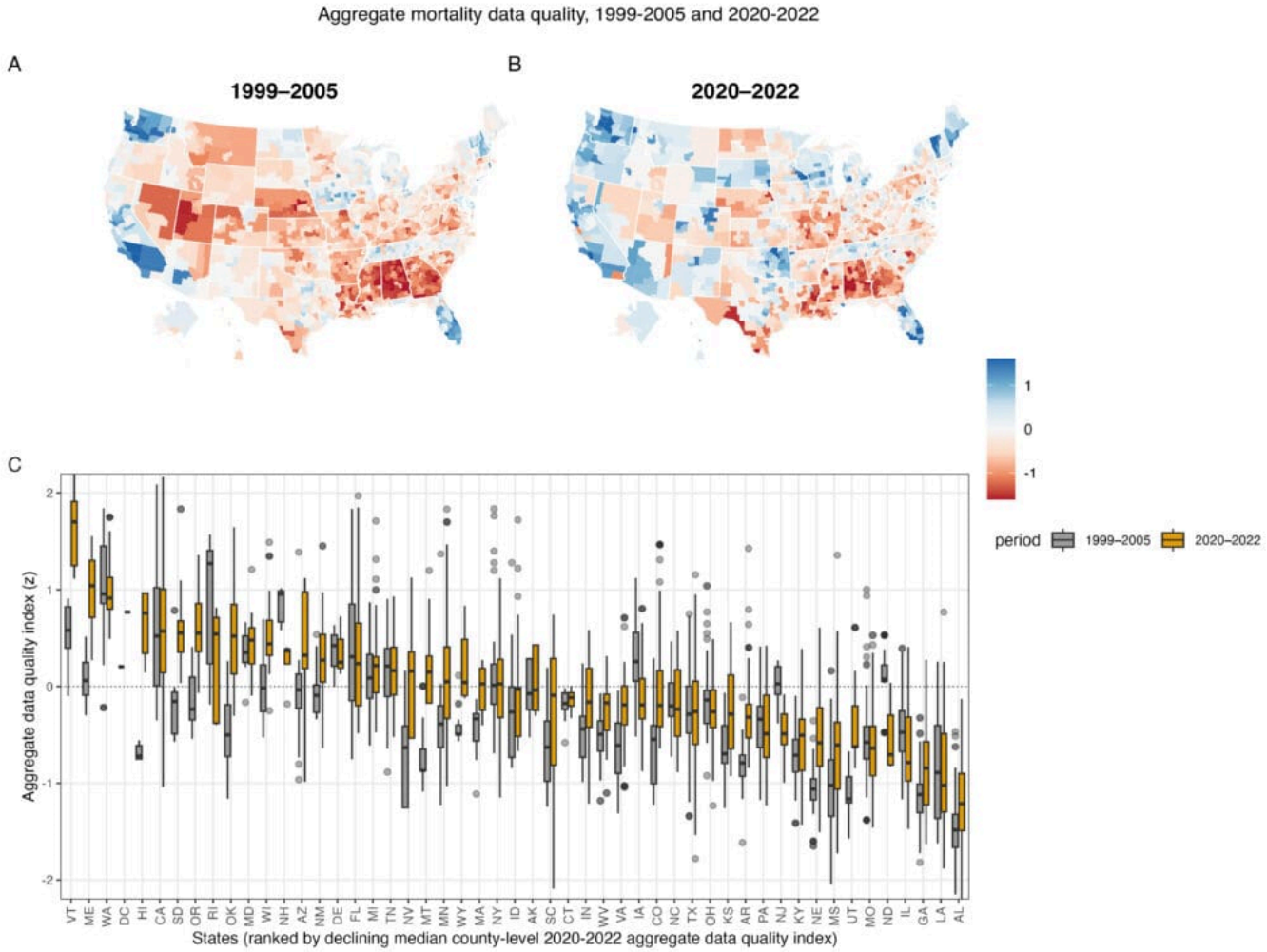
Geographic variation in the quality of US mortality data, 1999-2022 Amy Mann* Amy Mann Monica Alexander Mathew Kiang

Objectives: Cause-of-death data underpin public health surveillance, yet few tools quantify mortality data quality in high-income countries at a subnational level. We develop two metrics to measure mortality data quality and apply them to U.S. county mortality from 1999-2022.

Methods: We construct a Re-assignability Index (RI) that quantifies how confidently multiple-cause information can reclassify garbage-coded deaths into meaningful cause groups. We then define a standardized level-of-detail metric using entropy methods to measure coding diversity after accounting for differences in the underlying cause-of-death mix. We also estimate the proportion of deaths with garbage-coded underlying causes and combine these measures into an aggregate data quality index.

Results: Garbage coding declined nationally through 2019 but rose during the COVID-19 pandemic. Coding detail increased steadily, while RI declined modestly, consistent with growing cause-of-death diversity. All dimensions show persistent geographic inequalities, with lower-income counties exhibiting poorer data quality.

Conclusions: U.S. mortality data quality is multidimensional, geographically uneven, and systematically worse in socioeconomically disadvantaged areas. This framework enables scalable monitoring of subnational reporting quality and supports targeted investments to strengthen death certification and public health surveillance.


Aggregate mortality data quality, 1999-2005 and 2020-2022
A
1999–2005
B
2020–2022
1
0
-1
C
Aggregate data quality index (z)
2
1
0
-1
-2
VT ME WA DC HI CA SD OR RI OK MD WI NH AZ NM DE FL MI TN NV MT MN WY MA NY ID AK SC CT IN WV VA IA CO NC TX OH KS AR PA NJ KY NE MS UT MO ND IL GA LA AL
States (ranked by declining median county-level 2020-2022 aggregate data quality index)
period
1999–2005
2020–2022

Cancer

Measuring the uptake of screening mammography in populations using insurance claims: a problem of imperfect sensitivity Neal D. Goldstein* Neal Goldstein Yuchen Zhang Igor Burstyn Krishna Vasireddy Dawn Garland Matt Enright Scott D. Siegel

Background: Quantifying the uptake of screening mammography at a population level is challenged by suboptimal surveillance data. Insurance claims represent a potentially useful data source, however, claims data can be limited by underreporting. Using a quantitative bias analysis framework, we demonstrate an approach for dealing with imperfect sensitivity in an insurance claims database.

Methods: Insurance claims were obtained at the census tract level for screening mammography for the State of Delaware for 2019 and 2022. A measurement model related the observed uptake of mammography to the truth via two approaches: 1) the total number of medical claims, and 2) proportion of government funded health insurance. We then modeled how uptake of mammography predicts invasive breast cancer incidence and stage at diagnosis in Delaware.

Results: During the year 2022 and based on the observed measure, the statewide averaged uptake was 176 mammograms per 1,000 women aged 40 and above. This figure increased to a median of 234 mammograms per 1,000 women (95% simulation interval: 230, 239) following adjustment. Each additional 1,000 mammograms predicted an increase of 126 breast cancer cases using the observed data (95% confidence interval: 112, 140), whereas following adjustment, this number was attenuated to 77 cases (95% simulation interval: 63, 90). Mammography uptake was less predictive of more advanced stage disease following adjustment, in line with our hypothesis.

Conclusions: When working with administrative datasets for measuring the uptake of screening mammography in a population, researchers and healthcare administrators should account for potential underreporting.

Cancer

Tailored physical activity strategies and mortality among breast cancer survivors: a target trial emulation Emma McGee* Emma McGee Jinani Jayasekera Isaac J. Ergas Jacob Schneider Emma Tian Kaitlyn M. Wojcik Janise M. Roh Jacqueline B. Vo Lawrence H. Kushi Oliver W.A. Wilson

Background: Guidelines recommend individualized (i.e., tailored) physical activity strategies for cancer survivors. However, there is limited data on the causal effects of these strategies on long-term mortality outcomes for breast cancer survivors.

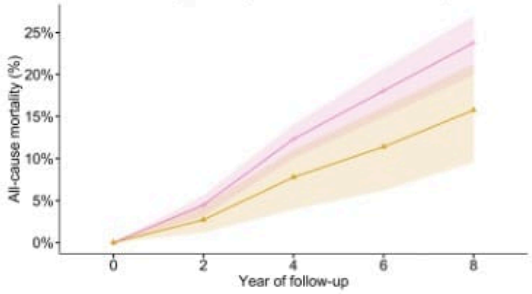
Methods: We specified the protocol of a target trial that approximately mirrored the Colon Health and Lifelong Exercise Change (CHALLENGE) randomized trial but was conducted among breast cancer survivors with stage II or III disease. We used observational data from the Pathways Study, a prospective cohort of individuals enrolled in the Kaiser Permanente Northern California health plan with invasive breast cancer, to emulate this first target trial. Then, we used data from the Pathways Study to emulate a second target trial examining the effects of more pragmatic, tailored physical activity strategies on mortality in a broader population of breast cancer survivors with stage I-III disease.

Results: In the first target trial, there were 959 eligible individuals and 183 deaths. Compared with a health-education strategy, a recreational aerobic activity strategy was associated with an 8.0 percentage point (95% CI: 3.4, 13.3) reduction in 8-year all-cause mortality, which was consistent with the CHALLENGE trial (7.1 percentage point reduction [95% CI: 1.8, 12.3]). In the second target trial, there were 2,107 eligible individuals and 321 deaths, 139 of which were due to breast cancer. Compared with no intervention, a strategy requiring tailored increases of 60 minutes of vigorous or 120 minutes of moderate aerobic activity per week was associated with a 3.1 percentage point (95% CI: 2.0, 4.6) reduction in 10-year all-cause mortality and a 2.4 percentage point (95% CI: 1.2, 3.5) reduction in 10-year breast cancer-specific mortality.

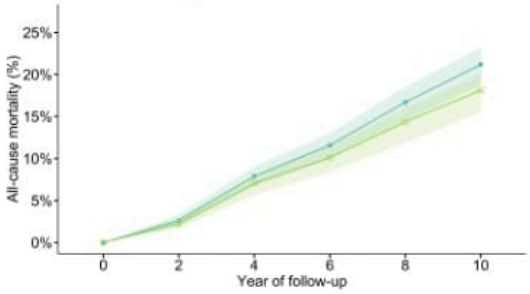
Conclusions: Pragmatic strategies requiring tailored increases in physical activity levels may reduce 10-year mortality among breast cancer survivors.

Estimated mortality risk curves among breast cancer survivors under different physical activity strategies in a) the first target trial that approximately mirrored the CHALLENGE trial and b-c) the second target trial of more pragmatic, tailored strategies in a broader population, Pathways Study (2005 – 2021).

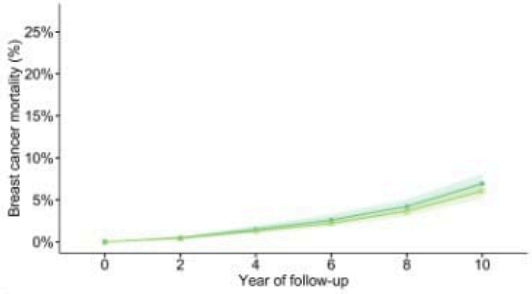
a) Target trial that approximately mirrored the CHALLENGE trial (N=959) – All-cause mortality

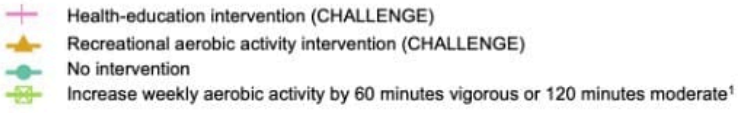


b) Target trial of more pragmatic strategies in a broader population (N=2,107)[a] – All-cause mortality



c) Target trial of more pragmatic strategies in a broader population (N=2,107)[a] – Breast cancer-specific mortality





[1]This pragmatic, tailored strategy requires individuals to increase their total aerobic physical activity beyond their normal levels for 8 years, unless they developed a serious comorbid condition (defined based on activity guidelines for cancer survivors and the available observational data). Abbreviations: CHALLENGE = Colon Health and Lifelong Exercise Change.

Cancer

Adherence to a healthy lifestyle and physical health decline after chemotherapy or endocrine therapy in breast cancer survivors Cassandra York* Cassandra York Lauren E. McCullough Alpa V. Patel Lauren R. Teras Clara Bodelon

Background. Women with a history of breast cancer (BC) experience greater physical health decline compared to age-matched cancer-free women. We investigated whether adherence to a healthy lifestyle could mitigate this decline.

Methods. This analysis included 1,862 women with BC (diagnosed 2015-2020) and 18,610 cancer-free women matched on age and date of returned survey from the Cancer Prevention Study 3. All were non-current smokers. Adherence to a healthy lifestyle was assessed using the American Cancer Society guideline for cancer survivors score, which includes body mass index (BMI), physical activity, and diet from the 2015 survey. The score (range: 0-8) was categorized as low (0-4) or high (5-8) adherence to a healthy lifestyle. Physical health was assessed using the Patient-Reported Outcomes Measurement Information System (PROMIS) Global Health Scale at three time points: before diagnosis, and <4 and ≥4 years post-diagnosis. We used multivariable linear regression adjusted for matching variables to estimate the association between a combined treatment-lifestyle variable and PROMIS score.

Results. Median age at diagnosis was 60 years (interquartile range [IQR]: 52-65). The median lifestyle score was 5 (IQR: 4-7) for BC survivors and 6 (IQR: 4-7) for cancer-free women. Patients who received chemotherapy and had a high lifestyle adherence score had better physical health after diagnosis compared to cancer-free women with a low adherence score (<4 years: β=0.83, 95% CI: 0.10, 1.56; ≥4 years: β=1.71, CI: 0.42, 3.01). In contrast, patients who received chemotherapy but had a low adherence score had significantly lower physical health than cancer-free women with a low adherence score (<4 years: β=-2.84, 95% CI: -3.86, -1.82; ≥4 years: β=-2.16, 95% CI: -3.90, -0.42).

Conclusion. High pre-diagnosis adherence to a healthy lifestyle was associated with greater physical health in BC survivors, including those who received chemotherapy.

Cancer

Longitudinal change in endocrine therapy adherence patterns in the Carolina Breast Cancer Study using latent class analysis Srijon Mukhopadhyay* Srijon Mukhopadhyay Sarah C. Van Alsten Terry Hyslop Melissa A. Troester

Background Lower endocrine therapy (ET) adherence worsens survival in less aggressive breast cancers and adherence barriers may change over time. We hypothesized that adherence patterns vary longitudinally and shifts are influenced by clinical and social characteristics.

Methods We identified women with Stage I-III HR+ tumors in the Carolina Breast Cancer Study who completed ET use surveys at 25 months and 84 months follow-up (n = 837). Surveys quantified adherence and assessed barriers such as affordability, side-effects, and risk tradeoffs. We applied latent class analysis at 25 and 84 months to identify adherence patterns. Adherence patterns at the two time points were compared to categorize shifts as “favorable” [improved adherence], or “unfavorable” [worsened adherence]. We estimated prevalence differences (PD) between adherence shifts and social and clinical factors using logistic regression with post-hoc estimated marginal means, adjusting for age, stage, and grade.

Results We identified 3 adherence patterns, consistent across time points: “High Adherence (HA)”, “Adherence Variability (AV)”, and “Substantial Barriers (SB)”. At 84 months, Black women were less represented in the HA group (PD= -8.4%; -15.5%, -1.3%) and experienced more unfavorable shifts (PD= 7.4%; -0.1%, 14.8%) than non-Black women. Chemo use was associated with more unfavorable shifts among non-Black women (PD= 13.5%; 5.8%, 21.2%) but not Black women. Compared to ≥50 women, younger women had higher unfavorable shifts, a trend observed in both Black (40-50: PD= 19.1%; 5.7%, 32.5%, <40: PD= 26.3%; 1.4%, 51.1%) and non-Black women (40-50: PD= 11.8%; 4.3%, 19.4%; <40: PD= 21.3%; 7.3%, 35.2%). Social factors did not influence adherence shifts.

Conclusion Longitudinal analyses show that latent adherence subtypes are stable across time, though individuals may transition between adherence states. Black women and younger women face more barriers maintaining adherence in later survivorship.

Cancer

Comparing neighborhood environment classifications with markers of chronic stress among breast cancer survivors Sarah Lima* Sarah Lima

Background: Neighborhood factors have been associated with adverse breast cancer endpoints, possibly through stress pathways. We evaluated which socioeconomic and environmental neighborhood measures were associated with markers of chronic stress among breast cancer survivors.

Methods: This cross-sectional study included 76 breast cancer survivors in Washington DC metro area. Neighborhood features included self-reported neighborhood stress, census-based socioeconomic measures (deprivation, racial and economic segregation) and satellite-based physical environment (greenspace, walkability, noise). Virtual audits of the street-level environment via Google Street View are ongoing. Participants reported perceived stress. Allostatic load and C-reactive protein (CRP) were available for a subset of participants (n=40). Quality of life (QoL) measures included general, functional, and social QoL. Correlations between neighborhood measures and outcomes were assessed. Neighborhood features were examined with chronic stress using box plots and linear regression. QoL was assessed by neighborhood as a potential intermediary.

Results: Correlations were moderate to strong within neighborhood domains but weak to moderate across domains. Neighborhood features were weakly correlated or uncorrelated with perceived neighborhood stress (r range: 0.00 for ADI to -0.21 for Gini index). Gini index and noise were consistently related to perceived stress. Perceived neighborhood stress, ADI, greenspace, and walkability were consistently associated with allostatic load and CRP. Perceived neighborhood stress, segregation, and noise were associated with QoL measures.

Conclusion: Socioeconomic and environmental features of neighborhood are related to chronic stress and QoL. Composite deprivation measures were less frequently related to chronic stress. Interventions within socioeconomic or environmental domains may be viable, however a comprehensive measure that encapsulates both domains is needed.

Cancer

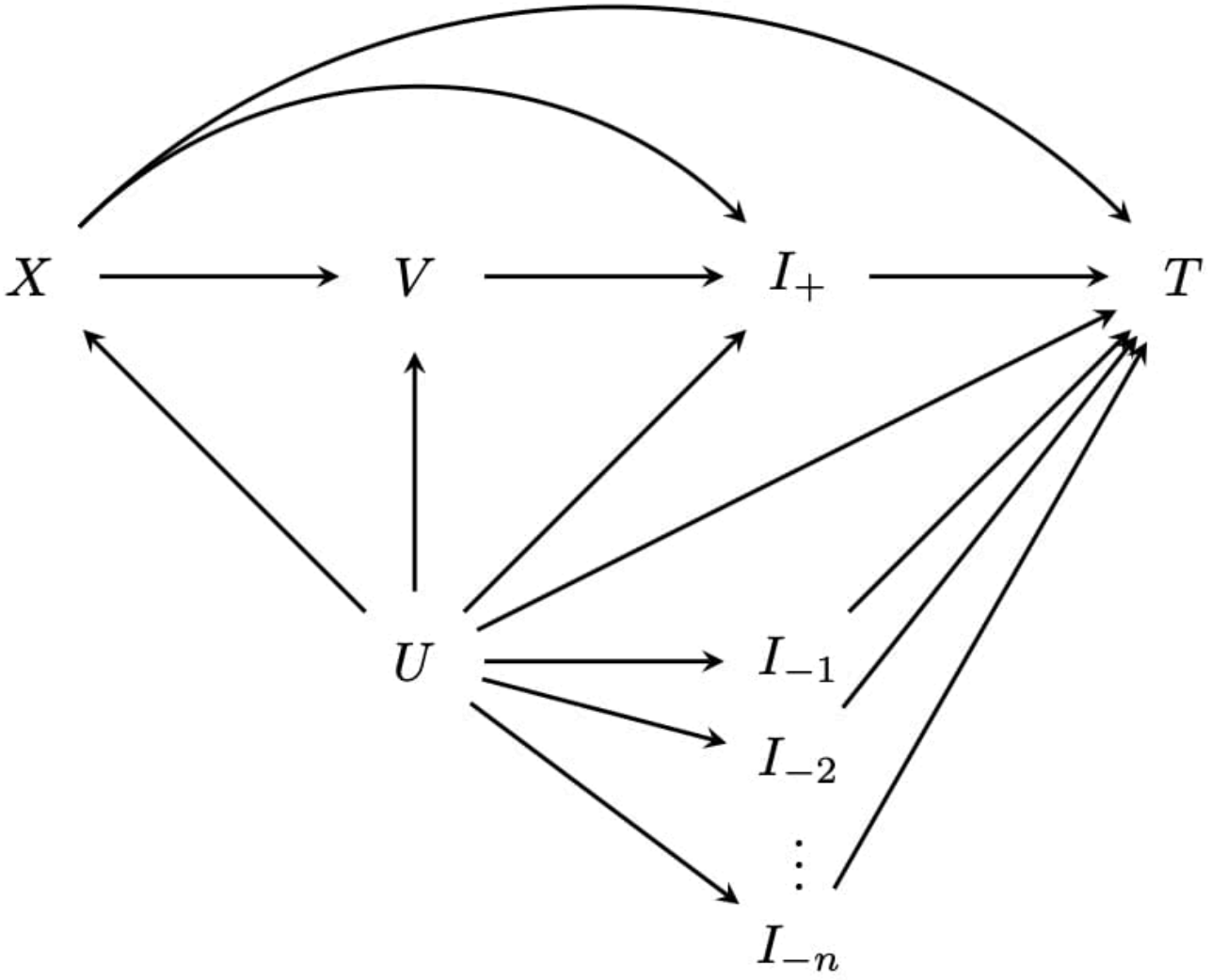
Educational attainment and mortality among World Trade Center Health Registry enrollees diagnosed with cancer after 9/11 Mst Afroza Parvin* Mst Afroza Parvin Rebecca D. Kehm James E. Cone Jiehui Li

Individuals exposed to the World Trade Center (WTC) terrorist attacks on 9/11/2001 have elevated risks for certain cancers, highlighting the need to identify determinants of mortality after cancer diagnosis in this population. Our prior work identified racial/ethnic disparities in cancer mortality among WTC-exposed individuals. It is unknown whether educational attainment, a determinant of cancer survival in the general population, also contributes to disparities. We used WTC Health Registry data to examine associations between educational attainment (≤high school (HS) degree, some college, bachelor's degree, graduate degree) and mortality among 6,603 individuals who were aged ≥25 at enrollment in 2003-2004 and were diagnosed with a first cancer after 9/11/2001. Cox proportional hazards models were used to evaluate all-cause mortality, with cause-specific Cox models assessing cancer-specific and non-cancer mortality. Person-time was calculated from cancer diagnosis to death or censoring on 12/31/2022, with left truncation applied for participants diagnosed before study enrollment. Premature mortality was also assessed among cases diagnosed before age 65 (n=4,467), with censoring at age 65. Models were stratified by age at diagnosis and adjusted for demographic, clinical, and prognostic factors. There were 1,965 deaths (817 premature) over follow-up. Compared to individuals with a graduate degree, those with ≤HS degree had higher risks of all-cause (HR=1.26, 95% CI=1.09-1.44) and cancer-specific (HR=1.23, 95% CI=1.04-1.47) mortality; no association was found for non-cancer mortality. Similar patterns were observed for premature mortality (all-cause: HR=1.37, 95% CI=1.08–1.74; cancer-specific: HR=1.36, 95% CI=1.04–1.79). Findings support that education is associated with cancer-specific mortality, including premature deaths, among 9/11-exposed individuals, highlighting the need for targeted monitoring and support for those with lower education in this population.

Infectious Disease

How should we select test-negative controls? A causal perspective in the era of multiplex respiratory testing Christopher Boyer* Christopher Boyer

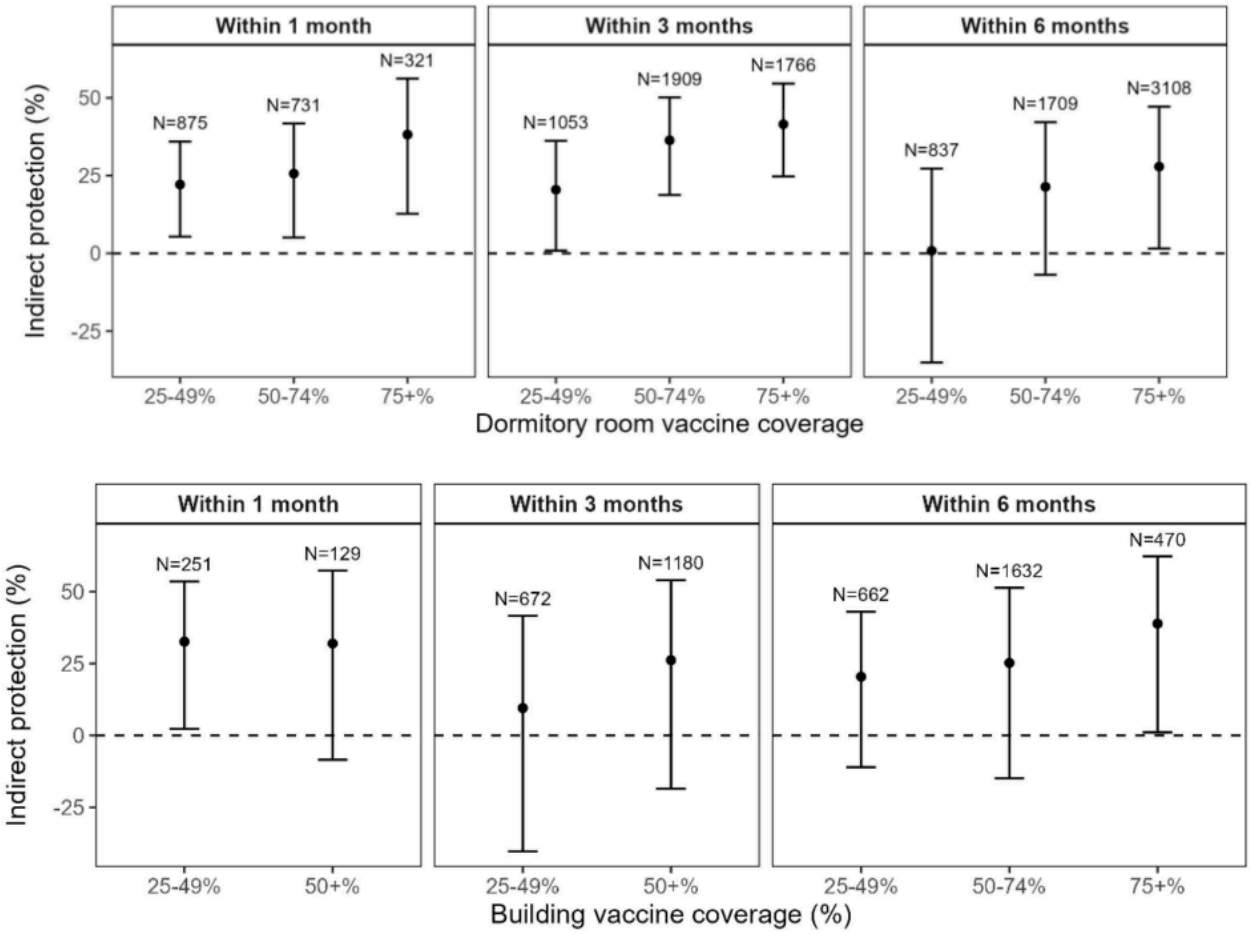
The test-negative design (TND) is widely used to estimate vaccine effectiveness (VE) for respiratory pathogens by comparing vaccination odds among symptomatic individuals who test positive (cases) versus those who test negative (controls). A central—and increasingly consequential—design choice is which test-negative illnesses constitute valid controls. With rapid multiplex PCR panels, investigators can now observe a rich spectrum of non-focal pathogens among test-negative patients, creating both opportunity (better characterization of control illness) and risk (including invalid controls that amplify bias). Building on recent work clarifying identifying assumptions under which the standard TND odds ratio recovers a causal estimand, we show how multiplex testing can inform the control-selection problem: “test-negative illness” becomes a mixture of pathogen-specific illnesses, each of which may violate assumptions differently. We propose a causal taxonomy of test-negative pathogens and a pragmatic selection strategy guided by (i) **vaccine irrelevance** (exclude pathogens affected by the focal vaccine, including plausible cross-protection), (ii) **vaccine-correlation threats** (exclude or adjust for pathogens influenced by other vaccines whose uptake is correlated with the focal vaccine), and (iii) **testing-process comparability** (avoid pathogens whose diagnosis or care-seeking is altered by alternative testing channels, such as at-home rapid tests). We also discuss differences between pathogens that serve as exposure proxies, i.e. proxies for unmeasured confounders of pathogen exposure and vaccination, versus testing proxies, i.e. proxies for unmeasured confounders of receiving a test and vaccination. Throughout, we illustrate how better information about test-negative illness can inform better design of test negative studies.


X
V
I_+
T
U
I_{-1}
I_{-2}
I_{-n}

COVID-19 Pandemic

Population-level indirect protection from COVID-19 vaccine-derived immunity across spatial scales Sophia T. Tan* Sophia Tan Hailey J. Park Isabel Rodríguez-Barraquer Ada T. Kwan Kate M. Bubar Tigist F. Menkir Samantha J. Bents Seth Blumberg Justine Hutchinson David Leidner Richard K.P. Sun Heidi M. Bauer David Sears Nathan C. Lo

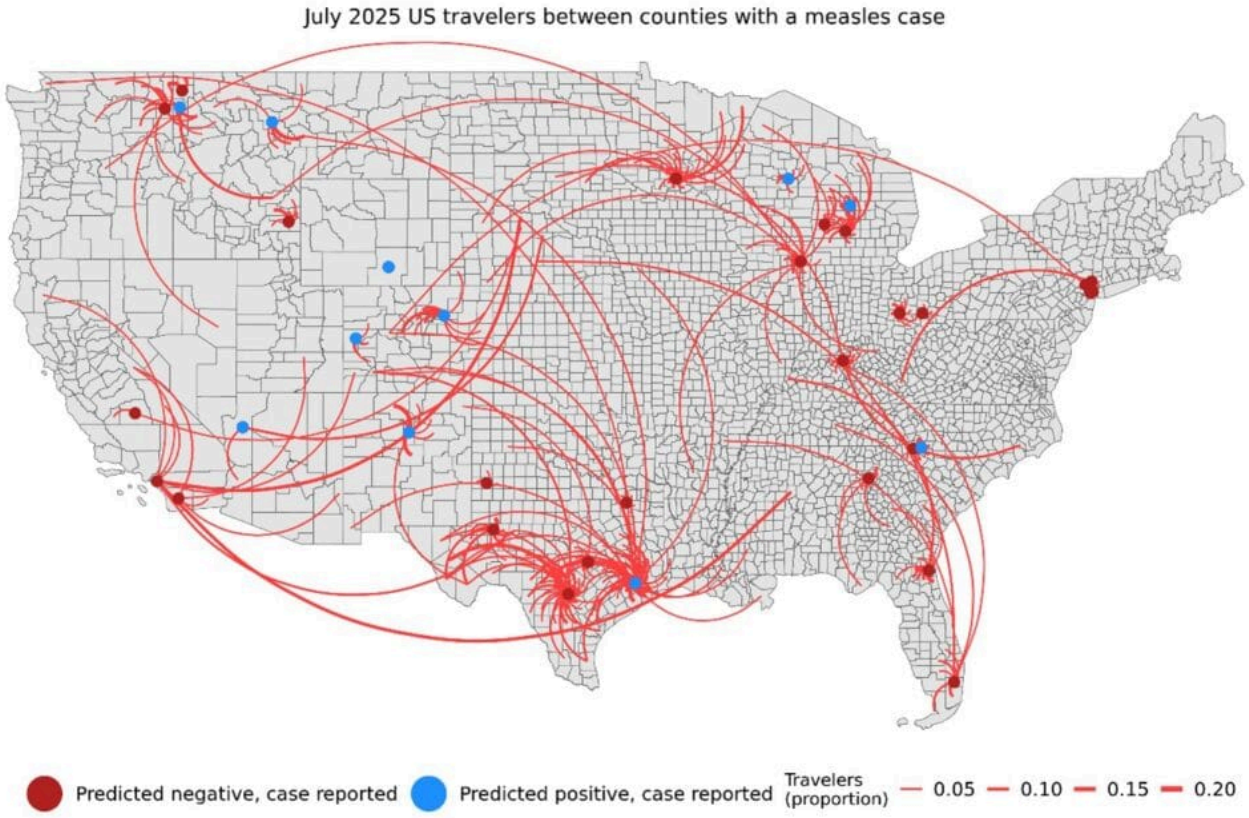
Despite years of COVID-19 vaccination, the extent to which COVID-19 vaccines confer indirect protection at the population level remains poorly characterized. Indirect protection, defined as reduced infection risk among close contacts of vaccinated individuals, is key to understanding population transmission and informing vaccine policy. While observational studies at small spatial scales (e.g., households, shared prison cells) have demonstrated moderate indirect protection from COVID-19 vaccines, there remains limited understanding of how vaccine-derived indirect protection shapes transmission at broader spatial scales. Here, we show that higher and more recent COVID-19 vaccination coverage was associated with progressively greater indirect protection against SARS-CoV-2 infection. Analyzing longitudinal de-identified surveillance data (December 2020–December 2022) from 35 California state prisons, we estimate indirect vaccine protection at two spatial scales defined as dormitory rooms (mean: 25 persons, IQR: 6-22) and large buildings (mean: 153 persons, IQR: 109-169). Compared to dormitory rooms with <25% vaccine coverage within the past 3 months, indirect protection was estimated to be 21% (95% CI: 1–36%) in dormitory rooms with 25–49% coverage, 36% (19–50%) with 50–74% coverage, and 42% (25–55%) with ≥75% coverage. Indirect protection was attenuated when using a 6-month vaccination window [28% (2–47%) with ≥75% coverage]. At the building level, we observed more variable protection, with 39% (1–62%) indirect protection at ≥75% vaccine coverage within 6 months. These findings provide evidence of population-level indirect protection from COVID-19 vaccination, estimating stronger indirect protection in settings facilitating closer social contacts (e.g., dormitory rooms) and potentially more variable protection at larger spatial scales with more diffuse and heterogeneous social mixing (e.g., building), with implications to public health policy and epidemic modeling.


Within 1 month
Within 3 months
Within 6 months
Indirect protection (%)
50
25
0
-25
N=875
N=731
N=321
N=1053
N=1909
N=1766
N=837
N=1709
N=3108
25-49%
50-74%
75+%
Dormitory room vaccine coverage
Within 1 month
Within 3 months
Within 6 months
Indirect protection (%)
50
25
0
-25
N=251
N=129
N=672
N=1180
N=662
N=1632
N=470
25-49%
50+%
25-49%
50+%
25-49%
50-74%
75+%
Building vaccine coverage (%)

Infectious Disease

A spatial graph neural network for predicting the 2022 polio and 2025measles outbreaks in the United States Dustin Hill* Dustin Hill Edem Fiatsonu Christopher Dunham Joe Moran Nicole Pulido Yifan Zhu Roma Agarwal Kayla Drucker Kirsten St. George Meghan Fuschino Michael Popowich Rafael Schulman David A. Larsen

For vaccine-preventable illnesses, identifying where a pathogen may spread next is a key public health concern. We use the Advan dataset of generalized movement patterns to model and predict the spread of polio in New York State in 2022 and measles in the US in 2025. We incorporate social network theory, machine learning, and infectious disease modeling to build a network contagion model called SPARC (spatial prediction analysis of the risk of contagion) based upon the premise that we can predict the location of where an infectious disease might be found next from generalized human movement patterns. We use a machine learning approach built on graph network data over time and across space. Weekly movement patterns between locations provide layers of data for the network. We use previous weeks to predict the visitors from one location to another in the next week to show the next place we might see a disease given an observed initial outbreak. SPARC has over 99 percent specificity in classifying counties as free from poliovirus circulation based on wastewater detection. The results support current monitoring plans that include counties with risk of polio re-emergence while excluding counties of low risk to maximize resources. However, the model only has 45 percent sensitivity in identifying counties with polio detections in wastewater. To improve the prediction of positives, we are including additional parameters like community vulnerability and wastewater detection method sensitivity. For identifying counties with and without measles cases, SPARC has 95 percent specificity but only 28 percent sensitivity. Our next step is to add estimates of vaccine uptake to improve the model’s predictive power. Combining the theory and methods of social networks, machine learning, and epidemiology shows that this interdisciplinary approach is relevant for building tools that harness the power of public health surveillance to proactively prepare for disease outbreaks.


July 2025 US travelers between counties with a measles case
Predicted negative, case reported
Predicted positive, case reported
Travelers (proportion)
0.05
0.10
0.15
0.20

Infectious Disease

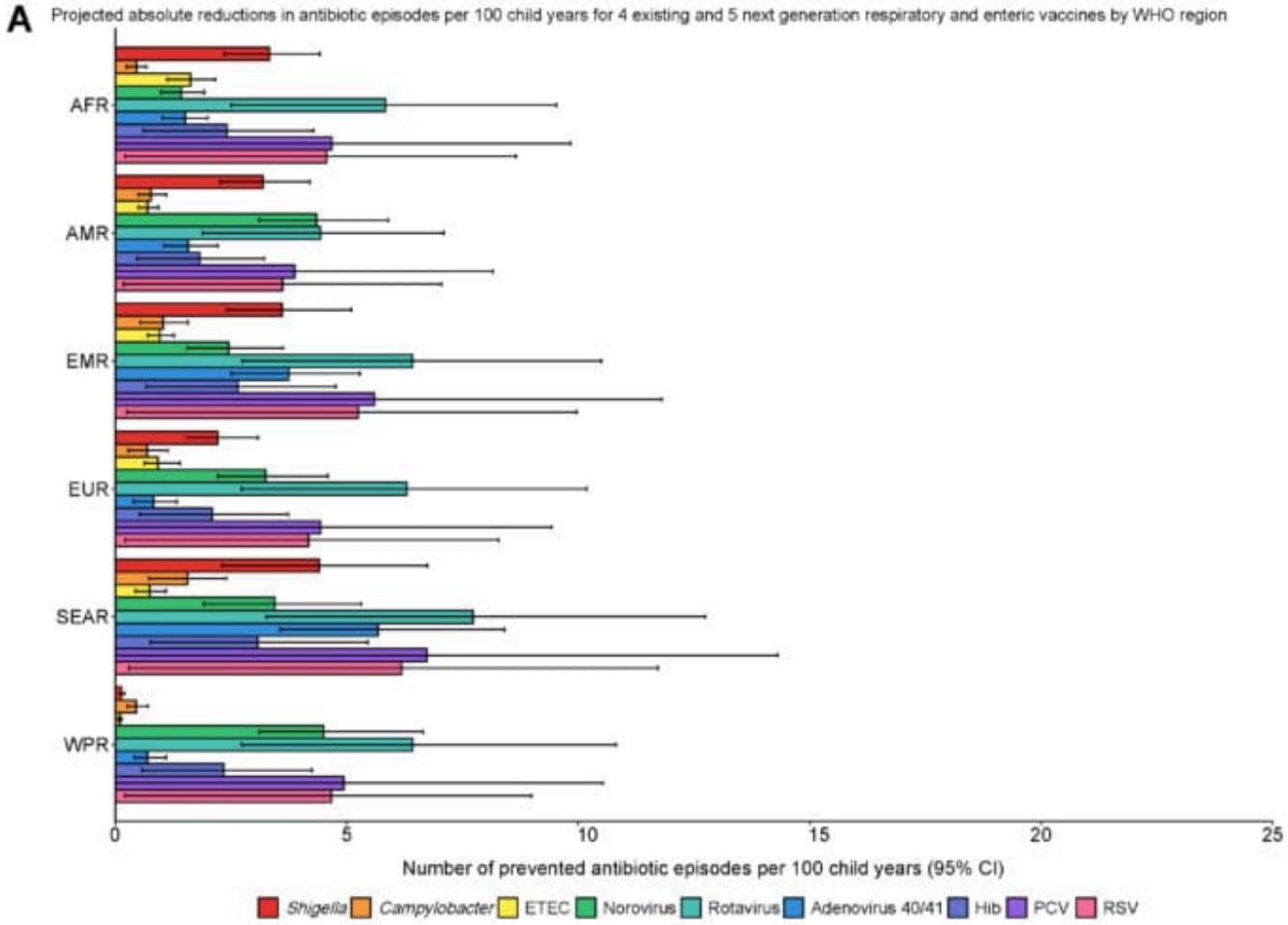
Projected worldwide impact of existing and next generation respiratory and enteric vaccines on antibiotic use and bystander pathogen exposures to antibiotics among children in 129 low- and middle- income countries Stephanie A. Brennhofer* Stephanie Brennhofer James A. Platts-Mills Joseph A. Lewnard Elizabeth T. Rogawski McQuade

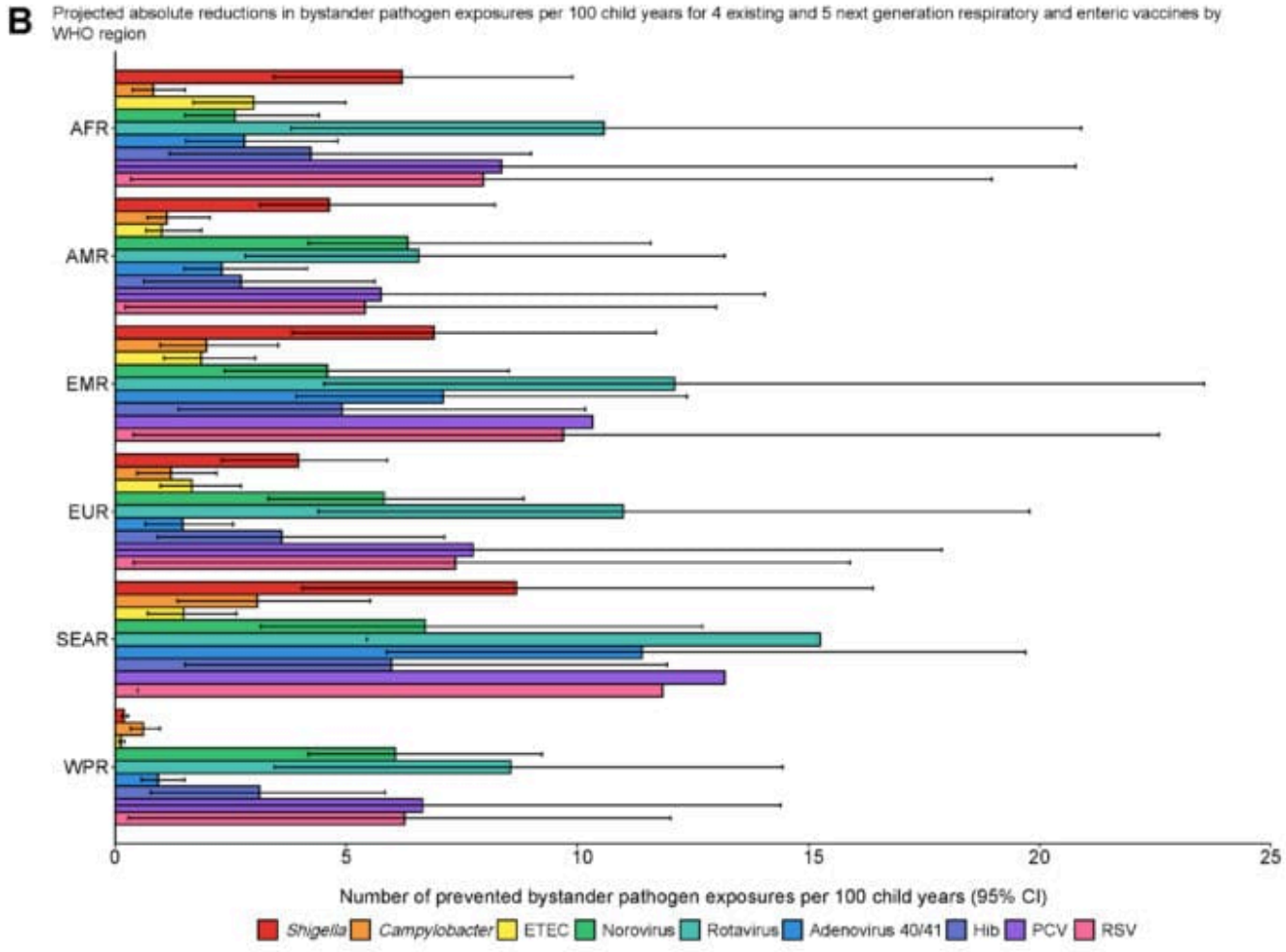
Vaccines could reduce selection pressure for antimicrobial resistance by reducing diarrhea and associated antibiotic use. We estimated the impact of existing Hib, PCV, RSV, and rotavirus vaccines, and hypothetical Shigella, Campylobacter, ETEC, norovirus, and adenovirus 40/41 vaccines on antibiotic use and antibiotic exposures to bystander pathogens among children in 129 low-resource countries.

Etiology-specific estimates of country-level incidence of antibiotic use for diarrhea were derived by combining antibiotic use data from the Demographic Health Surveys with WHO region-specific attributable fractions of diarrhea from the Global Pediatric Diarrhea Surveillance Study. Vaccine efficacy against etiology-specific antibiotic use was derived from the MAL-ED birth cohort study and applied equally across countries. Vaccine coverage was applied using averaged country-level data for rotavirus, Hib, and PCV vaccines from 2024. Bystander pathogen exposures were estimated from pathogen prevalence in asymptomatic and control stool samples from MAL-ED and the GEMS case-control study, respectively. Site level bystander pathogen data were aggregated regionally using GPDS-derived weights.

The largest reductions in antibiotic-treated respiratory illness incidence were projected to come from the existing PCV vaccine (3.87 [AMRO] to 6.72 [SEARO] episodes per 100 child years) (**Figure 1**), followed by the newly available RSV vaccine (3.62 [AMRO] to 6.19 [SEARO]). The largest reductions in antibiotic-treated diarrhea illness incidence were projected to come from the existing rotavirus vaccine (4.43 [AMRO] to 7.73 [SEARO] episodes per 100 child years). Projected reductions in diarrheal bystander antibiotic exposures amongst respiratory illnesses were greatest for PCV (5.75–13.19 per 100 child-years) and next for RSV (5.41–11.85). For diarrheal illnesses, the largest reductions in bystander exposures were projected from the existing rotavirus vaccine (6.57 to 15.25 per 100 child-years) with additional benefits from a simulated Shigella vaccine (0.19 to 8.68 per 100 child-years).

Existing vaccines drive the largest reductions in antibiotic use and bystander pathogen exposures, with new vaccines (e.g., RSV and Shigella) showing promise as the next high-priority target for vaccine implementation.


A
Projected absolute reductions in antibiotic episodes per 100 child years for 4 existing and 5 next generation respiratory and enteric vaccines by WHO region
AFR
AMR
EMR
EUR
SEAR
WPR
0
5
10
15
20
25
Number of prevented antibiotic episodes per 100 child years (95% CI)
Shigella
Campylobacter
ETEC
Norovirus
Rotavirus
Adenovirus 40/41
Hib
PCV
RSV


B
Projected absolute reductions in bystander pathogen exposures per 100 child years for 4 existing and 5 next generation respiratory and enteric vaccines by WHO region
AFR
AMR
EMR
EUR
SEAR
WPR
0
5
10
15
20
25
Number of prevented bystander pathogen exposures per 100 child years (95% CI)
Shigella
Campylobacter
ETEC
Norovirus
Rotavirus
Adenovirus 40/41
Hib
PCV
RSV

Infectious Disease

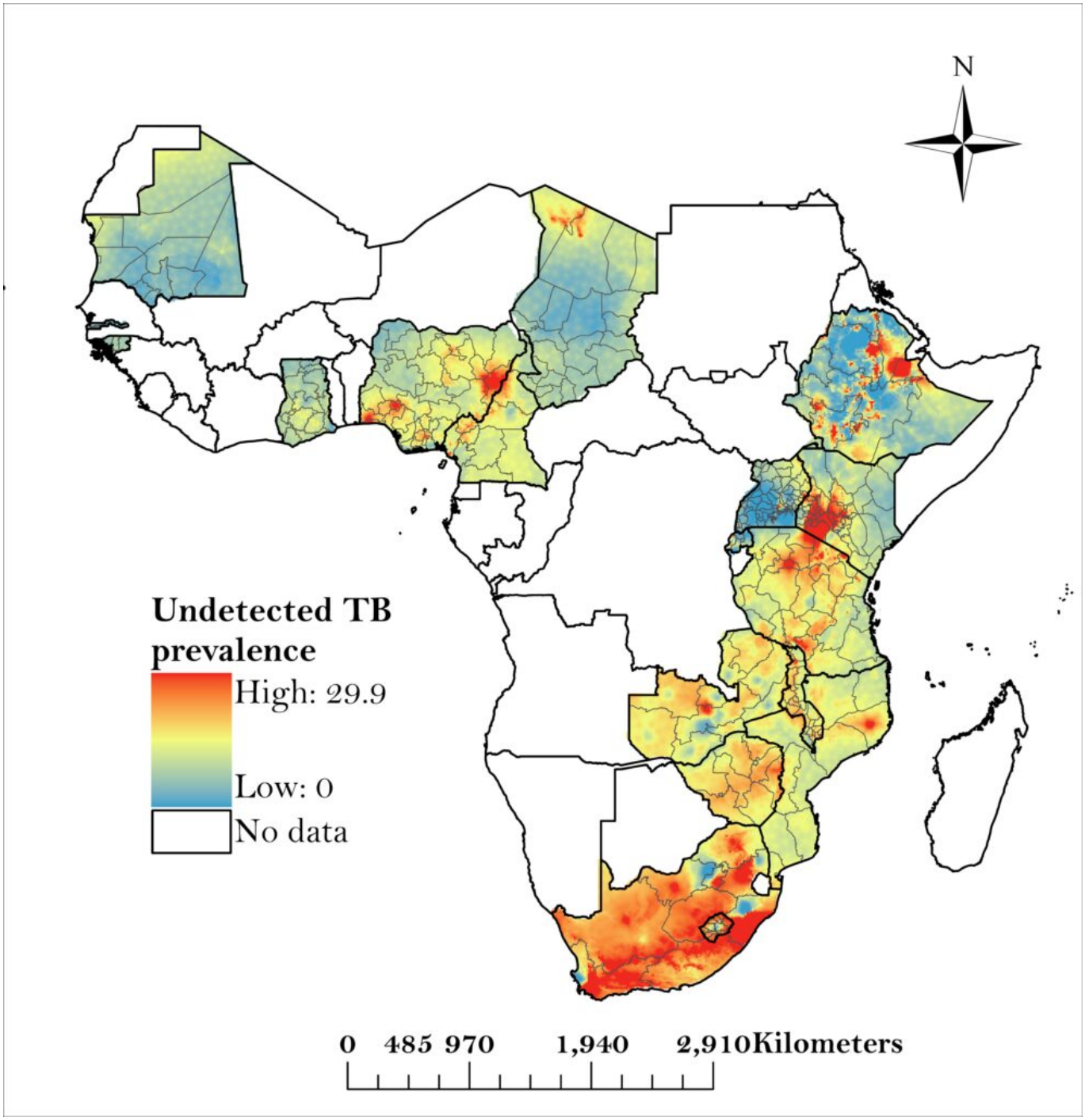
Spatial prediction of undetected tuberculosis in sub-Sahara Africa Haileab Fekadu Wolde* Haileab Fekadu Wolde Archie C A Clements Alemneh Mekuriaw Liyew Temesgen Yihunie Akalu Kefyalew Addis Alene

Background: Tuberculosis (TB) remains a major public health challenge in sub-Saharan Africa (SSA), with many cases undetected by routine healthcare systems. This study provides the first high-resolution, multi-country geospatial analysis of undetected TB prevalence in SSA, aiming to identify high-risk areas for targeted interventions.

Methods: Data on undetected TB prevalence were extracted from 75 surveys conducted across 18 SSA countries, containing 250 unique geographic locations and screening a total of 4,321,003 individuals. Undetected TB cases were defined as the proportion of newly diagnosed TB cases identified through community surveys that had not been detected by the routine healthcare system. A Bayesian geostatistical model was used to estimate the spatial variation of undetected TB prevalence at continental, national, sub-national and pixel levels.

Results: We found that an estimated 859,333 TB cases (95% CI: 232,136–2,256,603) remained undetected. Substantial spatial variations in the prevalence of undetected TB across SSA, with notable variation at national and local levels. Predicted national prevalence ranged from 0.13 (95% CrI: 0.03, 0.19) per 1000 population in Gambia to 4.08 (0.07, 6.11) in Lesotho. Longer walking distance to health facility (in minutes) (OR = 1.12, 95% CrI: 1.06, 2.31) and higher HIV prevalence (%) (OR=1.26, CrI: 1.10, 3.25) were positively associated with increased prevalence of undetected TB.

Conclusion: This study identified significant spatial disparities in undetected TB prevalence across SSA, with healthcare accessibility and HIV prevalence as key drivers. Targeted interventions, including active case-finding, improved access to health facilities, and integrated TB and HIV care are essential to enhance case detection and reduce transmission in the identified high-risk areas.


N
Undetected TB prevalence
High: 29.9
Low: 0
No data
0 485 970 1,940 2,910Kilometers

HIV / STI

HIV Transmission in a Declining African Epidemic: A Matched Case-Control and Contact-Tracing Study Griffin Bell* Griffin Bell Mary Kathryn Grabowski Josephine Mpagazi Francesco Di Lauro Aleya Khalifa Anthony Ndyanabo Hadijja Nakawooya Joseph Kagaayi Godfrey Kigozi Gertrude Nakigozi Ronald M Galiwango Grace Kigozi Michael A Martin Christophe Fraser David Bonsall Lucie Abeler-Dörner Tanya Golubchik Aaron Tobian Laura K. Beres Caitlin Kennedy Justin Lessler Thomas C Quinn Steven J Reynolds Maria J Wawer Ronald H Gray David Serwadda Larry W Chang Robert Ssekubugu

HIV incidence is declining throughout Africa. The dynamics of residual transmission in waning epidemics remain unclear, complicating allocation of novel prevention modalities such as long-acting pre-exposure prophylaxis.

We identified persons with incident HIV (cases) from a longitudinal population surveillance cohort in Uganda experiencing declining incidence. Cases were individually matched to persons without HIV (controls). Sexual partners were elicited, traced, and enrolled in both groups. Female sex workers (FSW) were enrolled from named venues of untraceable FSW partners. We used conditional logistic regression, transmission modeling, and phylogenetics to identify characteristics of incident case networks.

We administered 37,392 HIV tests to 27,013 people, identifying 4,653 people with HIV and 180 people with an incident HIV infection. We enrolled 164 (91%) of those with an incident HIV infection, including 79 (48%) men. Male cases reported more partners (mean=3.8) than male controls (2.2), female cases (1.9), and female controls (1.2). FSW partnerships were common among male cases (43%) and were associated with a 15.5-fold (95% CI: 3.7-64.8) increase in the odds of incident infection. The number of reported female non-SW partners was not significantly associated with incident infection in men. Most male cases with FSW partners also had female non-SW partners (91%), and female non-SW partners of cases had higher HIV seroprevalence (59.5% vs 33.7%) and population prevalence of viremia (15.0% vs 3.4%) than venue-enrolled FSWs, but transmission modeling still attributed 29.8% of all male incident infections to sex with FSWs. PrEP use among HIV-negative partners of cases was uncommon (5.4%).

Increased prioritization of male clients of FSWs in HIV programs in Africa, including for long-acting injectable PrEP, could be a highly efficient and effective strategy for HIV prevention and epidemic control.

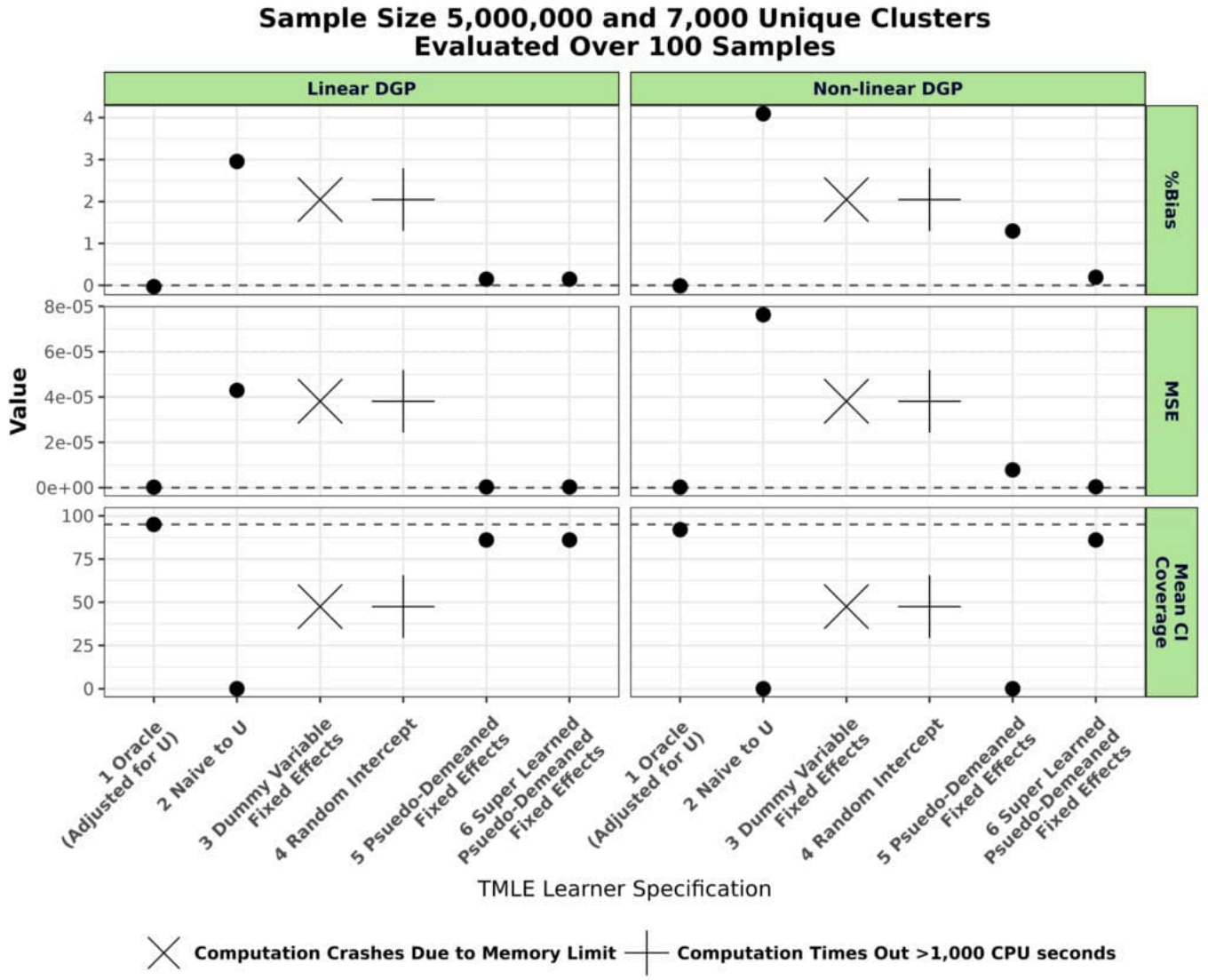
Social

Estimating Causal Effects of Community Drivers of Individual Health in the Presence of Unmeasured Between-Community Confounding in Large Data Settings John Halifax* John Halifax Laura B. Balzer Jennifer Ahern

Community characteristics, such as neighborhood violence, have been hypothesized as a driver of health and health disparities. However, causal effects remain insufficiently elucidated, in part due to analytical challenges: clustering within communities reduces the effective sample size; confounding occurs at multiple levels and is high-dimensional; unmeasured confounding between communities is often unaddressed. Additional challenges arise when using registry data. The large number of clusters make fixed effects regression (for between-community confounding) computationally infeasible, but clusters often have insufficient observations to support community-stratified estimation that resolves within-community confounding.

We extend TMLE for evaluating community effects with registry-scale data using pseudo-demeaned logistic regression to learn outcome and exposure mechanisms while addressing between-community unmeasured confounding. We evaluated performance with two synthetic multilevel, registry-scale data generating processes (DGP), one linear and one non-linear, with between-community unmeasured confounding (U). We compared 6 TMLEs using different learners: 1) oracle learners with correctly specified regressions including U as a benchmark, 2) naïve learners not accounting for between-community confounding, 3) dummy variable fixed effect learners, 4) random intercept learners, 5) pseudo-demeaned learners, and 6) super learned ensembles of pseudo-demeaned regressions.

The pseudo-demeaned and super learned pseudo-demeaned TMLE estimators matched performance with the oracle estimator in the linear DGP. In the non-linear DGP, only the super learned pseudo-demeaned TMLE matched oracle performance. The TMLE with dummy variable fixed effects failed computationally, while the random intercept TMLE failed to converge before a user-set time limit. This research suggests the super learned pseudo-demeaned TMLE is a flexible, scalable estimator for community determinants of health.


Sample Size 5,000,000 and 7,000 Unique Clusters
Evaluated Over 100 Samples
Linear DGP
Non-linear DGP
%Bias
MSE
Mean CI Coverage
Value
1 Oracle (Adjusted for U)
2 Naive to U
3 Dummy Variable Fixed Effects
4 Random Intercept
5 Psuedo-Demeaned Fixed Effects
6 Super Learned Psuedo-Demeaned Fixed Effects
TMLE Learner Specification
Computation Crashes Due to Memory Limit
Computation Times Out >1,000 CPU seconds

Social

A novel machine learning approach to identify neighborhood-level social phenotypes

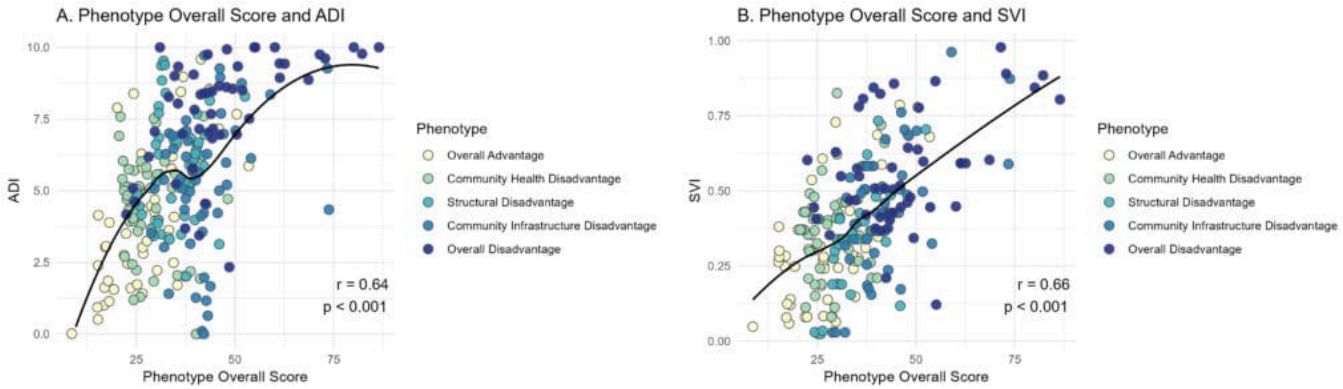
Madeline Brooks* Madeline Brooks Roger (Yi-Hsuan) Chen Michael Desjardins Amii Kress Bryan Lau

Measures of neighborhood-level disadvantage, like the Area Deprivation Index (ADI) and the Social Vulnerability Index (SVI), are widely used as measures of social determinants of health (SDOH) but were actually created for different purposes or represent only one SDOH domain. We used machine learning to identify multidimensional neighborhood phenotypes based on 60+ SDOH indicators and validated them against the ADI, SVI, and area-level health outcomes.

We collected data for Maryland related to neighborhood-level health, interpersonal, organization, economy, infrastructure, and structural factors; and aggregated these to spatially consistent hexagonal units (N=33,326). We applied four clustering algorithms, using 10-fold cross-validation and cluster fit statistics to choose the optimal number of phenotypes. Results were pooled using an adaptive clustering ensemble approach. Overall and domain summary scores were created to compare phenotypes and assign labels by the type and extent of relative advantage/disadvantage. Spatial regression models were used to estimate associations of phenotypes with tract-level prevalence of infant (preterm birth, low birthweight, stillbirth, and infant mortality) and adult (drug overdose and all-cause mortality) health outcomes.

Ensemble learning produced five phenotypes, corresponding to Overall Advantage (OA), Community Health Disadvantage (CHD), Structural Disadvantage (SD), Community Infrastructure Disadvantage (CID), and Overall Disadvantage (OD). The phenotype overall summary score was correlated with the ADI and SVI (r=0.64-0.66, p<0.05), suggesting convergent validity (Figure 1). The OD phenotype was associated with increased prevalence of all tract-level adverse health outcomes relative to the OA phenotype; other phenotypes were associated depending on outcome.

Neighborhood phenotypes derived from machine learning may capture spatial variation in SDOH and related health outcomes, beyond the commonly used ADI and SVI.



Social

Measuring neighborhood perception and social integration: a qualitative exploration of differential item functioning in the MIDUS study Sara Daniel* Sara Daniel Inez Adams Yusuf Ransome Ester Villalonga-Olives

Background: Differential Item Functioning (DIF) also referred to as lack of measurement invariance, is a key limitation in health equity research. It occurs when items used to collect data are not meaningful for certain populations, or when essential concepts are interpreted differently across groups. This leads to invalid comparisons and introduces measurement error. This study aims to understand potential sources of DIF between Black and White populations for select neighborhood perception and social integration questions in the Midlife in the United States (MIDUS) study.

Methods: In 2022, participants were recruited via Craigslist.com across five metropolitan areas. We conducted semi-structured interviews with 47 participants (53% White; 47% Black). To mimic the survey environment, participants were asked MIDUS questions related to neighborhood trust and safety, and community comfort and closeness. Open-ended follow-up questions were asked to identify potential sources of DIF. Using thematic analysis, item wording, interpretation, and perceived relevance were examined between the groups.

Results: Our findings suggest that while “neighborhood” is understood similarly by both groups as geographic, there were differences in the interpretation of “community,” as it could be both social and geographic. One-third of participants were unclear and asked a follow-up question about the meaning of the word “community.” Minority (race, sexual orientation, and/or gender identity) participants tended to mention social communities more often than white heterosexual participants.

Conclusions: This study highlights that items related to “community” are interpreted differently across racial and gender-identity groups and may affect the comparability and validity of results. Integrating contextual and cultural factors specific to minority groups into scale development strengthens test design and improves content and construct validity, helping to prevent future DIF.

Social

Is segregation bad for your heart?: A natural experiment for residential racial segregation exposure in childhood and cardiovascular disease Gabriel Schwartz* Gabriel Schwartz Mark Hernandez

Background: Residential racial segregation is hypothesized to be a driver of inequities in cardiovascular disease. A key manifestation of structural racism, residential segregation stratifies access to healthcare, education, food, and employment, as well as discretionary law enforcement and targeting for harmful product marketing. Yet despite ample cross-sectional data, little work has examined (A) the long-term implications of childhood residential segregation exposure for CVD, especially (B) using causal designs. Here, we use quasi-random urban planning decisions made by Northern cities prior to the Great Migration as an instrument for segregation as Black families moved to the North in search of opportunity, providing a natural experiment for the causal impact of childhood segregation exposure on CVD.

Methods: We followed Ananat's work identifying the degree to which early 1900s railway systems gridded cities as a valid instrument. We linked her data on segregation and train tracks to where participants in the Panel Study of Income Dynamics were born (1968-1994, n=829 Black & 1,262 White) and followed them through 2023. We fit race-stratified accelerated failure time models with an instrumental variables design and using a cluster bootstrap. Models controlled for parental socioeconomic status at birth.

Results: Given their distribution across PSID study cities, our instrument was stronger for White than Black participants. Point estimates for White (survival ratio = 1.16, 95% CI=1.02,1.75) and Black (SR = 0.67, 95% CI=0.29,5.10) participants suggest that childhood residential segregation exposure causally delays the onset of CVD for White individuals but speeds it up for Black individuals, though confidence intervals for our Black sample were uninformatively wide.

Conclusion: Segregation harms Black US Americans' heart health while protecting White US Americans, though larger studies are needed to estimate precise causal effects for Black communities.

Health Disparities

Cost-Constrained Dynamic Interventions for Health Equity Cuong* Cuong Pham Chidinma A. Ibe Emmanuel F. Drabo Jill A. Marsteller Lisa A. Cooper John W. Jackson

Hypertension is a leading risk factor for cardiovascular disease. In the United States, it disproportionately affects African Americans, Hispanics, and individuals living in underserved rural communities. These disparities are driven by social, cultural, and structural factors that impact disease risk and access to effective care.

Although multilevel interventions have been developed to reduce hypertension disparities, their implementation is constrained by limited resources. Hence, healthcare organizations face difficult decisions about how and whom to treat. These decisions require balancing the goal of optimizing health outcomes with equity and cost constraints. However, identifying optimal solutions to these trade-offs is challenging.

We address this challenge by incorporating the concept of allowability into the dynamic treatment regime (DTR) framework. A DTR is a set of decision rules that adapt treatment assignment over time based on patients' characteristics and evolving health status, while allowability permits adjustment for fair sources of variation when measuring health disparities. Although recent methods enable the estimation of outcome-optimal DTRs under cost constraints, such regimes do not necessarily reduce disparities. We extend the DTR framework to explicitly target disparity reduction while accounting for allowable covariates. This extension enables evaluation of existing care policies and construction of optimal, cost-constrained DTRs that improve health outcomes and reduce disparities.

We apply this framework to a collaborative care model for hypertension management that integrates community health workers (CHWs) within a care team. Our aims are to: (1) assess the extent to which existing care regimes improve hypertension outcomes and reduce disparities across racial, ethnic, and geographic groups; and (2) determine when and for whom adding CHWs yields the greatest population-level benefit while minimizing disparities under cost constraints.

Women’s Health

Infertility and long-term mortality among Mexican women Leslie V Farland* Leslie Farland William J Degan Marion Brochier Liliana Gomez-Flores-Ramos Jorge E Chavarro Gregory Talavera John M Ruiz Ellen C Caniglia Britton Trabert Martin Lajous Dalia Stern

Background: Evidence suggests that infertility may serve as an early-life marker for mortality; however most research is among high-income non-Hispanic White women (NHWW). Therefore, our goal was to estimate the relationship of infertility to mortality among Hispanic women, who are 70% more likely to experience infertility compared NHWW.

Methods: We followed 90,561 women in the Mexican Teachers Cohort study from 2008-2019, who were 44y at baseline. Women with infertility were compared to parous women without infertility. Infertility diagnoses (fallopian tube, polycystic ovary syndrome (PCOS), ovulatory, endometriosis, uterine factor, or male factor) were analyzed separately. Mortality was ascertained via cross-linkage with national registries. Cox proportional hazard models adjusted for a priori confounders were used to estimate hazard ratios and 95% confidence intervals for all-cause and cause-specific mortality (cardiometabolic [CM], breast cancer [BC], gynecologic cancer [GC; ovarian, endometrial]).

Results: At baseline, 22% reported infertility. Over 10.6 years of follow-up, there were 1,541 deaths (377 CM, 139 BC, and 65 GC). Women with infertility had a 17% higher rate of all-cause mortality compared to parous women without infertility (95% CI: 1.04-1.32). Infertility was associated with a 46% increased rate of CM mortality (95% CI: 1.16-1.83) and a 2.66-fold increased rate of GC mortality (1.61-4.41). There was no association with BC mortality (HR 0.67, 95% CI: 0.42-1.08). Infertility attributed to PCOS (HR 1.45, 95% CI: 1.06-1.98), fallopian tube (HR 1.26, 95% CI: 0.94-1.67), ovulatory (HR 1.19, 95% CI: 0.89-1.59), and endometriosis (HR 1.19, 95% CI: 0.78-1.82) were positively associated with all-cause mortality, but some estimates were imprecise.

Conclusions: Infertility was associated with increased all-cause, CM, and GC mortality. PCOS, fallopian tube, ovulatory, and endometriosis-related infertility may individually confer an elevated rate of death.

Health Disparities

Reduction of county-level socioeconomic inequity can partially remediate racial disparities in infant mortality and preterm birth Naria R. Z. Sealy* Naria Sealy Heather H. Burris Ellen C. Caniglia Aimin Chen Melody S. Goodman Katharine A. Rendle Stefanie N. Hinkle

Background: County-level inequities in socioeconomic indicators of structural racism may explain some of the racial disparities in infant mortality (IM) and preterm birth (PTB, <37 weeks' gestation).

Methods: We used vital statistics (2018-2020) in 1427 US counties (n=6,070,978 Black and White births). Census data were used to calculate poverty inequity by dividing each county's poverty rate for Black residents by the rate for White residents, dichotomized into excess Black poverty (ratio >1) vs. not (≤1). This was repeated for county-level income, education (proportion high school diploma), and unemployment. ICE race-income was dichotomized into privileged (>0) or disadvantaged (≤0). We estimated risk differences (RD) for Black-White disparities in IM and PTB. We used causal mediation models to estimate the IM and PTB inequity that would remain if Black disadvantage in each county-level structural racism indicator were eliminated; race as the exposure and socioeconomic structural racism indicators as the mediators (Figure 1). Inverse probability weighting accounted for mediator-outcome confounding (age, education, parity, payment method, urbanicity, hypertension and diabetes) and a linear probability model with robust standard errors estimated RDs (per 100 births) with 95% CI.

Results: There were 1,510,977 Black and 4,515,616 White births: the risk of IM was 0.9% vs. 0.4%, respectively (RD=0.53 [95% CI: 0.52, 0.55]), and the risk of PTB was 12% vs. 7%, respectively (RD=4.82 [4.76, 4.88]). Eliminating county-level Black disadvantage reduced the IM and PTB disparity for each indicator. Removal of excess Black poverty had the highest reductions in IM and PTB disparities: RD=0.24 (0.12, 0.37) and RD=3.20 (2.72, 3.67), respectively, corresponding to 34% and 55% of the disparities eliminated.

Conclusion: Policies focused on reducing county-level socioeconomic inequities driven by structural racism may substantially narrow racial disparities in IM and PTB.

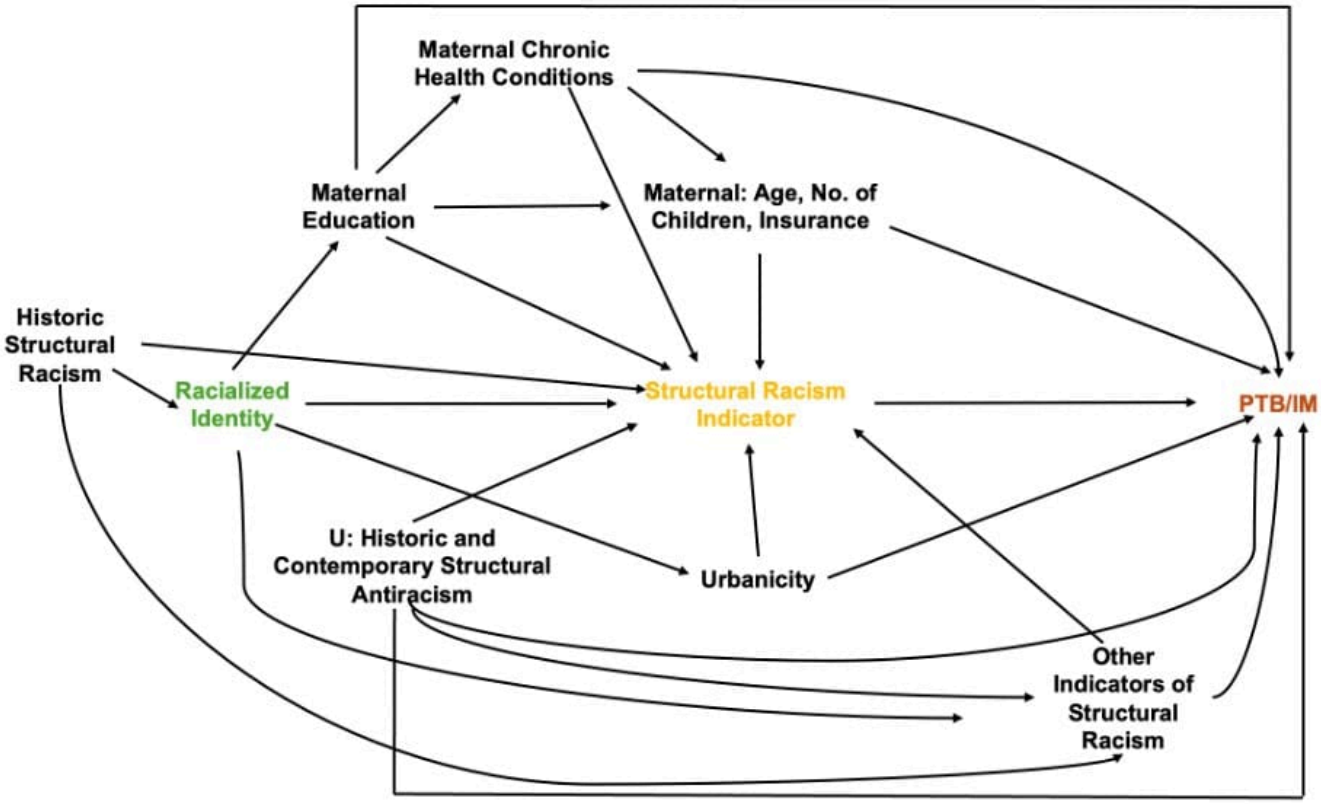


Figure 1. Directed Acyclic Graph for racialized identity (exposure) structural racism indicator (mediator) and preterm birth and infant mortality (outcomes). PTB = preterm birth. IM = infant mortality.

Health Disparities

Structural Intersectionality: Development of a policy-based measure of state-level discrimination Sara Daniel* Sara Daniel Lorraine Dean Bryan Lau

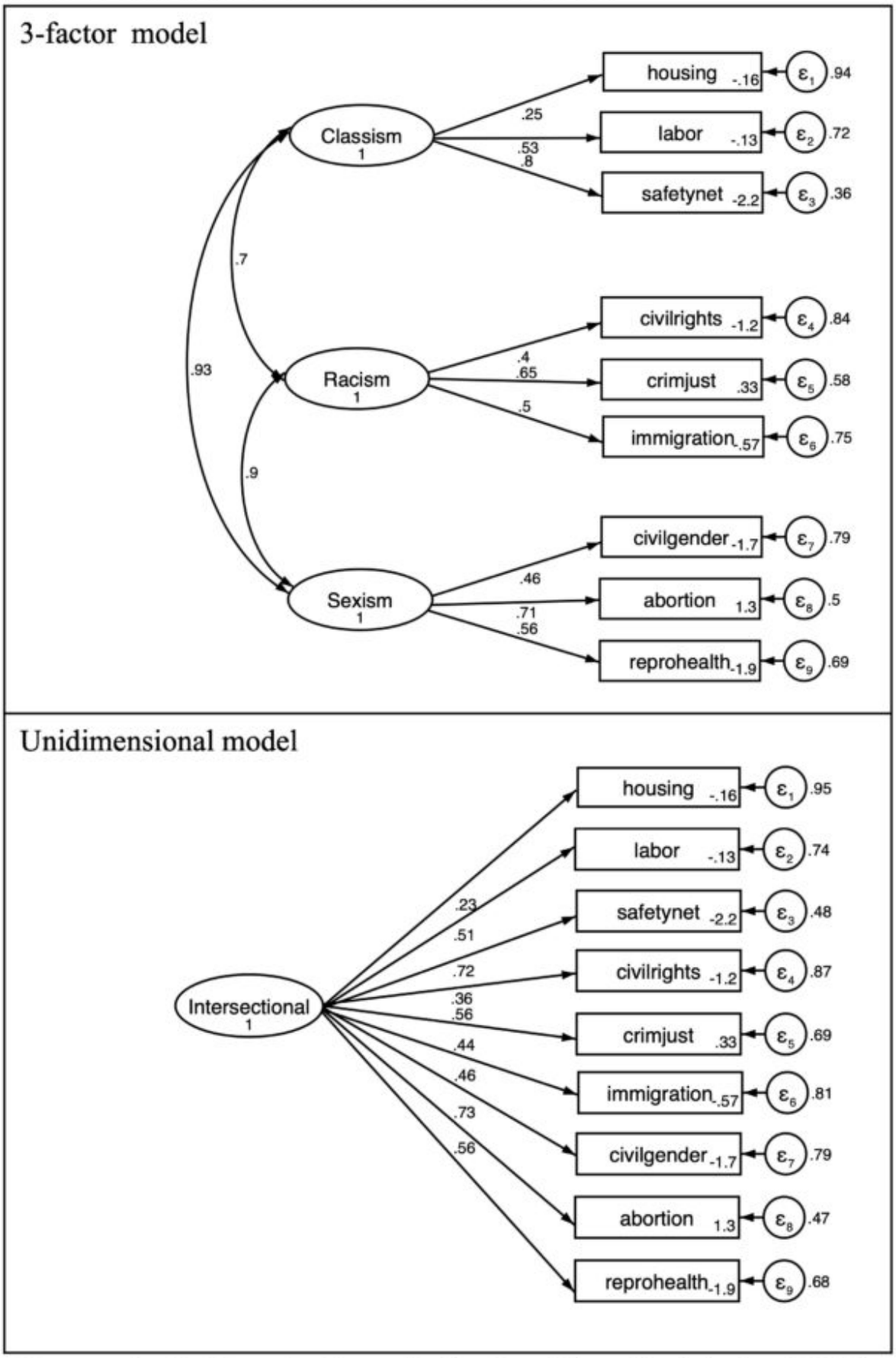
Background: Identifying methods to measure structural determinants of health is key to advancing health disparities research. However, few structural measures of discrimination consider the synergistic effects of racism, sexism, and classism on health inequities. Using intersectionality as an analytical tool to account for multiple axes of oppression, this study addresses key gaps in measurement of structural intersectionality by developing a novel policy-driven measure of state-level discrimination.

Methods: From an initial pool of 235 state-level policies from six databases, we coded and selected 88 thematically relevant policies across 10 domains as potential indicators of intersectional discrimination. We conducted a series of confirmatory factor analyses (CFA), including unidimensional, 3-factor, and second-order models, to evaluate the relationship between our policy domains and the underlying latent constructs of racism, sexism, and classism.

Results: We identified 2 models to quantify intersectional state-level discrimination (Figure 1). A 3-factor model for racism, sexism, and classism included 9 policy domain indicators and showed good fit (RMSEA: 0.026; CFI: 0.989; TLI: 0.983). A unidimensional model for intersectional discrimination also included 9 policy domains and showed good fit (RMSEA: 0.014; CFI: 0.996; TLI: 0.995). Top policy-drivers of intersectional structural discrimination were domains related to social safety net, criminal justice, and sexual and reproductive health.

Conclusions: This measure of state-level structural discrimination advances our understanding of the intersecting effects of structural racism, sexism, and classism to address health inequities by quantifying the combined effects of multiple policies and can be used to account for the policy environment in each state. Further development of this measure can include longitudinal trends and other forms of structural discrimination.

Figure 1. Path diagrams for 3-factor and unidimensional measurement models of intersectional structural discrimination.



Note: standardized factor loadings of Policy-Based State Discrimination (PBSD) are depicted above.

Health Disparities

Life-course Trajectories of Neighborhood Deprivation and Cognitive Consequences in Midlife: The Bogalusa Heart Study Eunsun Gill* Eunsun Gill Jeanette Gustat Katherine P. Theall Dohyeong Kim Owen T. Carmichael Soo Jung Kang Ileana De Anda-Duran Lydia A. Bazzano Camilo Fernandez Richard MacLehose David J. Libon Emily W. Harville

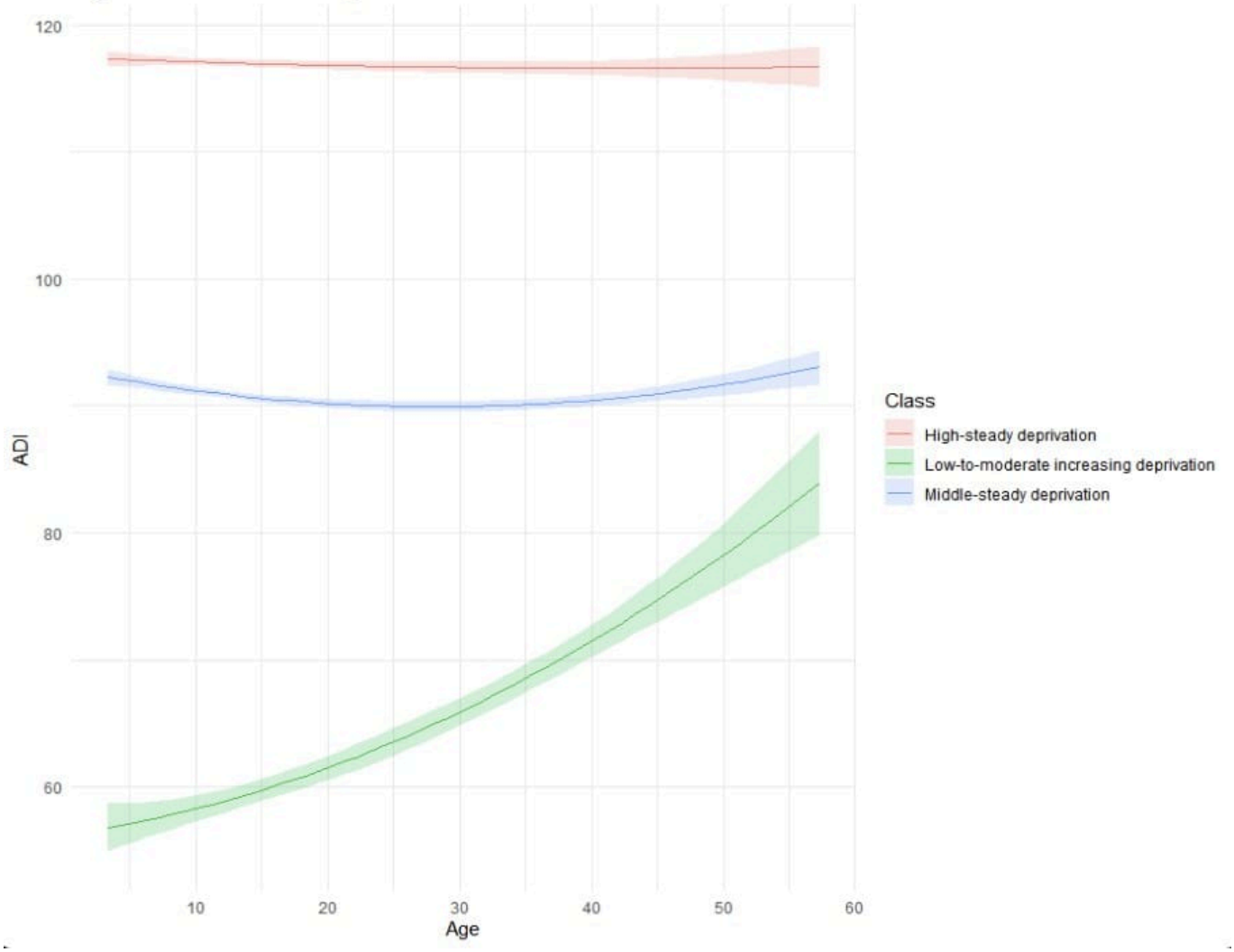
Introduction: Neighborhood socioeconomic deprivation contributes to cognitive function (CF) in middle-aged and older adults, yet life-course and longitudinal patterns remain understudied. We examined associations of cumulative and trajectory-based Area Deprivation Index (ADI) with midlife CF in the Bogalusa Heart Study.

Methods: We analyzed 1,052 adults (61% White, 39% Black; mean age at CF: 48±5.3). Residential addresses (1974–2016) were geocoded and linked to 17 census-based indicators. ADI was derived using weighted principal component analysis, with census/American Community Survey data (1990, 2000, 2006–2010, and 2013–2017) matched to address and year. Latent class growth curve models identified ADI trajectories, and cumulative ADI was estimated using the trapezoidal method. CF domains were age- and sex-standardized. Linear regression models estimated associations of cumulative and trajectory-based ADI with CF, adjusting for race, sex, parental education, adult education, and income. Multiple imputation was used to adjust for bias due to missing at random variables.

Results: Three ADI trajectories were identified: high-steady, middle-steady, and low-to-moderate increasing deprivation. Compared with the low-to-moderate increasing deprivation, high- and middle-steady deprivation had lower global CF (β= –0.36 [95% CI: –0.54, –0.18] and –0.23 [–0.41, –0.05]) and poorer verbal episodic memory and attention. The largest differences were observed in working memory (high: –0.47 [–0.71, –0.23]; middle: –0.30 [–0.50, –0.10]). No associations were found for processing speed. Cumulative ADI was inversely associated with global CF (–0.06 [–0.02, –0.10]), working memory (–0.07 [–0.13, –0.01]), and processing speed (–0.12 [–0.20, –0.04]), but not with verbal episodic memory.

Conclusions: Persistent high neighborhood deprivation and greater cumulative exposure across the life course were associated with poorer midlife CF, particularly working memory.

Figure. Lifecourse ADI Trajectories



Health Disparities

Harmonizing Mixed-Scale Public Data to Build Ecological Indices of Institutional and Economic Barriers for Health Disparities Research Zonggui Li* Zonggui Li Sara Daniel Nneka Okeke Jennifer Contreras Ester Villalonga Olives

Background: Institutional and economic barriers shape access to resources and opportunities and lead to health disparities for Black and Hispanic populations in the U.S. Prior qualitative work identified 70 candidate ecological-level indicators to measure institutional and economic barriers across 4 domains (behavioral, physical/built environment, sociocultural, and healthcare system) and 3 levels (interpersonal, community, and societal). We conducted a data-availability review and identified 60 indicators that could be quantified using publicly available data.

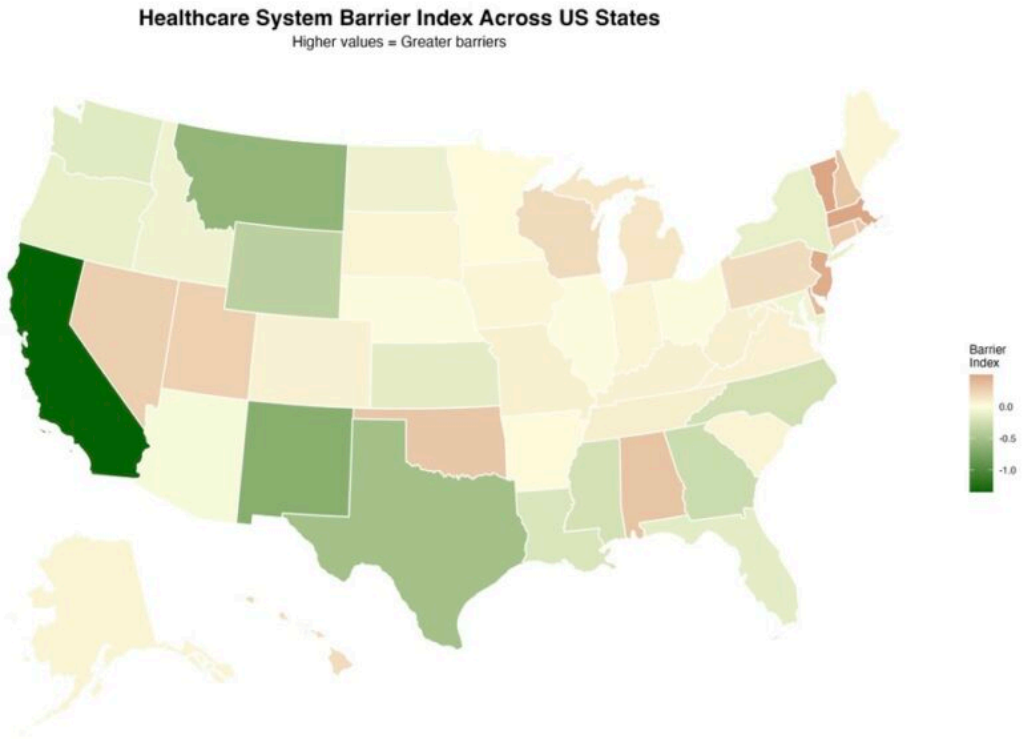
Objectives: To systematically link public data sources to each indicator and generate multidimensional-multilevel (4 domains × 3 levels), ecological-level indices across geographic areas and years.

Methods: For each indicator, we: 1) cataloged data source, variable selection, temporal coverage, reporting frequency, and geographic resolution; 2) harmonized measures by aligning geographic identifiers; 3) standardized indicators and aligned indicator direction so higher values indicate greater barriers; 4) computed indices by domain using expert-derived weights; and 5) conducted sensitivity analyses varying standardization approach, weighting methods, and missing-data rules to assess robustness of spatial and temporal change in the developed index.

Results: We present the indicator–data source crosswalk, data coverage by geography and year, and state-level indices for each of the 4 domains for selected years. Figure 1 presents a preliminary heatmap for one of the domains, healthcare-system. The index (weighted z-score) was constructed using the most recent available data and ranged from -1.35 (California, least barriers) to 0.50 (Vermont, most barriers).

Conclusions: This project developed ecological-level indices and a data pipeline that advance methods for measuring institutional and economic barriers for Black and Hispanic populations, while documenting limitations due to statistical and data constraints.

Figure 1 State-level Barrier Index for Healthcare System Domain Across US States



Health Disparities

Sleep regularity and other sleep dimensions in relation to incident cardiovascular disease among middle- to older-aged US women Symielle A. Gaston* Symielle Gaston Rupsha Singh Wensu Zhou Dale P. Sandler Chandra L. Jackson

Sleep health is increasingly recognized as a pillar of cardiovascular health. Yet, few studies have examined multiple sleep dimensions, including regularity, in relation to cardiovascular disease (CVD). Also, few have assessed racial-ethnic differences in women. We investigated multiple sleep dimensions in relation to incident CVD overall and by race-ethnicity among 42,542 women (mean age 55±8.9 years; 86% non-Hispanic White, 8.4% non-Hispanic Black [NHB], 3.3% Latina, 2.6% another race-ethnicity group) in the Sister Study without prior CVD. At enrollment (2003–2009), participants reported bed and wake times over 7 days, from which we derived mean sleep duration (hours), duration regularity (SD of durations), mean sleep timing (sleep midpoint), timing regularity (SD of midpoints), and social jet lag (midpointnon-workdays – midpointworkdays). Insomnia symptoms (IS: difficulty falling/staying asleep ≥3 nights/week) and frequent napping (≥3 times/week) were also reported (yes vs. no). Incident CVD (i.e., ischemic heart disease, heart failure, myocardial infarction, stroke, or related procedures) was captured through October 2022. Cox proportional hazards models estimated associations (HRs [95% CIs]) between multiple sleep dimensions simultaneously (given weak correlations: $|r| \leq 0.10$) and CVD, adjusting for relevant confounders. Effect modification (EM) was tested with cross-product terms. Over a median follow-up of 14.4 years, 3,132 incident CVD events occurred. With small variation across participants, mean sleep duration was 7.5±1.1 hours and mean sleep midpoint was 2:24 (1:06–3:42) AM. IS and frequent napping were more prevalent among CVD cases and NHB women. After adjustment, only IS were associated with higher CVD risk, observed only among NHB women (HR=1.81 [1.12–2.92] vs. HRrange: 0.71-1.05; pEM=0.02). IS—not sleep regularity—emerged as a key CVD risk factor, particularly among Black women, highlighting a potential target for reducing disparities in CVD risk.

Mental Health

Maternal antenatal depression and offspring DNA methylation Diane Putnick* Diane Putnick Akhgar Ghassabian Weihua Guan Pauline Mendola Rajeshwari Sundaram Edwina Yeung

Antenatal depression may affect child development through prenatal programming of the Hypothalamic-Pituitary-Adrenal axis by epigenetic modifications. Research on the link between antenatal depression and alterations in offspring DNA methylation is sparse and inconsistent. We aimed to test the association between maternal antenatal depression and offspring DNA methylation in neonatal and middle childhood periods.

Moderate to severe maternal antenatal depression was identified via a combination of diagnosis codes from outpatient and inpatient encounters during pregnancy and self-reported symptom severity on birth certificates. Offspring DNA methylation was quantified from dried blood spot and venous blood samples in the neonatal and middle childhood periods, respectively. Robust linear regression models with antenatal depression as the exposure and CpG M-values as outcomes were run adjusted for covariates and corrected for false discovery rate (FDR).

Of 733 mothers with available data in the neonatal period, 53 (7%) experienced moderate to severe antenatal depression. In middle childhood, 15 (9%) of the 161 mothers with available data experienced moderate to severe antenatal depression. In the neonatal period, no probes passed FDR correction. In middle childhood (Table 1), antenatal depression was associated with hypomethylation at two probes after adjustment and FDR correction: cg06112204 (in MAD1L1; β=-1.68, SE=0.29) and cg17830140 (in POLRMT, β=-1.94, SE=0.36). Both probes had a similar direction and magnitude when adjusting postnatal depression (β=-1.71, SE=0.34 and β=-1.78, SE=0.42, respectively). cg06112204 was also hypomethylated in the neonatal sample (β=-0.49, SE=0.21), but cg17830140 was not (β=0.07, SE=0.22).

Hypomethylation in the MAD1L1 gene has previously been associated with depression phenotypes in adolescents and adults, lending credibility to the finding that antenatal depression is associated with hypomethylation of cg06112204 in offspring.

Table 1
Top ten CpG probes in middle childhood

Probe	Estimate	SE	*p*	FDR *p*	Position	UCSC Gene Name	Gene region	Relation to CpG Island
cg06112204	-1.6810	0.2926	9.32E-09	0.007091	Chr7:2078981	MAD1L1	intron	OpenSea
cg17830140	-1.9440	0.3586	5.89E-08	0.022427	Chr19:626119	POLRMT	intron	S_Shelf
cg07511721	0.3818	0.0746	3.04E-07	0.077207	Chr7:5335697	SLC29A4	intron	N_Shore
cg15008725	0.3971	0.0809	9.21E-07	0.155530	Chr17:48133686	ITGA3	exon	Island
cg12936983	0.3271	0.0671	1.08E-06	0.155530	Chr1:151299782	PI4KB	exon	N_Shore
cg10924908	-0.2022	0.0417	1.23E-06	0.194856	Chr19:50380558	AKT1S1	exon & intron	Island
cg22766025	-0.2475	0.0516	1.59E-06	0.248822	Chr5:90650061	--	--	OpenSea
cg10863036	0.2585	0.0544	2.05E-06	0.007091	Chr11:82769278	RAB30	intron	OpenSea
cg10291205	0.5943	0.1275	3.14E-06	0.022427	Chr13:46856182	LINC00563	intron	OpenSea
cg24569116	-0.3154	0.0678	3.27E-06	0.248821	Chr3:119416332	--	--	OpenSea

Note. CpG β-values were transformed to M-values for analysis. Estimates can be interpreted as log2 fold changes in methylation between groups with negative estimates indicating lower methylation in the depressed than non-depressed group and positive estimates indicating higher methylation in the depressed than non-depressed group. Adjusted for batch, estimated cell types (naïve and memory B cells, naïve and memory CD4 + and CD8 + T cells, neutrophils, eosinophils, basophils, monocytes, natural killer cells, and T regulatory cells), maternal age, education (college or higher vs. less than college), pre-pregnancy BMI, pregnancy smoking (yes/no), and child sex, age, and twin status (vs. singleton).

Neurology

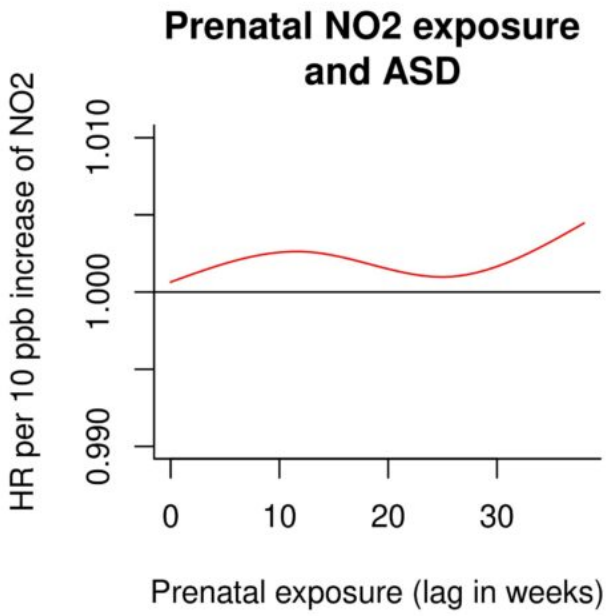
Prenatal exposure to nitrogen dioxide and neurodevelopmental delays in children among Medicaid recipients: a national cohort study Wanyu Huang* Wanyu Huang Xinye Qiu Krista Huybrechts Sonia Hernandez-Diaz Matthew Shupler Hayon Michelle Choi Michael Leung Yaguang Wei Joel Schwartz Antonella Zanobetti Marc Weisskopf Stefania Papatheodorou

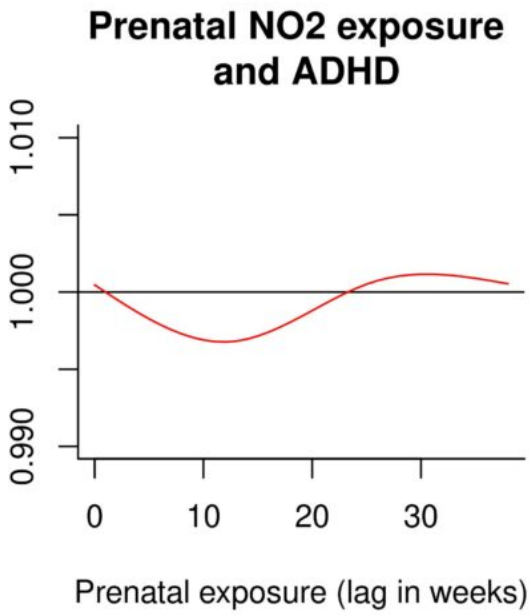
Objective: Prenatal period is critical for brain formation and children's neurodevelopment, yet few epidemiologic studies have examined the effects of prenatal exposure to gaseous pollutants, compared to PM2.5, particularly in underprivileged populations. Nitrogen dioxide (NO2) is one of the gaseous pollutants, also deemed as a traffic emission tracer.

Methods: We assigned ambient NO2 concentrations at the residential zip code of mother-infant pairs in a longitudinal cohort from the Medicaid Analytic eXtract (MAX). Identification of autism spectrum disorder (ASD) and attention-deficit/hyperactivity disorder (ADHD) were based on ICD-9 codes. Weekly prenatal NO2 levels from spatiotemporal models were calculated over the gestational period. We applied distributed lag models (DLM) coupled with stratified Cox models (by county, birth year, race), adjusting for temperature, relative humidity, maternal age, behavioral risk factors (e.g. smoking, alcohol, drug use), SES (area-level), as well as season of delivery.

Results: We included 1,616,197 births from 2001 to 2014. We observed a positive association between a 10 ppb increase of prenatal NO2 exposure and the hazard of ASD across lag0 to 38 weeks during the gestational period, with a cumulative HR of 1.08 (95% CI: 1.01, 1.15) as the overall effect. We observed no association between NO2 exposure and ADHD (cumulative HR: 0.97, 95% CI: 0.94 – 1.00) (**Fig. 1**).

Conclusion: Among the Medicaid population, prenatal exposure to NO2 was associated with increased risk of ASD but not ADHD. This is the first and largest study providing evidence on gaseous pollutants and neurodevelopment delays, among the US socioeconomically disadvantaged population.


Prenatal NO2 exposure and ASD
HR per 10 ppb increase of NO2
1.010
1.000
0.990
0
10
20
30
Prenatal exposure (lag in weeks)


Prenatal NO2 exposure and ADHD
1.010
1.000
0.990
0
10
20
30
Prenatal exposure (lag in weeks)

Pharmacoepidemiology

Systematic Surveillance of Maternal and Neonatal Outcomes Following Antipsychotic Use in Pregnancy Using Tree-Based Scan Statistics Motohiko Adomi* Motohiko Adomi Loreen Straub Shirley V. Wang Seanna M. Vine Sonia Hernandez-Diaz Krista F. Huybrechts

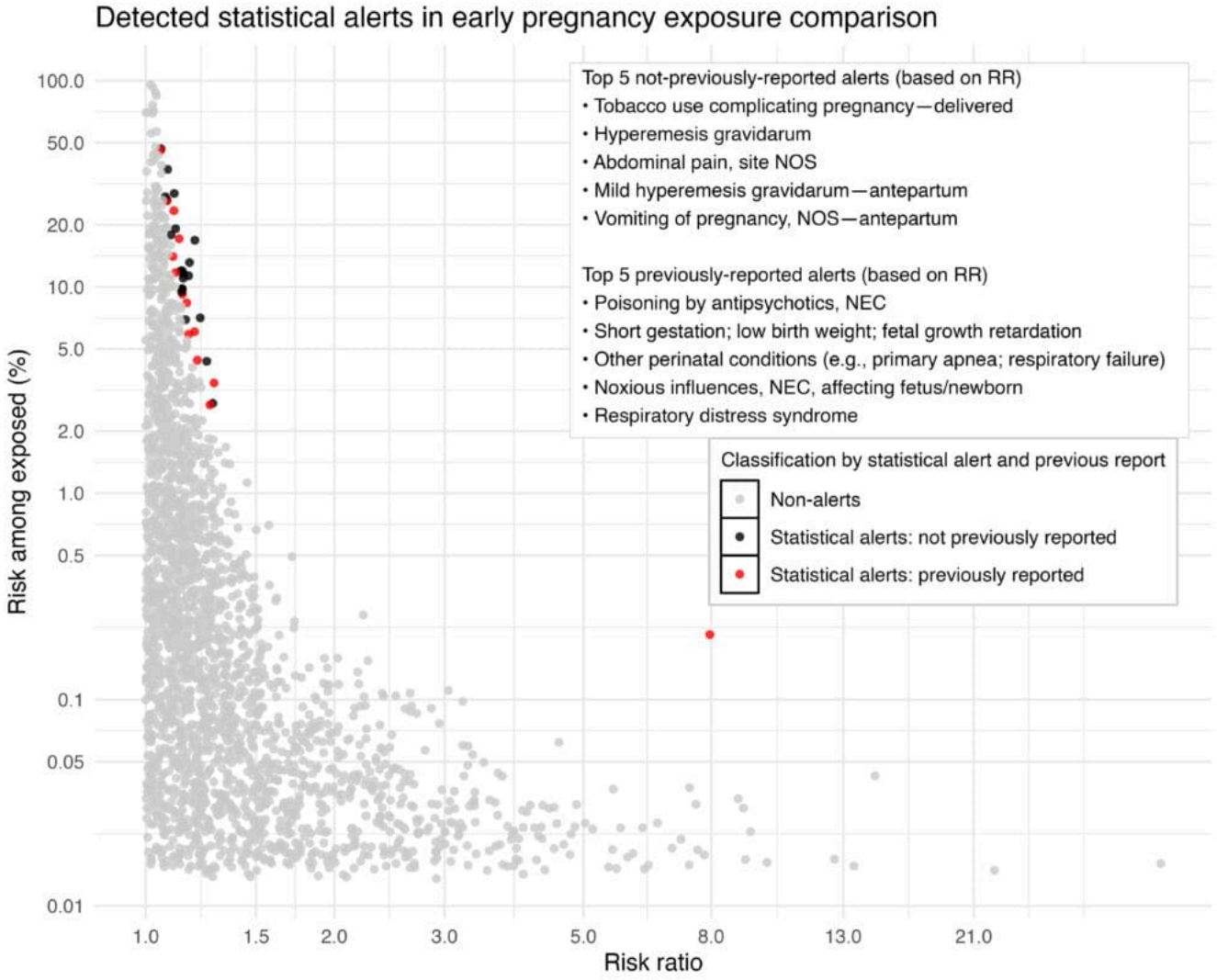
Background: Antipsychotics are used to treat severe psychiatric disorders, and their use has increased in recent years. Despite guideline recommendations for continuation during pregnancy, patients often discontinue treatment due to safety concerns. Prior studies have mainly focused on congenital malformations and prematurity-related outcomes, leaving limited evidence for other maternal/neonatal outcomes.

Objectives: To conduct hypothesis-free safety surveillance of atypical antipsychotic use in pregnancy using tree-based scan statistics.

Methods: Using Medicaid (2000–2018) and MarketScan (2003–2021) databases, we identified a cohort of pregnant individuals linked to live-born infants. Three exposure patterns during pregnancy were evaluated: (i) early exposure (regardless of late exposure), (ii) both early and late exposure, and (iii) late exposure (without early exposure), each compared with no exposure during the respective window. Outcomes included all ICD-9/10 diagnosis codes, excluding congenital malformations, and were organized into a hierarchical tree comprising 9,151 nodes. Exposed pregnancies were propensity score–matched to unexposed pregnancies on the first dispensing date of interest, and follow-up began the next day. Tree-based scan statistics using a Poisson model were implemented, with p-values obtained via permutation tests.

Results: The early (N=17,653), early and late (N=6,458), and late (N=3,375) exposed pregnancy comparisons identified 36, 21, and 0 statistical alerts based on $p < 0.05$, respectively; 40–60% of alerts corresponded to outcomes previously reported in the literature (e.g., preterm birth, neonatal respiratory distress syndrome).

Conclusions: Tree-based scan statistics enabled systematic surveillance of maternal and neonatal outcomes, identifying known safety signals and additional potential signals. This approach could serve as a scalable screening tool to prioritize outcomes for targeted follow-up studies using refined study designs.


Detected statistical alerts in early pregnancy exposure comparison
Top 5 not-previously-reported alerts (based on RR)
• Tobacco use complicating pregnancy—delivered
• Hyperemesis gravidarum
• Abdominal pain, site NOS
• Mild hyperemesis gravidarum—antepartum
• Vomiting of pregnancy, NOS—antepartum
Top 5 previously-reported alerts (based on RR)
• Poisoning by antipsychotics, NEC
• Short gestation; low birth weight; fetal growth retardation
• Other perinatal conditions (e.g., primary apnea; respiratory failure)
• Noxious influences, NEC, affecting fetus/newborn
• Respiratory distress syndrome
Classification by statistical alert and previous report
Non-alerts
Statistical alerts: not previously reported
Statistical alerts: previously reported
Risk among exposed (%)
100.0
50.0
20.0
10.0
5.0
2.0
1.0
0.5
0.1
0.05
0.01
1.0
1.5
2.0
3.0
5.0
8.0
13.0
21.0
Risk ratio

Perinatal & Pediatric

Development and Validation of the Adverse Pregnancy Outcomes Population Risk Tool (PregPoRT): A Population-Based Model for Predicting Maternal Risk in Canada Sabrina Chiodo* Sabrina Chiodo Sonia M. Grandi Jessica Gronsbell Laura C. Rosella

Introduction: Adverse pregnancy outcomes (APOs), including gestational diabetes, preeclampsia, and placental abruption, are major contributors to maternal and fetal morbidity. Existing prediction models rely on biomarkers and clinical records, limiting their utility for population health planning. We developed and validated the Adverse Pregnancy Outcomes Population Risk Tool (PregPoRT), a model integrating clinical, social, and environmental determinants to predict APO risk in Canada.

Methods: We conducted a retrospective cohort study using linked Canadian Community Health Survey (2000–2017) and Discharge Abstract Database records, with environmental exposures from national datasets. The cohort included females aged 15–49 who delivered within two years of survey participation. We compared three models: (1) full model (sociodemographic, behavioural, clinical, and environmental predictors); (2) survey-only model (self-reported sociodemographic, behavioural, and clinical predictors); and (3) clinical-only model (administrative and self-reported clinical predictors). Models were fit using a Weibull accelerated failure time framework with bootstrap validation. Performance was assessed via discrimination, calibration, and predictive accuracy.

Results: Among 13,603 pregnancies, 7.9% experienced ≥1 APO. The full model showed good discrimination (C-statistic: 0.72 development; 0.71 validation) and strong calibration (ICI: 0.03), The survey-only model demonstrated comparable discrimination (C-statistic: 0.70 validation), supporting population-level surveillance, while the clinical-only model performed less well (C-statistic: 0.68 validation).

Conclusions: PregPoRT is the first Canadian APO risk tool integrating routinely collected population-based data. It demonstrates robust calibration and good discrimination, outperforming models limited to clinical variables alone. PregPoRT enables identification of high-risk groups and advances precision public health in maternal care.

Environment/Climate Change

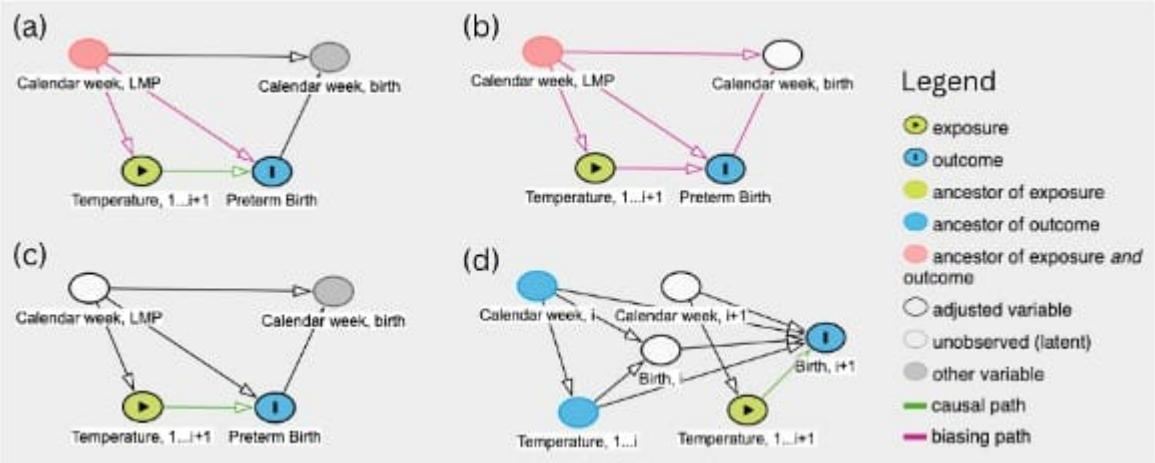
Misspecified seasonality adjustment in temperature and birth outcomes studies may introduce severe bias: A real birth cohort-based simulation Raanan Raz* Raanan Raz Selin Girgin Offer Erez Daniel Nevo

Background: Seasonality is typically controlled for to mitigate potential confounding by seasonally varying variables in environmental epidemiology research. We aimed to illustrate that correctly specifying the seasonality variable is crucial for effectively controlling confounding by seasonality in the context of prenatal temperature exposure and preterm birth.

Methods: We conducted a simulation study based on a real cohort of 131,599 births in Southern Israel, 2005-19. Weekly mean temperature exposures throughout pregnancy and last menstrual period date (LMP) were taken from the original cohort, while gestational age at birth was simulated using a Cox model under four causal scenarios: no seasonal confounding and no effect of temperature; seasonal confounding only; causal effect of temperature only; and seasonal confounding and a causal effect. Within each scenario, we compared four seasonality-adjustment approaches: no adjustment; fixed birthdate-based adjustment; fixed LMP-based adjustment; and time-varying seasonal adjustment. Finally, we compared these methods using our original cohort analysis to examine their divergence in real epidemiological study settings.

Results: Birthdate-based adjustment induced strong collider bias across all scenarios and in the real study setting. In the absence of seasonal confounding, the other three adjustment methods were comparable and produced valid estimates. In the presence of seasonal confounding, however, fixed LMP-based adjustment was inferior to the use of a time-varying seasonal covariate.

Conclusion: Birthdate-based seasonal adjustment in studies of temperature and birth outcomes may introduce severe collider bias and should be avoided, particularly when examining outcomes strongly associated with the duration of pregnancy.



Health Disparities

Hypertensive Disorders of Pregnancy and Black–White Racial Disparities in Severe Maternal Morbidity Rashida S. Smith-Webb* Rashida S. Smith-Webb Samantha E. Parker Martha M. Werler Christina D. Yarrington M. Maria Glymour Collette N. Ncube

Background: Limited research has examined the contribution of hypertensive disorders of pregnancy (HDP) to racial disparities in severe maternal morbidity (SMM); however, quantifying the role of HDP more precisely could help prioritize strategies to reduce disparities in SMM. We used mediation analysis to estimate the contribution of HDP to Black–White racial disparities in SMM.

Methods: We identified Black and White birthing people aged 12–55 years with deliveries in Massachusetts from 1998 to 2021 using the Pregnancy to Early Life Longitudinal Data System (N = 1,242,574). We estimated the total absolute effect of maternal race, as a proxy for exposure to racism, on SMM using generalized linear models, and applied G-estimation of a structural nested mean model to estimate the counterfactual disparity measure for the direct effect. We then calculated the proportion of the Black–White racial disparity in SMM that could be eliminated by preventing all HDP and severe HDP, separately.

Results: Black birthing people had a higher rate of SMM than White birthing people (114.0 vs. 50.4 per 10,000 in-hospital deliveries), corresponding to an excess of 63.6 events per 10,000 in-hospital deliveries (95% confidence interval [CI]: 57.9, 69.3). Under complete prevention of all HDP, the SMM disparity was reduced to 38.4 events per 10,000 in-hospital deliveries (95% CI: 33.4, 44.8), suggesting that 39.7% of the absolute Black–White racial disparity in SMM could be eliminated. Preventing severe HDP reduced the SMM disparity to an excess of 45.8 events per 10,000 in-hospital deliveries (95% CI: 40.2, 51.5), representing elimination of 27.9% of the disparity.

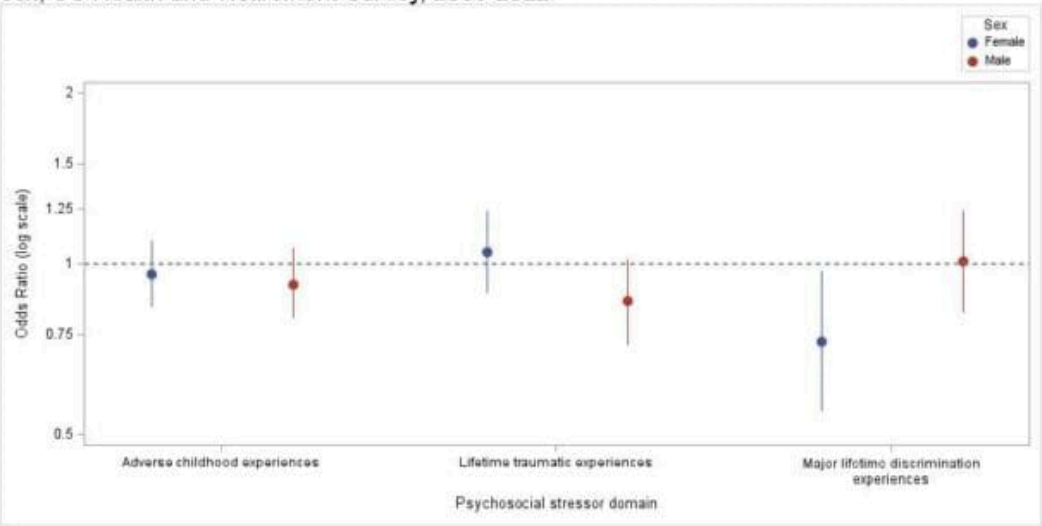
Conclusion: Preventing HDP could reduce Black–White racial disparities in SMM. These findings highlight the need for further research on preventive strategies among Black birthing people, with specific attention to effective messaging and adherence to prenatal aspirin, which has been shown to reduce the incidence of preeclampsia.

Substance Use

Psychosocial stressors and high-volume drinking in later life: Sex-specific associations in the Health and Retirement Study, 2006–2022 Suzanne G. McLone* Suzanne McLone Jillian Hebert Shelli Vodovozov Rebecca E. Graff Stacy Sterling Hélène Choquet David Kapaon Suzanna M. Martinez Scott C. Zimmerman Yvette C. Cozier M. Maria Glymour

Major lifecourse psychosocial stressors may affect the risk of high-volume drinking in later life. We used US Health and Retirement Study data from 2006–2022 (up to 9 waves per respondent), restricting the sample to respondents age ≥50 years in 2006 with no missing psychosocial data (women: n=8,630; men: n=5,952). Exposures were self-reported of three psychosocial stressors occurring prior to 2006: 1. Adverse childhood experiences (9 items); 2. Lifetime traumatic experiences (7 items), and; 3. Major lifetime discrimination experiences (7 items). Our longitudinal outcome was high-volume drinking based on NIAAA standards, but excluding heavy episodic drinking (>7 drinks/week for women; >14 for men). We ran sex-stratified mixed models with random intercepts and a logit link to assess associations between each psychosocial stressor and high-volume drinking, adjusting for sociodemographic, health, and lifestyle variables. Separate models were estimated to include stressor-by-age interactions. Ages were centered at age 50 for all models. Among women, major lifetime discrimination experiences were associated with lower odds of high-volume drinking (OR=0.73; 95% CI: 0.55–0.97) on average during follow-up. Among men, lifetime traumatic experiences were associated with lower odds of high-volume drinking (OR=0.86; 95% CI: 0.72-1.02) on average during follow-up. No stressor-by-age interactions were observed for women. There was equivocal evidence that adverse childhood experiences was associated with age-related cchange in the odds of high-volume drinking for men (interaction per decade: OR=0.91; 95% CI: 0.83-1.01). Findings suggest that certain psychosocial stressors are associated with lower high-volume alcohol use patterns in middle- and older-aged adults. Additionally, findings demonstrate that associations between psychosocial stressors and high-volume drinking in later life differ by sex and stressor domain and may change from middle age to older adulthood.

Figure 1. Associations between life course psychosocial stressors and high-volume drinking by sex, US Health and Retirement Survey, 2006-2022



Adjusted for: Year, age, race, ethnicity, education, marital status, smoking status, income, assets, US Census Division, religion, lagged self-rated health, and lagged self-rated memory.

Substance Use

Lifecourse frequency of heavy episodic drinking from adolescence to late midlife in NLSY79: a sequence and cluster analysis Jillian Hebert* Jillian Hebert Scott C. Zimmerman Peter Buto Anusha M. Vable Lucia Pacca Suzanna M. Martinez Rebecca E. Graff Stacy A Sterling Felicia Chi Cynthia I. Campbell M. Maria Glymour Laura Schmidt

Emerging research suggests that even small amounts of drinking affect health but this is complicated by reverse causation ("sick quitter" effects) and conflation of lifetime abstainers with former problem drinkers. Few data sources include longitudinal information on participants' use across the lifespan. Evidence regarding the health effects of heavy episodic drinking (HED) has been hampered by the complexity of characterizing lifecourse alcohol use. Sequence analysis groups thousands of individual trajectories into similar clusters, retaining substantive differences between trajectories. We used this method to capture lifecourse alcohol use.

We used 1979-2018 data from the National Longitudinal Surveys 1979 study (NLSY79), which recruited U.S. participants 14-22 years old in 1979 (N=2,732 male; N=2,871 female). NLSY79 assessed alcohol use beginning in 1982, when participants were 18+ years old. We characterized lifecourse alcohol use trajectories into three mutually exclusive HED states based on frequency in the past 30 days ([6+ drinks on one occasion]: No HED, Occasional HED [1-3 times/mo], Frequent HED [4+ times/mo]) – from ages 18-61. We used the Hamming method to calculate dissimilarity between all individuals' trajectories and agglomerative hierarchical clustering with a Ward linkage to cluster trajectories. All analyses were sex stratified.

Overall, from ages 18-61, males were more likely than females to engage in occasional (15% vs 8%) or frequent (11% vs 3%) HED. We found evidence for 5 clusters for males and 7 clusters for females, characterized by differences in timing of HED (Fig 1). While several clusters had similar patterns of HED after age 50 (Fig 1, females 1-2; 3-4), these clusters differed in early-life drinking patterns.

Confining analyses to current alcohol use may miss important lifecourse risk factors for health in older adults. Measuring lifecourse trajectories of alcohol use using sequence analysis can inform problems with reverse causation.

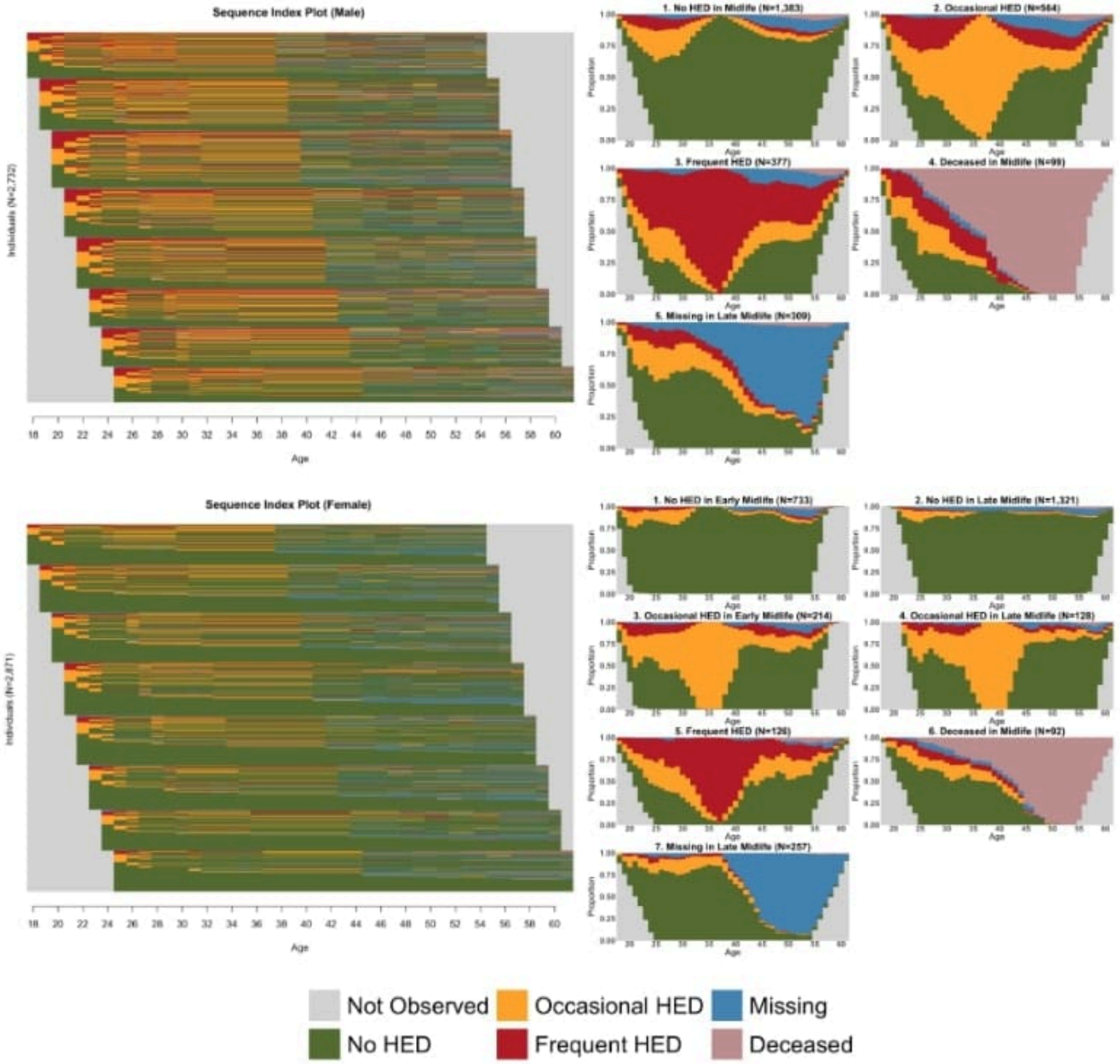


Figure 1 Index plots and chronograms of alcohol binging trajectories across the lifecourse, by sex

Notes: Index plots show individual trajectories for each participant from ages 18 to 61 (unclustered). Chronogram plots show the proportion of each binging status at every age for recommended clusters (5 for males and 7 for females) based on Hamming dissimilarity matrix and agglomerative hierarchical clustering with Ward linkage. The "Not Observed" sequence analysis state refers to ages when participants were not in the survey. The "Missing" sequence analysis state includes participants who were dropped from the survey, lost from the survey, refused to respond to the survey, or were unavailable to respond to the survey that year.

Substance Use

Alcohol use from adolescence into adulthood: the role of state-level alcohol policy and contextual factors on alcohol use trajectories Lynsie Ranker* Lynsie Ranker Ziming Xuan

While we know familial and environmental forces influence adolescent alcohol initiation and use, the literature is limited regarding the role of such factors experienced in adolescence on drinking patterns into adulthood. We examined associations between several contextual factors and past 30-day drinking frequency trajectories from age 12-35 years within the National Longitudinal Survey of Youth (1997) cohort. Specifically, we assessed the role of: a) the stringency of the state policy environment (measured via Alcohol Policy Scale, APS), b) parenting style, c) youth mental health, and d) recent stressful life events (e.g., parental divorce, crime victimization, homelessness, and family member hospitalization, incarceration, or death). Five drinking trajectories were identified within the cohort (N=8,984) using latent class growth curve modeling: high frequency (12.0%), moderate use surrounding age 21 (17.5%), late escalating (19.4%), no/infrequent (21.4%), and consistent low frequency (29.6%). In multinomial models with low frequency as the comparison trajectory, a 10-unit higher APS score was associated with reduced odds of moderate drinking membership (adjusted OR [aOR]=0.82, 95%CI 0.72, 0.93) after adjustment for covariates. Associations between APS score and other trajectory memberships were null. Similar effect magnitudes were seen for the influence of parenting style and youth mental health on trajectory membership. Experiencing stressful events in early adolescence had the largest effect magnitudes for high frequency drinking (aOR 1.20, 95%CI 1.04, 1.39) and moderate drinking (aOR 1.17, 1.02, 1.35) memberships. Results demonstrate the distinct roles of stringent state alcohol policy, parenting practices, and positive youth mental health in reducing risk of normative drinking (e.g., limiting escalation prior to age 21). However, stress and upheaval increase the risk of drinking trajectories characterized by early initiation and high frequency.

Substance Use

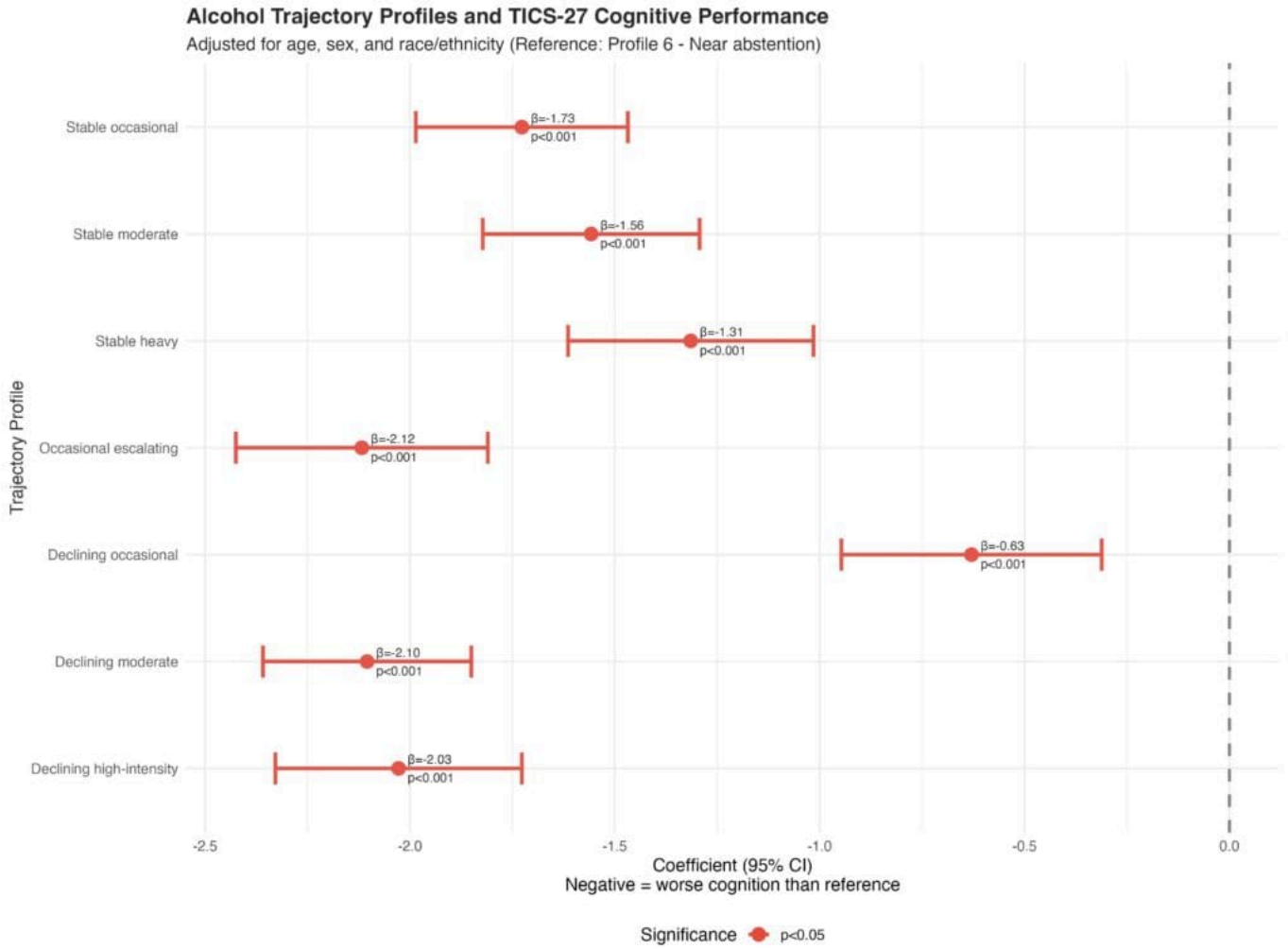
Lifecourse alcohol use profiles and cognitive health among older US adults Jonathan Platt*
Jonathan Platt Katrina Kezios Sarah McKetta

For many older adults, a lifetime of alcohol consumption may influence cognitive health. Despite substantial lifecourse variability in drinking behavior, research often relies on cross-sectional designs or recent recall periods among older populations, and is thus unable to account for reverse causation, prior drinking history, and other key sources of bias. This analysis aimed to identify distinct lifecourse trajectories of alcohol use behaviors and estimate their longitudinal associations with cognitive health in older adulthood.

The study sample included 14 waves (1982-2018) of the National Longitudinal Survey of Youth 1979 Cohort (n=12,686, ages 18–61). Latent profile analysis of six person-level alcohol use behaviors (i.e., means and linear slopes for binge drinking frequency, drinking days/week, and drinks/day) identified distinct drinking trajectories over time. Cognitive health was measured using the Modified Telephone Interview for Cognitive Status (TICS-M) (range=0-27). Continuous TICS-M scores were regressed on drinking profiles, adjusting for sex, race/ethnicity, and age.

Eight drinking profiles were identified: near abstention (7.4%), stable occasional use (19.8%), declining occasional use (6.9%), stable moderate use (17%), to stable heavy use (9.1%), declining moderate use (23.4%), high-intensity declining use (8.6%), occasional escalating use (7.8%). Compared with the near abstention group, all alcohol use trajectories were associated with significantly lower TICS-M scores. The largest deficits were seen for occasional escalating ($\beta = -2.12$, 95% CI: -2.42, -1.81), declining moderate ($\beta = -2.10$, 95% CI: -2.36, -1.85), and declining high-intensity use ($\beta = -2.03$, 95% CI: -2.33, -1.73).

The cognitive consequences of alcohol use depend on the timing, intensity, and direction of change across the lifecourse. Conceptualizing alcohol use as a dynamic, heterogeneous process will inform prevention efforts to maximize cognitive health in aging populations.


Alcohol Trajectory Profiles and TICS-27 Cognitive Performance
Adjusted for age, sex, and race/ethnicity (Reference: Profile 6 - Near abstention)
Trajectory Profile
Stable occasional
Stable moderate
Stable heavy
Occasional escalating
Declining occasional
Declining moderate
Declining high-intensity
β=-1.73
p<0.001
β=-1.56
p<0.001
β=-1.31
p<0.001
β=-2.12
p<0.001
β=-0.63
p<0.001
β=-2.10
p<0.001
β=-2.03
p<0.001
-2.5
-2.0
-1.5
-1.0
-0.5
0.0
Coefficient (95% CI)
Negative = worse cognition than reference
Significance
p<0.05

Substance Use

Resilience to Alcohol Use Disorder Despite High Genetic Risk: Evidence from a Nationally Representative U.S. Sample Haitao Zhang* Haitao Zhang

Background: Alcohol use disorder (AUD) is strongly influenced by genetic liability, yet many individuals at elevated genetic risk never develop the disorder. Identifying phenotypic characteristics associated with resilience under high genetic risk may clarify non-genetic factors that differentiate outcomes among vulnerable individuals.

Methods: Data were drawn from the National Epidemiologic Survey on Alcohol and Related Conditions–III (2012–2013). Analyses were restricted to genotyped current or former drinkers in the top quartile of AUD polygenic risk scores. Resilience was defined as absence of lifetime AUD within this high-risk group. Survey-weighted logistic regression models were estimated using SUDAAN with domain analysis to account for the complex sampling design. To reduce concerns about reverse causation, primary predictors were limited to early-life adversity, ages of substance initiation, and adult characteristics considered relatively stable or behaviorally anchored, including religious service attendance. Models adjusted for genetic ancestry principal components and key sociodemographic factors.

Results: Among 5,141 high–genetic-risk drinkers (weighted N ≈ 31.9 million), older age (per year: OR = 1.02, 95% CI 1.01–1.03) and female sex were consistently associated with higher odds of resilience. Greater childhood trauma (OR = 0.55) and earlier initiation of alcohol, tobacco, or other drugs were strongly associated with lower odds of remaining AUD-free. Religious or spiritual importance and binary indicators of religious service attendance were not independently associated with resilience. More frequent religious service attendance showed a modest positive association (OR = 1.22, 95% CI 1.00–1.49) with resilience in minimally adjusted models, but this association was attenuated after adjustment for sociodemographic characteristics. Several sociodemographic factors, including region of residence, were also associated with resilience.

Conclusions: In this nationally representative sample of individuals with high genetic liability for AUD, belief-based religiosity and some commonly studied early-life factors were insufficient to independently distinguish resilience. Earlier substance initiation and childhood trauma emerged as robust correlates of non-resilience, while regular participation in structured adult social contexts showed limited and context-dependent associations. These findings highlight the importance of developmentally anchored behavioral exposures over attitudinal characteristics in buffering genetic risk for AUD.

Global Health

Evaluating Waning Vaccine Effectiveness: Methods Applied to Rotavirus Vaccine in Low-Resource Settings Using Observational Data Adiba Hassan* Adiba Hassan Eleanor Burnett Jacqueline E. Tate Umesh Parashar

Background: Accurately assessing waning vaccine effectiveness (VE), or declining VE post-vaccination, is crucial for public health policy and implementation. However, statistical approaches have relied on simulated or trial data with limited application to real-world data. We applied two survival-based methods to detect waning VE using observational rotavirus data and compared findings with traditional approaches.

Methods: We pooled data from 22 low- and middle-income countries with test-negative case-control VE studies including 13,863 children aged <2 years hospitalized for acute diarrhea with confirmed rotavirus vaccination status. Case-patients had rotavirus-positive stool tests and control-patients were rotavirus-negative. VE was assessed for a period of 18-months following vaccination by first fitting a logistic model (1-odds ratio) at 3-month time intervals since vaccination and a Cox model for a fixed VE estimate (1-hazard ratio). We then varied the hazard ratio over time using: 1) Scaled Schoenfeld residuals averaged over time categories, and 2) Time-vaccine interaction term, then plotted using a LOESS curve. All models were adjusted for country and stratified by age group at hospitalization (<1 vs. 1 to <2 years) to account for confounding and effect modification, respectively. Logistic models were additionally adjusted for continuous age at hospitalization.

Results: Waning was identified only in age-stratified logistic model among children aged 1 to <2 years, while the Cox model didn't differ in VE by age groups. Conversely, Schoenfeld residuals and time-vaccine interaction methods identified comparable waning VE among both age groups. VE in children <1 year peaked at 59% at 6 months of age and waned to 21% by 11 months; in children 1 to <2 years, VE waned by >40 percentage points.

Conclusions: Both time-varying survival frameworks detected waning VE compared with traditional approaches. To improve VE accuracy using observational data, investigators should incorporate time-varying confounders into these frameworks to further differentiate effects of waning from such biases.

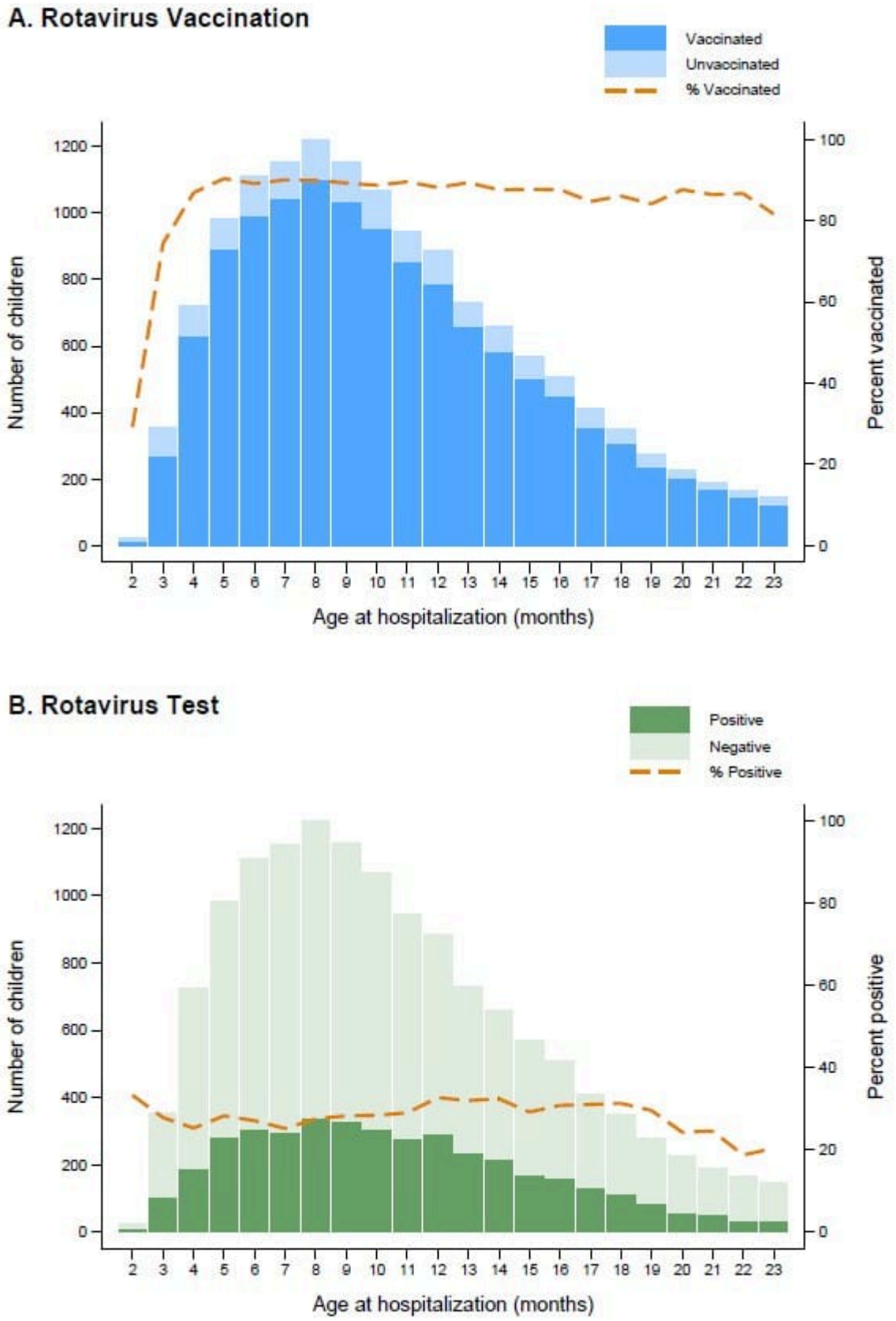


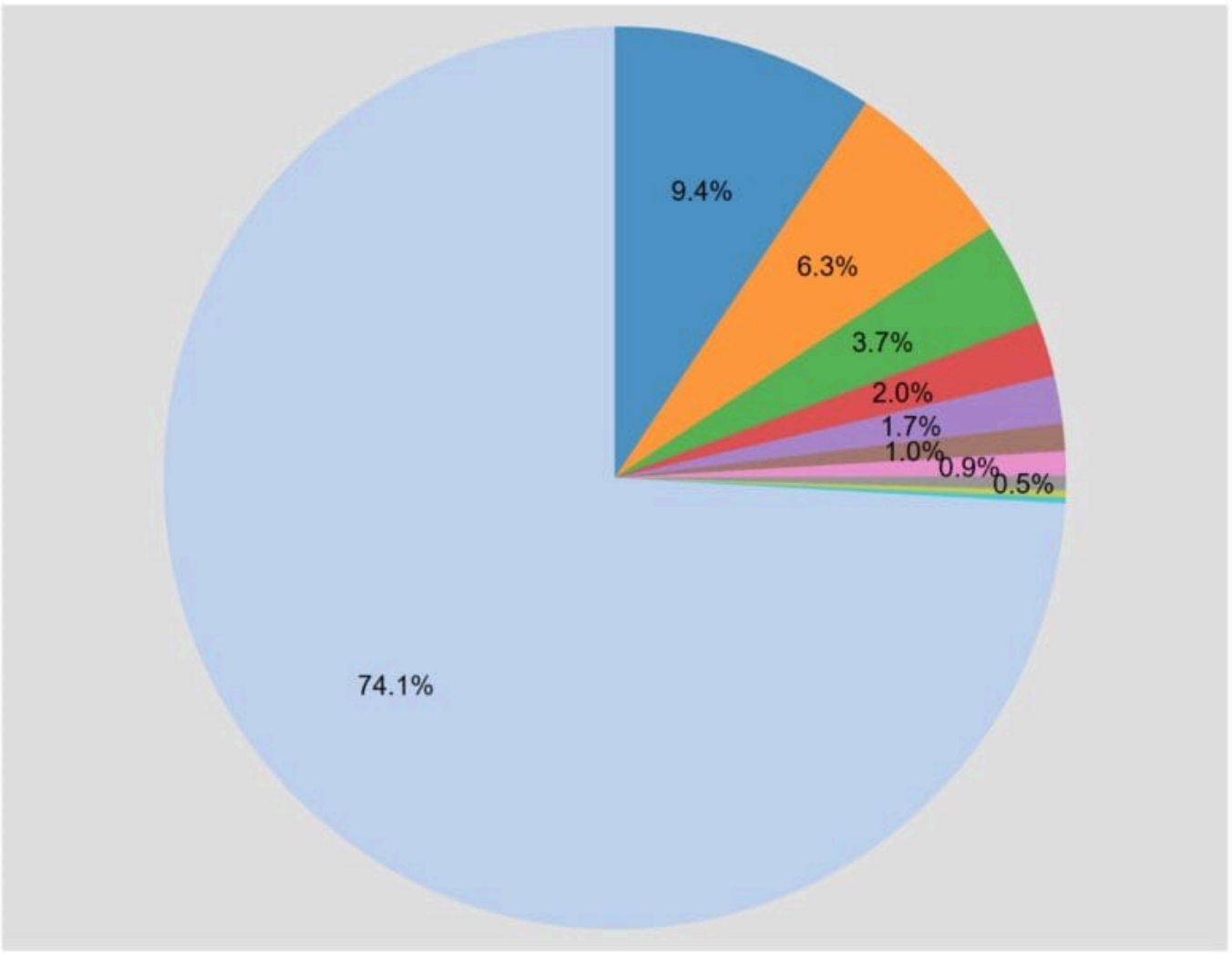
Figure 2. Number and proportion of children aged <2 years (A) fully vaccinated within 10-24 weeks of age and (B) tested for rotavirus at hospitalization.

Infectious Disease

Etiology-specific population attributable fractions for Acute Febrile Illness in the Peruvian Amazon: Findings from the first three years of the RIVERA case-control study, 2021 – 2024

Josh Colston* Josh Colston Maribel Paredes Olórtegui Francesca Schiaffino Pablo Peñataro Yori Margaret N. Kosek

Acute febrile illness (AFI) is a major cause of primary care-seeking in the Peruvian Amazon and across the Tropics and caused by a range of bacterial, viral, and parasitic pathogens. Due to diagnostic limitations AFI cases are seldom attributed to specific etiologies, leading to a large diagnostic gap. RIVERA is a health facility-based prospective case-control surveillance study conducted in and around the Peruvian city of Iquitos. 1,898 AFI cases were enrolled and matched 1:1 with afebrile controls. Baseline and follow-up (3-4 weeks later) questionnaires were administered, and blood, saliva, and nasal swab samples collected and tested for 36 pathogen targets by PCR. Clinical characteristics, risk factors, and pathogen detections were compared using odds ratios (ORs) and population attributable fractions (PAFs) from univariate conditional logistic regression models. Statistically and clinically significant variables were included in a final, multivariable models, from which adjusted ORs (aORs) and PAFs (aPAFs) were derived. AFI cases had increased odds of recent travel by river (OR=7.72 [95% CI: 4.99, 11.95]), or other mode (4.68 [1.83, 11.94]), and of reporting ticks (2.58 [1.61, 4.14]) but not fleas (0.82 [0.49, 1.36]) on their bodies, and bats (1.65 [1.29, 2.11]) but not rats (1.14 [0.97, 1.34]) in their homes. The most prevalent pathogen in the study population was SARS-CoV-2 followed by dengue virus (DENV), Plasmodium, influenzas B and A, cytomegalovirus (CMV) and Oropouche virus (OROV), all of which were detected in asymptomatic controls as well as AFI cases. Over a third of the AFI burden in this setting is attributable to just five pathogens – DENV, OROV, SARS-CoV-2, Plasmodium spp. and CMV – after adjustment for temporal variation, background asymptomatic carriage and various comorbidities, risk factors and confounders. A large fraction of the AFI burden remains unattributed despite the extensive, contextually tailored panel of pathogen tested.



Target	OR (95% CI)	PAF% (95% CI)
DENV	8.82*** (5.67, 13.70)	9.40 (8.74, 9.83)
Plasmodium spp.	8.67*** (5.08, 14.79)	6.26 (5.68, 6.59)
SARS-CoV-2	1.75*** (1.34, 2.29)	3.72 (2.21, 4.87)
CMV	2.67*** (1.61, 4.40)	1.99 (1.21, 2.46)
Influenza A	1.56* (1.01, 2.40)	1.71 (0.06, 2.78)
OROV	2.42* (1.23, 4.74)	0.98 (0.32, 1.32)
HIV	2.67* (1.04, 6.81)	0.87 (0.06, 1.18)
Leptospira spp.	3.50* (1.15, 10.63)	0.53 (0.10, 0.67)
Influenza B	1.04 (0.69, 1.57)	0.24 (-2.52, 2.08)
Other etiology	1.18 (0.67, 2.09)	0.21 (-0.68, 0.71)
Unattributed	-	-

Global Health

Household Food Insecurity and child anthropometry, cognition and behavioral outcomes: Insights from the MAASTHI Birth Cohort in India Giridhara Rathnaiah Babu* Giridhara Rathnaiah Babu Deepa Ravi Zaineb Attarwala Sumathi Swaminathan Debarati Mukherjee

Background: Globally, 2.4 billion people are facing moderate or severe food insecurity, which is a critical social determinant of child health. However, its impact in urban India remains understudied. We examined longitudinal associations between household food insecurity (measured by FAO's FIES) and child health outcomes in a birth cohort in urban Bengaluru, India. We hypothesized that higher food insecurity would be associated with poorer growth and psychosocial outcomes in early childhood.

Material and Methods: We analyzed data from 985 mother–child dyads (child age: 6.6 ± 1.1 years) in the Maternal Antecedents of Adiposity and Studying the Trans-generational role of Hyperglycaemia and Insulin (MAASTHI) cohort. Household food insecurity in 2023 was measured using the FIES, with moderate and severe insecurity classified according to FAO thresholds. Child outcomes assessed at the 2024–25 follow-up included anthropometry (weight-for-age z-score [WAZ]) and behavioral difficulties (internalizing and externalizing subscales of the Strengths and Difficulties Questionnaire). We used multivariable linear regression adjusting for maternal and paternal education and occupation, household socioeconomic status, family size, marital status, maternal social support, and the child's school type.

Results: Moderate and severe food insecurity prevalence was 20.5% and 3.6%, respectively. After adjustment, a higher FIES score was significantly associated with lower WAZ (β = –0.28 per unit; 95% confidence interval [CI]: –0.54, –0.01; p = 0.03). Higher food insecurity was also associated with greater behavioral difficulties: internalizing score (β = 0.042; 95% CI: 0.012–0.073; p = 0.007) and externalizing score (β = 0.030; 95% CI: 0.001–0.060; p = 0.046).

Conclusion: In this urban cohort, food insecurity was common and prospectively linked to undernutrition and adverse behavioral outcomes. Urban households experienced high levels of food insecurity. The association between higher FIES scores and lower weight-for-age underscores the need for targeted urban interventions to address undernutrition. Additionally, the significant associations with adverse behavioural outcomes highlight the impact of food insecurity on children's mental well-being beyond physical growth.

Global Health

The Association between Minimum Dietary Diversity and Unhealthy Food Consumption among Women in Ghana David Owiredu* David Owiredu Penias Tembo Sherry Price Monique Brown James Hebert

Background: The Minimum Dietary Diversity for Women (MDD-W) is a proxy for micronutrient adequacy, but its association with diet quality in settings undergoing a nutrition transition is underexplored. We examined the association between MDD-W and consumption of unhealthy foods among females aged 15-49 years in Ghana.

Methods: We analyzed cross-sectional data from the 2022 Ghana Demographic and Health Survey. Using the Food and Agriculture Organization's definition, meeting MDD-W threshold was operationalized as the consumption of ≥5 of 10 food groups in the prior 24 hours. Unhealthy food consumption was defined as the intake of sweetened beverages, sugary snacks, fried foods, or processed packaged foods. We used 1:1 nearest-neighbor propensity score matching with a caliper of 0.1 on age, education (none, primary, secondary, higher), household wealth (asset-based quintiles), marital status, region, rural/urban residence, employment, and media exposure, followed by logistic regression in the matched sample. E-values were calculated to assess sensitivity to unmeasured confounding.

Results: Among 15,008 women, 47.9% met the MDD-W threshold, and 7.5% reported consuming at least one unhealthy food. Consumption of starchy staples (98.9%) and green vegetables (71.8%) was high, but intake of dairy products (15.4%) was low. Matching produced 5,846 balanced pairs, and achieving MDD-W was associated with higher odds of consuming unhealthy foods (OR: 1.33, 95% CI: 1.15-1.54). Based on the E-value, an unmeasured confounder would need to be associated with both the exposure and outcome by an odds ratio of at least 1.99 to fully account for the observed association.

Conclusion: Women who achieved minimum dietary diversity were more likely to consume unhealthy foods. Our findings suggest that dietary diversity alone may not adequately capture overall diet quality in this setting. However, given the moderate E-value, residual confounding cannot be ruled out.

Global Health

Crisis Methods for Crisis Settings: Flexing Our Randomised Controlled Trials to Flexibly Test Behavioural Interventions in War Sydney Tucker* Sydney Tucker Susan Hillis Oliver Ratmann Seth Flaxman Jamie Lachman Nicole Baldonado Nisreen Hawatmeh Maher Abu Lail

Background

Two-thirds of the world's children live in conflict-affected countries. War-time threats present challenges for rigorously evaluating interventions – including loss-to-follow-up and ethical challenges such as urgency to deliver potentially beneficial interventions without delay. Epidemiologists must develop rigorous yet flexible methodologies to identify effective solutions to protect children in war.

Methods

We conducted a two-armed parallel-group randomised controlled trial among N=350 displaced Palestinians in Jordan. We utilised rolling recruitment with a randomised roll-out design. Participants were 1:1 randomised to Hope Groups – a mental health, parenting, and violence prevention support group intervention – or waitlist control. The primary analysis estimates the effectiveness of Hope Groups post-intervention on parent mental health and violence against children. Our primary model is a two-level generalised linear mixed-effects model nesting person within timepoint to estimate incidence rate ratios, with confidence intervals estimated via wild bootstrapping. Building on theory from Rolled-Entry Matching, we conduct a secondary analysis estimating the intervention's effects at 3, 6, and 12 months follow-up, comparing previous intervention participants to newly enrolling untreated participants at each timepoint.

Results

We observed high response rates: 91.2% of participants completed endline surveys. After the intervention, the control arm's parental depression and anxiety rate was 1.85 (95%CI=1.52,2.17) times the rate in the intervention arm. Similarly, the control arm's rate of violence against children was 1.41 (95%CI=1.16,1.72) times the intervention arm's rate. Our innovative long-term follow-up design shortened control arm wait-times by 4-8x compared to traditional RCT approaches. Follow-up results are pending and will be reported at SER.

Discussion

In an era of polycrisis, developing innovative impact evaluation methods is a public health priority.

Methods/Statistics

Causal Inference in Real-World Dementia Research: A Systematic Review Yi Yang* Yi Yang Jiamin Du Hongen Ma Ivan Koychev Vanessa Raymont

Background: Dementia presents major challenges for causal inference due to its multifactorial aetiology, long preclinical phase, and heterogeneous progression. Randomized controlled trials are often impractical or unethical for many dementia-related exposures, leading to heavy reliance on observational studies. However, traditional observational designs, particularly prevalent exposure designs, are highly susceptible to bias, including survivor bias, misaligned time zero, time-varying confounding, and poorly defined interventions. To address these limitations, dementia research has increasingly adopted causal inference frameworks that aim to emulate hypothetical interventions and improve causal interpretability. This systematic review critically evaluates how causal inference methods are applied in observational dementia research, assesses their methodological rigor, and identifies emerging trends and gaps.

Methods: To address the urgent need for a field-level evaluation of how causal inference methods are applied in dementia research, an issue not amenable to single empirical studies, we conducted a systematic review. Following PRISMA guidelines, we searched MEDLINE, EMBASE, Web of Science, PsycINFO, Scopus, and the Cochrane Library for studies published between 1960 and 2024. Eligible studies were observational in design and explicitly applied causal inference methods to investigate dementia-related outcomes, including cognitive decline, disease onset or progression, mortality, and quality of life. Data extraction captured study characteristics, causal frameworks, assumptions, analytical methods, and reporting practices. Risk of bias was assessed using ROBINS-I. Findings were synthesized narratively, with meta-analysis conducted where methodological homogeneity permitted.

Results: From 11,009 records identified, 345 studies were included. Mendelian randomization was the most used causal method, followed by marginal structural models and instrumental variable analyses, with increasing use of hybrid approaches integrating machine learning. Substantial heterogeneity was observed in the definition of causal estimands, handling of time-varying confounding, and transparency of assumptions. Risk of bias varied widely, with frequent concerns related to residual confounding, weak instruments, selection bias, and limited sensitivity analyses. Despite these limitations, several studies demonstrated the potential of causal methods to address questions not amenable to randomized trials.

Conclusions: Causal inference methods offer essential tools for strengthening causal interpretation in dementia research where experimental evidence is limited. However, their application remains inconsistent. Greater alignment with explicit causal frameworks, improved reporting standards, and more rigorous sensitivity analyses are needed to enhance validity and reproducibility. This review highlights both the promise and current limitations of causal inference in dementia research and informs future methodological development.

Systematic review registration PROSPERO (CRD42024619228).

Causal Inference

Graphical insights into exposure-induced mediator–outcome confounders in causal mediation analysis Etsuji Suzuki* Etsuji Suzuki Tomohiro Shinozaki Eiji Yamamoto

As has been well appreciated in the causal mediation literature, the total effect can be decomposed into natural direct and indirect effects in the counterfactual framework. If certain assumptions about confounding are met, we can use the so-called mediation formula to identify these effects under the nonparametric structural equation models with independent errors (NPSEM-IE). However, natural direct and indirect effects have been criticized because these rely on a specific cross-world quantity, and the so-called cross-world independence assumption is not empirically verifiable. In this context, previous studies have highlighted challenges posed by exposure-induced mediator–outcome confounders for identifying natural direct and indirect effects. In this presentation, we discuss the implications of exposure-induced mediator–outcome confounders for causal mediation analysis, providing visualized explanations using causal directed acyclic graphs (DAGs). To achieve this, we incorporate potential outcomes and error terms into the causal DAGs under NPSEM-IE. Then, we visually demonstrate that the absence of the exposure-induced mediator–outcome confounder is a sufficient but not a necessary condition for identification of the natural direct and indirect effects. Indeed, if there is an exposure-induced mediator–outcome confounder, the natural direct and indirect effects are not generally identified irrespective of whether data are available on it, except under strong assumptions, such as no interaction between the exposure and mediator at the individual level. Furthermore, we identify additional settings in which the natural direct and indirect effects can be identified even in the presence of an exposure-induced mediator–outcome confounder. Our visual illustration provides clear insight into the implications of exposure-induced mediator–outcome confounders for causal mediation analyses.

Causal Inference

Characterizing the Causal Structure of Lead Time Bias in Screening Studies with Causal Diagrams and Causal Estimands Matthew Coates* Matthew Coates Onyebuchi Arah

Lead-time bias refers to the phenomenon that comparing post-diagnosis survival time between screen-detected and symptom-detected cancers can create the appearance of longer survival in the screened group, even without a true survival benefit, because screening reduces the lead time between onset and diagnosis. In prior literature, lead-time bias has been discussed as confounding, as information bias due to measurement error, and as selection bias. Despite being discussed in great detail, particularly in the cancer literature, lead-time bias has not been commonly described using tools from formal causal inference frameworks, such as counterfactual language and causal diagrams. Using causal diagrams and causal estimands that specify the definition, timing, and measurement of the target population, exposure, and outcome, we describe the mechanisms underlying lead-time bias. Randomized trials can be used to avoid lead-time bias through a combination of (1) creating an often-implicit target population that includes people without the disease, (2) balancing time since disease onset between treatment and control arms, and (3) aligning the start of follow-up in the arms. Some analyses susceptible to lead-time bias, including trial-based analyses, restrict the study population to individuals who are diagnosed, perhaps implying a target population of those who are diagnosed who may benefit from screening. Identifying and estimating the effect of screening in this target population, defined after intervention, is challenging and requires data beyond those diagnosed. Explicitly defining survival since disease onset as the outcome clarifies the measurement error that arises when using time since diagnosis and which generates lead-time bias. We use causal diagrams to demonstrate that multiple other biasing mechanisms, including confounding and selection bias, often co-occur in studies subject to lead-time bias.

Causal Inference

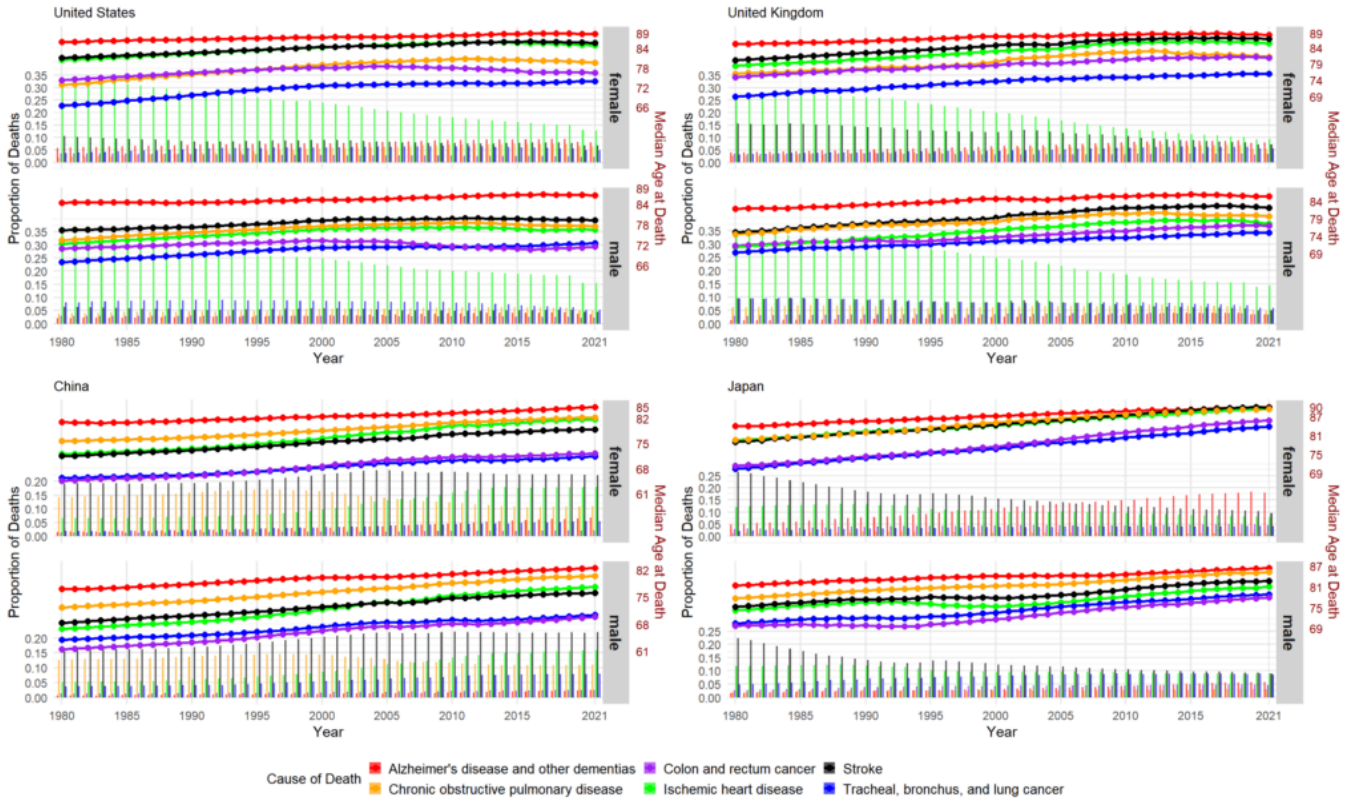
Age-at-Death Patterns as a Source of Heterogeneity in Mendelian Randomization Studies Across Countries Hong Tang* Hong Tang Catherine Mary Schooling

Mendelian randomization (MR) is a powerful tool for estimating the causal effect of exposure on outcomes because it is less susceptible to confounding compared to conventional observational study. However, MR studies often recruit middle-aged and older adults, whose survival to recruitment is affected by genetic endowment and occurrence of the outcome or competing risk of the outcome, which can introduce internal bias due to collider selection. In addition, disease-specific age-at-death patterns may vary by country and over time, making MR estimates susceptible to net-external bias related to the transportability of effect estimates, creating apparent effect modification. These two types of selection bias are less considered in MR study.

To address this gap, we compared cause-specific age-at-death patterns over 40 years to identify potential sources of heterogeneity in MR effect estimates across countries. Since this bias is especially concerning in multi-country MR studies with differing age-at-death patterns, we focused on countries with large publicly available genome-wide association studies. Figure 1 compares cause-specific median ages at death and the proportion of deaths across four countries. In the United States and the United Kingdom, individuals tend to die at an older age from stroke compared to chronic obstructive pulmonary disease (COPD), whereas in China and Japan, the pattern is reversed, with higher median ages at death from COPD than from stroke. These country-specific differences in age-at-death patterns may contribute to heterogeneity in MR estimates for the same exposure-outcome relationships.

Age-at-death patterns may vary due to country-specific factors, such as healthcare systems or environmental exposures, which could influence individual survival status and, consequently, who is available for recruitment in MR studies. We explore how differential age-at-death patterns may contribute to heterogeneity in MR studies conducted across countries.

Figure 1: Median age at death by sex from six major causes in four countries from 1980 to 2021, along with the proportion of deaths from each of these causes during the same period



Causal Inference

Thinking Beyond Simulation: Benchmarking as an Empirical Tool for Method Comparison
Haidong Lu* Haidong Lu Kaicheng Wang Lindsey Rosman

Background and Objective: Simulation studies dominate methodological comparisons of propensity score estimators, yet their conclusions depend heavily on design choices that may not reflect the complexity of real-world data. In contrast, benchmarking, defined as comparing observational estimates against results from randomized trials addressing the same question, offers an empirical alternative for evaluating causal methods. We used the benchmarking approach to assess whether machine learning-based propensity score estimation outperforms conventional logistic-regression method in practice.

Methods: Using electronic health record data from the Veterans Affairs health system, we emulated a target trial comparing sacubitril–valsartan with angiotensin-converting enzyme inhibitors and angiotensin receptor blockers on all-cause mortality among patients with heart failure and implantable cardioverter-defibrillators between 2016 and 2020. We compared three propensity score approaches: (1) logistic regression with pre-specified confounders; (2) generalized boosted models (GBM) using the same pre-specified confounders; and (3) GBM with expanded covariates and automated feature selection. Observational effect estimates were benchmarked against results from an existing randomized trial addressing the same research question.

Results: The logistic regression–based propensity score approach yielded estimates closest to the randomized trial (HR = 0.93, 95% CI: 0.61–1.42 vs. trial HR = 0.81, 95% CI: 0.61–1.06; 23-month RR = 0.86, 95% CI: 0.57–1.24). Despite superior predictive performance, GBM with pre-specified confounders showed no improvement over logistic regression (HR = 0.97, 95% CI: 0.68–1.37; RR = 0.96, 95% CI: 0.89–1.98). In contrast, GBM with expanded covariates and data-driven feature selection substantially increased bias (HR = 0.61, 95% CI: 0.30–1.23; RR = 0.69, 95% CI: 0.36–1.04).

Conclusions: Machine learning–based propensity score estimation does not inherently outperform conventional approaches and may exacerbate bias due to overfitting or causal model misspecification. These findings underscore the value of benchmarking against randomized trials as an innovative and important empirical tool for comparing causal inference methods using real-world data. Rather than serving as stand-alone solutions, machine learning algorithms should be embedded within principled causal frameworks, such as doubly robust estimators with cross-fitting, while retaining explicit, subject-matter–driven confounder specification.

Causal Inference

Causal effects of plant-based diet indices on incident obstructive sleep apnoea: TMLE and AIPW analyses in UK Biobank Yohannes Adama Melaku* Yohannes Adama Melaku Zegeye Abebe Abitew Tefera Mekonnen Anteneh Mengist Dessie Robert Adams Yohannes Adama Melaku

Background: Plant-based dietary patterns may reduce obstructive sleep apnoea (OSA) risk through pathways related to adiposity, inflammation, and cardiometabolic health, but causal evidence remains limited. We estimated the causal effects of healthy, overall, and unhealthy plant-based diet indices on incident OSA in UK Biobank.

Methods: We analysed 114,990 UK Biobank participants, with incident OSA identified via linked hospital admissions and primary care records (1,438 cases). Exposures were three plant-based diet indices—healthy plant-based diet (hPDI), overall plant-based diet (PDI), and unhealthy plant-based diet (uPDI)—evaluated using percentile-based contrasts (>25% vs ≤25%, >50% vs ≤50%, and >75% vs ≤75%). We estimated causal risk ratios (RRs) using targeted maximum likelihood estimation (TMLE) and augmented inverse probability weighting (AIPW), adjusting for baseline sociodemographic and behavioural confounders.

Results: Higher adherence to healthier plant-based diets was associated with lower incident OSA risk. For hPDI, high versus low adherence was associated with reduced risk at >25% (AIPW RR 0.77, 95% CI 0.68–0.86; TMLE RR 0.76, 0.68–0.86) and >50% (AIPW RR 0.88, 0.79–0.99; TMLE RR 0.78, 0.80–0.98), with attenuation at >75% (AIPW RR 0.88, 0.76–1.03; TMLE RR 0.88, 0.75–1.02). For PDI, high adherence was consistently protective at >25% (both methods RR 0.82, 0.73–0.92) and >50% (AIPW RR 0.86, 0.78–0.96; TMLE RR 0.86, 0.77–0.95), with weaker evidence at >75% (AIPW RR 0.89, 0.78–1.02; TMLE RR 0.88, 0.77–1.01). In contrast, uPDI showed no evidence of benefit and suggested a trend toward increased risk at higher thresholds (e.g., >75%: AIPW RR 1.11, 0.98–1.26; TMLE RR 1.13, 0.99–1.27).

Conclusions: Using two doubly robust causal estimators, greater adherence to healthy and overall plant-based diets was associated with lower incident OSA risk, whereas adherence to an unhealthy plant-based diet was not protective and may increase risk at higher levels. These findings highlight the importance of diet quality within plant-based eating patterns for OSA prevention.

Health Disparities

Estimating causal effects of hypothetical interventions to reduce health inequality Lauren Zalla* Lauren Zalla Catherine Lesko Jessie Edwards Stephen Cole John Jackson

Modern estimation of causal effects has focused on health outcomes, rather than on health inequality. We propose a framework for estimating the effects of hypothetical interventions on health inequality, as well as on population-average health, using observational data. First, to build intuition, we define three causal mechanisms through which an intervention can affect inequality: by targeting a determinant of health that has a different average causal effect on the outcome across social groups; by altering the distribution of a determinant of health across social groups; and/or by allocating the intervention according to modifiers of the average causal effect of the determinant of health that are differentially distributed across groups. Second, building on prior work, we define measures of the population intervention effect of a hypothetical intervention on absolute and relative inequality in a health outcome. These measures can be estimated from observational data under the same set of assumptions needed to estimate population-average causal effects. Our proposed measures incorporate an allocation rule that defines eligibility for the intervention and thus permits comparison of different intervention strategies (e.g., dynamic or stochastic interventions). We illustrate our proposed measures using simple examples and a real-world data example comparing the effects of different treatment strategies on the mortality inequality between non-Hispanic Black and non-Hispanic White people in HIV care in the United States. Finally, we discuss the limitations of our proposed approach and key considerations for its application. Our focus is on developing a deeper understanding of how public health and policy interventions shape health inequality and providing a framework for estimating effects on inequality using existing data and tools.

Health Disparities

Disparities in spatial access to Hepatitis C treatment providers, Los Angeles County Jacob M Gizamba* Jacob Gizamba Darren Ruddell Jeffrey D Klausner

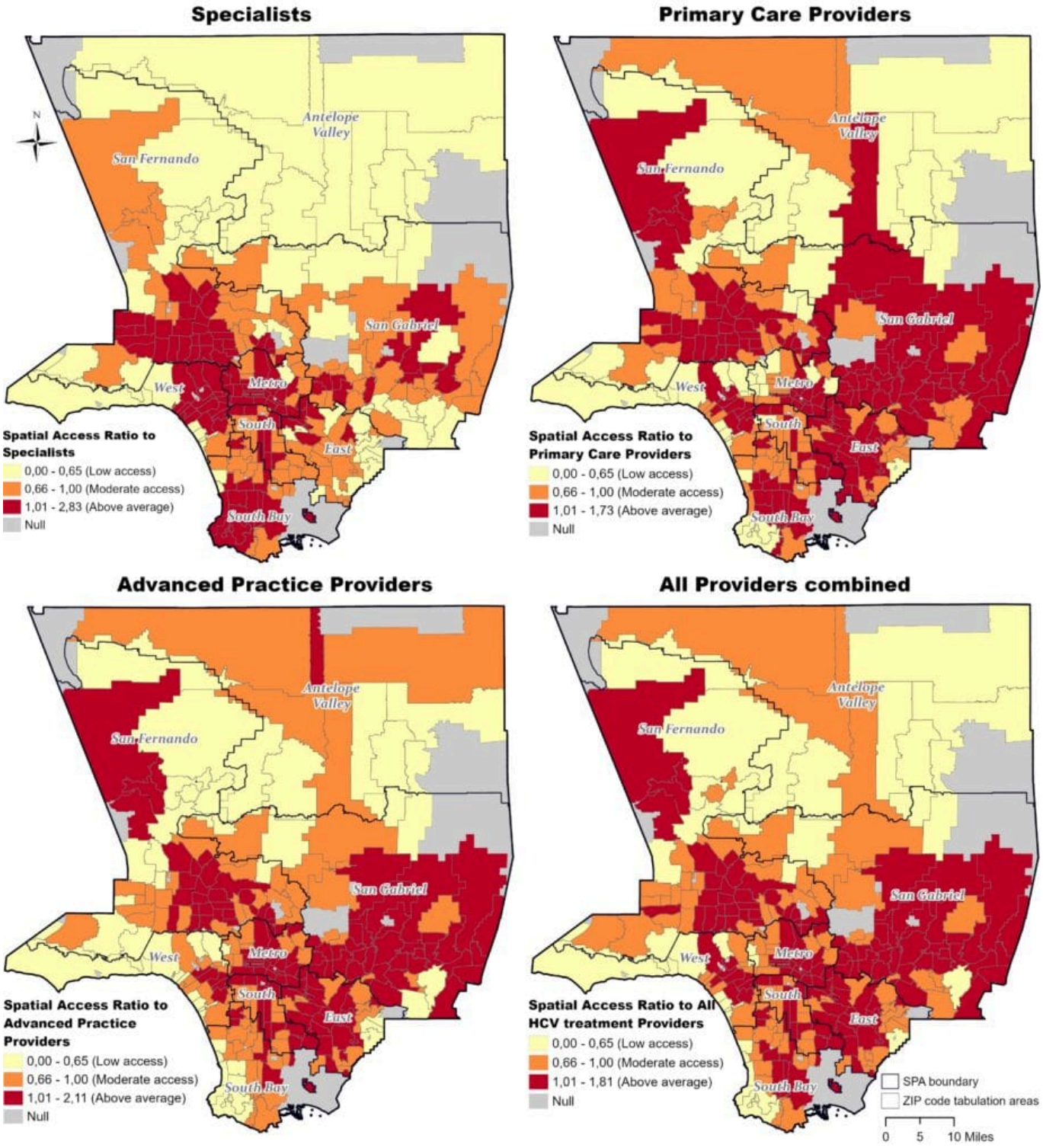
Background: Access to hepatitis C virus (HCV) treatment is essential for patients to get a cure, prevent transmission, and advance elimination efforts in the United States, yet evidence on spatial access to HCV treatment remains limited.

Objective: To assess variation in spatial access to HCV treatment providers across zip code tabulation areas in Los Angeles County and socioeconomic factors correlated with low access.

Methods: In this cross-sectional study, we combined provider location data, the reported rate of HCV infection, and American Community Survey data to assess spatial access to treatment providers. Potential treatment providers were identified through the National Plan and Provider Enumeration System, which included specialists (hepatologists, gastroenterologists, and infectious disease specialists) and non-specialists, such as primary care physicians and advanced practice providers, 2023. For each zip code, spatial access ratios to providers were calculated using the Enhanced 2-step Floating Catchment Area method. Hotspot analysis (Getis-Ord Gi*) was employed to identify and visualize clusters of low and high spatial access. Zip codes were classified into three access categories (low, moderate, and high-access areas) based on the mean and standard deviation of the spatial access ratios. Multinomial regression assessed socioeconomic factors associated with low spatial access, defined as a spatial access ratio more than one standard deviation below the county mean.

Results: A total of 6,826 providers were included in the analysis, comprising 614 specialists, 2,531 primary care physicians, and 3,682 advanced practice providers. Among the 255 zip codes examined, 13% were classified as low-access areas, 34% as moderate-access, and 53% as high-access, considering access to all providers combined. Considering spatial access to provider types separately, access to non-specialists was generally higher than access to specialists. Notably, for access to specialists, 20% of the zip codes were classified as low-access; for advanced practice providers and primary care providers, 17% and 15% of zip codes were classified as low-access, respectively. High-access areas for specialists were primarily located on the west side of the county, whereas high-access areas for non-specialists were distributed more broadly throughout the county. Factors correlated with increased likelihood of low-access to all providers were higher poverty levels, uninsured residents, and a higher share of Hispanic residents.

Conclusion: Spatial access to HCV treatment providers in Los Angeles County reveals significant disparities; while access to non-specialists is relatively geographically equitable, specialists are concentrated in specific areas. This highlights the potential of non-specialists to enhance treatment coverage in underserved regions. The Enhanced 2-step Floating Catchment Area offers a valuable approach for assessing geographic disparities in access to HCV treatment providers.


Specialists
N
Antelope Valley
San Fernando
San Gabriel
West
Metro
South
East
South Bay
Spatial Access Ratio to Specialists
0,00 - 0,65 (Low access)
0,66 - 1,00 (Moderate access)
1,01 - 2,83 (Above average)
Null
Primary Care Providers
Spatial Access Ratio to Primary Care Providers
0,00 - 0,65 (Low access)
0,66 - 1,00 (Moderate access)
1,01 - 1,73 (Above average)
Null
Advanced Practice Providers
Spatial Access Ratio to Advanced Practice Providers
0,00 - 0,65 (Low access)
0,66 - 1,00 (Moderate access)
1,01 - 2,11 (Above average)
Null
All Providers combined
Spatial Access Ratio to All HCV treatment Providers
0,00 - 0,65 (Low access)
0,66 - 1,00 (Moderate access)
1,01 - 1,81 (Above average)
Null
SPA boundary
ZIP code tabulation areas
0 5 10 Miles

Health Disparities

Measuring Policy Effects on Health Inequities Hidden by Compositional Change Colleen A. Reynolds* Colleen Reynolds Jeremy A. Labrecque Joost Oude Groeniger

Background

Reducing socioeconomic inequalities in health is a major public health priority. However, when policies affect socioeconomic status, estimating changes in health inequalities becomes more challenging because the composition of the groups being compared changes.

For example, imagine we want to understand how a policy aimed at increasing educational attainment affects educational inequalities in life expectancy. Educational attainment is an intercurrent event between exposure and outcome. Stratifying on this variable would obscure the effect of the policy on life expectancy through educational attainment, the primary mechanism.

Methods

Utilizing the principal stratification framework, we propose a new estimand relevant to policy evaluation: the effect of the policy on health inequalities across the distribution of education that would have existed in the absence of the policy. Using the example described above, we apply this estimator on simulated data and outline the interpretation and policy relevance.

Results

In our simulation we observe a 3.3-year increase in overall life expectancy. When we stratify on observed educational attainment, the policy is not associated with a change in educational inequalities in life expectancy. When we stratify on educational level that would have been attained in the absence of intervention, the policy is associated with a 5-year reduction in educational inequalities in life expectancy.

Conclusion

We demonstrate that our approach can capture changes in health inequalities that are obscured by compositional changes in the disparity population, overcoming post-treatment bias that results from simple stratification on the disparity population of interest This approach has broad potential applications to scenarios where the exposure of interest alters the composition of the disparity population, and offers a new methodological tool for health inequalities research.

Figure 1. Comparison of Effect Estimates			
	Total Effect of Policy	Effect of Policy on Observed Inequities	Change in Inequity, Defined by Pre-Policy Groupings
Estimand	$E[Y^{a=1}] - E[Y^{a=0}]$	$(E[Y^{a=1}\|M^{a=1} = 1] - E[Y^{a=1}\|M^{a=1} = 0]) - (E[Y^{a=0}\|M^{a=0} = 1] - E[Y^{a=0}\|M^{a=0} = 0])$	$(E[Y^{a=1}\|M^{a=0} = 1] - E[Y^{a=1}\|M^{a=0} = 0]) - (E[Y^{a=0}\|M^{a=0} = 1] - E[Y^{a=0}\|M^{a=0} = 0])$
Estimator	$E[Y\|A = 1] - E[Y\|A = 0]$	$E[Y\|M = 1, A = 1] - E[Y\|M = 0, A = 1] - E[Y\|M = 1, A = 0] + E[Y\|M = 0, A = 0]$	$E[Y\|M = 0, A = 0] + \left(E[Y\|M = 0, A = 1] + \frac{E[Y\|M = 0, A = 0] - E[Y\|M = 0, A = 1]}{\left(\frac{\Pr[M = 0\|A = 0] - \Pr[M = 0\|A = 1]}{\Pr[M = 0\|A = 0]}\right)} + \frac{E[Y\|A = 1] - E[Y\|A = 0]}{\Pr[M = 0\|A = 0] - \Pr[M = 0\|A = 1]} \right) \times \frac{\Pr(M = 0\|A = 0) - \Pr(M = 0\|A = 1)}{\Pr(M = 0\|A = 0)} + E[Y\|M = 0, A = 1] \times \frac{\Pr(M = 0\|A = 1)}{\Pr(M = 0\|A = 0)}$
Assumptions	Exchangeability: $A \perp\!\!\!\perp Y^a$ Consistency: if $A_i = a, then\ Y_i^a = Y_i^A = Y_i$	Exchangeability: $A \perp\!\!\!\perp Y^a\|M^a$ Consistency: if $A_i = a, then\ M_i^a = M_i^A = M_i$; if $A_i = a, then\ Y_i^a = Y_i^A = Y_i$	Exchangeability: $A \perp\!\!\!\perp Y^a\|M^a$; $A \perp\!\!\!\perp Y^a\|M$; $M \perp\!\!\!\perp Y^{a,m}$; $S \perp\!\!\!\perp A$ Consistency: if $A_i = a, then\ M_i^a = M_i^A = M_i$; if $A_i = a, then\ Y_i^a = Y_i^A = Y_i$; if $M_i = m, then\ Y_i^{a,m} = Y_i^{a,M} = Y_i^a$ Monotonicity: $M^{a=1} \geq M^{a=0}$ Exclusion: $Y^{a,m} = Y^{a^*,m}$
Estimate	3.3 years	0 years	-5 years
Interpretation	The policy increases overall life expectancy by 3.3 years.	The policy has no effect on observed health inequities.	The policy causes a 5-year reduction in life expectancy inequities between those who would have had high and those who would have had low education in the absence of the policy.
Implications	The policy has a positive effect on the life expectancy of the population overall	The policy does not have a direct effect, not through educational attainment.	The policy reduces health inequities by improving educational attainment.

Health Disparities

Income-related differences in pediatric asthma hospitalization cost and risk in the United States Luke Barry* Luke Barry Luke Barry Nicola Churchill Roch Nianogo

Why children from lower-income areas incur lower costs per asthma hospitalization despite a higher overall inpatient cost burden remains unclear. This study identifies modifiers of socioeconomic differences in pediatric inpatient costs and estimates income-related differences in asthma hospitalization risk. Using the Healthcare Cost and Utilization Project, National Inpatient Sample (2016–2019), we identified U.S. asthma hospitalizations among children aged 5–17 years. Exposure was residence in the lowest ZIP Code–level income quartile, and the outcome was inpatient service delivery cost (2020 USD). Causal forests were used to estimate average and heterogeneous effects of lower versus higher income on hospitalization costs across patient, admission, and hospital characteristics. We estimated income-stratified asthma hospitalization risks by dividing age, sex, year, census division, and income-specific inpatient counts by corresponding population counts from the American Community Survey. Among hospitalized children (n=28,634), admissions from lower-income areas had modestly lower average costs (−$207; 95% CI: −375,−39). However, cost differences were heterogeneous, with the largest reductions observed among admissions with major or extreme illness severity (−$1,282; 95% CI: −2,184,−380) and in the Pacific region (−$950; 95% CI: −1,563,−337). In contrast, children from lower-income areas were 1.91 (95% CI: 1.86, 1.96) times more likely to be hospitalized than those from higher-income areas. Socioeconomic disparities in pediatric asthma-related hospital cost burden are therefore driven primarily by higher hospitalization rates rather than greater costs per admission. Lower per-admission costs among lower-income children are most pronounced in settings characterized by greater clinical discretion. Distinguishing hospitalization risk from inpatient resource use clarifies socioeconomic patterns in pediatric asthma costs and highlights settings where equity-relevant differences are most evident.

Health Disparities

Time-Varying Effects of Health Technology on Racial Disparities: Why When We Measure Matters Chloe R. Bennett* Chloe Bennett Louisa H. Smith

Evaluations of health technology interventions increasingly consider effects on health disparities, yet typically rely on summary measures, like hazard ratios, that may obscure how intervention effects on disparities evolve over time. Health technologies do not confer benefits passively—they require users to interpret data, modify behaviors, and access follow-up care to translate information into health improvements. Health technologies present unique evaluation challenges: user engagement evolves as individuals learn from and adapt to devices, and the technologies themselves change rapidly through software updates. Well-established critiques note that collapsing effects over time obscures meaningful variation; such concerns are amplified when both engagement patterns and structural barriers change over follow-up. We used target trial emulation to examine continuous glucose monitor (CGM) effects on White-Black disparities in hospitalization among adults with type 2 diabetes using All of Us Research Program data. The White-Black risk difference among CGM users was -0.10 at 12 months (White lower risk), 0.01 at 24 months (no difference), and 0.11 at 72 months (Black lower risk)—a reversal that a summary hazard ratio of 1.88 (Black lower risk) would entirely mask. Early CGM use may reveal the need for clinical intervention, while sustained benefits depend on determinants that are socially and structurally shaped (e.g., access to healthy foods). While findings require cautious interpretation given wide confidence intervals and small samples of Black CGM users, results illustrate how the equity implications of a technology can shift across follow-up. Substantial investment in health technology as a tool for reducing disparities requires rigorous evidence, yet single-time-point evaluations risk premature conclusions about whether technologies narrow or widen inequities.

Substance Use

Assessing Racial Heterogeneity in the Effects of State-Level Drug Harm Reduction Law Enactments on fatal drug overdose John Pamplin* John Pamplin Chinelo Onyebeke Daniel Neill Magdalena Cerda Silvia Martins

Drug harm reduction laws have been widely enacted to address the overdose crisis, but the specific provisions included in the enactments vary greatly from state to state and may also have different effects on different populations. This study aimed to identify the set of harm reduction law provisions that were associated with the greatest reductions in opioid overdose mortality overall, and for Black people specifically. We calculated monthly fatal overdose rates from 2000-2022 using data from the National Vital Statistics System and linked them with state-level harm reduction law data from the Prescription Drug Abuse Policy System. We estimated difference-in-difference (DID) models to estimate the average 12-month effect of each policy enactment on rates of opioid-involved overdose deaths, weighted across differences in the pre-and co-enacted policy landscape in the12 months before enactment and a 12-month period after. Separate models were built to estimate the effects of enactment 1-12, 13-24, and 25-36 months post enactment. Predicted effects from each set of models were assessed via post-hoc decision tree regressions. This process was repeated, restricting the outcome to opioid-involved overdose among Black people. There were 114 enactments during the observation period. Decision tree regressions found no enactment scenarios that predicted reductions in overall overdose in any of the assessed post-enactment periods. However, preliminary results suggest that enactment scenarios that included NAL dispenser criminal and civil immunity, and that did not include GSL protection from arrest for drug paraphernalia predicted a .09 deaths per 100,000 reduction in Black overdose deaths 25-36 months post enactment (mse = 0.097; sample = 7). Findings suggest that harm reduction laws may have heterogeneous effects across racial groups; however, very few enactments were associate with reduced overdose, and data did not support differences beyond chance.

Substance Use

US state fentanyl laws and opioid overdose mortality trends Erin Annunziato* Erin Annunziato Matthew R. Lamb Silvia S. Martins Pia M. Mauro Deborah S. Hasin

Aims: As of June 2023, 43 states enacted or introduced laws increasing penalties for fentanyl distribution to reduce overdose mortality. We examined the impact of fentanyl laws on overdose trends.

Methods: The outcome was state-month opioid (ICD-10 T40.0-T40.4, T40.6) overdose deaths from 2013-2024 Multiple Cause of Death CDC Data. The exposure was fentanyl law enactment date from Legislative Analysis and Public Policy Association's "Fentanyl-specific criminal provisions: Summary of state laws" dataset. Interrupted time series analyses with linear regression tested overdose changes following enactment lagged 1, 2, and 3 years.

Results: From 2016-2023, 23 states enacted fentanyl laws as opioid overdose mortality rates increased from 2016-2021 and declined after 2022. Among 14 states that enacted laws before 2022, 1-year lag models showed overdoses increased significantly in 7 states immediately after enactment and no significant changes in 10 states. Significant increases did not persist over time post-enactment. For example, Florida's 2017 law was associated with 117 (95% CI=64, 169) more overdoses immediately after enactment, with overdoses predicted to decrease by 6.4 per month post-enactment. Among 9 states that enacted laws after 2022, overdoses significantly decreased immediately after enactment in 5 states that enacted laws in 2023 after overdose deaths had started declining. Models testing 2 and 3 year lags showed almost all pre-2022 laws were associated with immediate increases in overdoses.

Conclusions: Results do not provide evidence that fentanyl criminalization caused overdose mortality declines. Pre-2022 fentanyl laws were associated with increased overdoses 1, 2, and 3 years after enactment. Post-2022 fentanyl laws were associated with decreased overdoses, but declining overdose trends preceded fentanyl law enactment. Understanding the impact of fentanyl laws is necessary for policymakers considering strategies to sustain overdose mortality declines.

Substance Use

Trends in opioid-related overdose outcomes by county-level rurality and measures of OUD treatment availability, Florida, 2015-2024 Melissa Ward* Melissa Ward Grace Schimenti Saurya Dhungel

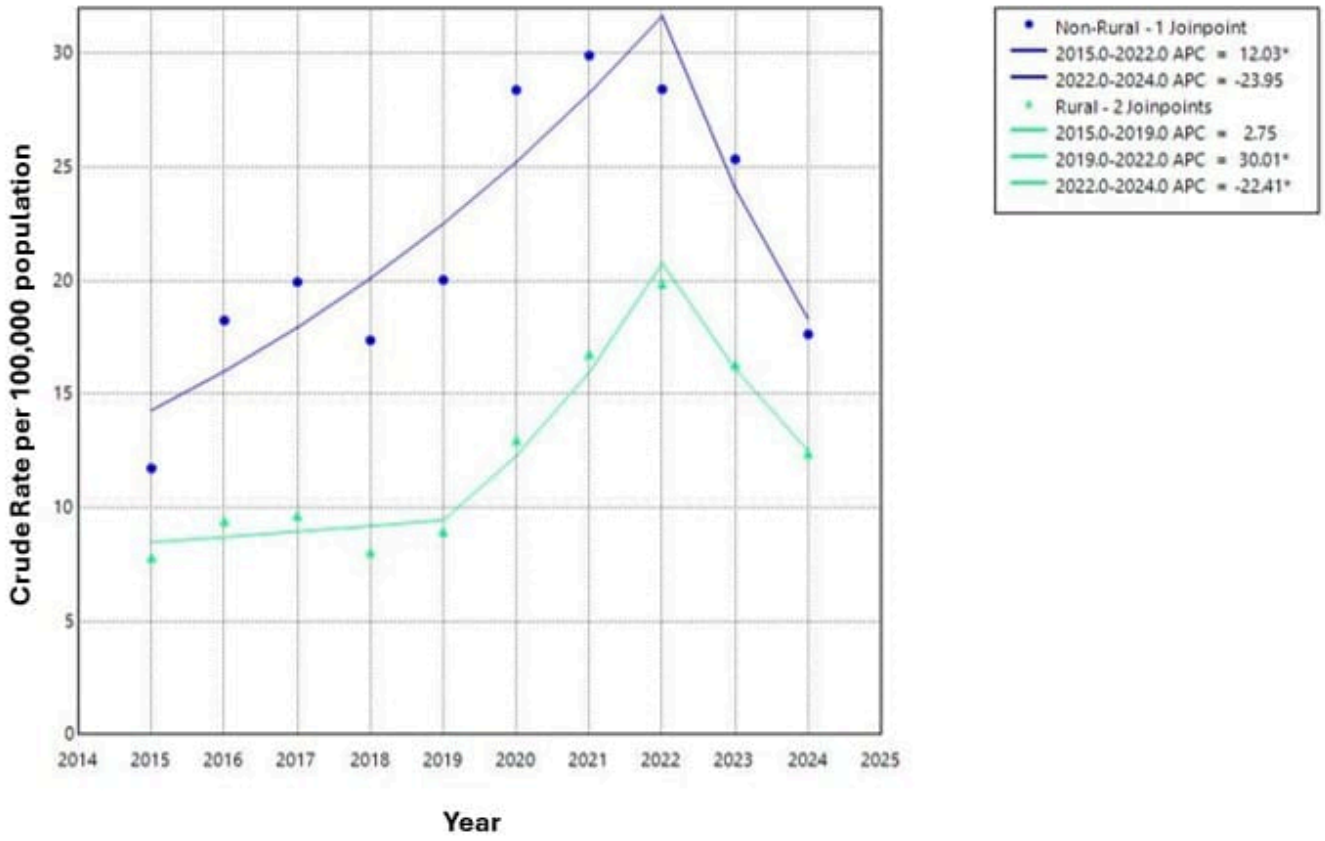
Introduction: Floridians experience substantial harm from opioid misuse, and access to opioid use disorder (OUD) treatment differs markedly across the state. This study examined how trends in rates of opioid-related overdoses (ODs) in Florida varied by county-level classifications of rurality and OUD treatment availability from 2015 to 2024.

Methods: Counts of opioid-involved OD deaths and emergency medical service (EMS) responses to suspected opioid-involved ODs were obtained from the Florida Department of Health Substance Use Dashboard. Population denominators were derived from 2023 American Community Survey 5-year estimates. Counties were classified as rural or nonrural according to HRSA designations, and according to measures of treatment availability derived from SAMHSA data including availability of medications for OUD and rates of buprenorphine prescribers. The National Cancer Institute's Joinpoint Trend Analysis Software was used to identify significant changes in linear trends over time and estimate annual percentage change (APC).

Results: While nonrural counties had the highest rates of opioid-related ODs, rural counties experienced more accelerated increases in rates over shorter time periods, including significant increased APCs of 30% for fatal ODs from 2019-2022 and 55% for EMS responses from 2018-2021. In comparison, nonrural counties showed significant increased APCs of 12% from 2015-2022 and 36% from 2015-2021 for fatal ODs and EMS responses, respectively. Similar results were observed for counties classified at the lowest levels of OUD treatment availability compared to counties classified at the highest levels of availability.

Conclusion: Rural counties and counties with the lowest levels of treatment availability experienced significant increases in opioid-related ODs over short periods of time. Decision makers should ensure under-resourced counties have adequate support to identify and respond to rapid changes in the opioid crisis.

Rates of Fatal Opioid Overdoses in Florida Counties by Rurality, 2015-2024



Substance Use

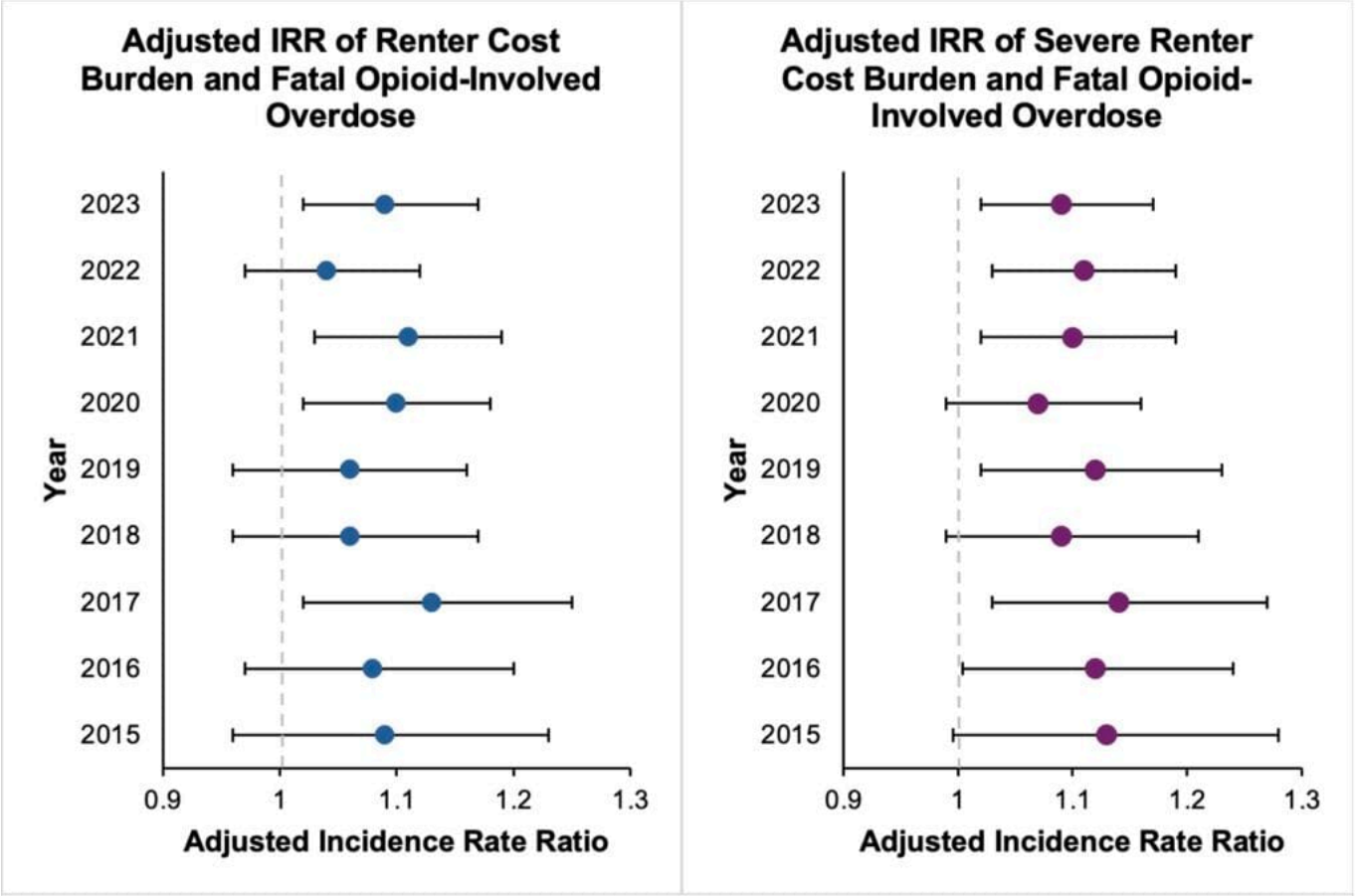
Examining Neighborhood-Level Renter Cost Burden and Opioid-Involved Overdose Fatalities in Chicago, IL, 2015-2023 Morgan Watson* Morgan Watson Kechna Cadet Gabrielle Zuckerman Elizabeth Nesoff

Background: Housing insecurity, including homelessness and eviction, is linked to higher fatal overdose risk. However, the relationship between renter cost burden and fatal opioid-involved overdose remains unclear. This study examined the neighborhood-level association between renter cost burden and fatal opioid-involved overdose in an urban setting.

Methods: We conducted a cross-sectional spatial analysis of Chicago census tracts using locations of opioid-involved fatal overdoses from the Cook County Medical Examiner's Office, 2015-2023 (n = 7,926). Renter cost burden (percentage of renter households spending ≥ 30% of income on housing) and severe renter cost burden (≥ 50%) were obtained for Chicago census tracts from the American Community Survey. We mapped spatial patterns of renter cost burden and fatal overdose and assessed spatial autocorrelation using bivariate Global Moran's I plots. We used negative binomial regression to estimate the association between renter cost burden and severe cost burden and fatal overdose rate by year, controlling for neighborhood variables (e.g., income, segregation, population density).

Results: Our findings demonstrate positive spatial autocorrelation, indicating spatial clustering of census tracts with a high proportion of cost-burdened renters and fatal overdose rates. We found consistent positive associations between fatal overdose rates and renter cost burden and severe cost burden over time, controlling for neighborhood demographics. For example, in 2023, each 10% increase in the proportion of cost-burdened renters was associated with a 9% increase in fatal overdose rate (aIRR = 1.09, 95% CI [1.02, 1.17]).

Conclusions: Neighborhoods with higher proportions of cost-burdened renter households experience higher fatal overdose rates, with consistent associations over time. Upstream housing interventions (e.g., rental assistance) may mitigate fatal overdose risk.



Adjusted for: population density, proportion of renters:owners, median household income, and ICE

Substance Use

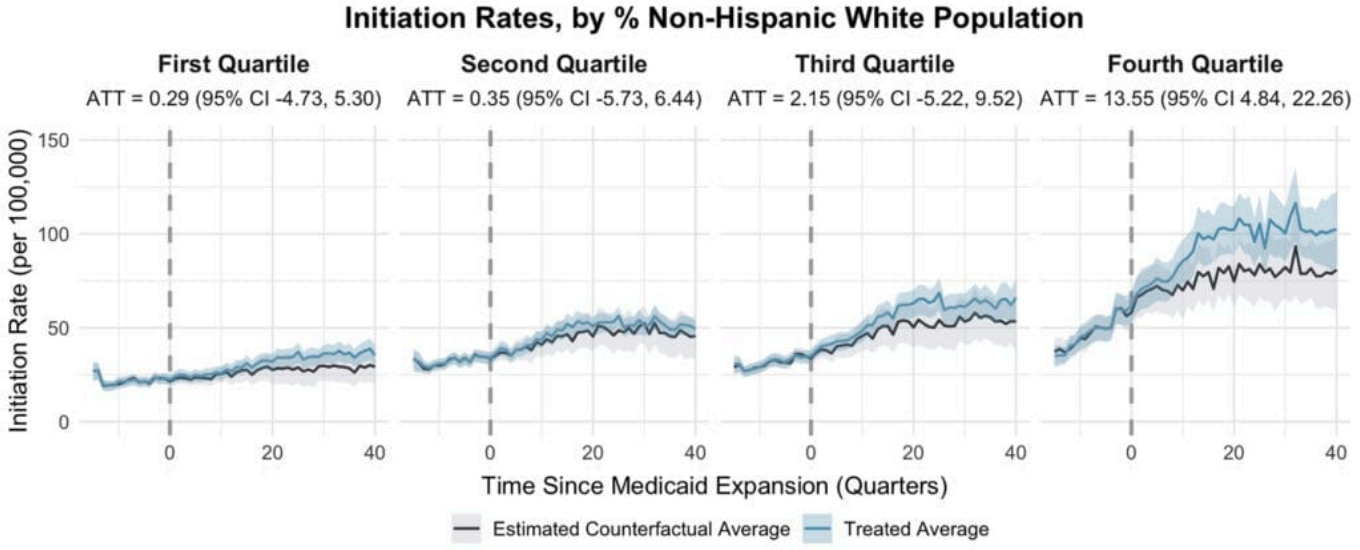
Racial Disparities in Buprenorphine Initiation and Retention Following Medicaid Expansion Anna T Nguyen* Anna Nguyen Esther E Velasquez Mathew V Kiang

Introduction: Buprenorphine is an effective treatment for opioid use disorder but is particularly underutilized among non-White populations. Medicaid Expansion under the Affordable Care Act increased buprenorphine access, but it is unclear how expansion impacted treatment disparities. Here, we use quasi-experimental methods to assess heterogeneity in the effect of Medicaid expansion on buprenorphine use by area-level racial composition.

Methods: We identified 154 million buprenorphine prescriptions across 4.7 million patients between Jan 2010 and Dec 2023 in the IQVIA longitudinal prescriptions database. We used generalized synthetic control models to estimate the effect of Medicaid Expansion on buprenorphine initiation (new prescription after ≥180 days of no treatment) and retention (continuous treatment for ≥180 days). We compared effect estimates between areas (ZIP3s) with small vs large Non-Hispanic White populations, based on quartiles estimated from 2010 Census data. We incorporated area-level educational attainment, household income, and poverty levels into the synthetic controls, and weighted effect estimates by population size.

Results: Following Medicaid Expansion, we found an overall increase of 5.7 (95% CI 2.1, 9.3) buprenorphine initiations per 100,000 people. This increase was driven by areas with the largest Non-Hispanic White populations, where initiations increased by 13.6 (95% CI 4.8, 22.3) per 100,000 people. There was no increase in areas with the smallest Non-Hispanic White populations (+0.3 per 100,000, 95% CI -4.7, 5.3). Buprenorphine retention declined starting five years after expansion, but we found no differences in this trend by area-level racial composition.

Conclusion: Medicaid Expansion only increased buprenorphine initiation in areas with large Non-Hispanic White populations. Additional efforts are needed to improve retention across all new users and address structural barriers that limit medication access in non-White populations.



Substance Use

Decomposing the US drug overdose crisis Mathew Kiang* Mathew Kiang Monica Alexander Antonino Polizzi

Despite recent modest declines, the US continues to experience high drug-related mortality at over 30 deaths per 100,000 population in 2023. Previous work has found variation in drug-related mortality across geography, sociodemographic characteristics, and underlying drug. However, this work has largely focused on describing these patterns across a single axis and using overlapping drug categories, limiting their ability to inform health policy.

Here, we address these limitations by using demographic decomposition methods on the NCHS restricted-access multiple cause of death data from 1999 to 2023. Using Kitagawa decomposition, we quantify the contribution of mutually-exclusive drug categories to the change in age-standardized national drug-related mortality rate by both geographic (states) and sociodemographic (race-ethnicity-age-sex-specific) subgroups.

When examining the contribution of different drugs to the change in the national drug-related mortality rate, we found distinct geographic patterns. Since 2020 xylazine-involved mortality contributed approximately 0.25 to 0.5 deaths per 100,000 population to the national drug-related mortality rate with the majority limited to just two states (NY, PA). In contrast, deaths involving both methamphetamine and fentanyl contributed 0.4 to 1.4 deaths per 100,000 to the national rate and the majority of this contribution came from West Coast states (CA, WA, OR). Similarly, deaths involving cocaine and fentanyl contributed between 0.3 to 0.8 deaths per 100,000 but were spread across Eastern US states (e.g., NY, MI, OH, PA, MD, VA). While 2023 saw a 1.25 deaths per 100,000 decline in the national rate, this decline was driven primarily by six states (IL, IN, OH, PA, NC, FL) and almost entirely by reductions in fentanyl-involved deaths.

Demographic decomposition methods provide actionable insights into the US drug overdose crisis, revealing not only who and where people are most impacted, but also which substances are driving change.

Pharmacoepidemiology

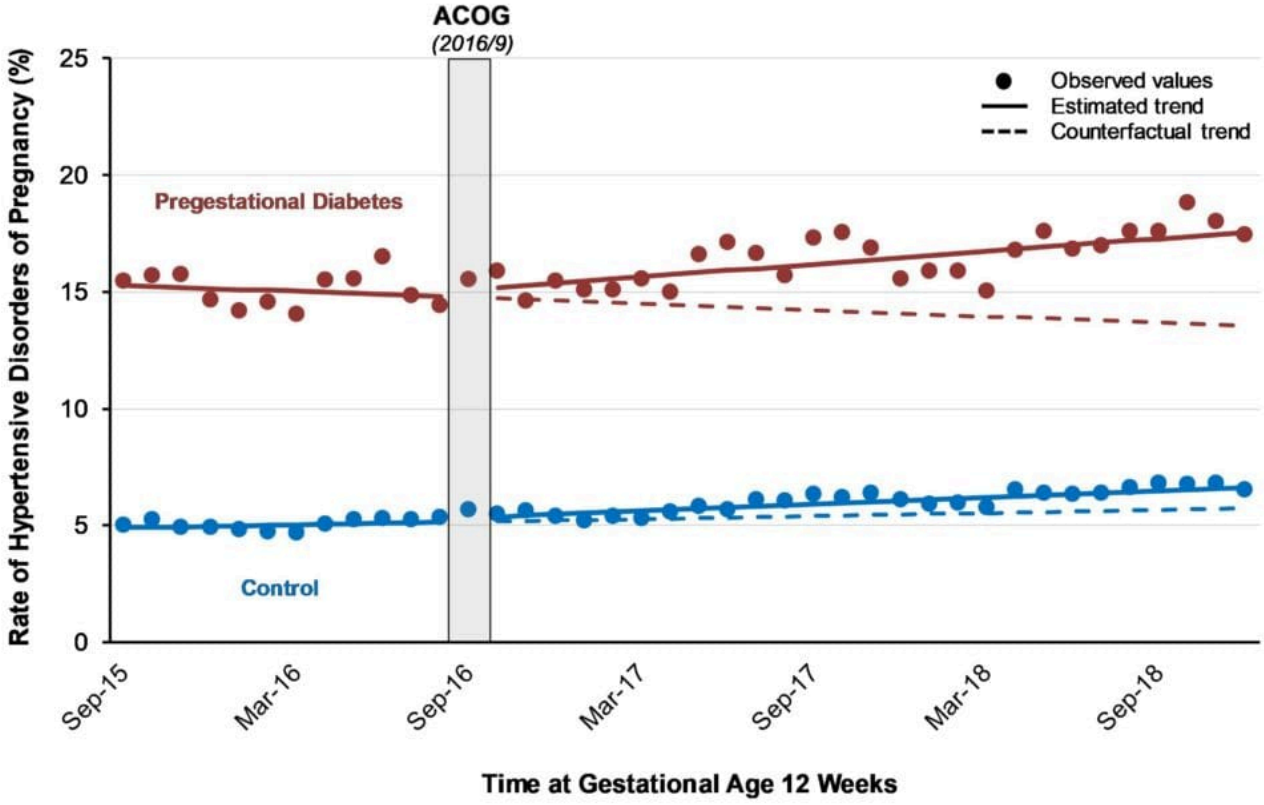
From Guideline to Practice: A Quasi-Experimental Evaluation of Hypertensive Disorders of Pregnancy Following the ACOG Low-Dose Aspirin Recommendation in Pregnancies With Pregestational Diabetes Ellen C Caniglia* Lin-Chieh Meng Charles E Leonard Beth Pineles Brian Lee Viktor H. Ahlqvist Cecilia Magnusson Enrique F Schisterman Stefanie N Hinkle Sunni L Mumford

Background: The American College of Obstetricians and Gynecologists (ACOG) recommends low-dose aspirin (LDA) for the prevention of preeclampsia among high-risk pregnancies, including those complicated by pregestational diabetes (PGD). However, recent randomized controlled trials (RCTs) have questioned the efficacy of LDA in this population. We leveraged the 2016 ACOG guideline update as a natural experiment to evaluate the real-world impact of guideline adoption on maternal outcomes among pregnancies with PGD.

Methods: We conducted a controlled interrupted time-series (CITS) analysis using US National Vital Statistics System birth certificate data. Time was indexed by calendar month at gestational age 12 weeks, spanning September 2015 through December 2018, with the September 2016 ACOG guideline update treated as the intervention point. Pregnancies with PGD were compared with a low-risk control group defined as nulliparous individuals younger than 35 years with a normal pre-pregnancy body mass index and no history of PGD, chronic hypertension, or assisted reproductive technology use. This control group was used to address potential confounding from concurrent interventions or underlying temporal trends. The primary outcome was hypertensive disorders of pregnancy (HDP) recorded on the birth certificate, defined as a composite of gestational hypertension and preeclampsia. Segmented regression models were used to estimate between-group differences in immediate level changes and post-guideline trend changes on the absolute risk scale.

Results: The analysis included 75,123 pregnancies with PGD and 993,450 low-risk control pregnancies. The CITS analysis showed no evidence of a between-group, guideline-associated change in HDP, with an estimated immediate level change of 0.18% (95% CI, −1.13 to 1.48) and no differential post-guideline trend change (0.12% per month; 95% CI, −0.06 to 0.30).

Conclusion: In this population-based CITS analysis, real-world uptake of the 2016 ACOG recommendation for LDA was not associated with a reduction in HDP, including preeclampsia, among pregnancies with PGD. These findings are consistent with recent RCT evidence and underscore the need for further research to evaluate the effectiveness of LDA and alternative preventive strategies in this population.


ACOG
(2016/9)
Observed values
Estimated trend
Counterfactual trend
Pregestational Diabetes
Control
Rate of Hypertensive Disorders of Pregnancy (%)
25
20
15
10
5
0
Sep-15
Mar-16
Sep-16
Mar-17
Sep-17
Mar-18
Sep-18
Time at Gestational Age 12 Weeks

Pharmacoepidemiology

Application of Disease Risk Scores to Obtain Individualized Estimates of Ibuprofen Associated Acute Kidney Injury in Hospitalized Patients Corey He* Haedi Thelen Corey He Wei Yang Sean Hennessy Jordana Cohen Wensheng Guo Todd Miano

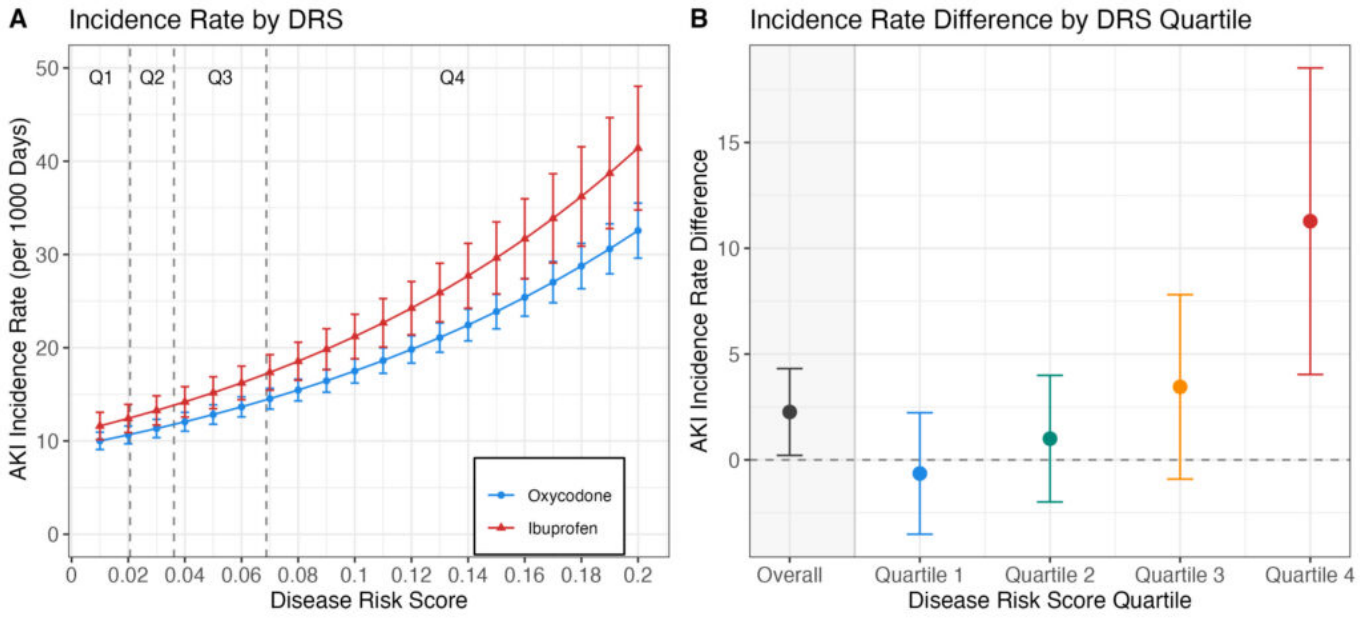
Background: Non-steroidal anti-inflammatory drugs (NSAID) are key opioid-sparing options in hospitals but may increase acute kidney injury (AKI) risk. Prior studies evaluated heterogeneous treatment effects (HTE) by individual characteristics (e.g., age, kidney function), but do not capture how multiple factors combine to modify treatment effects. Disease risk score (DRS) approaches can address this limitation by summarizing multiple AKI risk factors into a single measure.

Objective: To determine whether NSAID effects on AKI vary by baseline AKI risk.

Methods: We conducted an active comparator cohort study of patients hospitalized in the University of Pennsylvania Health System treated with the NSAID ibuprofen versus those treated with oxycodone. Using split-sample estimation, we estimated an AKI DRS with logistic regression on 68 baseline covariates in a randomly selected half of oxycodone patients (training set). Using this model, we estimated DRS on the remaining patients and stratified patients into DRS quartiles. We estimated inverse probability of treatment weights within each DRS stratum and estimated stratum-specific incidence rate differences (IRD). We also estimated treatment effects as a continuous function of the DRS.

Results: The DRS development set included 36,171 patients who experienced 2,243 AKI events. The outcome analysis included 42,485 patients (ibuprofen = 6,313, oxycodone = 36,172) with 2,556 AKI events. The overall adjusted AKI incidence rate was 16.41 and 14.14 per 1000 days in the ibuprofen and oxycodone groups, respectively (IRD = 2.26 per 1000 days, 95% CI [0.21, 4.31]). The IRD was 11.28 per 1000 days (95% CI [4.04, 18.52]) in the highest DRS quartile and -0.64 per 1000 days (95% CI [-3.52, 2.23]) in the lowest DRS quartile.

Conclusion: Our results suggest the effect of ibuprofen on AKI varies >10-fold across levels of baseline AKI risk. DRS stratification may be a useful tool for individualized NSAID treatment in hospitalized patients.



Treatment effects across disease risk score (DRS). Panel A: AKI incidence rate per 1,000 patient days by DRS for ibuprofen and oxycodone. Vertical dashed lines mark quartile boundaries (Q1: 0-0.021, Q2: 0.021-0.036; Q3: 0.036-0.069; Q4: 0.069-0.936), error bars represent 95% confidence intervals. Panel B: AKI incidence rate difference between ibuprofen and oxycodone treatment groups per 1,000 patient days by overall and within quartile of DRS. The continuous curves (Panel A) show treatment effect heterogeneity across the spectrum of risk, while the stratified estimates (Panel B) show treatment effects in clinically interpretable groups of equal size.

Cancer

Comparative Effects of GLP-1 Receptor Agonists and Other Glucose-Lowering Drugs on Kidney Cancer Risk: A Target Trial Emulation in Post-Bariatric Patients Jesus Hernandez* Jesus Hernandez Omer Abdelgadir Mohanad Albayyaa Deepali Ernest Jing Chen Stacia M. DeSantis Arthur S. Hong Lindsay G. Cowell Jaime P. Almandoz Sara E. Messiah David S. Lopez

Importance: Kidney cancer (KC) is an obesity-related malignancy with rising incidence. Metabolic and bariatric surgery (MBS) has been shown to reduce the risk of some obesity-related cancers, yet the effect of post-surgical glucose-lowering therapies on the incidence of KC remains poorly understood. Use of glucagon-like peptide-1 receptor agonists (GLP-1 RA) is rising after MBS for weight and glycemic control; however, little is known about its effect on the incidence of KC among patients who underwent MBS.

Objective: To assess whether initiation of GLP-1 RA compared with other glucose-lowering agents is associated with KC risk in post-MBS patients with overweight, obesity, or type 2 diabetes (T2D).

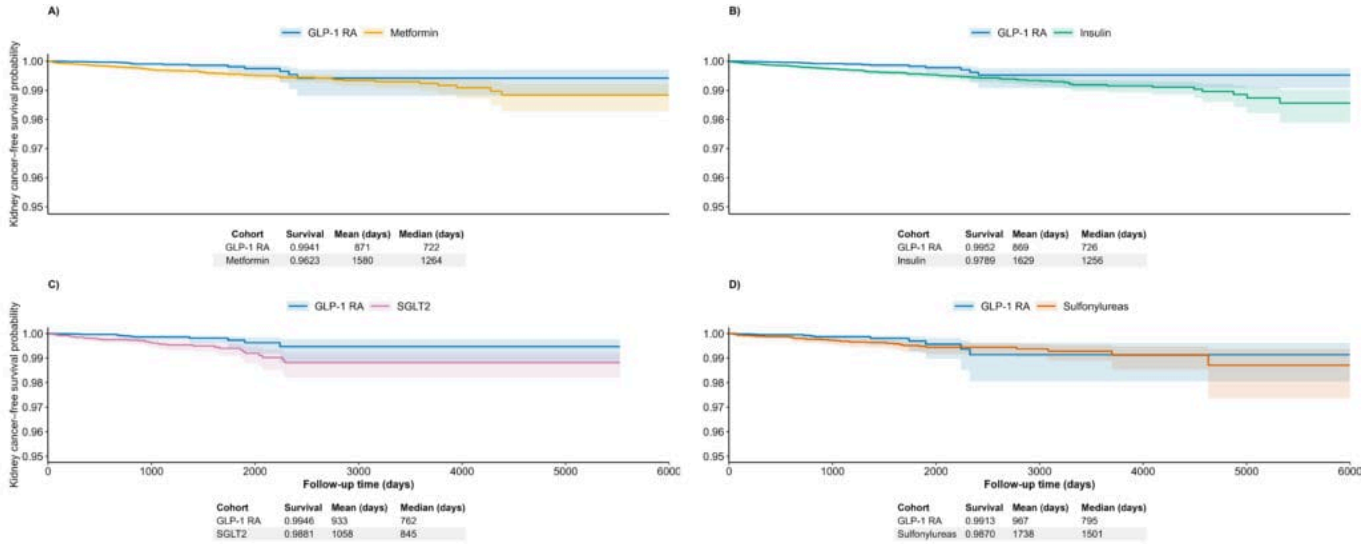
Design, Setting, and Participants: This retrospective cohort study followed a target trial emulation design that included adults (≥18 years) with prior MBS between January 1, 2006, and January 1, 2025. Individuals with prior cancer, type 1 diabetes, or severe comorbidities were excluded.

Exposures: Initiation of GLP-1 RA (semaglutide, dulaglutide, liraglutide, exenatide, lixisenatide, albiglutide, or tirzepatide) was compared separately with metformin, insulin, sodium–glucose cotransporter 2 inhibitors (SGLT2i), or sulfonylureas. Time zero was defined as the first post-surgical prescription after a 365-day period without use of the study drug class to ensure a new-user design.

Main Outcomes and Measures: Incident KC (renal or renal pelvis; ICD-10 C64, C65, C79.0) after time zero. Propensity score matching (1:1) balanced baseline characteristics. We estimated 19-year risk differences (RDs), risk ratios (RRs), and hazard ratios (HRs).

Results: After matching, 20,662 GLP-1–metformin, 28,358 GLP-1–insulin, 9,745 GLP-1–SGLT2i, and 7,118 GLP-1–sulfonylurea pairs were included. GLP-1 RA initiation was associated with lower KC risk compared with metformin (RD, −0.25%; 95% CI, −0.35% to −0.15%), insulin (RD, −0.31%; 95% CI, −0.39% to −0.23%), SGLT2i (RD, −0.29%; 95% CI, −0.43% to −0.14%), and sulfonylureas (RD, −0.27%; 95% CI, −0.44% to −0.09%). Results were consistent across temporal and diabetes-duration–restricted analyses and were further supported by a negative control outcome.

Conclusions: Among post-MBS patients, GLP-1 RA initiation was associated with a lower risk of KC when compared with several active glucose-lowering drugs. These findings provide insight about reducing the incidence of KC with use of GLP-1 RA after MBS and highlight the need for further investigation among patients with different types of bariatric surgery and more diverse populations.


A)
GLP-1 RA
Metformin
Kidney cancer-free survival probability
1.00
0.99
0.98
0.97
0.96
0.95
Cohort Survival Mean (days) Median (days)
GLP-1 RA 0.9941 871 722
Metformin 0.9623 1580 1264
B)
GLP-1 RA
Insulin
Cohort Survival Mean (days) Median (days)
GLP-1 RA 0.9952 869 726
Insulin 0.9789 1629 1256
C)
GLP-1 RA
SGLT2
Kidney cancer-free survival probability
0
1000
2000
3000
4000
5000
6000
Follow-up time (days)
Cohort Survival Mean (days) Median (days)
GLP-1 RA 0.9946 933 762
SGLT2 0.9881 1058 845
D)
GLP-1 RA
Sulfonylureas
Follow-up time (days)
Cohort Survival Mean (days) Median (days)
GLP-1 RA 0.9913 967 795
Sulfonylureas 0.9870 1738 1501

Pharmacoepidemiology

Choices and Consequences of Alternative Estimands in Time-to-Event Safety Analyses Joy Zora Nakato* Joy Zora Nakato Laura B. Balzer Laura Telep Nicholas Williams Carrie Nielson Andrew Mertens

In pharmacoepidemiology, some post-authorization studies aim to assess the effects of treatment exposures (where multiple are available) on the risk of adverse events using electronic health records or insurance claims retrospectively comparing patients who initiated the treatment of interest versus an active comparator. Common challenges in these analyses include treatment switching, incomplete outcome ascertainment, and irregular monitoring (e.g., due to changes in insurance or healthcare provider). These challenges are exacerbated for time-to-event endpoints, where treatment switching and other intercurrent events affect risk sets, censoring mechanisms, and the interpretation of hazard-based estimands. Traditional approaches for time-to-event safety analyses allow the estimator (e.g., Cox proportional hazards) to implicitly determine the causal estimand and rely on strong causal and statistical assumptions. In contrast, alternative causal estimands address different scientific questions in the presence of treatment switching and other intercurrent events. We present several such estimands, including the treatment policy estimand (contrasting initial treatments regardless of subsequent changes), a hypothetical estimand under no treatment switching, a composite that incorporates switching into the outcome, a while-on-treatment estimand that censors at switching, and a principal stratum estimand defined among individuals unlikely to switch under either treatment. Following the Causal Roadmap, we discuss how each estimand fits into a wider research framework. Using simulations, we demonstrate the practical consequences of alternative choices for estimands and their corresponding estimators by comparing traditional parametric and modern machine-learning approaches (e.g., TMLE). We conclude that following the Causal Roadmap when designing safety analyses can help define a set of potentially interesting estimands that can be robustly estimated with modern methods.

Big Data/Machine Learning/AI

Virtual Pooling: Accurate, Scalable, and Privacy-preserving Analytics Without Aggregating Patient Data Ishtiyaque Ahmad* Trinabh Gupta Kunlong Liu Goktug Onal Ishtiyaque Ahmad Vivek Rudrapatna Trinabh Gupta

Background: Concerns regarding patient privacy and data security preclude many important medical studies that require multicenter datasets for maximal robustness. Although federated learning methods address this problem, existing implementations are often complex to use, less accurate, and lack support for common biostatistical and multi-iterative analyses. Here we test Virtual Pooling (VP), a new approach for analyzing multicenter data without aggregating patient data into a single repository.

Methods: We used VP to replicate a high impact study that measured the association between chronic immunosuppressant use and in-hospital outcomes among COVID-19 patients using the N3C dataset from 59 health systems (N=334,754). The study used a common biostatistical analytical pipeline involving propensity score matching followed by Cox proportional hazards model. We compared VP results against direct pooling, the gold standard. We selected two covariates and induced center-specific correlations (positive, negative, or none) via probabilistic patient assignment to test VP's robustness under imbalanced cross-center data distributions.

Results: VP generated an identical matched cohort to that obtained via direct pooling. Following propensity score matching, Cox regression analyses produced the same covariate coefficients and p-values under both approaches. This concordance persisted in simulations with extreme distributional imbalances. VP required only 17 seconds of additional computation time relative to direct pooling.

Conclusions: Virtual pooling enables accurate, scalable multicenter data analysis without sharing patient-level data, ensuring strong privacy. It achieves accuracy comparable to direct data pooling, while supporting advanced time-to-event analyses such as Cox proportional hazards model. Thus, VP can accelerate multicenter collaborations and enhance the robustness and generalizability of medical research.

Comparison of Cox Proportional Hazards Model Estimates After Propensity Score Matching: Direct Pooling vs. Virtual Pooling (VP).

Covariate	Coefficient		P value	
	Pooling	VP	Pooling	VP
immuno_flag	-0.05	-0.05	1.83E-02	1.83E-02
transplant_any	-0.18	-0.18	<5.00E-07	<5.00E-07
pulmonary	0.11	0.11	<5.00E-07	<5.00E-07
renal	0.15	0.15	<5.00E-07	<5.00E-07
CHF	0.14	0.14	<5.00E-07	<5.00E-07
rheumatic	0.04	0.04	0.13	0.13
rx_other_pulm	0.04	0.04	0.04	0.04
rx_renal	-0.20	-0.20	<5.00E-07	<5.00E-07
rx_laba	-0.02	-0.02	0.52	0.52
dmcx	0.04	0.04	0.15	0.15
diabetes	-0.04	-0.04	0.14	0.14
rx_inhaled_cs	-0.09	-0.09	6.61E-06	7.00E-06
cancer	0.13	0.13	<5.00E-07	<5.00E-07
liver_mild	-0.04	-0.04	0.07	0.07
mets	0.06	0.06	0.05	0.05
rx_insulin	0.09	0.09	1.11E-05	1.10E-05

Big Data/Machine Learning/AI

Evaluating the Performance of the Parametric G-formula Relative to Causal Forest in Identifying Effect Modifiers and Estimating Subgroup Effects: A Simulation and Application using Look AHEAD trial Yulin Gong* Roch Nianogo Yulin Gong

Causal machine learning algorithms like causal forest have gained popularity for estimating heterogeneous treatment effects (HTEs) at the individual level. However, such models can have low interpretability but high flexibility. The parametric and semi-parametric frameworks such as the generalized heterogeneous treatment effect (G-HTE) approach based on the G-computation algorithm, emphasize interpretability but have limited flexibility in capturing complex interactions. We compared G-computation and causal forest to examine trade-offs between the two methods using simulation studies and data from the Look AHEAD trial of adults with type 2 diabetes evaluating the effectiveness of intensive lifestyle vs education. G-computation identified two effect modifiers (EM) and four subgroups: baseline fasting glucose (FG) and HbA1c as candidate EM and estimated effects. E.g., Estimated effects HbA1c < 8.5% (RD= -9%, 95%CI [-28% to 10%]) vs HbA1c ≥ 8.5% (RD= 28%, 95%CI [-14% to 69%]); P-for interaction = 0.10). In contrast, causal forest revealed more complex EM (n=3) and subgroups (n=6): HbA1c, systolic blood pressure (SBP), and cardiovascular disease (CVD) history. Individuals with lower HbA1c (HbA1c <8%) and no prior CVD derived the greatest benefit from the intervention (RD = -2% [-4% to -1%]) whereas those with higher HbA1c (HbA1c ≥ 8%) and elevated SBP ≥ 140 mmHg experienced the least benefit (RD = 7%, 95%CI, [2% to 11%]). G-computation emphasized simplicity and interpretability by identifying a small number of single-variable EM with clear conclusion: the less advanced (late) the diabetes is, the more effective in reducing FG/HbA1c the intensive lifestyle intervention tends to be (Figure). Causal forest prioritized flexibility and accuracy, revealing multivariable HTEs but complex conclusions. Methodological choice substantially influences HTE characterization and should align with analytic objectives and clinical context.

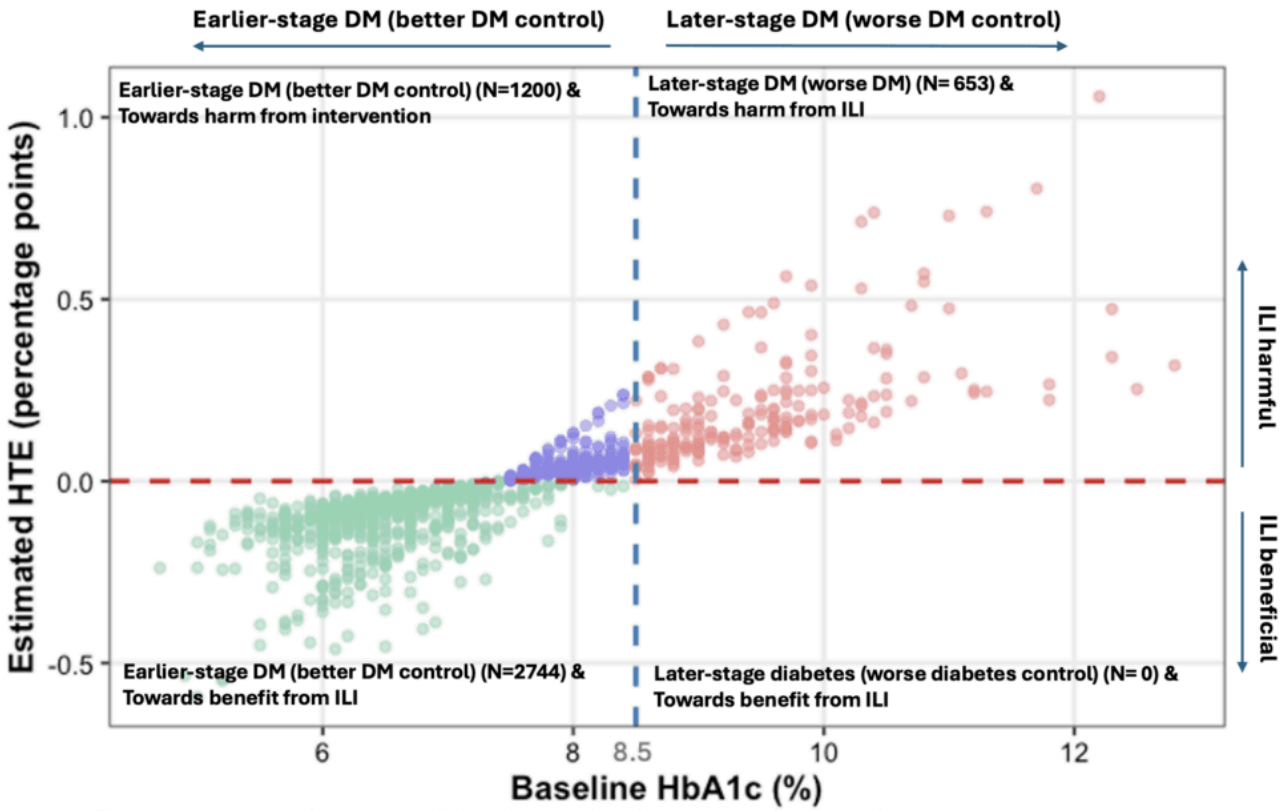


Figure. Association between individual conditional average treatment effect estimated using g-computation and glycated hemoglobin (HbA1c). HTE: heterogeneous treatment effect; DM: Type 2 diabetes mellitus, ILI: Intensive lifestyle intervention. 8.5% HbA1c cutoff from the generalized-HTE approach

Big Data/Machine Learning/AI

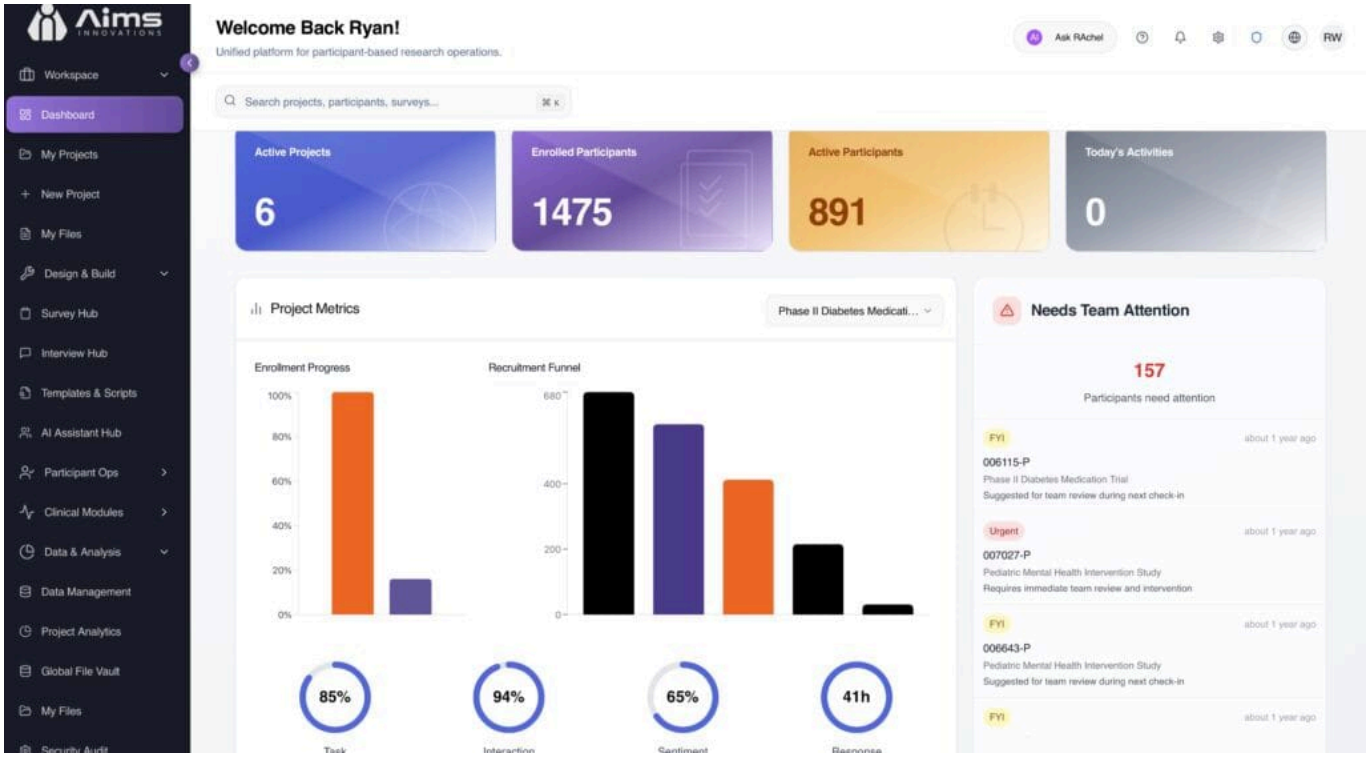
Governance-First AI Research Platform Accelerates Epidemiologic Studies: Multi-Site Implementation Allison Curry* Allison Curry Ryan Warren Johnathon Ehsani Dominique Ruggieri Joel Hillier

Epidemiologic research infrastructure remains fragmented across design, recruitment, engagement, data collection, and analysis—creating operational barriers. Rising personnel costs, compliance requirements, and funding instability mean fewer studies, longer timelines, and staff effort diverted from science to documentation—inefficiencies that compound in under-resourced settings where disease burden is highest.

We developed a HIPAA-compliant Research Management System (RMS) to accelerate participant-based epidemiologic studies while meeting institutional governance requirements. The RMS consolidates operations across the study pipeline with role-based access, immutable audit trails, and IRB-ready documentation. Protocol-grounded AI capabilities enable: multilingual participant recruitment; automated consent with comprehension validation; and real-time tracking of progress, participant engagement, and metrics. Security architecture and study-level isolation were designed for academic implementation. We evaluated feasibility and preliminary performance, with ongoing validation comparing response rates, representativeness, and data quality to traditional methods.

Five institutions—Harvard, Johns Hopkins, UWash, UIowa, Nationwide Children’s—completed security/IRB reviews and initiated projects. The UIowa feasibility study (n=20 survey) showed clear AI interactions, 2-day completion vs. 4-week conventional estimate, and staff effort reduced from 50 to 4 hours. Other validations will be completed in Spring 2026.

A governance-first AI platform successfully implemented across diverse academic settings demonstrated feasibility for accelerating epidemiologic operations. Preliminary findings suggest substantial efficiency gains; larger studies are evaluating methodological validity, representativeness, and equity implications. The RMS enables epidemiologic research in resource-constrained settings and accelerates evidence generation for time-sensitive public health decisions.


Aims
INNOVATIONS
Welcome Back Ryan!
Unified platform for participant-based research operations.
Ask RAchel
RW
Workspace
Dashboard
My Projects
New Project
My Files
Design & Build
Survey Hub
Interview Hub
Templates & Scripts
AI Assistant Hub
Participant Ops
Clinical Modules
Data & Analysis
Data Management
Project Analytics
Global File Vault
My Files
Search projects, participants, surveys...
⌘ K
Active Projects
6
Enrolled Participants
1475
Active Participants
891
Today's Activities
0
Project Metrics
Phase II Diabetes Medicati...
Enrollment Progress
100%
80%
60%
40%
20%
0%
Recruitment Funnel
680
400
200
0
85%
94%
65%
41h
Needs Team Attention
157
Participants need attention
FYI
about 1 year ago
006115-P
Phase II Diabetes Medication Trial
Suggested for team review during next check-in
Urgent
about 1 year ago
007027-P
Pediatric Mental Health Intervention Study
Requires immediate team review and intervention
FYI
about 1 year ago
006643-P
Pediatric Mental Health Intervention Study
Suggested for team review during next check-in
FYI
about 1 year ago

Big Data/Machine Learning/AI

Secure extraction of structured epidemiologic data from multilingual pathology reports using on-premise large language models Janos Tibor Fekete* Janos Tibor Fekete Mate Posta Aida Figler Zsofia Dobolyi Balazs Gyorffy

Background: The transformation of unstructured clinical text into structured, analysis-ready data remains a major bottleneck in epidemiology and cancer research. Although large language models (LLMs) offer substantial potential for clinical data extraction, their adoption is limited by concerns related to data sovereignty, multilingual performance, and infrastructure requirements. We introduce CIDER (ClinIcal Data ExtractoR), an open-source, on-premise LLM-based pipeline designed for secure, scalable extraction of structured epidemiologic variables from multilingual pathology reports.

Methods: CIDER employs an asynchronous FastAPI architecture combined with a vLLM inference engine to deploy the Qwen3-VL-32B-Instruct-FP8 model within an air-gapped institutional environment. System performance was evaluated using 2,073 real-world Hungarian-language histopathology reports from an institutional OnkoBank. Extraction accuracy was assessed against expert-curated registry data for seven key variables (sex, year of surgery, T stage, N stage, primary tumor site, histology, and tumor size). Technical reproducibility was evaluated across three independent runs (temperature = 0.1).

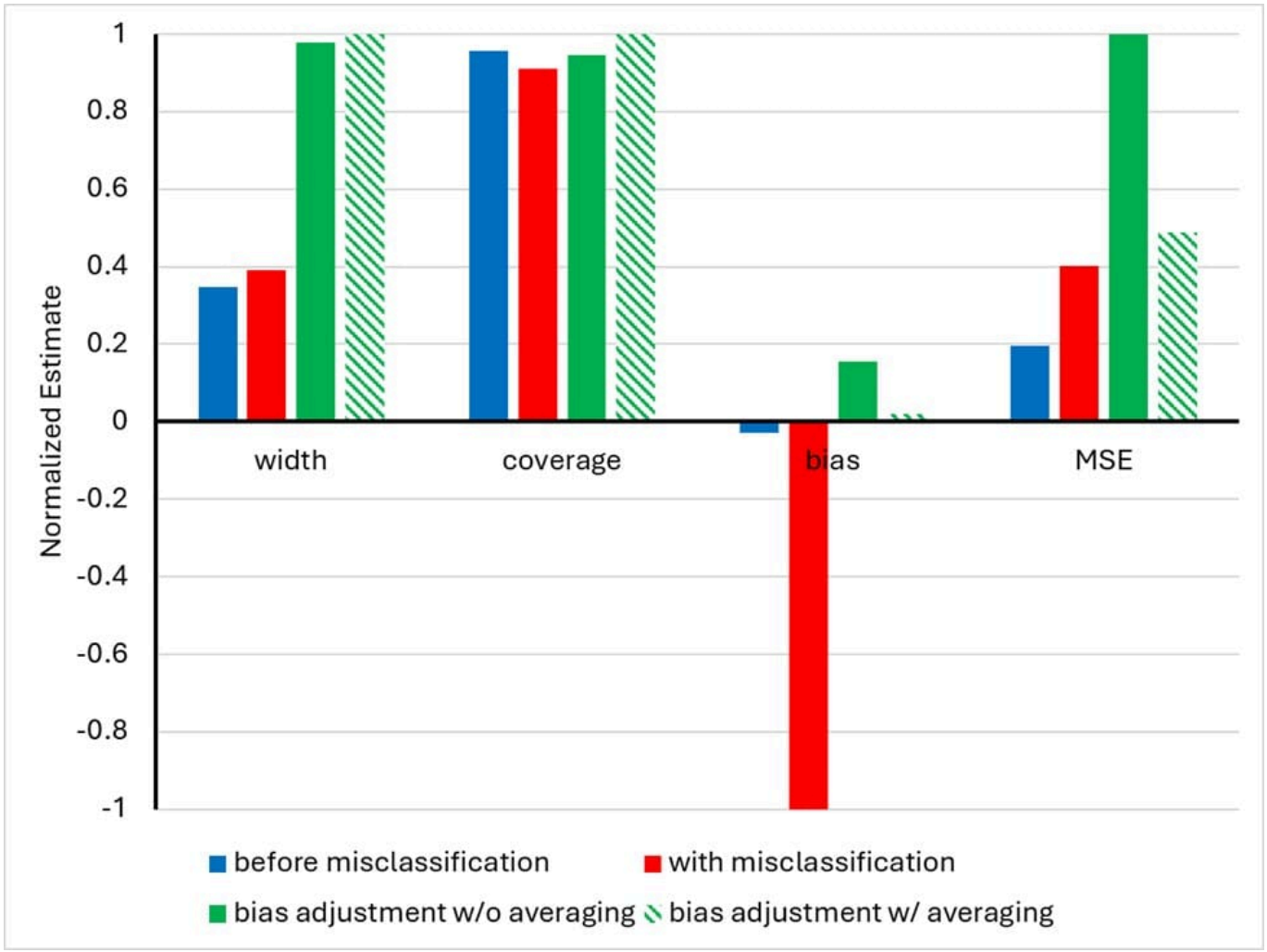
Results: CIDER demonstrated high concordance with expert-curated data, exceeding 98% accuracy for demographic variables and maintaining >95% accuracy for T stage and >92% for N stage. Importantly, the system recovered clinically valid information missing from manual curation, including 62.8% of previously unrecorded T stages (n = 713) and 91.5% of missing tumor size values (n = 289). Performance was highly stable across repeated runs and remained robust even at extreme temperature settings.

Conclusions: CIDER shows that locally deployed, open-source LLMs can achieve near–expert-level performance in extracting structured epidemiologic data from complex, English and non-English clinical narratives while fully preserving data sovereignty. CIDER is publicly accessible at: https://llm.gyorffylab.com/cider.

Methods/Statistics

Optimizing Use of Sparse Internal Validation Data Timothy L. Lash* Timothy L. Lash Richard F. MacLehose Huda Bashir Thomas P. Ahern Lindsay J. Collin

Internal validation sub-studies compare an observed imperfect measurement of an exposure, outcome, or covariate with its gold standard measurement in a sample of the study's participants. The gold standard measurement is usually expensive or otherwise difficult to collect, so the validation subsample—constrained by the costs—is typically small. To improve the information density of the validation subsample, validation studies usually sample conditional on disease status and the observed (misclassified) measurement rather than using a simple random sample. This conditional sampling allows valid direct estimation of predictive values within cases and non-cases but does not allow valid direct estimation of sensitivity or specificity. Reweighting the validation sample to account for the sampling fractions allows indirect estimation of sensitivity and specificity within cases and non-cases. If non-differential misclassification is expected, weighted averages of these sensitivities and specificities may yield more efficient estimators. We propose, for the first time, to take advantage of these pairs of indirect estimates by averaging them, then recalibrating the estimates of the predictive values used in quantitative bias analysis. Our hypothesis is that the recalibrated predictive values derived from the average of the pairs of independent estimates of sensitivity and specificity will yield better-performing bias adjustments. In our simulation of 10,000 cohorts each with 100,000 iterations of bias adjustments, we show that this new method optimizes the use of sparse validation data for bias adjustment. The averaged estimates yielded lower bias, lower mean squared error, similar simulation interval widths, and better interval coverage. Future work will vary the simulation, extend the method to misclassification involving outcomes, confounders, and modifiers, and combine it with other strategies that might improve the utility of sparse validation data.


Normalized Estimate
1
0.8
0.6
0.4
0.2
0
-0.2
-0.4
-0.6
-0.8
-1
width
coverage
bias
MSE
before misclassification
with misclassification
bias adjustment w/o averaging
bias adjustment w/ averaging

Methods/Statistics

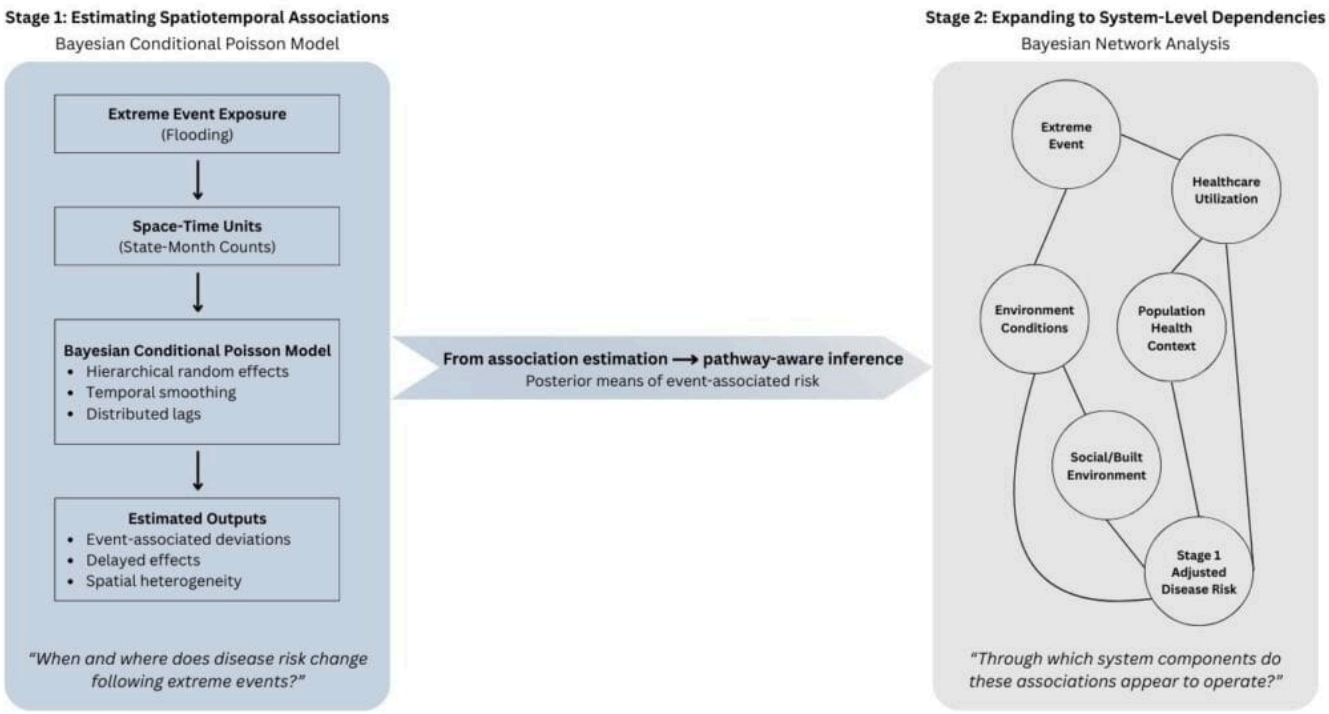
A Two-Stage Bayesian Framework for Pathway-Aware Inference of Infectious Disease Risk Following Extreme Weather Events Brittany L. Morgan Bustamante* Brittany L. Morgan Bustamante Simon K. Camponuri Aidan Lee Lisa Couper Mark Hoffman Theodore C. White Justin V. Remais

Background: Extreme weather events can influence infectious disease risk through pathways involving exposure, built and social environments, and healthcare utilization. Standard regression approaches often estimate associations but treat pathways as independent. This limits pathway-aware inference—whether associations operate directly or indirectly through intermediate system components—and the ability to identify effective interventions.

Methods: We developed a two-stage Bayesian framework to evaluate the influence of extreme weather events on infectious disease outcomes. First, we modeled spatio-temporal disease counts using a Bayesian conditional Poisson model with hierarchical random effects, temporal smoothing, and distributed lag terms to estimate changes in disease incidence associated with extreme weather events while accounting for spatial heterogeneity and secular trends. Second, we applied Bayesian Network Analysis (BNA) to integrate posterior estimates of event-associated risk from the Poisson model with measures of flood exposure, social/built environment, population health, and healthcare utilization, allowing the BN to characterize relationships among system components after accounting for spatio-temporal patterns. We demonstrate the framework using U.S. surveillance and electronic health record data from 2016-2023 to evaluate flooding-aspergillosis associations.

Results: In the flooding-aspergillosis case study, conditional Poisson models indicated that moderate-severe flooding events were associated with increased incidence of aspergillosis, with elevated risk following exposure and a subsequent decline at longer lags (7-12 months). BNA further highlighted complex pathways through which flooding may influence aspergillosis risk.

Conclusions: This work advances a systems-oriented epidemiologic framework that combines conditional Poisson regression with BNA to evaluate infectious disease risk following extreme weather events. Together, this approach supports more pathway-aware inference by distinguishing direct and indirect associations operating through interconnected system components that are difficult to assess using single-equation models and is broadly applicable across environmental exposures and health outcomes.


Conceptual Overview of a Two-Stage Bayesian Framework for Pathway-Aware Inference of Disease Risk Following Extreme Events
Stage 1: Estimating Spatiotemporal Associations
Bayesian Conditional Poisson Model
Extreme Event Exposure
(Flooding)
Space-Time Units
(State-Month Counts)
Bayesian Conditional Poisson Model
• Hierarchical random effects
• Temporal smoothing
• Distributed lags
Estimated Outputs
• Event-associated deviations
• Delayed effects
• Spatial heterogeneity
"When and where does disease risk change following extreme events?"
From association estimation ⟶ pathway-aware inference
Posterior means of event-associated risk
Stage 2: Expanding to System-Level Dependencies
Bayesian Network Analysis
Extreme Event
Healthcare Utilization
Environment Conditions
Population Health Context
Social/Built Environment
Stage 1 Adjusted Disease Risk
"Through which system components do these associations appear to operate?"

Causal Inference

Practical hands-on guidance for creating directed acyclic graphs in epidemiologic sub-fields where they are under-utilized Rachel R Yorlets* Rachel Yorlets Ana Karina Millones Gomez Eleanor Murray Hortencia Campos Sembrera Alicia Pilar Condeso Cynthia Celeste Vargas Chuan-Chin Huang Sonya Shin Judith Jimenez Leonid Lecca Helen E Jenkins Courtney M Yuen

Background

Directed acyclic graphs (DAGs) are essential for communicating epidemiologists' assumptions about context-specific data-generating processes. DAGs are underutilised in tuberculosis (TB) research and global health more broadly because implementation is challenging: TB research involves complex social factors that are difficult to represent on a DAG. We aimed to develop and document a reproducible process for creating DAGs for TB.

Methods

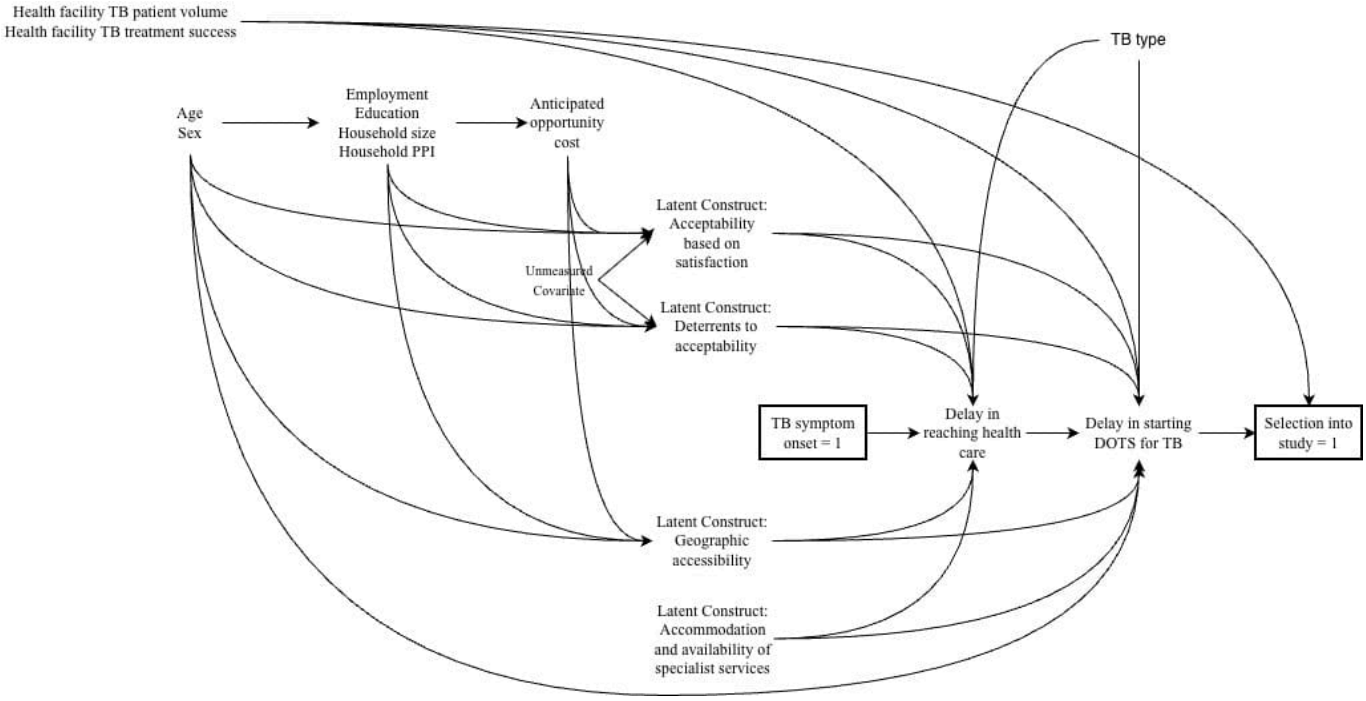
In our underlying study, we aimed to understand how care-seeking factors are associated with time to TB treatment initiation in Lima, Peru; we surveyed participants on exposures representing pre-TB care access. We began with an initial DAG drafted by a TB expert who works in Lima. Next, we undertook an iterative decision-making process on how to 1) operationalize the exposures and outcome, 2) depict study selection, 3) represent symptomaticity as an effect measure modifier, and whether to include 4) mediators, 5) measurement error, or 6) multiple time points. Finally, we created a structured process for identifying, defining, and assessing the inclusion of measured and unmeasured covariates. We illustrated each step with annotated interim DAGs.

Results

We provide documentation and templates for collaborative decision-making steps that multidisciplinary teams can use to develop DAGs. Our documented process includes a scoping literature review, consultations with context experts, systematic revision of covariate definitions, and consensus-building on DAG structure with a focus on omitted edges and nodes. At each step, we focus on DAG-building aspects common to implementation-heavy fields where causal inference methods are uncommon. We share the final DAG.

Discussion

With increased transparency on how to apply DAGs to complex research questions, we help make foundational methods translational to fields like TB. We emphasize processes for DAG development that allow analyses to be grounded in evidence and subject-matter expertise.


Health facility TB patient volume
Health facility TB treatment success
TB type
Age
Sex
Employment
Education
Household size
Household PPI
Anticipated opportunity cost
Latent Construct: Acceptability based on satisfaction
Unmeasured Covariate
Latent Construct: Deterrents to acceptability
TB symptom onset = 1
Delay in reaching health care
Delay in starting DOTS for TB
Selection into study = 1
Latent Construct: Geographic accessibility
Latent Construct: Accommodation and availability of specialist services

Methods/Statistics

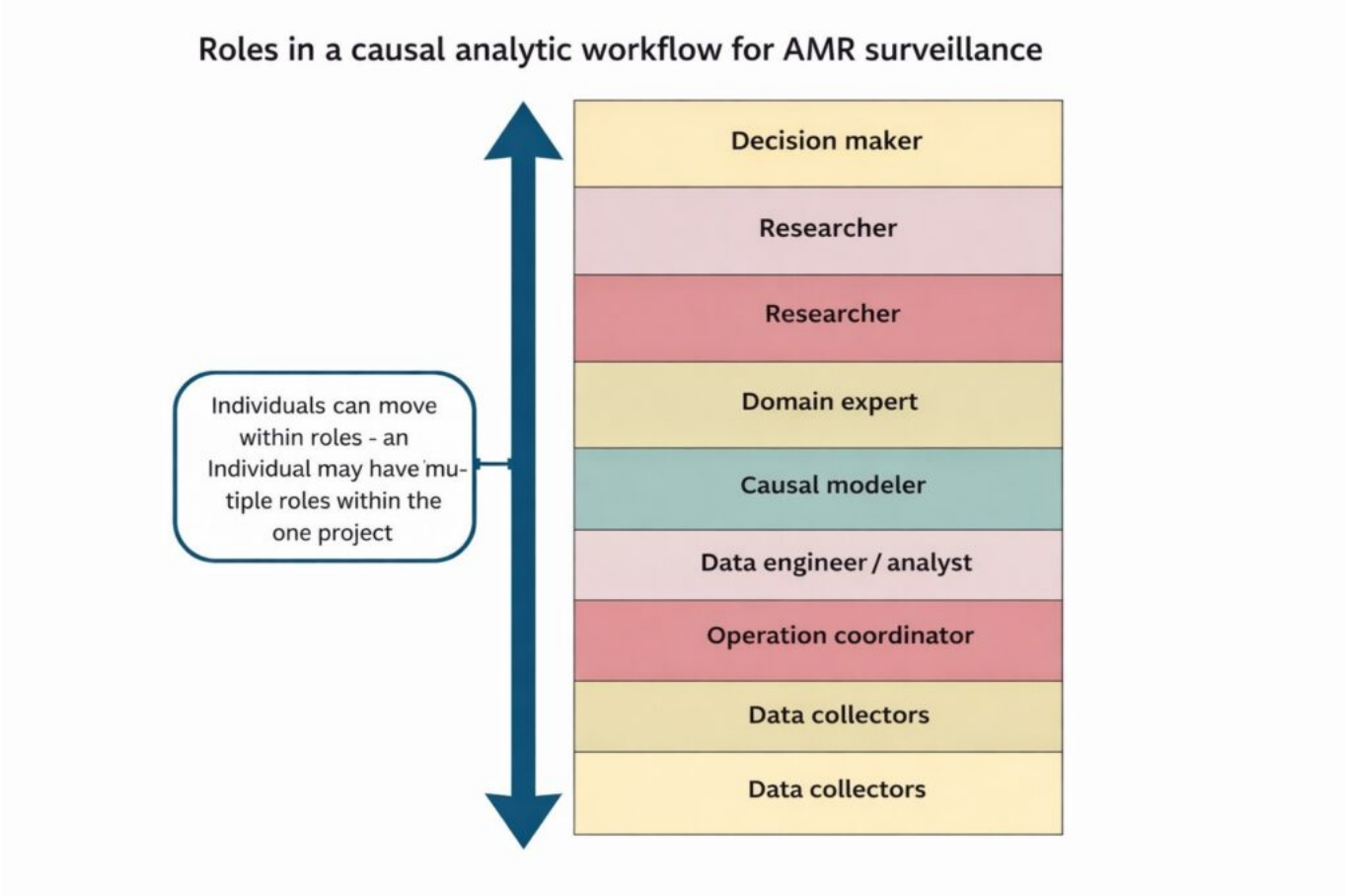
A Causal Analytic Workflow for Processing Clinically Linked Antimicrobial Resistance Surveillance Data Mengyao Tang* Mengyao Tang Michelle

Background:
Antimicrobial resistance (AMR) surveillance is essential for understanding disease burden and informing policy, yet analytic efforts are often constrained by fragmented data structures, inconsistent denominators, and limited linkage between microbiological and clinical data—particularly in low- and middle-income settings and neonatal populations. These challenges hinder reproducibility, comparability, and valid causal inference.

Methods:
We developed a standardized causal analytic workflow to guide the processing of clinically linked AMR surveillance data into a reproducible and generalizable analytic structure. Using data from two neonatal AMR surveillance systems—the ACORN2 project in the Philippines and the multicenter NeoSEAP study across South and Southeast Asia—we applied a directed acyclic graph (DAG)–informed approach to identify key variables along the causal pathway to resistant infection. Raw laboratory and clinical data with differing formats (long and wide) were transformed into a unified data architecture organized around four epidemiologic concepts: persons, episodes, specimens, and organisms. Reproducible R scripts were used to standardize data linkage, account for contaminants using a pathogenicity classification, and summarize antimicrobial use through WHO AWaRe categories.

Results:
The proposed workflow enabled consistent handling of multiple infection episodes, appropriate denominator selection, and systematic integration of clinical and microbiological information across heterogeneous data sources. Data monitoring reports identified missingness, data entry errors, and enrollment patterns, while analytic outputs supported epidemiologic analyses of pathogen distribution, antimicrobial use, and clinical outcomes. Applying the workflow across two structurally distinct datasets demonstrated its generalizability and scalability.

Conclusions:
This causal analytic workflow provides a practical framework for processing AMR surveillance data that enhances reproducibility, supports valid epidemiologic inference, and reduces analytic burden. By aligning data processing with causal structure and surveillance objectives, this approach facilitates higher-quality AMR reporting and can be adapted for diverse infectious disease surveillance settings.


Roles in a causal analytic workflow for AMR surveillance
Individuals can move within roles - an Individual may have mutiple roles within the one project
Decision maker
Researcher
Researcher
Domain expert
Causal modeler
Data engineer / analyst
Operation coordinator
Data collectors
Data collectors

Methods/Statistics

Mode effects on survey item measurement: A systematic review of the experimental evidence Georgia Tomova* Georgia Tomova Richard Silverwood Liam Wright

Survey data are increasingly collected using mixed-mode designs (e.g., face-to-face and online). However, item measurement may differ between modes, introducing ‘mode effects’, a form of systematic measurement error. While the literature discusses the theoretical mechanisms behind this in detail, empirical evidence on the occurrence and magnitude of mode effects is fragmented. Further, some statistical approaches for handling mode effects, such as quantitative bias analysis, remain underused due to the need for such external evidence. Motivated by these issues, we conducted a systematic review of experimental studies of mode effects. We searched multiple bibliographic databases and the grey literature, with backward and forward citation screening. Eligible studies had random allocation of survey mode, sampled from the general population (or age-, sex-, or region-specific strata thereof), and reported mode effect estimates on item measurement. We extracted comprehensive details on the study design, sampling, mode effect estimates, and reporting. Ninety experiments published from 1967 to 2024 met the inclusion criteria, comprising 4,113 mode effect estimates for 3,545 variables. Mode effects were generally small (typically under 0.2 SD). However, larger mode effects were more commonly observed when modes differed by direct interviewer involvement or by question delivery (i.e., visual vs aural), and when variables were sensitive (e.g., sexual behaviour, social life), aligning with pre-existing theory on the causes of mode effects. Generally, mode effects were variable-, mode-, and population-specific. However, reporting quality varied substantially. Post-randomisation non-response and compliance were commonly not reported or not addressed, and may have therefore introduced bias. We collated all mode effect estimates into a free online database to inform future study design and analysis, and provide a set of recommendations to improve the reporting of future research.

Big Data/Machine Learning/AI

Epidemiology in space! Reproduce your research anywhere Malcolm Barrett* Malcolm Barrett

Voyager I and II, launched in 1977, each have about 70 kilobytes of memory, less than most of the smallest files on our phones. Although 50 years old, scientists that maintain these probes sometimes make impressive code maneuvers to keep the probes communicating with Earth. Yet, here on Earth, we often have trouble running analysis code from last week. Why is it so hard to reproduce code, and how can we make ours more resilient to changing technology? At the Health Policy Data Science Lab, we have cultivated a framework of thinking about reproducibility, durability and duration of code. We provide guidance to our scientists on what techniques to apply, including reproducible documents, version control, package management, and containerization, as well as when to apply them. Our comprehensive approach to reproducibility provides both a way of thinking about reproducibility and practical applications that has been applied to papers in population health, statistical methods, decision science, and more. In this talk, I'll share our framework and techniques as well as guidance on getting started in your own lab.

Science Communication & Media

“This article may be too technical for most readers to understand. Please help improve it.” – Improving epidemiology content on Wikipedia. Anna Palmer* Anna Palmer Peter Socha

Wikipedia is one of the most widely used reference sources in the world, and is increasingly used to train large language models that shape how medical and public health information is accessed and summarized. At the same time, many articles describing fundamental epidemiologic concepts are incomplete, outdated, or misleading. Building on our symposium at the 2026 SER Mid Year Meeting, we aim to (1) provide background on how Wikipedia functions as part of the modern health information ecosystem, (2) highlight successful efforts from other scientific and medical fields that improved content through coordinated editing, and (3) describe ongoing initiatives focused on strengthening articles in epidemiology and related disciplines. Using examples from society-led programs, including the International League Against Epilepsy’s Wikipedia Epilepsy Project, we illustrate how organized participation has improved article quality while creating opportunities for student training and professional recognition. We then summarize efforts to improve epidemiology content since the 2026 SER Mid Year Meeting. The poster is intended as an information and engagement space, offering practical resources for getting involved in editing and an opportunity for discussion about how epidemiologists can collaboratively improve the reliability and visibility of epidemiologic knowledge on Wikipedia.

Cardiovascular

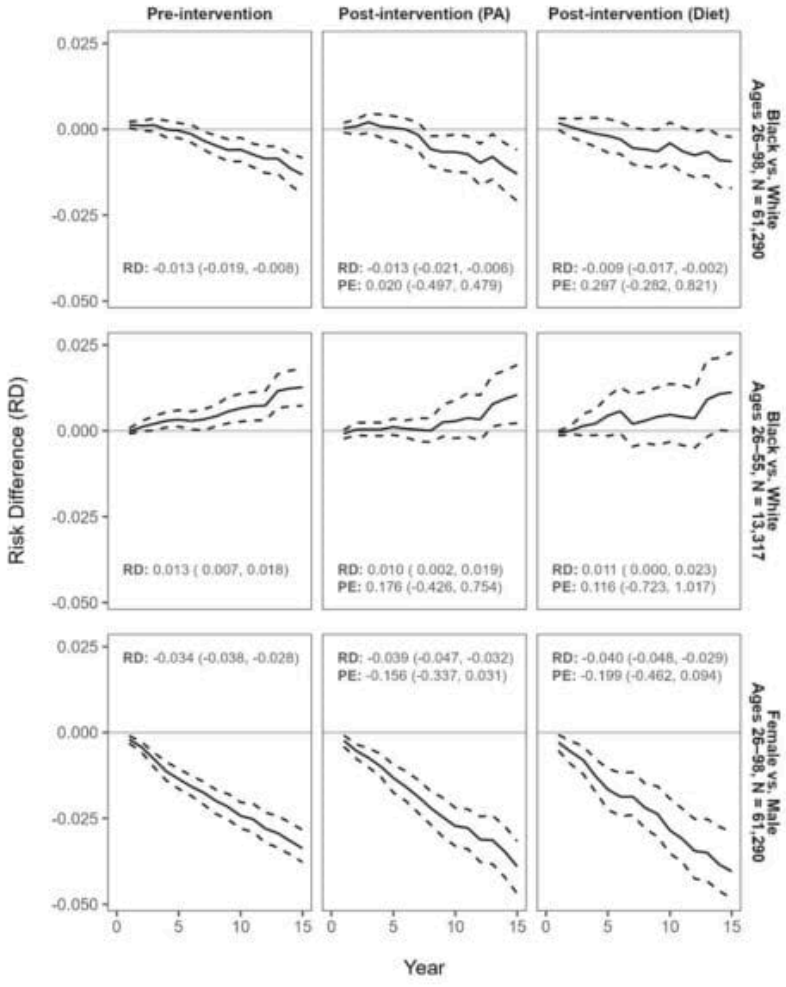
Hypothetical interventions on lifestyle factors to reduce racial and sex differences in incident heart failure: a causal mediation analysis Han-Chih Hsieh* Chanelle Howe Jason Gantenberg Han-Chih Hsieh Mir Moafi Mandani Mary Roberts James Newburg Faraz Ahmad Norrina Allen Daniel Forman David Jacobs Jorge Kizer Emily Levitan Anna Kucharska-Newton Wayne Rosamond Vanessa Xanthakis Michael LaMonte Charles Eaton

Race and sex differences in incident heart failure (HF) remain substantial in the US. Modifiable lifestyle factors (e.g., physical activity (PA) and diet) may be mediators. We quantified the extent to which hypothetical interventions that achieved recommended PA levels or yielded healthier diets reduced race and sex differences in incident HF.

A causal mediation analysis was performed among Black and White males and females included in harmonized data from 8 US cohorts (i.e., WHI, FHS, ARIC, Health ABC, REGARDS, CARDIA, CHS, and MESA). We used Aalen-Johansen estimators—inverse probability weighted based on lifestyle, clinical, or sociodemographic factors—to estimate RDs for incident HF by race or sex for the first 15 years of follow-up. This estimator accounted for measured sources of selection and confounding bias, and the competing risk of death. Time zero was study entry or a later time when necessary data were available. RDs were calculated before and after a hypothetical intervention on PA or diet. The PA intervention set all participants at time-zero to exercise moderately or vigorously for 150 mins/wk, or vigorously for 75 mins/wk. The diet intervention set all participants at time zero to be in the top two quintiles of the Alternative Healthy Eating Index 2010. RDs before and after the intervention were used to calculate a PE, the proportion of the pre-intervention race or sex difference that would be eliminated due to the intervention. Race and sex analyses were performed among participants who were 26-98 years old at time zero (n=61,290). Race analyses were also among participants who were <=55 at time zero (n=13,317).

Among participants of all ages at time zero, race differences at year 15 of follow-up were reduced after both interventions. The same result was observed among participants aged <=55 at time zero. Sex differences at year 15 were not reduced (Figure). Real world interventions on PA or diet may reduce race differences in incident HF in the US.

Figure. Risk Differences (RDs) for incident heart failure by race or sex among Black and White males and females included in harmonized data from 8 US cohorts (i.e., WHI, FHS, ARIC, Health ABC, REGARDS, CARDIA, CHS, and MESA). RDs refer to before and after a given hypothetical intervention at time-zero. Numeric RD values refer to year 15. The RDs at year 15 were used to calculate the proportion eliminated (PE) at year 15. Solid lines represent point estimates and dashed lines represent the upper and lower bound of pointwise 95% confidence limits (CLs) estimated at one-year intervals. 95% CLs were estimated using the non-parametric bootstrap percentile method based on 200 bootstraps.



Cardiovascular

Sex-Specific Differences in Premature Cardiovascular Disease Subtypes in Adults from East Asia Yuichiro Mori* Yuichiro Mori Hokyou Lee Dasom Son Ryuichiro Yagi Yuichiro Yano Hyeon Chang Kim Sadiya S. Khan Kosuke Inoue

Background: While it is well-established that women experience atherosclerotic cardiovascular disease (ASCVD) at later ages compared with men, sex-specific data on premature onset of heart failure (HF) and its antecedent risk factors, are limited. This is of unique interest in East Asia where rapid epidemiologic transitions are shifting the burden of cardiovascular disease.

Methods: This bi-national cohort study used data from the Japan Health Insurance Association (JHIA) and the Korean National Health Insurance Service (KNHIS). We included adults aged 35–59 years at baseline without prior ASCVD or HF. The primary outcome was premature CVD defined as ASCVD or HF occurring before age 65. We calculated differences by sex in the age-of-onset with cumulative incidence functions. We also calculated hazard ratios (HRs) by sex for traditional risk factors and incident CVD using Cox proportional hazards models and evaluated differences in these associations between women and men.

Results: Among 5,442,337 participants in the JHIA and 5,226,414 participants in the KNHIS, mean age was 46.2 (7.0) and 46.7 (6.7) years, and 33.2% and 42.6% were women, respectively. Women developed incident premature CVD 11.4 years and 7.3 years later than men in the JHIA and the KNHIS, respectively, with similar patterns for ASCVD and HF. Traditional risk factors were significantly associated with premature ASCVD and HF in both sexes. Notably, the magnitude of association between each risk factor and HF was largely similar for women and men.

Conclusions: While women experience HF at older ages compared with men, antecedent risk factors and the magnitude of association between traditional risk factors and HF were largely similar underscoring prioritization of preventive efforts earlier in the life course for both women and men.

Study Overview
A Bi-National Cohort Study

10.6 Million Adults from East Asia

5.4M adults from Japan

5.2M adults from Korea

Outcome

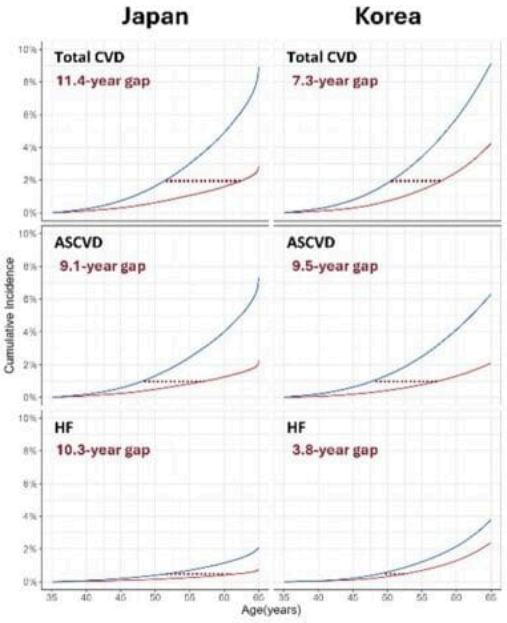
Total CVD (ASCVD or HF) before age 65

Baseline Profile

Women had more favorable profiles

- ✓ Lower BMI
- ✓ Lower blood pressure
- ✓ Lower prevalence of smoking
- ✓ Lower prevalence of diabetes

Age-of-Onset Gap
Women Experience a Later Onset of Premature CVD Compared with Men



Associations Between Risk Factors and Premature CVD

✓ Significant association between major risk factors and premature CVD in both sexes

e.g.,
- Smoking
- Diabetes
- Systolic BP

✓ **Largely similar magnitude of associations** in women and men.

Clinical Implications

Later premature CVD onset in women is likely driven by a more favorable baseline risk factors.

⚠ **Targeting traditional risk factors early** is essential for both women and men.

Cardiovascular

Effect of Smoke-Free Laws on Cardiovascular Disease (CVD) Mortality in US counties, 2000–2018: An Application of the Generalized Synthetic Control Method Chuyue Wu* Chuyue Wu Mina Habib Nathan D. Wong Tony Kuo May C Wang Roch A. Nianogo

Comprehensive smoke-free laws reduce secondhand smoke exposure and may lower cardiovascular disease (CVD) risk, but long-term effects on cardiovascular disease (CVD) mortality and the distribution of benefits across subgroups remain uncertain. We estimate the long-term impact of comprehensive smoke-free laws on county-level CVD mortality and assess heterogeneity by age, sex, and race/ethnicity. We conducted a quasi-experimental study of U.S. counties from 2000–2018 using the generalized synthetic control method (GSCM) with staggered policy adoption. Treated counties (n=38) implemented comprehensive 100% smoke-free laws in workplaces, restaurants, and bars between 2007 and 2018, while control counties (n=103) never adopted such laws. The outcome was annual age-adjusted CVD mortality per 100,000 population (ICD-10 I00–I99), analyzed overall and stratified by age (25–64 years, ≥65 years), sex, and race/ethnicity. We estimated year-specific and 12-year averaged average treatment effects on the treated (ATTs) with bootstrapped 95% confidence intervals. Smoke-free laws were associated with sustained reductions in overall CVD mortality (12-year averaged ATT −12.0 per 100,000; 95% CI, −21.3 to −2.7). Larger reductions were observed among adults aged ≥65 years (ATT −84.4; 95% CI, −146.0 to −22.7), men (ATT −16.8; 95% CI, −26.5 to −7.0), and non-Hispanic White populations (ATT −12.6; 95% CI, −21.5 to −3.7). Effects among adults aged 25–64 years, women, and non-Hispanic Black populations were smaller and imprecise. Year-specific post-policy ATTs are shown in the **Figure**. Comprehensive smoke-free laws were associated with meaningful and durable declines in county-level CVD mortality, but benefits were uneven across demographic groups. Equity-focused implementation and enhanced protections are needed to address persistent disparities in second-hand smoke exposure and cardiovascular outcomes.

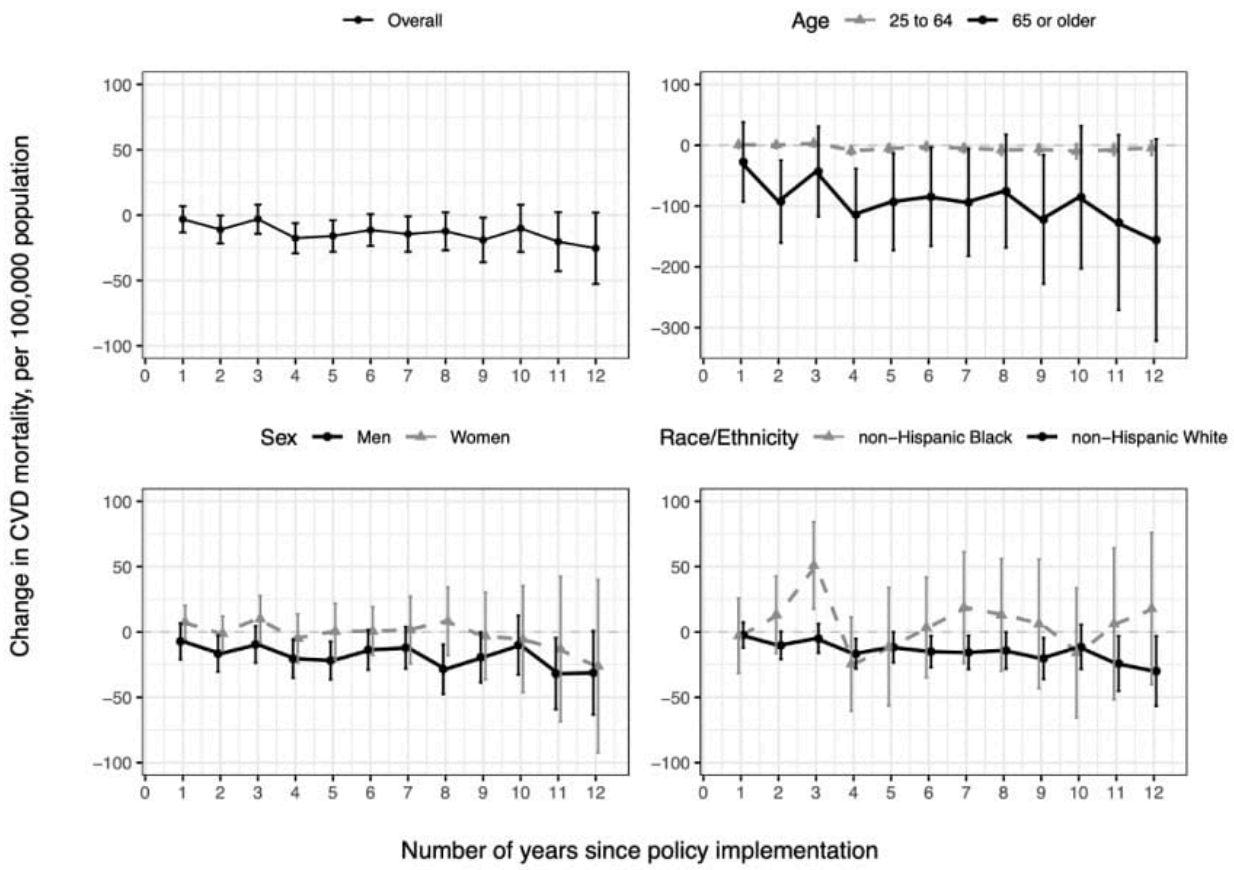


Figure. Post-policy year-specific effects of comprehensive 100% smoke-free laws on age-adjusted cardiovascular disease (CVD) mortality per 100,000 population overall and by age, sex, and race/ethnicity. Points represent average treatment effects on the treated (ATT) by year since policy implementation, with vertical lines indicating 95% confidence intervals.

Cardiovascular

Serum Metabolomics and the Risk of Ischemic Heart Disease Death: Evidence from the Golestan Cohort Study Mahdi Nalini* Mahdi Nalini Hossein Poustchi Cristian C Abnet Arash Etemadi Reza Malekzadeh

Background: Established cardiovascular risk factors do not fully explain the burden of atherosclerotic cardiovascular disease. We evaluated associations between 250 serum metabolomic measures and ischemic heart disease (IHD) mortality to identify prediagnostic biomarkers.
Methods: We conducted a case-cohort nested within the population-based Golestan Cohort Study (n = 50,045; ages 40–75 years; 58% women; enrollment 2004–2008) in northeastern Iran. Metabolites were quantified using nuclear magnetic resonance spectroscopy by Nightingale. After excluding participants with prior cardiovascular events, the analysis included 387 IHD deaths and 458 subcohort noncases. Associations were estimated between standardized (z-score) biomarker measures and IHD death through 2018 using Cox regression models with age as the time scale and stratified/adjusted for sex, residence, ethnicity, education, wealth, physical activity, fruit and vegetable intake, tobacco smoking, opium use, obesity, hypertension, and diabetes. Bonferroni correction was applied for multiple testing.
Results: The mean (SD) age at baseline was 57.5 (9.5) years, and the median follow-up was 9.1 years. An increased risk of death from IHD was associated with higher apolipoprotein B-to-A1 ratio [HR, 1.49; 95% CI, 1.19–1.86; P=0.0006], large-size high-density lipoprotein free cholesterol (% of total lipids) [1.44; 1.15–1.80; 0.0017], tyrosine [1.40; 1.13–1.72; 0.0019], and creatinine [1.54; 1.17–2.03; 0.0021], whereas albumin [0.75; 0.62–0.89; 0.0012] and medium-size high-density lipoprotein cholesteryl ester [0.74; 0.62–0.90; 0.0021] were inversely associated. Additional adjustment for routine blood lipids did not materially change these associations.
Conclusion: Specific biomarkers—including lipoprotein subclass composition, tyrosine, albumin, and creatinine—were independently associated with death from IHD, highlighting their potential value in risk assessment beyond traditional cardiovascular risk factors.

Pharmacoepidemiology

Target Trial Emulation of Semaglutide vs Tirzepatide on Cardiovascular Outcomes in Patients with Obesity and Established CVD Rafeya Raquib* Rafeya Raquib Gwen Aubrac Minh Le Andrew C. Stokes

Introduction: Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) and the dual glucose-dependent insulinotropic polypeptide and GLP-1 RA tirzepatide have shown cardiovascular benefits in patients with diabetes. Recently, semaglutide was indicated for cardiovascular risk management in patients without diabetes. Direct comparative evidence on cardiovascular protection between semaglutide and tirzepatide in patients with obesity but without diabetes remains limited.

Methods: We used an active comparator new user design and target trial emulation framework to compare 5-point and 3-point MACE risk in new users of semaglutide and tirzepatide with obesity and CVD but without diabetes from Komodo Health (11/8/2023-5/31/2025). We used a per-protocol approach over 18 months of follow-up, censoring those with ≥90 day-gaps in supply or treatment switching. We applied inverse probability of treatment weights (IPTW) and inverse probability of censoring weights (IPCW). We estimated hazard ratios from weighted Cox proportional hazards models and incidence rate differences from weighted Kaplan-Meier curves with 1,000 bootstrap samples.

Results: We identified 6,903 new users of semaglutide and 6,937 new users of tirzepatide. Semaglutide users tended to be older, have more comorbidities, and were more likely to have commercial insurance, but balance was achieved after weighting. Risk of 5-point MACE was 18% higher in semaglutide compared to tirzepatide users (HR=1.18, 95% CI: 1.09 to 1.3), while risk of 3-point MACE did not differ (HR=1.09, 95% CI: 0.94 to 1.27).

Conclusions: MACE risk was lower for tirzepatide compared to semaglutide in those with obesity and CVD but without diabetes. Given the proven cardiovascular benefit of semaglutide compared to placebo from clinical trials, these findings suggest tirzepatide can be a promising alternative treatment option. Future research should confirm these results, which may have implications for expanding the indication of tirzepatide.

Outcome	Weighted incidence rate per 1,000 py in Semaglutide group	Weighted incidence rate per 1,000 py in Tirzepatide group	HR (95% CI)
5 point MACE	255.1 (238.7, 271.6)	203.9 (187.8, 219.9)	1.18 (1.09 to 1.31)
Ischemic stroke	89.5 (79.7, 99.3)	78.2 (66.7, 85.6)	1.11 (0.95 to 1.29)
Myocardial infarction	33.1 (27.5, 38.7)	31.7 (25.4, 38.0)	0.99 (0.77 to 1.30)
Heart failure	11.6 (10.6, 12.6)	9.5 (8.5, 10.6)	1.29 (1.14 to 1.46)
Coronary revascularization	10.9 (9.8, 11.9)	7.2 (6.2, 8.1)	1.64 (1.40 to 1.93)
All-cause mortality	-	-	-
3 point MACE	94.8 (84.9, 104.8)	81.7 (71.9, 91.6)	1.09 (0.94 to 1.27)





Cardiovascular

Diet quality and incident heart failure among individuals with preclinical heart failure: a prospective UK Biobank cohort study Fang Zhu* Fang Zhu Gretell Henriquez Santos Carolina Downie Jungnam Joo Mercedes Sotos Prieto Maryam Hashemian Veronique Roger

Background: The preclinical stage of heart failure (HF), affecting over half of adults, represents a critical window for preventive intervention, yet the effects of diet quality on subsequent HF risk in this population remain unexplored.

Objective: To examine the association of the alternative Mediterranean diet (AMED) score with incident clinical HF among preclinical HF individuals.

Methods: Using UK Biobank data (2006-2010), we analyzed 93,541 participants (51.1% women) with preclinical HF with ≥2 valid 24-hour dietary recalls, followed through 2023. AMED scores (0-9 points) were calculated from 9 food items, with higher scores indicating greater adherence. Cause-specific hazard models were used to examine the associations of AMED scores with incident clinical HF, accounting for competing risk and adjusting for potential confounders. We examined potential interaction effects with age, sex, Townsend Deprivation Index (TDI), and baseline10-year predicted HF risk.

Results: During a median of 13.7-year follow-up, 2,801 incident HF events occurred. Each one-point increase in AMED score was associated with a 6% lower risk of HF (HR: 0.94; 95% CI: 0.92-0.96). Compared with the lowest adherence group (scores 0-2), those with the highest adherence (scores 7-9) had a 25% lower HF risk in the fully adjusted model (HR: 0.75; 95% CI: 0.65-0.86). A significant interaction with TDI was observed (p for interaction=0.006). Subgroup analyses indicated that the association between AMED scores and HF risk was present only among the most deprived participants (HR: 0.56; 95% CI, 0.44-0.72 for scores 7-9 compared with scores 0-2). No significant interaction effects between AMED score and sex, age, and HF risk were observed.

Conclusion: In preclinical HF, higher adherence to the AMED was associated with a lower risk of HF, particularly among those who live in more deprived areas. Higher adherence to a healthy dietary pattern supports diet as a potential strategy for early HF prevention.

Perinatal & Pediatric

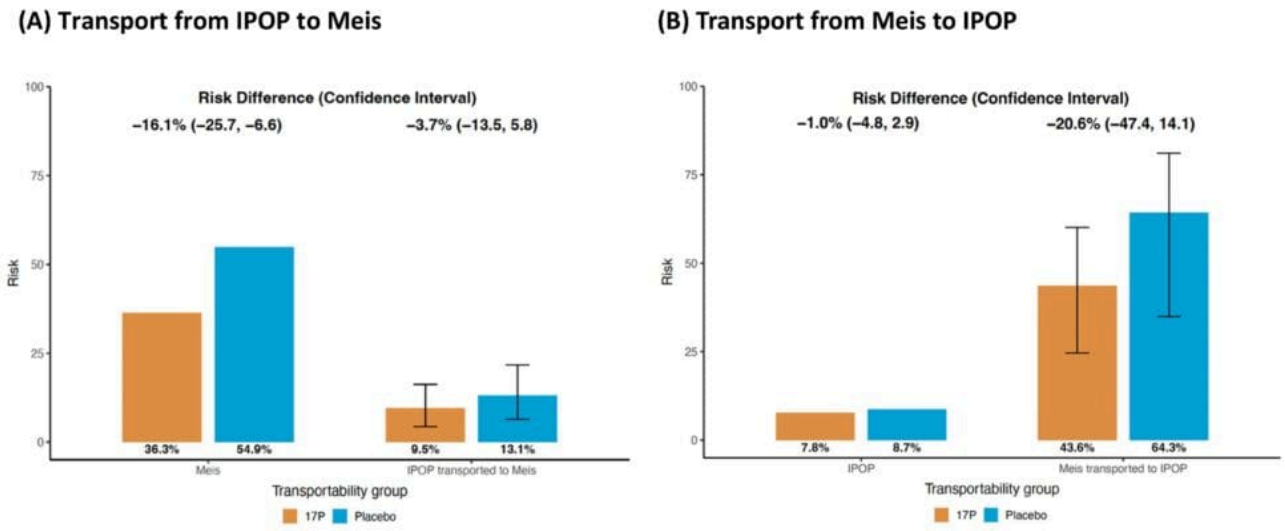
When high risk is not one category: Transportability of 17 alpha-hydroxyprogesterone caproate trial results in preterm delivery Ellen C Caniglia* Lin-Chieh Meng Enrique F Schisterman Eric Tchetgen Tchetgen Daniel Xu Stephen R Cole Jeffrey S A Stringer Stefanie N Hinkle Sunni L Mumford

Background: The 2003 Meis trial found that 17α-hydroxyprogesterone caproate (17OHP-C) reduced recurrent preterm birth among individuals with a prior spontaneous preterm delivery (RD, −18.6%; 95% CI, −28.2% to −9.1%). In contrast, the 2021 IPOP trial found no benefit of 17OHP-C for preventing preterm birth among pregnant individuals living with HIV without a history of preterm birth (RD, −1.0%; 95% CI, −4.8% to 2.9%). Although both populations are considered at high risk for preterm birth, the trials differed not only in eligibility pathways but also in age, education, and other sociodemographic factors. These conflicting findings have raised questions about whether differences in population characteristics may explain the inconsistency in 17OHP-C's effectiveness across high-risk groups.

Methods: We conducted bidirectional transportability analyses, transporting treatment effects from Meis to IPOP and from IPOP to Meis, using individual participant data from both trials. In the original trials, weekly intramuscular injections of 17OHP-C or placebo were administered. The primary outcome in this study was preterm delivery before 37 weeks' gestation. We used doubly robust estimators combining outcome modeling with inverse odds of trial selection weighting to transport treatment effects between trials while accounting for differences in baseline covariates.

Results: Transporting the Meis results to the IPOP population yielded an RD of −20.6% (95% CI, −47.4% to 14.1%), indicating a more protective effect than the original IPOP estimate, although with a wide CI overlapping the IPOP result. Transporting the IPOP results to the Meis population produced an RD of −3.7% (95% CI, −13.5% to 5.8%), moving closer to but not aligning with the Meis estimate. Restricting Meis participants to those with documented infections during pregnancy attenuated the result (RD, −8.0%; 95% CI, −24.3% to 8.4%) and more closely matched the IPOP findings.

Discussion: These findings indicate that differences in measured baseline characteristics did not explain the inconsistency between trials. The effectiveness of 17OHP-C may vary by underlying biological pathways and may not generalize across distinct high-risk populations.


(A) Transport from IPOP to Meis
Risk Difference (Confidence Interval)
−16.1% (−25.7, −6.6)
−3.7% (−13.5, 5.8)
Risk
100
75
50
25
0
36.3%
54.9%
9.5%
13.1%
Meis
IPOP transported to Meis
Transportability group
17P
Placebo
(B) Transport from Meis to IPOP
Risk Difference (Confidence Interval)
−1.0% (−4.8, 2.9)
−20.6% (−47.4, 14.1)
Risk
100
75
50
25
0
7.8%
8.7%
43.6%
64.3%
IPOP
Meis transported to IPOP
Transportability group
17P
Placebo

Perinatal & Pediatric

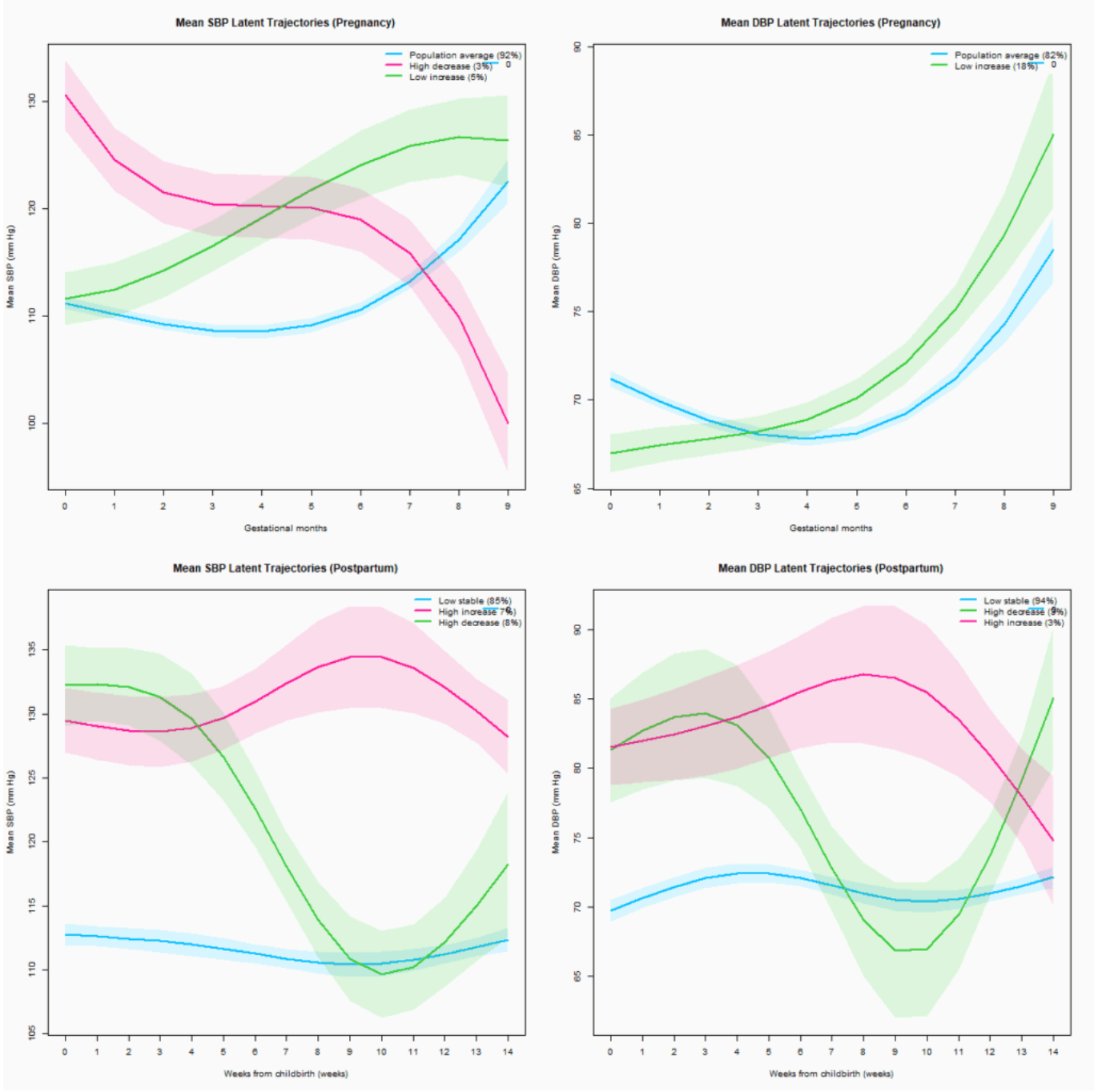
Blood pressure trajectories from early pregnancy through early postpartum: A descriptive Latent Class Growth Model analysis Rui Ling* Rui Ling Mengling Liu Yu Chen Anais Hausvater Shilpi S. Mehta-Lee Leonardo Trasande Linda G. Kahn

Background: Average blood pressure (BP) in pregnancy follows a shallow U-shape, but individual trajectories vary. This study used electronic medical records (EMR) data to investigate characteristics of latent classes of systolic (SBP) and diastolic (DBP) BP from early pregnancy through “the fourth trimester” postpartum, a critical but less studied period of cardiovascular (CV) risk.

Methods: We included women with singleton live births or stillbirths in the NYU Children’s Health and Environment Study (2016–2023). BP from EMR during nonurgent encounters was modeled with latent class growth models separately for pregnancy (N=1,563) and ≤14 weeks postpartum (N=1,326). Inclusion required a baseline and ≥2 additional BP measures per period. We used Bayesian Information Criterion, class sizes, and entropy for model selection; and Chi-square tests and Kruskal–Wallis tests for group differences.

Results: In pregnancy, we identified three classes for SBP: ‘Population average’ (92%), ‘High decrease’ (3%), and ‘Low increase’ (5%); and two for DBP: ‘Population average’ (82%) and ‘Low increase’ (18%). Both ‘Low increase’ SBP/DBP were associated with higher risk of hypertensive disorders of pregnancy (HDP). The SBP ‘High decrease’ class was enriched with prior chronic hypertension. Postpartum SBP and DBP each had three classes: ‘Low stable’ (85% for SBP; 94% for DBP), ‘High decrease’ (8% SBP; 3% DBP), and ‘High increase’ (7% SBP; 3% DBP); both ‘High increase’ and ‘High decrease’ were associated with prior HDP and chronic hypertension. We also observed class differences by race/ethnicity and other sociodemographic factors; and prenatal smoking was more prevalent in higher-risk postpartum DBP classes.

Conclusions: In a diverse, urban pregnancy cohort we identified distinct BP trajectories in pregnancy and early postpartum associated both with HDP as well as sociodemographic and behavioral characteristics that may help identify women at risk of short- and long-term CV complications.


Mean SBP Latent Trajectories (Pregnancy)
Population average (92%)
High decrease (3%)
Low increase (5%)
Mean SBP (mm Hg)
Gestational months
Mean DBP Latent Trajectories (Pregnancy)
Population average (82%)
Low increase (18%)
Mean DBP (mm Hg)
Gestational months
Mean SBP Latent Trajectories (Postpartum)
Low stable (85%)
High increase (7%)
High decrease (8%)
Mean SBP (mm Hg)
Weeks from childbirth (weeks)
Mean DBP Latent Trajectories (Postpartum)
Low stable (94%)
High decrease (3%)
High increase (3%)
Mean DBP (mm Hg)
Weeks from childbirth (weeks)

Perinatal & Pediatric

Precision Medicine Approach to Elective Induction Decisions: Secondary Analysis of A Randomized Trial of Induction Versus Expectant Management (ARRIVE) Yuri Sebastião* Yuri Sebastião Katelyn J. Rittenhouse Jackie K. Patterson Teeranan Pokaprakarn John M. Thorp Jr. Stephen R. Cole

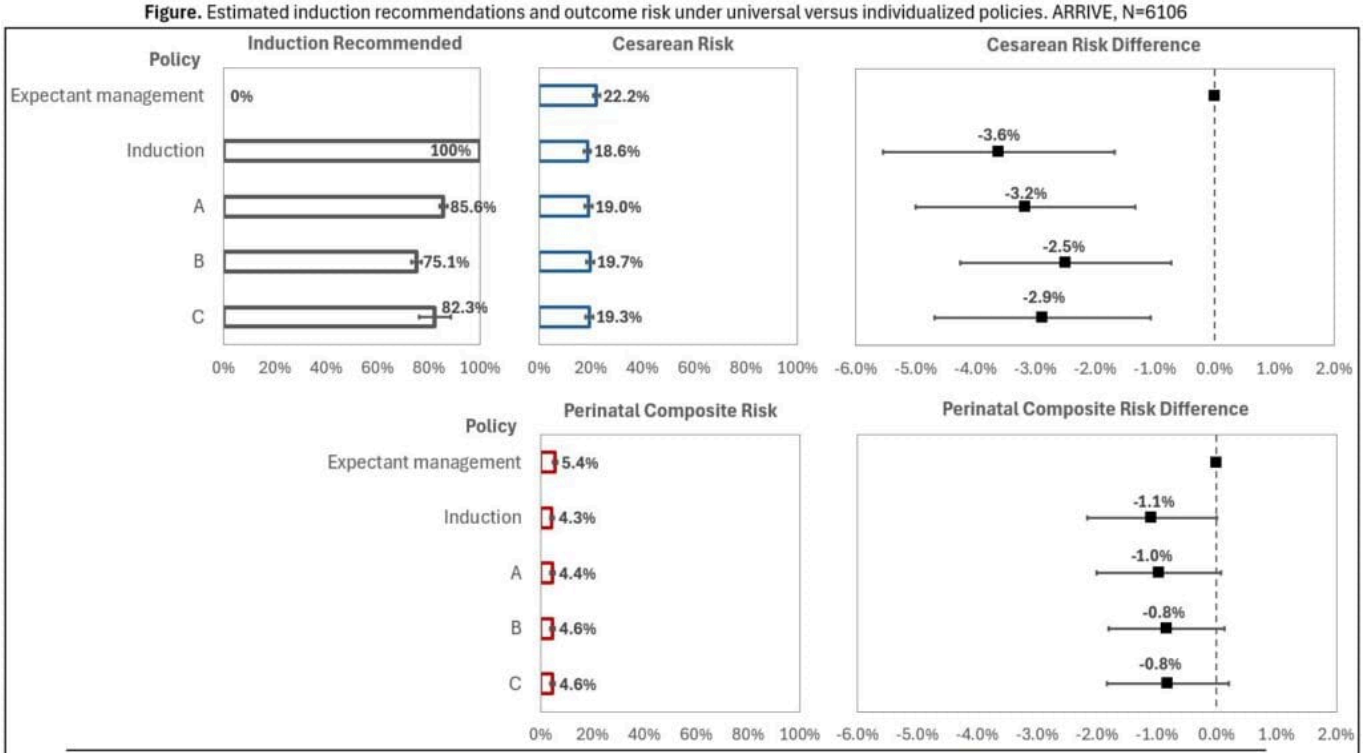
Elective induction at 39 weeks reduces cesarean risk among low-risk pregnancies, but outcome heterogeneity may be masked. We evaluated whether individualized treatment rules could improve outcomes.

We analyzed ARRIVE trial data (N=6,106 low-risk nulliparas randomized at 38 weeks' gestation to undergo either elective induction at 39 weeks or expectant management) using intention-to-treat. Baseline covariates included maternal age, height, weight, BMI, cervical dilation, Bishop score, assisted conception, substance use, marital status, employment, insurance, prior pregnancy loss, and fetal anomaly. We estimated individualized treatment effects on cesarean delivery and a perinatal (fetal/neonatal) morbidity/mortality composite using causal forests. Three individualized policies were defined: (A) induce if lower cesarean risk for induction versus expectant management, (B) induce if lower perinatal composite risk, and (C) induce if lower cesarean risk without increased perinatal risk. Expected risks under each policy, including universal induction and expectant management, were estimated via augmented inverse-probability-weighting with 5-fold cross-fitted SuperLearner. Missing data were replaced by 20 imputations using chained equations.

Compared to universal expectant management, universal induction had 18.6% cesarean (RD: −3.6% [95% CI: -5.6, -1.7]) and 4.3% perinatal composite risk (RD: -1.1% [-2.2, 0.0]). Individualized policies (A-C) recommended induction for 75.1-85.6% of participants, achieving 19.0-19.7% cesarean and 4.4-4.6% perinatal risk (Figure).

In ARRIVE, universal induction achieved the lowest cesarean risk, but individualized policies reduced inductions by 14–25 percentage points while maintaining lower cesarean and perinatal risks than universal expectant management. Individualized strategies may support patient-centered decision-making by identifying patients for whom elective induction is unlikely to provide cesarean or perinatal risk reduction.

Figure. Estimated induction recommendations and outcome risk under universal versus individualized policies. ARRIVE, N=6106



	Universal		Individualized		
	Expectant Management	Induction	A	B	C
Induction Recommended	0%	100%	85.6% (84.0%, 87.2%)	75.1% (73.2%, 77.0%)	82.3% (76.1%, 88.5%)
Difference	-100%	0% (Reference)	-14.4% (-16.0%, -12.8%)	-24.9% (-26.8%, -23.0%)	-17.7% (-23.9%, -11.5%)
Cesarean Risk	22.2% (20.7%, 23.6%)	18.6% (17.2%, 19.9%)	19.0% (17.6%, 20.6%)	19.7% (18.2%, 21.2%)	19.3% (17.9%, 20.9%)
Difference	0% (Reference)	-3.6% (-5.6%, -1.7%)	-3.2% (-5.0%, -1.3%)	-2.5% (-4.3%, -0.7%)	-2.9% (-4.7%, -1.1%)
Perinatal Composite Risk	5.4% (4.6%, 6.2%)	4.3% (3.6%, 5.0%)	4.4% (3.7%, 5.2%)	4.6% (3.8%, 5.4%)	4.6% (3.8%, 5.4%)
Difference	0% (Reference)	-1.1% (-2.2%, 0.0%)	-1.0% (-2.0%, 0.1%)	-0.8% (-1.8%, 0.1%)	-0.8% (-1.8%, 0.2%)

Perinatal composite outcome defined as in ARRIVE (perinatal death or severe neonatal morbidity)

A: Induce if predicted cesarean benefit (individualized cesarean risk difference<0 for induction vs expectant management)

B: Induce if predicted perinatal composite outcome benefit

C: Induce if predicted cesarean benefit without increase in perinatal composite risk

Perinatal & Pediatric

Pregnancy and Infant Outcomes Following Opioid Overdose During Pregnancy Among Individuals with an Opioid Use Disorder Michelle Ann Caesar* Michelle Ann Caesar Gretchen Bandoli Kathryn Hollenbach Karen Ferran John Alcaraz Christina Chambers

Objective: The objective of this study was to evaluate the effect of having an opioid overdose on pregnancy and infant outcomes among pregnant individuals with an opioid use disorder.

Methods: This retrospective study consisted of singleton, livebirths among individuals with an opioid use disorder in California between 2007 and 2021. Infant records (birth through one year of life) and maternal records (one year before delivery through one year postpartum) were linked to vital statistics birth records. Adjusted risk ratios and risk differences were calculated to estimate the association between opioid overdose among pregnant individuals with an opioid use disorder and preterm birth, neonatal abstinence syndrome, and admission to the NICU.

Results: Overall, 14,073 birthing individuals in California had an opioid use disorder and 190 (1.35%) had an opioid overdose during pregnancy. In those who had an opioid overdose, 50.79% occurred in 1st trimester, 23.81% in the 2nd, and 25.40% in the 3rd. There was no statistically significant difference in the risk of preterm birth, admission to the neonatal intensive care unit, or neonatal abstinence syndrome among individuals with an opioid use disorder who had an opioid overdose during pregnancy compared to those who did not. Additional analyses examining timing showed an increased risk of preterm birth among individuals who had an opioid exposure during the second trimester of pregnancy compared to individuals who did not have an opioid overdose (aRR=2.29, 95%CI: 1.44, 3.65; aRD=0.26, 95% CI: 0.05, 0.47).

Conclusion: This study did not find an increased risk of preterm birth, neonatal abstinence syndrome, or admission to NICU among individuals with an opioid use disorder who experienced an opioid overdose during pregnancy. These findings may suggest that acute overdose events during pregnancy does not confer additional risk beyond the already elevated risk of these adverse outcomes among individuals with an opioid use disorder.

Perinatal & Pediatric

Nonparametric Estimation of Elevated Blood Pressure Tracking Throughout Childhood and Adolescence Lucia Petito* Lucia Petito Abigail Gauen Ngoc Duong Norrina Allen

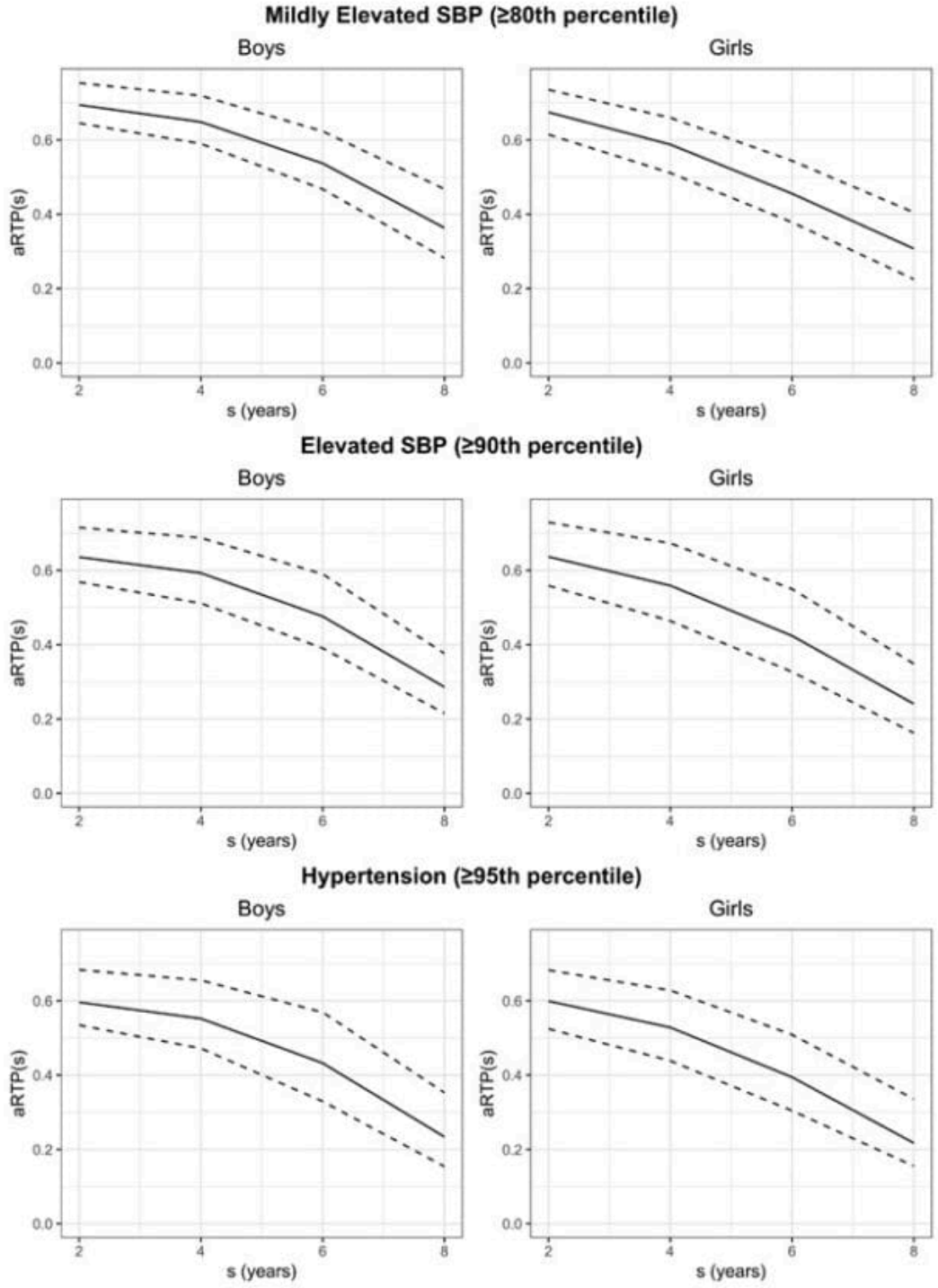
Introduction. Elevated blood pressure (BP) affects approximately 1 in 12 US children and adolescents, a condition that may persist into adulthood and is linked to increased risk of hypertension and subsequent cardiovascular events. Here we aimed to better understand how BP percentiles track over childhood.

Methods. We used data from children aged 3-19 years from the Environmental influences on Child Health Outcomes (ECHO) Consortium with ≥2 systolic BP (SBP) measurements. We estimated clinically-relevant estimands called age-integrated rank-tracking probabilities (aRTP(s)), which reflect the current risk of elevated SBP (at age a) among those who had elevated SBP s years ago (at age a – s), integrated over childhood (ages 5-19). This reflects how consistently children maintain their sex-age-height specific SBP percentile, answering the question “what is the chance a child still has elevated SBP given they had elevated SBP s years ago?” Sex-specific estimates of aRTP(s) were generated for mildly elevated SBP (SBP percentile ≥80th), elevated SBP (≥90th), and hypertension (≥95th) separately using a nonparametric kernel-based method. We estimated 95% confidence intervals using clustered bootstraps with 200 resamples.

Results. We included 2,484 girls and 2,481 boys (observed 5,278 and 5,211 times, respectively; median age 4 years; 55% non-Hispanic White) with prevalences of mildly elevated SBP of 26.2% and 24.4%, respectively. For mildly elevated SBP, aRTP declined as look-back periods increased from 2 to 8 years, decreasing from 0.67 (95% CI 0.61-0.74) to 0.31 (0.23-0.41) and 0.69 (0.65-0.75) to 0.36 (0.28-0.47) among girls and boys, respectively. This pattern was consistent for elevated SBP and hypertension (Figure).

Conclusions. Childhood BP measurements taken closely together in time track more strongly than those taken further apart, supporting population-wide rather than individualized healthy lifestyle interventions to promote early maintenance of optimal BP.

Figure. Estimated age-integrated rank-tracking probabilities (aRTP(s)), which reflect risk of elevated blood pressure among those previously with elevated blood pressure s years ago, integrated over all ages, for mildly elevated BP (SBP percentile ≥80), elevated BP (≥90) and hypertension (≥95) and their respective 95% bootstrap percentile confidence intervals for boys and girls.



Perinatal & Pediatric

Predicting Infant Nonattendance at the Next Recommended Well-Child Visit: Model Development and External Validation Amanda Luff* Amanda Luff Marybeth Ingle Clare Crosh Melanie Marsh Francois Modave Veronica Fitzpatrick

Background: Well-child visits (WCVs) are critical for infant preventive care, yet missed visits are common and are associated with delayed diagnoses and increased acute care use. A tool to predict next-visit nonattendance at the current visit could enable proactive support.
Methods: Using EHR data from two Chicago-area pediatric clinic groups, we developed models to predict nonattendance at the next recommended WCV among infants who attended the current WCV. Clinic A (training/internal validation) contributed 1,215 patients (3,654 visits) and Clinic B (external validation) 1,271 patients (3,044 visits). Features captured visit context (timepoint, visit delay, scheduling lead days, provider type, new to clinic), prior utilization (ED use, prior no-show, prior missed WCV, immunization refusal), and patient indicators (sex, insurance, in-system birth; low birth weight, preterm birth, NICU admission). We compared regularized logistic regression, random forest, and XGBoost. Nested group k-fold cross-validation (by patient) optimized average precision. We estimated SHAP values and report threshold-specific metrics using F1-maximizing cutoffs.
Results: Missed-next-visit rates were 16.2% (Clinic A) and 20.7% (Clinic B). Discrimination and average precision were modest and similar across models: internal AUC 0.69–0.72 and average precision 0.36–0.41; external AUC 0.66–0.68 and average precision 0.36–0.38. At the F1-maximizing threshold, recall (sensitivity) ranged 0.40–0.51 internally and 0.54–0.71 externally, with precision (positive predictive value) 0.30–0.37; negative predictive value remained high (~0.86–0.89). In all models, SHAP values identified timepoint, visit delay, schedule lead days, and prior no-show as among the top 6 most influential features.
Conclusion: Predicting next-WCV attendance is feasible using routinely available EHR features, though performance is modest. A parsimonious LASSO logistic regression model performed comparably to more complex models.

Mental Health

Toward scalable and equitable risk prediction for internalizing disorders in adolescence

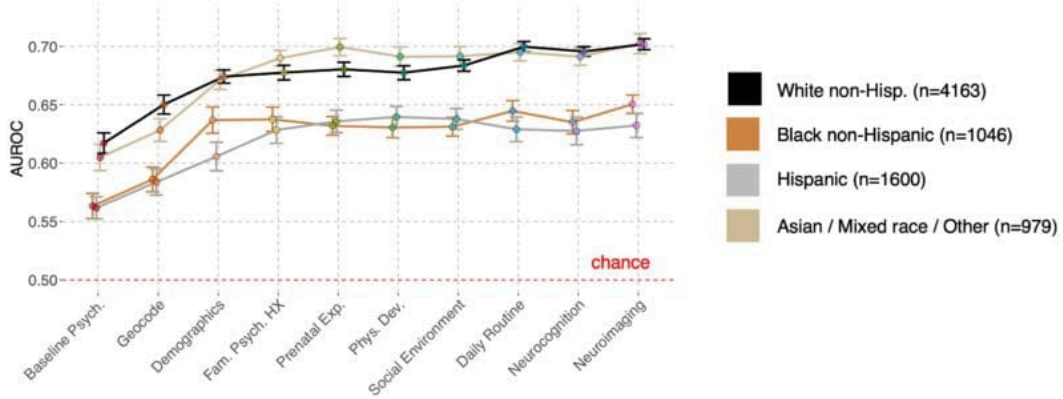
Nana Okada* Nana Okada Divyangana Rakesh Heather Mattie Kate McLaughlin Henning Tiemeier

Adolescence is the peak period for onset of internalizing disorders (e.g. anxiety, depression) and a critical intervention window. Scalable intervention requires prospectively identifying high-risk youth using information feasible to obtain in clinical care. Progress in risk prediction is slowed by disciplinary silos, minimal attention to feasibility of collecting predictors in clinical settings, scarce evaluation of algorithmic fairness, and arbitrary dichotomizations of continuous psychiatric phenomena.

We use multimodal data collected at ages 9-10 from ~10k participants in the Adolescent Brain and Cognitive Development Study to predict internalizing symptom severity by ages 14-15. >300 predictors are grouped into “layers” and ordered by anticipated feasibility: baseline psychopathology, neighborhood features, familial psychiatric history, prenatal exposures, anthropometrics, social environment, daily routine, cognition, hormones, genomics and neuroimaging. Machine-learning models (gradient-boosted trees, random forest, LASSO) are fit with nested cross-validation, adding layers stepwise to quantify incremental gains from higher-cost modalities. To evaluate fairness, we test whether overall performance and the added value of costly layers differ by racial identity. Initial analyses using a binary internalizing outcome at age 12 (Fig. 1) show modest discrimination (AUROC ~ 0.55-0.7), limited improvement from layers beyond familial history, and lower performance for Black and Hispanic youth than White youth. Ongoing work extends these models to a continuous symptom outcome at ages 14-15, when incidence peaks, and incorporates hormonal and genomic predictors. Updated results will be presented.

Rather than proposing a deployable risk calculator, this work delineates practical limits of prediction, clarifies when high-cost modalities meaningfully improve performance, and informs cautious development of scalable, equitable risk-stratification tools in youth mental health.

Figure 1: Incremental predictive value of multimodal information for incident internalizing disorders at age 12, stratified by race / ethnicity



Mental Health

Trends in Suicide Mortality by Method among US Individuals aged 10-24 Years from 1999 to 2024 Anne Bischops* Anne Bischops Marie-Laure Charpignon Kenneth D. Mandl Maimuna Majumder

Background

For over a decade, suicide has been the second leading cause of death among individuals aged 10-24 in the United States (US). From 1999 to 2019, suicide rates increased by 46%. However, recent temporal trends after the COVID-19 pandemic remain unclear. We examined suicide mortality patterns, focusing on method use by sex and age group.

Methods

Using publicly available mortality data from the National Center for Health Statistics (NCHS), we analyzed national-level suicide rates from 1999 to 2024 by method. Four suicide method categories were considered: firearm, poisoning, asphyxiation, and other. For each method, both crude and age-standardized suicide mortality rates were estimated and stratified by sex and age group. Changing trend time points and annual percent change (APC) were determined via Joinpoint regression models, using R and the NCI Joinpoint software.

Results

Following a downward trend from 2018 to 2020, suicide mortality rates have since plateaued. Rates declined among ages 15-19 (APC 2017-2024: -3.3, p=0.027) and 20-24 (APC 2021-2024: -5.8, p=0.038), but not among ages 10-14. Although rates were three times higher among males in 1999-2017, the sex gap decreased by 9.3% since 2017. Firearms remained the leading method, predominantly used by males and 15-to 24-year-olds, although their use was increasing among females and 10-to 14-year-olds. Asphyxiation was most common among females and ages 10-14. Poisoning and other methods showed a steady rise. Results were robust to age standardization.

Discussion

Adolescent suicide mortality rates have plateaued, suggesting that earlier progress in prevention efforts may have leveled off during the pandemic. Firearm-related suicides are rising among individuals aged 10-14 and females. Further, suicides by poisoning are increasing across all age groups and both sexes. The implementation of targeted, sex- and age-sensitive approaches will be key to reinforcing the effectiveness of suicide prevention efforts.

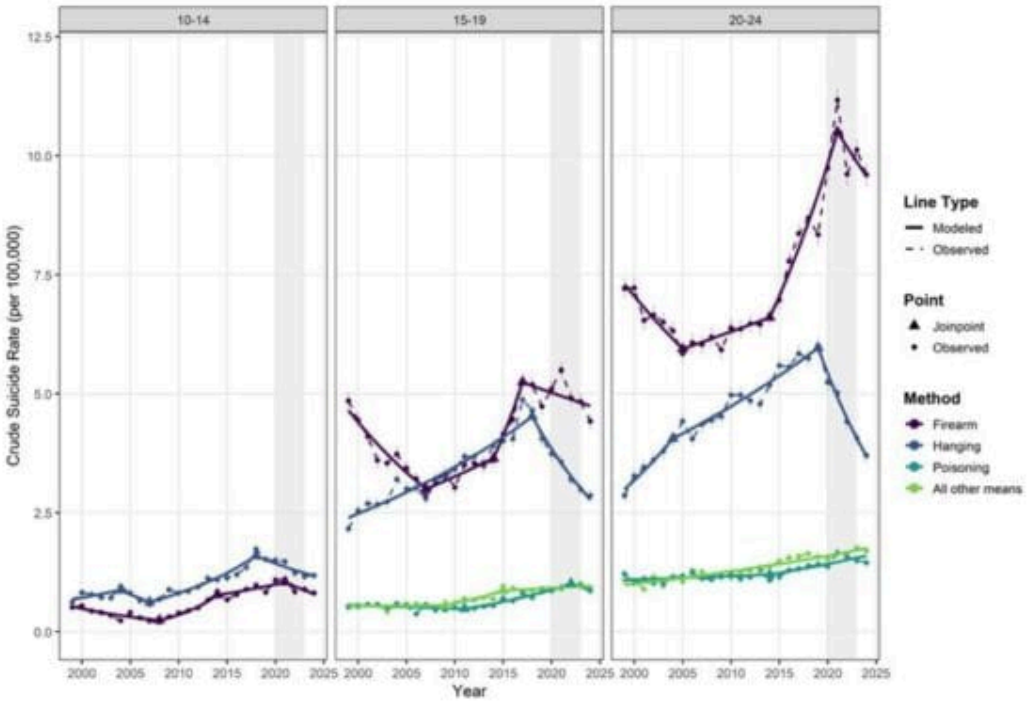


Figure: Trends in Crude Suicide Mortality Rates among Individuals aged 10-24 Years in the United States, by Method and Age Group

The three panels correspond to the 10-14, 15-19, and 20-24 age groups, respectively. The grey shading denotes the COVID-19 pandemic period (2020-2023). Error bars represent 95% confidence intervals. Of note, in the 10-14 age group, data were suppressed for suicides by poisoning and by other means owing to limited sample sizes (i.e., less than 10 deaths).

Mental Health

Machine learning and natural language processing for the early detection of potential mental disorders among school-age children: a prospective birth cohort study Shanquan Chen* Shanquan Chen Ting Dang Mengjie Qian Quinette Abegail Louw

Background This study aimed to assess whether integrating natural language processing (NLP) of children's essays with traditional risk factors could enhance the early detection of potential mental health disorders compared with models using either data type alone.

Methods We conducted a prospective analysis using data from the UK-based National Child Development Study (NCDS), a national birth cohort initiated in 1958. Data from birth, age 7, and age 11 assessments were analyzed. The final sample included 8,981 children (4,428 [49.3%] female) who completed a creative writing essay at age 11 describing their imagined life at age 25. Predictors comprised traditional risk factors (perinatal, socioeconomic, and parental engagement variables) and linguistic features computationally extracted from the essays. The primary outcome was potential mental health disorder at age 11, defined as scoring above the 95th or 90th percentile on the teacher-completed Bristol Social Adjustment Guide (BSAG). The mother-completed Rutter A Scale was used for sensitivity analysis. Machine learning models incorporating various predictor combinations were developed, and their predictive performance was evaluated using receiver operating characteristic (ROC) curves.

Results Using BSAG 95th percentile threshold, models combining top five selected variables with essay features achieved significantly higher predictive capability (ROC:0.77, 95%CI:0.71-0.83) compared to models using all variables (ROC:0.70, 95%CI:0.63-0.76) or essay features alone (ROC:0.67, 95%CI:0.60-0.74). At 90th percentile threshold, this integrated approach showed similar improvement (ROC:0.81, 95%CI:0.78-0.85). Key predictors included gestational length, maternal parity, parental age, residential characteristics, parental engagement metrics, and children's BMI. Sensitivity analyses using Rutter A Scale confirmed these findings.

Conclusions In this prospective birth cohort study, integrating NLP analysis of children's essays with a small set of key risk factors substantially improved the prediction of potential mental health disorders. This integrated approach represents a potential paradigm for developing scalable, objective screening tools.

Figure 2. Relative importance of predictors for childhood mental health risk.

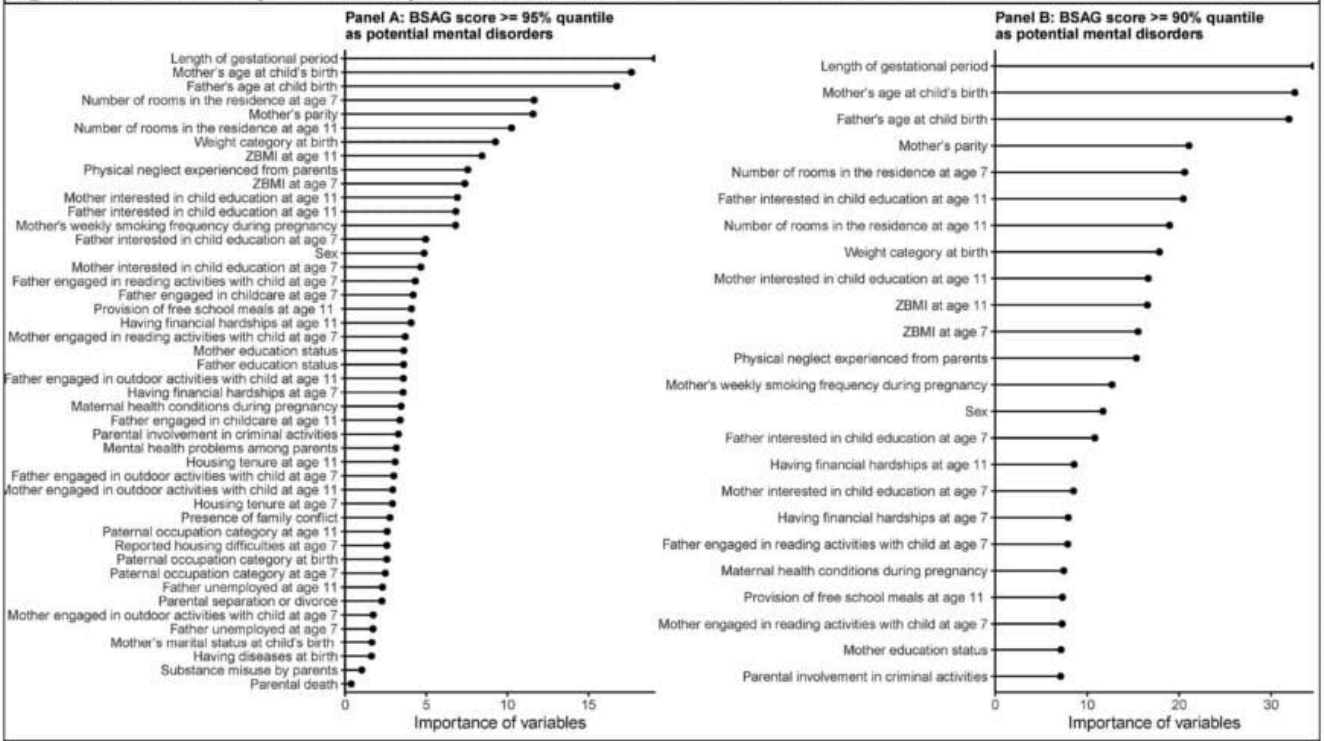
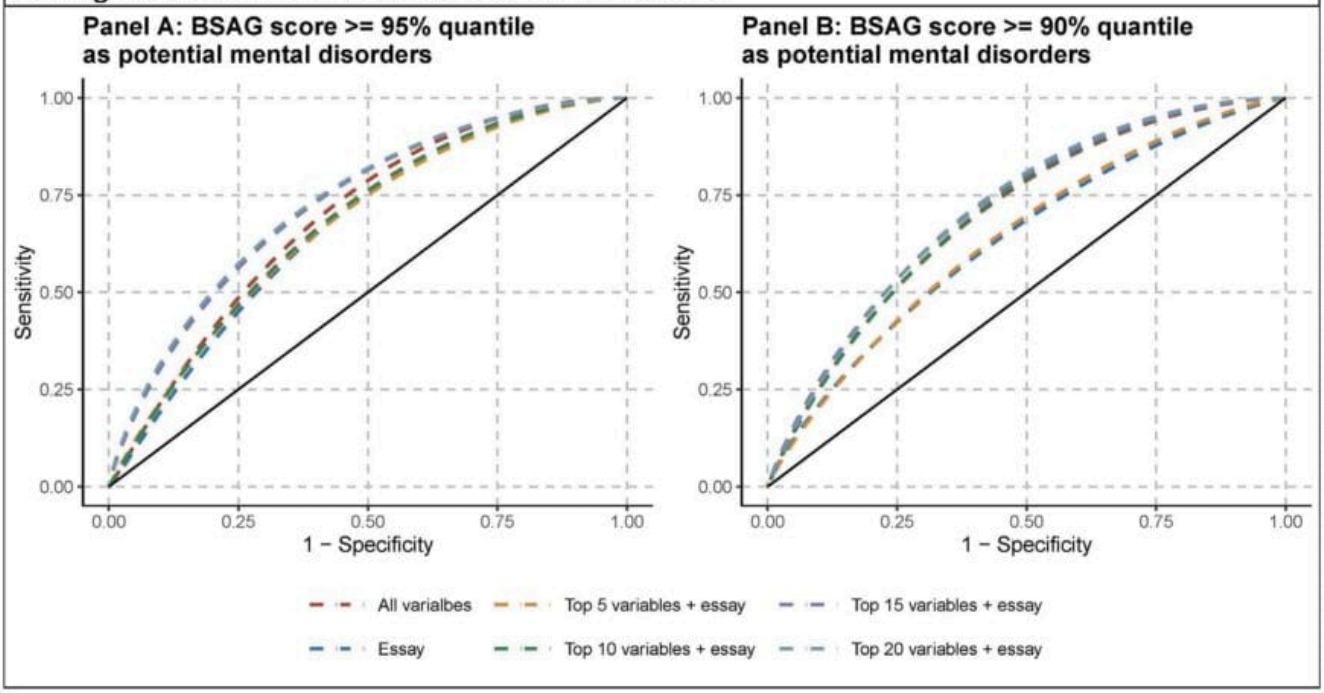


Figure 3. Receiver operating characteristic (ROC) curves comparing predictive performance of machine learning models for childhood mental health assessment.



Mental Health

Intersectional inequalities in measurement and outcomes in youth mental health: evidence from a UK birth cohort Darío Moreno-Agostino* Darío Moreno-Agostino Helen L. Fisher Praveetha Patalay Emla Fitzsimons Thomas Steare George B. Ploubidis Clare R. Evans

Youth mental (ill-)health, the leading contributor to the global burden of disease in young people, is shaped by intersecting social identities such as gender, ethnicity, sexuality, and socioeconomic position (SEP). Yet most research examines these factors in isolation, and even when intersectionality is acknowledged, systematic differences in measurement and missing data across intersectional positions are rarely addressed.

This pre-registered study, shaped by the involvement of young people with lived experience of mental ill-health and/or social discrimination, will apply an innovative analytic framework combining Intersectional Multilevel Analysis of Individual Heterogeneity and Discriminatory Accuracy (I-MAIHDA), measurement invariance testing (alignment), and bootstrapping with multiple imputation. Using an intersectional framework, we will analyse inequalities in both measurement and levels of three complementary mental health outcomes: psychological distress (Kessler-6), wellbeing (Short Warwick-Edinburgh Mental Well-Being Scale), and self-harm and attempted suicide. We will use data from age 23 sweep (2023-24) of the Millennium Cohort Study, a nationally representative birth cohort study of around 19,000 people born in the UK in 2000-02. Inequalities will be analysed at the intersection of gender (2 categories), ethnicity (4), sexuality (2), and SEP (2).

This study will deliver an up-to-date, comprehensive, and multifaceted sociodemographic mapping of youth mental health inequalities available at a critical period of transition into adulthood. Findings will inform policymakers aiming to reduce health inequities, guide data producers on potential measurement bias in widely used instruments, and provide health equity researchers with a methodological exemplar for addressing intersectional complexity in both outcomes and measurement.

Social

Intersectional mental health disparities among sexual and gender minority adults: an I-MAIHDA analysis of the All of Us Research Program Junjie Lu* Junjie Lu David Rehkopf

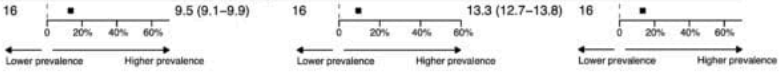
Background: Sexual and gender minority (SGM) adults experience elevated mental health burden, yet traditional modeling assumes identity categories (sex assigned at birth, sexual orientation, gender identity) operate independently. Intersectional Multilevel Analysis of Individual Heterogeneity and Discriminatory Accuracy (I-MAIHDA), which fits mixed-effects models with intersectional strata as random effects, can reveal how multiple marginalized identities interplay to shape health outcomes beyond additive effects.

Methods: We analyzed 60,769 participants from the NIH All of Us Research Program who completed the Emotional Health Survey. Using Bayesian multilevel models, we examined depression (PHQ-9≥10), anxiety (GAD-7≥10), and probable PTSD (PCL-6≥14) across 16 intersectional strata defined by sex assigned at birth (male, female), sexual orientation (heterosexual, bisexual, gay/lesbian, other sexual minority), and gender identity (cisgender, gender minority). We compared traditional logistic regression and I-MAIHDA models.

Results: The highest prevalence was observed among Female-Other sexual minority-Gender minority individuals for depression (55.8%) and PTSD (60.6%), and among Female-Bisexual-Gender minority individuals for anxiety (49.3%). Male-Heterosexual-Cisgender individuals showed the lowest prevalence (13.6%, 9.5%, 13.3%, respectively). Variance Partition Coefficients indicated 4.9-6.8% of outcome variance was attributable to stratum membership. Notably, 62% (depression), 69% (anxiety), and 43% (PTSD) of between-stratum variance was attributable to interactions. Traditional regression showed significant sex and sexual orientation coefficients, but I-MAIHDA revealed these reflect intersectional interactions rather than independent contributions.

Conclusions: I-MAIHDA reveals SGM mental health disparities are driven by intersectional interactions, supporting precision mental health interventions.

Sex assigned at birth	Sexual orientation	Gender identity	N	Depressive symptoms (PHQ–9 >=10) % (95% CrI)	Rank	Anxiety symptoms (GAD–7 >=10) % (95% CrI)	Rank	Probable PTSD (PCL–6 >=14) % (95% CrI)	Rank
Female	Other sexual minority	Gender minority	496	55.8 (51.4–60.1)	1	42.1 (37.7–46.5)	3	60.6 (56.4–64.8)	1
Female	Bisexual	Gender minority	341	52.4 (47.3–57.6)	2	49.3 (44.3–54.3)	1	60.1 (54.9–65.1)	2
Male	Gay/Lesbian	Gender minority	92	50.3 (40.9–59.9)	3	40.3 (31.5–50.1)	5	53.4 (43.9–63.1)	4
Female	Gay/Lesbian	Gender minority	139	49.4 (41.7–57.2)	4	45.4 (37.6–53.2)	2	56.4 (48.6–64.3)	3
Male	Other sexual minority	Gender minority	97	45.9 (37.1–55.0)	5	35.3 (26.9–44.2)	8	48.9 (39.8–58.0)	6
Female	Other sexual minority	Cisgender	980	44.7 (41.6–47.9)	6	37.3 (34.1–40.4)	6	45.8 (42.7–49.0)	7
Female	Bisexual	Cisgender	3,055	42.1 (40.3–43.9)	7	36.6 (34.9–38.4)	7	43.0 (41.2–44.8)	8
Male	Bisexual	Gender minority	99	41.8 (33.2–50.9)	8	40.4 (31.8–49.6)	4	49.7 (40.7–58.8)	5
Female	Heterosexual	Gender minority	77	36.8 (27.6–46.8)	9	30.5 (22.1–40.1)	9	33.7 (24.8–43.0)	9
Male	Heterosexual	Gender minority	66	30.9 (22.2–41.1)	10	27.3 (18.6–37.5)	10	23.9 (15.7–33.0)	13
Male	Bisexual	Cisgender	609	28.3 (24.8–31.9)	11	19.4 (16.5–22.7)	12	26.4 (23.1–30.0)	10
Male	Other sexual minority	Cisgender	187	26.9 (21.2–33.1)	12	16.2 (11.7–21.1)	14	25.9 (20.1–32.0)	11
Female	Gay/Lesbian	Cisgender	1,043	25.3 (22.7–28.0)	13	21.0 (18.6–23.5)	11	24.8 (22.1–27.5)	12
Male	Gay/Lesbian	Cisgender	1,784	23.4 (21.5–25.4)	14	18.9 (17.1–20.8)	13	23.1 (21.2–25.1)	14
Female	Heterosexual	Cisgender	34,496	20.0 (19.6–20.4)	15	16.0 (15.6–16.4)	15	19.1 (18.7–19.6)	15
Male	Heterosexual	Cisgender	17,208	13.6 (13.1–14.1)	16	9.5 (9.1–9.9)	16	13.3 (12.7–13.8)	16



Category definitions: Sex assigned at birth: female, male. Sexual orientation: heterosexual, gay/lesbian, bisexual, other sexual minority (including asexual, queer, and other non-heterosexual identities). Gender identity: cisgender (gender identity aligns with sex assigned at birth), gender minority (including transgender, genderqueer, non-binary, and other gender-diverse identities). Strata sorted by depressive symptoms prevalence (highest to lowest). Rank: 1 = highest prevalence for each outcome.

Abbreviations: CrI, credible interval; GAD-7, Generalized Anxiety Disorder 7-item scale; PCL-6, PTSD Checklist 6-item version; PHQ-9, Patient Health Questionnaire 9-item scale; PTSD, post-traumatic stress disorder.

Mental Health

Bridging Divides: Working with Young People to Coproduce a Better Understanding of Gender Inequalities in Youth Mental Health Gemma Knowles* Gemma Knowles Daniel Stanyon Syudo Yamasaki Haruka Goto Koraima Sotomayor-Enriquez Ulrich Reininghaus Junko Niimura Vanessa Pinfold Devi Khanna Esther Putzgruber Yutaka Sawai Daiki Nagaoka Zhuo Li Leonie Ader Kiyoto Kasai Jonas Kitisu Adna Hashi Thai-Sha Richards Zui Narita Dario Moreno-Agostino Atsushi Nishida The Bridging Divides Study Group

This presentation introduces Bridging Divides, a new five year research programme funded by the Wellcome Trust that investigates the causes of gender inequalities in youth mental health in London and Tokyo. Although teenage girls consistently report higher rates of depression and anxiety than boys, the mechanisms underlying this ‘gender gap’ – and whether it is preventable – remain poorly understood.

Bridging Divides is grounded in meaningful youth involvement at every stage. Guided by young people’s priorities, the programme asks a central question: in a world free of sexism, misogyny, and gender inequality (SMGI), would gender differences in youth mental health exist?

To address this, Bridging Divides integrates secondary data analysis with several novel data generation work packages:

1. A new longitudinal cohort study of thousands of young people in London and Tokyo, completing annual questionnaires to understand the extent, nature, and mental health impacts of SMGI over time.
2. A nested qualitative study exploring how adolescents from diverse backgrounds experience SMGI in their daily lives.
3. The development of a youth informed measure of SMGI for 11-18 year olds.
4. An intensive longitudinal (or ‘digital diary’) study capturing daily and momentary data to examine how ‘everyday’ SMGI interacts with puberty, periods, and the menstrual cycle to shape mental health.

The presentation will provide an overview of the programme and highlight emerging insights from the ongoing pilot phase (Dec 2025-Feb 2026), which has already recruited around 800 participants in London. Full pilot results are expected by April/May 2026, offering a timely opportunity for conference attendees to engage with and critically shape the project. We warmly invite critical, multidisciplinary perspectives to shape the main phase.

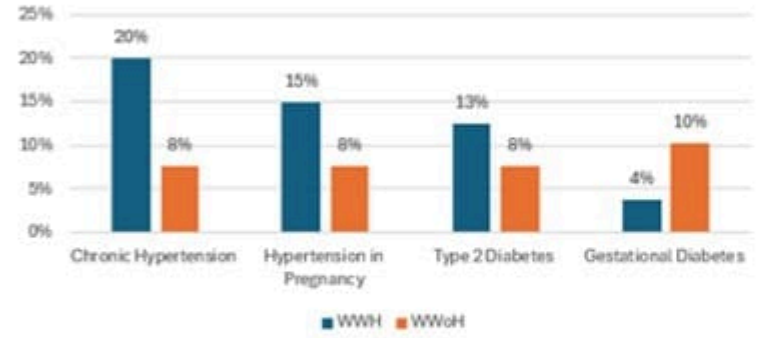
Perinatal & Pediatric

HIV Status And Cardiometabolic Health During Pregnancy: A Cross-Sectional Analysis From A Prospective Southeast US Based Cohort Danielle Carson* Danielle Carson Lauren Collins Christina Mehta Seble Kassaye Aadia Rana Daniel Westreich Elizabeth Topper Maria Alcaide Anandi Sheth Angela Bengtson

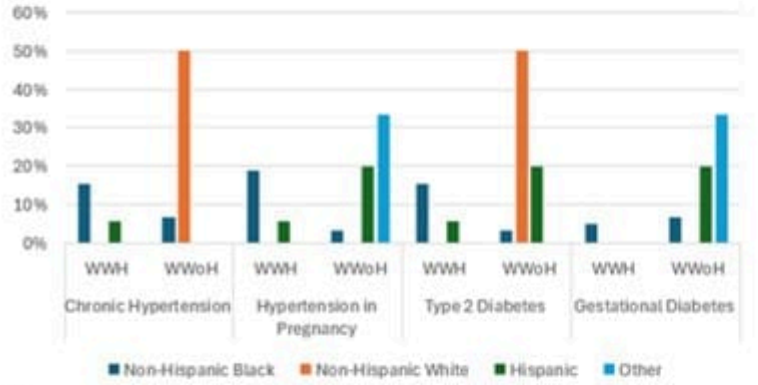
Cardiometabolic complications during pregnancy have increased in the past decade and pose heightened risks for women with HIV (WWH), who face compounded vulnerabilities from chronic inflammation, antiretroviral therapy (ART) exposure, and intersecting health disparities. We conducted a cross-sectional analysis of baseline data from pregnant participants at enrollment into STAR. We assessed associations between HIV status and cardiometabolic indicators (blood pressure, glucose, HbA1c, lipids) using linear regression and prevalent conditions (chronic hypertension (BP ≥140 or ≥90, medication use, or self-report diagnosis <20 weeks), hypertension in pregnancy (BP ≥140 or ≥90, medication use, or self-report diagnosis ≥20 weeks), type 2 diabetes (HgbA1c ≥6.5% or FBG ≥126 mg/dL, medication use, or self-report diagnosis < 24 weeks), and gestational diabetes (self-report diagnosis or study ascertainment)) using log-binomial regression. Prevalence was also examined overall and stratified by race and age group. Among 119 pregnant participants (80 WWH, 39 women without HIV (WWoH)), characteristics were: 73% identified as Non-Hispanic Black, median age 30.6 years, and 55% were obese, and most participants were multiparous, with 68% reporting two or more prior pregnancies. WWH vs WWoH had higher mean systolic blood pressure (112.6 vs 112.5 mmHg), diastolic blood pressure (70.3 vs 63.0 mmHg) and glucose levels (83.0 vs 75.8 mg/dL) but lower total (209.0 vs 231.0 mg/dL), HDL (68.0 vs 69.7 mg/dL), and LDL cholesterol (12.6 vs 131.7 mg/dL). Chronic hypertension was more prevalent among WWH (20% vs 8%, PR: 2.60, 95% CI: 0.81, 8.40), as was hypertension in pregnancy (15% vs 8%, PR: 1.95, 95% CI: 0.58, 6.51) and type 2 diabetes (13% vs 8%, PR: 1.65, 95% CI: 0.47, 5.57), while gestational diabetes was more prevalent among WWoH (4% vs 10%, PR: 0.37, 95% CI: 0.09, 1.55). Although overall prevalence ratios were higher among WWH, stratified analyses showed heterogeneity by age and race, with some older strata exhibiting high prevalence regardless of HIV status. These findings highlight substantial cardiometabolic vulnerability during pregnancy and the need for longitudinal follow up to assess age and race specific impacts of HIV.

Figure 1. Prevalence of cardiometabolic outcomes at enrollment into the STAR cohort among N=119 reproductive aged women living with HIV (WWH) and women without HIV (WWoH) A) overall B) stratified by race group C) stratified by age group

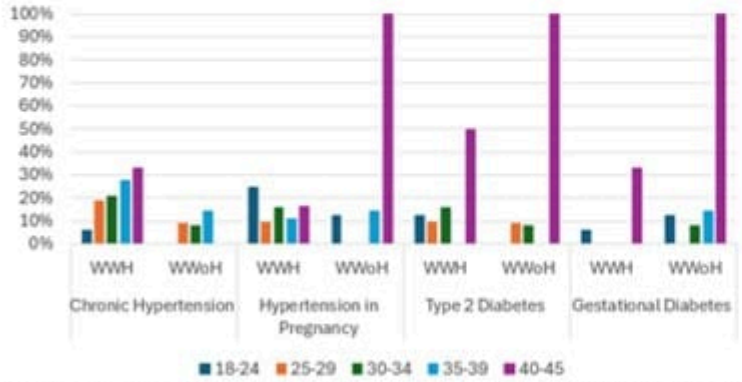
A.



B.



C.



Chronic hypertension defined as systolic blood pressure (BP) ≥140 or diastolic BP ≥90, or medication use, or self-report diagnosis <20 weeks. Hypertension in pregnancy defined as systolic BP ≥140 or diastolic BP ≥90, or medication use, or self-report diagnosis ≥20 weeks. Type 2 diabetes defined as HgbA1c ≥6.5% or FBG ≥126 mg/dL, or medication use, or self-report diagnosis < 24 weeks. Gestational diabetes defined as self-report diagnosis or study ascertainment.

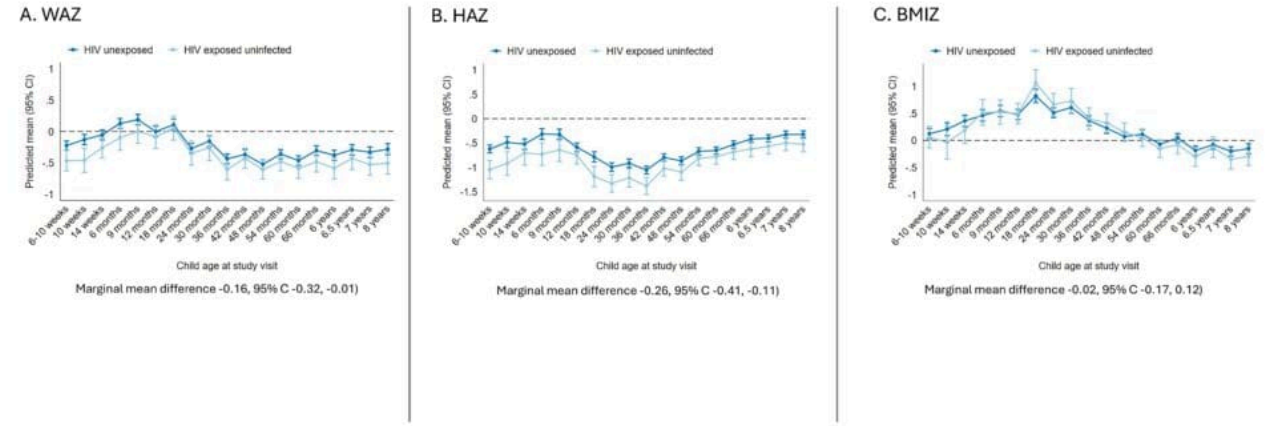
HIV / STI

In utero HIV exposure and anthropometry trajectories from birth through 8 years of age: findings from a prospective birth cohort in South Africa Angela Bengtson* Angela Bengtson Jennifer Pellowski Maresa Botha Tiffany Burd Lesley Workman Elizabeth Goddard Dan J Stein David Burgner Toby Mansell Heather J Zar

Children who are HIV-exposed but uninfected (CHEU) may have suboptimal growth, but few data are available beyond infancy to inform public health strategies. We investigated anthropometry trajectories from 6 weeks to 8 years in a South African birth cohort, the Drakenstein Child Health study. Anthropometry was assessed at least annually by trained study staff and converted to weight-for-age (WAZ), height-for-age (HAZ), and body mass index (BMIZ) z-scores. Stunting (HAZ <-2SD from 12 months) and overweight (BMIZ score >2 SD from 6 months) were secondary outcomes. Multivariable linear mixed effects models were used to estimate associations between HIV exposure status and anthropometry trajectories and explore the impact of maternal HIV factors among CHEU. Among 1,072 children (CHEU n= 236 (22%), children unexposed to HIV (CHU) n= 836 (78%)) mean birthweight (CHEU 3012g (SD 598) vs CHU 3041g (SD 590)) and preterm birth status (CHEU 18.3% CHEU vs CHU 15.0%) were similar. Among pregnant women with HIV, 99% were on antiretroviral therapy (ART; 80% efavirenz-based ART), and 65% had an undetectable viral load. In multivariable analyses, CHEU had lower marginal WAZ (marginal difference (MD) -0.16 (95% CI -0.32, -0.01) and marginal HAZ (MD -0.26, 95% CI -0.41, -0.11) scores, compared to CHU. Differences in WAZ and HAZ were largest before 3 years of age, but similar between CHEU and CHU thereafter. There was no association between HIV exposure and BMIZ scores (MD -0.02, 95% CI -0.17, 0.12), stunting (MD 0.05, 95% CI -0.04, 0.13) or overweight (MD 0.05, 95% CI -0.04, 0.13) overall or at specific time points. Among CHEU, timing of maternal ART initiation, ART regimen, and viral load in pregnancy were not associated with anthropometry outcomes. Compared to CHU, CHEU had lower marginal weight and height from birth to 8 years, driven by differences before 3 years of age. Among CHEU, maternal HIV factors did not drive anthropometry outcomes.

Figure 2. Weight for Age (WAZ), Height for Age (HAZ) and Body Mass Index (BMIZ) scores by HIV exposure status from 6 weeks to 8 years of age.

Individual time points and marginal (overall) estimates from linear mixed effects models adjusted for clustering by child and for parental employment, household income, maternal education, household asset score, maternal BMI, maternal age, maternal depression, maternal IPV, maternal alcohol use, maternal smoking at cohort enrollment, birthweight zscore, birth length zscore, and site.



HIV / STI

Intimate Partner Violence, Food Insecurity, and HIV Incidence Among Women Aged 15–49 Years in Wakiso and Hoima, Uganda: A Population-Based Longitudinal Cohort Study (2018-2023) Alex Daama* Alex Daama Shira Goldenberg Stephen Mugamba Robert James Nkale Menya Joan Madihah Nakakande Emmanuel Kyasanku Godfrey Kigozi Fred Nalugoda Gertrude Nakigozi Stephen Watya Doreen Tuhebwe Susan Kiene Amanda P Miller

Intimate Partner Violence, Food Insecurity, and HIV Incidence Among Women Aged 15–49 Years in Wakiso and Hoima, Uganda: A Population-Based Longitudinal Cohort Study (2018-2023)

Background

Sub-Saharan Africa accounts for nearly two-thirds of global HIV incidence, with women disproportionately affected. Despite Uganda’s progress in HIV prevention, recent community-based estimates of HIV incidence remain scarce. Previous research has largely emphasized individual-level factors, overlooking broader socio-ecological determinants. We examined interpersonal, community, and structural determinants of HIV incidence among women in two Ugandan districts.

Methods

We analyzed data from the Africa Medical and Behavioral Sciences Organization (AMBSO) Population Health Surveillance (PHS) longitudinal research cohort, between 2018 and 2023. Participants were HIV seronegative women aged 15–49 years .Person-time was calculated from baseline to follow-up HIV testing to estimate incidence per 100 person-years (PY). Poisson regression models were used to compute incidence rate ratios (IRR) and 95% confidence intervals (CI) for primary exposures: intimate partner violence (IPV), district of residence, food insecurity and water insecurity.

Results

Among participants (N=3,603), median age was 29 years [IQR 23- 37]. Over 54 sero-conversions occurred over 3,608 PY, yielding an incidence rate of 1.50/100 PY, with higher incidence observed in the Hoima district (1.61/100 PY) vs. Wakiso (1.38/100 PY). In separate adjusted models, IPV was significantly and strongly associated with HIV incidence (Adjusted Rate Ratio (aRR)=3.25; 95% CI: 1.10, 9.56, as was food insecurity (ARR= 3.43; 95% CI: 1.10, 10.67). Both water insecurity and residing in Hoima (vs. Wakiso) were associated with a higher HIV incidence, rate though these associations were null (aRR= 1.56, 95%CI: 0.44-5.46 and adjusted RR= 1.01; 95% CI: 0.45, 2.24, respectively).

Conclusion

Despite declining HIV incidence in Uganda, persistent interpersonal and structural vulnerabilities

faced by women, including those related to both gendered violence and food insecurity, may act as critical drivers of new infections amongst women. IPV and food insecurity substantially elevate the risk of HIV among women, underscoring the need for integrated prevention strategies addressing gender-based violence and resource insecurity.

Table showing Bivariate and Multivariable analysis for the four main exposures on HIV incidence among women 15-49 years 2018-2023 (N=3,603).

Primary exposures	Outcome	IRR	Adjusted IRR
Model 1			
Experienced IPV*			
Yes	HIV incident cases	2.53(1. 01, 6.35)	3.25(1.1(32)0, 9.56)
No	No HIV incident cases	1 (ref)	1 (ref)
Model 2			
Food insecurity*			
Yes	HIV incident cases	1.75(0.97, 3.18)	3.43(1.10, 10.67)
No	No HIV incident cases	1 (ref)	1 (ref)
Model 3			
Water insecurity*			
Yes	HIV incident cases	1.41(0.56, 3.54)	1.56(0.44, 5.46)
No	No HIV incident cases	1 (ref)	1 (ref)
Model 4			
District			
Hoima	HIV incident cases	1.17(0.69, 2.01)	1.01(0.45, 2.24)
Wakiso	No HIV incident cases	1 (ref)	1 (ref)

*Within the past 12 months

HIV / STI

Characterization of sexual partnerships and prediction of future age distribution and HIV burden in Botswana and Zambia: preliminary findings from the EPIPLAN-HIV model Divya Hosangadi* Divya Hosangadi Meagan C. Fitzpatrick Hope Sabao Kesalefa Elliam Kesalefa Wilbroad Mutale Billy Tsima Ndwapi Ndwapi Lillian Okui Kristen Stafford

Introduction: HIV prevalence has shifted to older ages due to longer lifespans among people with HIV and lower incidence in younger ages. Past modeling has underestimated this age shift and has underassessed sexual partnerships in older adults. Using repeated population-based surveys in Botswana and Zambia, we describe sexual partnerships and model HIV prevalence by 2040.
Methods: Using Population-based HIV Impact Assessment (PHIA) survey data from Botswana (2013, 2021) and Zambia (2016, 2021), participants age ≥15 years (y) reported sexual partnerships in the past year and underwent HIV testing. We report weighted mean and 95% CIs for sexual partners by sex, age, and HIV status (Fig 01). Extending an age-based cohort model to include HIV acquisition risk stratified by age and sex based on partner profiles, we projected HIV prevalence by age for each country independently.
Results: In Botswana 2021, people with (vs. without) HIV had fewer partnerships [men: 0.97 (95% CI: 0.89, 1.04) vs 1.27 (1.22, 1.31); women: 0.85 (0.81, 0.89) vs 0.96 (0.92, 0.99)]. In Zambia 2016, men with (vs. without) HIV had more partnerships [1.13 (1.06, 1.21) vs 1.00 (0.97, 1.03)]. From 2013 to 2021 in Botswana, serodifferent partnerships decreased and seroconcordant partnerships increased (Fig 01). In Zambia 2021, adults ≥50y had higher prevalence of serodifferent partnerships versus adults <50y [10.85% (7.86%, 13.84%) vs 6.29% (5.34%, 7.24%)]. Trends were similar but with overlapping confidence intervals in Botswana 2021. By 2040, we predict the HIV prevalence in Botswana and Zambia will be 6% and 2%, respectively and HIV prevalence among adults ≥50y will be 32% and 30%, respectively.
Conclusions: Older age was associated with serodifferent partnerships in Zambia. We predict by 2040, ≥30% of adults ≥50y in each country will have HIV. HIV testing and prevention programs may need to include programming for older adults to achieve and maintain epidemic control.

Figure 01: Heatmaps of the difference in mean number of sexual partnerships between 2021 and 2013 Botswana surveys.

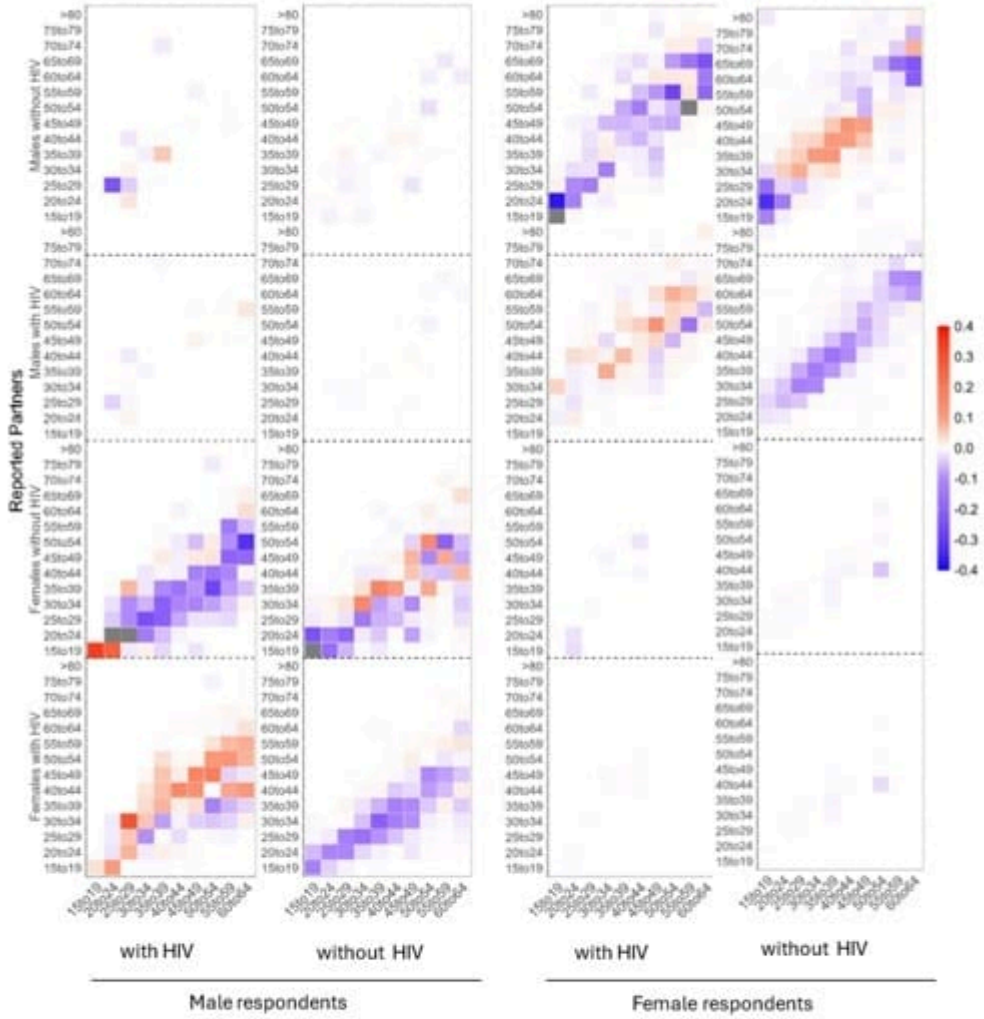


Figure 01: Heatmaps of the difference in mean number of sexual partnerships between 2021 and 2013 Botswana surveys. Cell colors represent the absolute difference in mean number of partners for a given age, sex, HIV status category between 2021 and 2013 Botswana survey years (Botswana 2021 – Botswana 2013). Gray boxes indicate the difference was an outlier of the color scale range.

HIV / STI

Mental health disparities in HIV Viral Suppression Before and During the COVID-19 Pandemic Among People With HIV: A Nested Cohort Study in NA-ACCORD, 2018–2021 Yue Zhang* Yue Zhang Brenna Hogan Xianming Zhu Sarita Shah Michael A Horberg Jennifer O Lam Kathleen Akgun Sonia Napravnik Keri N Althoff Angela M Parcesepe

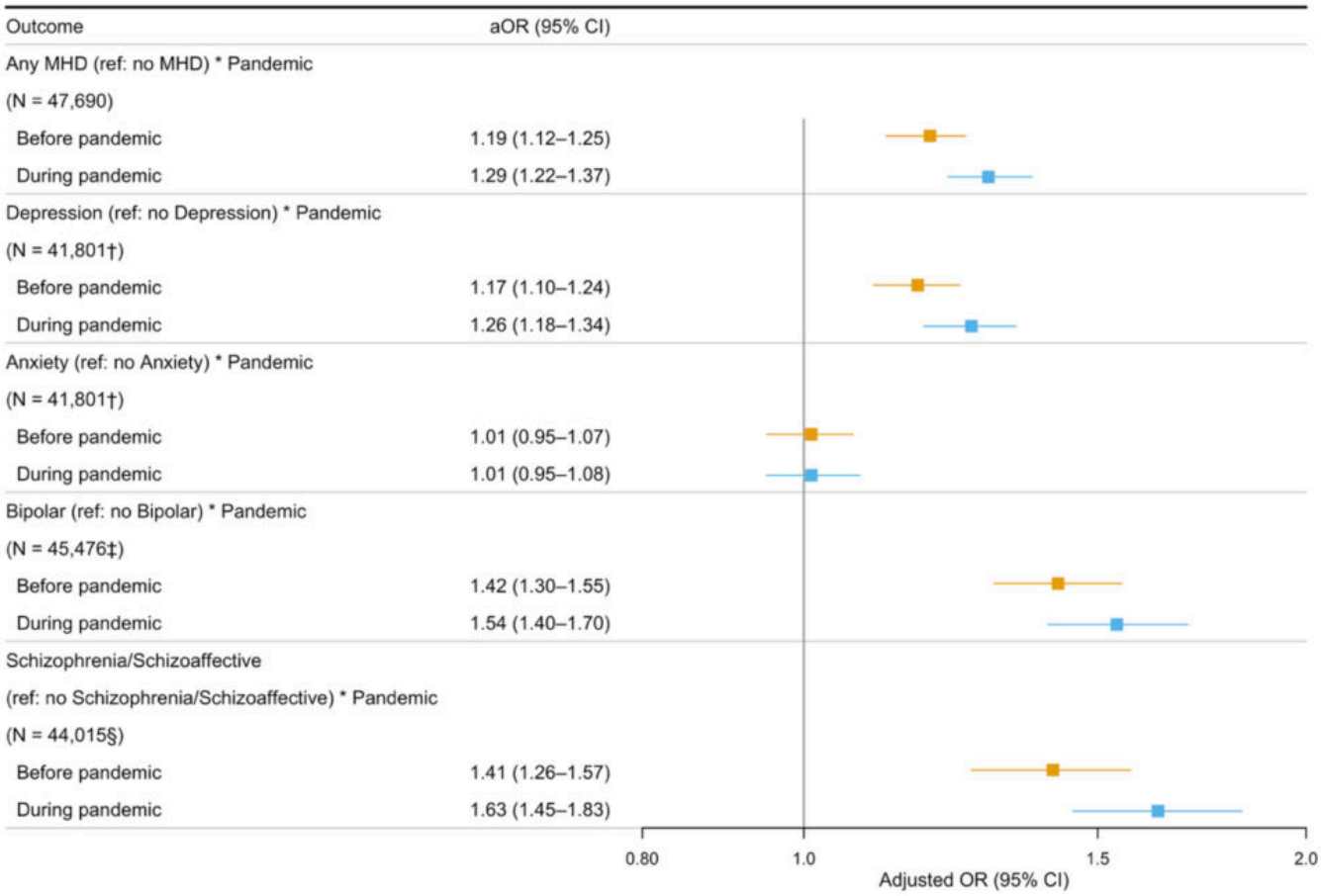
Background: Mental health disorders (MHD) are common among people with HIV (PWH) and associated with viral non-suppression. During the COVID-19 pandemic, increases in MHD and disruptions in healthcare services may have affected both MHD diagnosis and HIV care. We evaluated the association between four MHD and unsuppressed VL among PWH before and during the pandemic.

Methods: We included PWH (≥18 years) enrolled in 11 U.S. cohorts in the North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD) with available MHD data. Eligible participants were engaged in HIV care (≥1 clinical encounter or viral load [VL]) during both intervals: 09/01/2018–02/29/2020 (before pandemic) and 06/01/2020–12/31/2021 (during pandemic) . MHD of interest were clinical diagnoses (both prevalent and new diagnoses) of depression, anxiety, bipolar disorder, and schizophrenia/schizoaffective disorder (SCZ/SZA) based on ICD-10 codes. Logistic regression models with general estimating equations estimated adjusted ORs of unsuppressed VL (>200 copies/mL) for each MHD. Models included a term for pandemic period (before vs during), an interaction term between MHD and the pandemic period, and were adjusted for age, sex, race/ethnicity, HIV acquisition group, and baseline CD4 count.

Results: A total of 47,690 PWH (median age of 54 years, 88% male, 43% non-Hispanic Black) were included, with median follow-up time of 32 months. Diagnosis of any of the MHDs of interest (vs. no MHD) was associated with higher odds of unsuppressed VL before the pandemic and the magnitude of this association increased during the pandemic (Figure). Diagnosis of depression (vs. no depression, bipolar or SCZ/SZA), bipolar (vs. no bipolar or SCZ/SZA), or SCZ/SZA (vs. no SCZ/SZA or bipolar) were each independently associated with higher odds of unsuppressed VL before the pandemic, and the magnitude of all these associations increased during the pandemic. There was no association of anxiety and unsuppressed VL before or during the pandemic.

Conclusions: Disparities in unsuppressed VL widened among those with depression, bipolar disorder, or SCZ/SZA during the pandemic highlighting a need for targeted support of PWH with these MHD during future public health emergencies.

Figure. Adjusted odds ratios for unsuppressed HIV viral load associated with mental health disorders before and during the COVID-19 pandemic



Footnotes:

New to care classification required an unsuppressed (>200 copies/mL) at entry into care. Viral load measurements at the date an individual was new to care and for the subsequent 3 months were removed from this analysis.

P-value for interaction was determined by comparing QICu values between GEE models (with and without interaction term) using a Chi-square test, with degrees of freedom equal to the difference in the number of model parameters. All p-values for interaction are less than 0.05, except for anxiety (p = 0.95).

†Individuals with diagnosis of bipolar disorder or schizophrenia/schizoaffective disorders were excluded from the analysis of depression and anxiety.

‡Individuals with diagnosis of schizophrenia/schizoaffective disorders were excluded from the analysis of bipolar disorders.

§Individuals with diagnosis of bipolar disorder were excluded from the analysis of schizophrenia/schizoaffective disorders.

Substance Use

Fatal and non-fatal overdoses among people with HIV enrolled in care in an urban clinic in Baltimore, Maryland, USA, 2019-2025 Catherine Lesko* Catherine Lesko Michael Chiu Oluwaseun Falade-Nwulia Jarratt Pytell Lauren Zalla Joyce Jones Lorraine Dean Y. Joseph Hwang Richard Moore LaQuita N. Snow Jeanne Keruly Nicholas Schweizer Anthony T. Fojo

Background: We described incidence of and risk factors for fatal and non-fatal overdose in a cohort of people with HIV (PWH) in routine care in Baltimore, Maryland.

Methods: We included PWH in the Johns Hopkins HIV Clinical Cohort from June 2019-March 2025. Fatal overdoses were identified with cause of death codes. Non-fatal, medically involved overdoses were identified by diagnoses from clinical encounters. A subset of patients also self-reported past-6-months, non-fatal overdoses on tablet-based patient reported outcomes (PRO) surveys. We fit multivariable logistic models for self-reported, non-fatal overdose, after applying inverse odds weights to remove selection bias due to participation in the PROs.

Results: We included 2,549 people, median age 55 years (interquartile range [IQR]: 44, 61), 64% male, 77% Black, and 23% with a history of injection drug use. 1,402 people completed ≥1 PRO. There were 43 fatal overdoses (rate=3.28 per 1000 person-years (PY)), 102 non-fatal, medically involved overdoses (rate=7.7/1000 PY), and 320 self-reported, non-fatal overdoses (rate=78.2/1000 PY). Most fatal overdoses (91%) implicated opioids, although 37% also listed cocaine. 55% of non-fatal, medically involved overdoses were linked to opioids, 22% to psychoactive substances, and 24% to an unspecified drug. Independent risk factors for non-fatal, self-reported overdose included younger age, male sex, unsuppressed viral load, household income >300% of federal poverty level, prior opioid use disorder diagnosis, recent cocaine or opioid use, and recent receipt of MOUD or ever been prescribed a non-MOUD opioid. Non-fatal overdose increased the hazard of fatal overdose by 69% (95% CI: 0.55, 5.18).

Conclusions: Self-reported, non-fatal overdoses are about 10 times as common as non-fatal, medically involved overdoses and 20 times as common as fatal overdoses. We confirmed previously identified risk factors for non-fatal overdose, including stimulant (cocaine) involvement.

Health Services/Policy

Preventable Healthcare Encounters in Transgender and Non-Transgender Adults at an Integrated Health System. Cynthia N. Ramirez* Cynthia N. Ramirez Michael Goodman Varada Sarovar Wendy Leyden Alexandra Lea Michael J. Silverberg

Purpose: Preventable healthcare encounters (PHE) are defined as avoidable hospitalizations and emergency department visits for conditions that can be effectively managed in outpatient care. Transgender and gender diverse (TGD) patients may face elevated risk for PHE due to care disruptions, stigma, and higher rates of mental health and substance use conditions. However, PHE have not been examined in TGD compared with non-TGD patients.

Methods: We conducted a cross-sectional analysis in a matched cohort of TGD and non-TGD adults at Kaiser Permanente Northern California from January 1, 2023, to December 31, 2024. PHE were identified using a validated metric developed by the Agency for Healthcare Research and Quality for measuring ambulatory care-sensitive conditions, which examines PHE for seven conditions: diabetes, chronic obstructive pulmonary disease, hypertension, heart failure, pneumonia, urinary tract infection, and asthma. Associations between TGD status and PHE (any vs none) were evaluated using prevalence ratios (PRs) estimated from modified Poisson regression, sequentially adjusting for sociodemographic factors, primary care engagement, clinical comorbidities, and mental health and substance use conditions.

Results: Among 7,181 TGD and 121,188 non-TGD adults, PHE prevalence was higher among TGD patients (6% vs. 4%). TGD patients had higher unadjusted prevalence of PHE (PR = 1.52; 95% CI, 1.38–1.68), which remained elevated after adjustment for sociodemographic factors, primary care engagement, and clinical comorbidities (PR = 1.24; 95% CI, 1.12–1.36). After additional adjustment for mental health and substance use conditions, the association was attenuated (PR = 1.10; 95% CI, 1.00–1.21).

Conclusion: TGD patients experience a higher prevalence of PHE overall, but this appears to be explained by diagnosis of mental health and substance use conditions. Efforts to reduce PHE among TGD patients may benefit from integrating mental health and substance use services within affirming outpatient care.

Table 1. Prevalence ratios and 95% confidence intervals for the association between transgender and gender-diverse (TGD) status (TGD vs non-TGD) and preventable healthcare encounters (any vs none), estimated using sequentially adjusted nested models.

		Preventable Healthcare Encounters			
Model	Predictor variables	PR	95% CI		p-value
1	Unadjusted	1.52	1.38	1.68	<.0001
2	+ Sociodemographic	1.38	1.25	1.52	<.0001
3	+ Primary care engagement	1.28	1.16	1.41	<.0001
4	+ Clinical comorbidities	1.24	1.12	1.36	<.0001
5	+ Mental health and substance use conditions	1.10	1.00	1.21	0.06

Sociodemographics include age, sex assigned at birth, race and ethnicity, insurance type, and Neighborhood Deprivation Index.
Primary care engagement analyzed using total number of primary care encounters in year prior.
Clinical comorbidities include a modified Charlson comorbidity index score (excludes diabetes, chronic pulmonary disease, and congestive heart failure) and body mass index.
Mental health and substance use conditions include anxiety and depression diagnosis in year prior, history of smoking, and diagnosis of alcohol substance use disorder in year prior.
Abbreviations: CI - confidence interval; PR - prevalence ratio.

Health Services/Policy

Length of stay risk adjustment for patients with acute pancreatitis using a large U.S. cohort Tahmina Begum* Tahmina Begum Laura H Gunn Helia Hadavi John Martin Michael Korvink

Background: Acute pancreatitis (AP) is a common gastrointestinal cause of hospitalization. Gaps remain in population-based risk adjustments leveraging large, commonly available datasets across U.S. hospital systems, often ignoring non-clinical factors, competing in-hospital mortality risks, and discharges against medical advice (AMA). We examine patient and facility factors associated with hospital length of stay (LOS), and hypothesize that commonly available variables beyond clinical factors can enhance risk-adjustments of LOS among AP patients, adjusting for AMA and in-hospital mortality.

Methods: A retrospective cohort study of 63,970 hospitalized patients was used with AP principal diagnosis discharged in 2024 over 784 U.S. facilities, using administrative claims data. The outcome was time to clinical discharge, with in-hospital mortality as competing risk and AMA discharge a censoring event. Two separate facility-clustered Fine-Gray models were used to estimate LOS, one with Elixhauser index (EI) and another using individual comorbidities, adjusting for patient and facility variables. C-statistics were estimated within an 80:20 derivation-validation cohort split.

Results: Patient and facility factors were associated with LOS. For example, women (hazard ratio; HR=0.978), count of secondary diagnoses (HR=0.941), and procedures (HR=0.851) were associated with longer LOS ($p<0.03$), while smaller facilities (≤250 beds) were associated with shorter LOS ($HR\geq1.07$; $p<0.05$). The individual comorbidity-based model demonstrated substantial HR differences across comorbidities vs. HRs implied from the EI-based model. Both models demonstrated moderate out-of-sample performance ($C\geq0.67$).

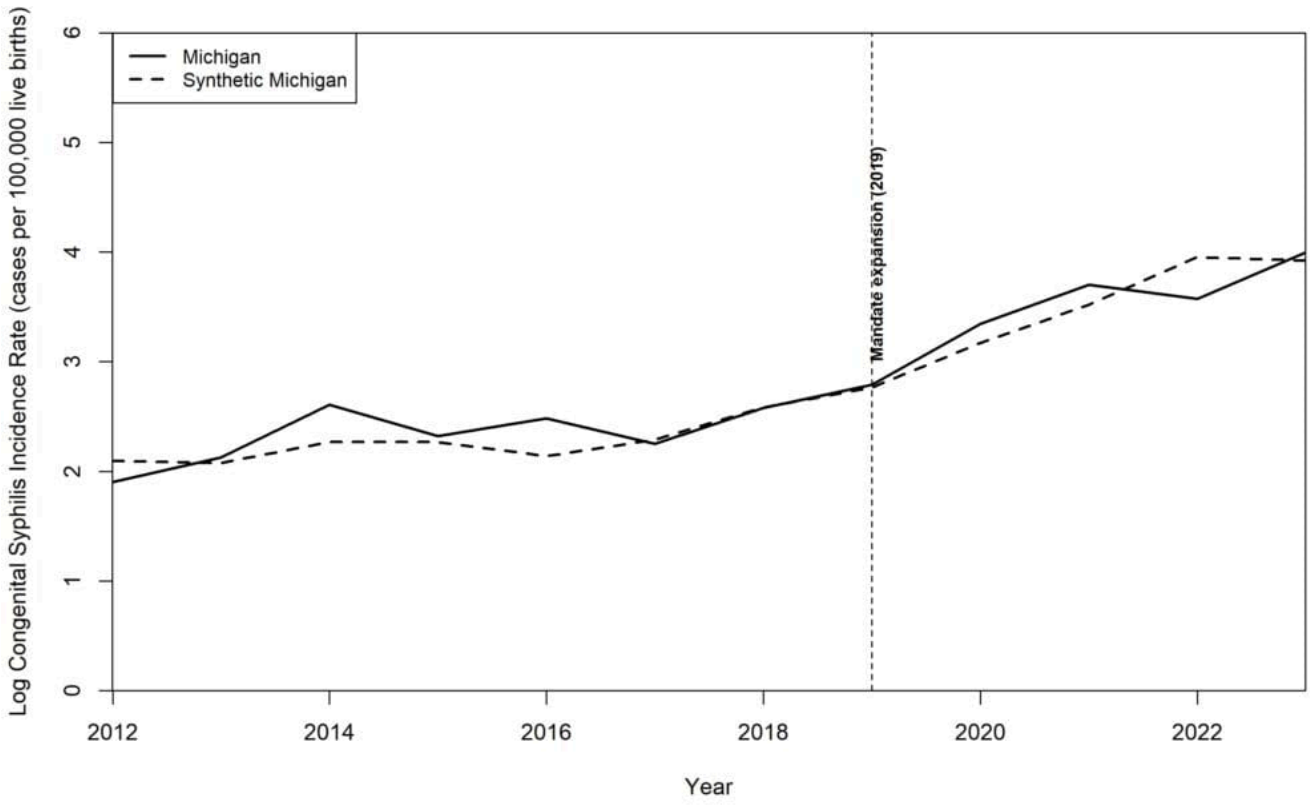
Conclusions: Risk-adjustment of national administrative data can identify additional non-clinical determinants of AP LOS, with implications of informing interventions to optimize care and refining processes for more equitable payments, particularly for hospitals caring for underserved communities.

Health Services/Policy

Quasi-Experimental Evaluation of Michigan’s Prenatal Syphilis Screening Mandate Expansion Meredith Cahill* Meredith Cahill Claire E. Margerison

Michigan’s congenital syphilis incidence increased by over 1000% from 2012-2023, mirroring national trends. Because testing and treatment during pregnancy can prevent most cases of congenital syphilis, prenatal screening is a key prevention strategy. In 2019, Michigan expanded its prenatal syphilis screening mandate (MCL §333.5123), adding a 3rd trimester screening requirement to the existing 1st prenatal visit requirement. We evaluated the impact of this expansion on Michigan’s congenital syphilis incidence using a synthetic control design. We constructed a state-year panel (2012–2023) using congenital syphilis incidence data from the CDC and natality data for Michigan and 18 U.S. states that maintained the same screening requirement as Michigan’s pre-expansion requirement across the study period. We fit a synthetic Michigan using pre-expansion log-transformed congenital syphilis incidence and the percentages of Medicaid-covered births and births receiving first-trimester prenatal care. We estimated post-expansion effects as differences in log incidence and reported them as percent change beginning in 2020 to account for gestational timing. The synthetic control closely approximated Michigan’s pre-expansion trends (root mean squared prediction error [RMSPE]=0.19; Figure 1). Post-expansion divergence modestly exceeded pre-period error (post/pre RMSPE ratio=1.23). Initially, Michigan’s mandate expansion appeared to increase congenital syphilis incidence by 19% (2020) and 20% (2021) relative to the synthetic control, but in 2022 the trend reversed and incidence was 32% lower. Augmented synthetic control models and placebo tests supported the robustness of these findings. Our study provides one of the first quasi-experimental evaluations of state prenatal syphilis screening mandates and offers initial evidence of the population-level effects of expanded state screening requirements amid the current congenital syphilis epidemic.

Figure 1. Observed vs. Synthetic Michigan Log Congenital Syphilis Incidence: 2012–2023



Health Services/Policy

Expiration of SNAP Emergency Allotments and Food Insecurity among Adults with Disabilities Banushree Jawaharlal Nehru* Tarang Parekh Banushree Jawaharlal Nehru

Background
During the COVID-19 pandemic, Supplemental Nutrition Assistance Program (SNAP) emergency allotments (EA) increased food benefits for low-income households. These allotments ended nationwide by March 2023, raising concerns about food insecurity, particularly among adults with disabilities who face heightened economic vulnerability.

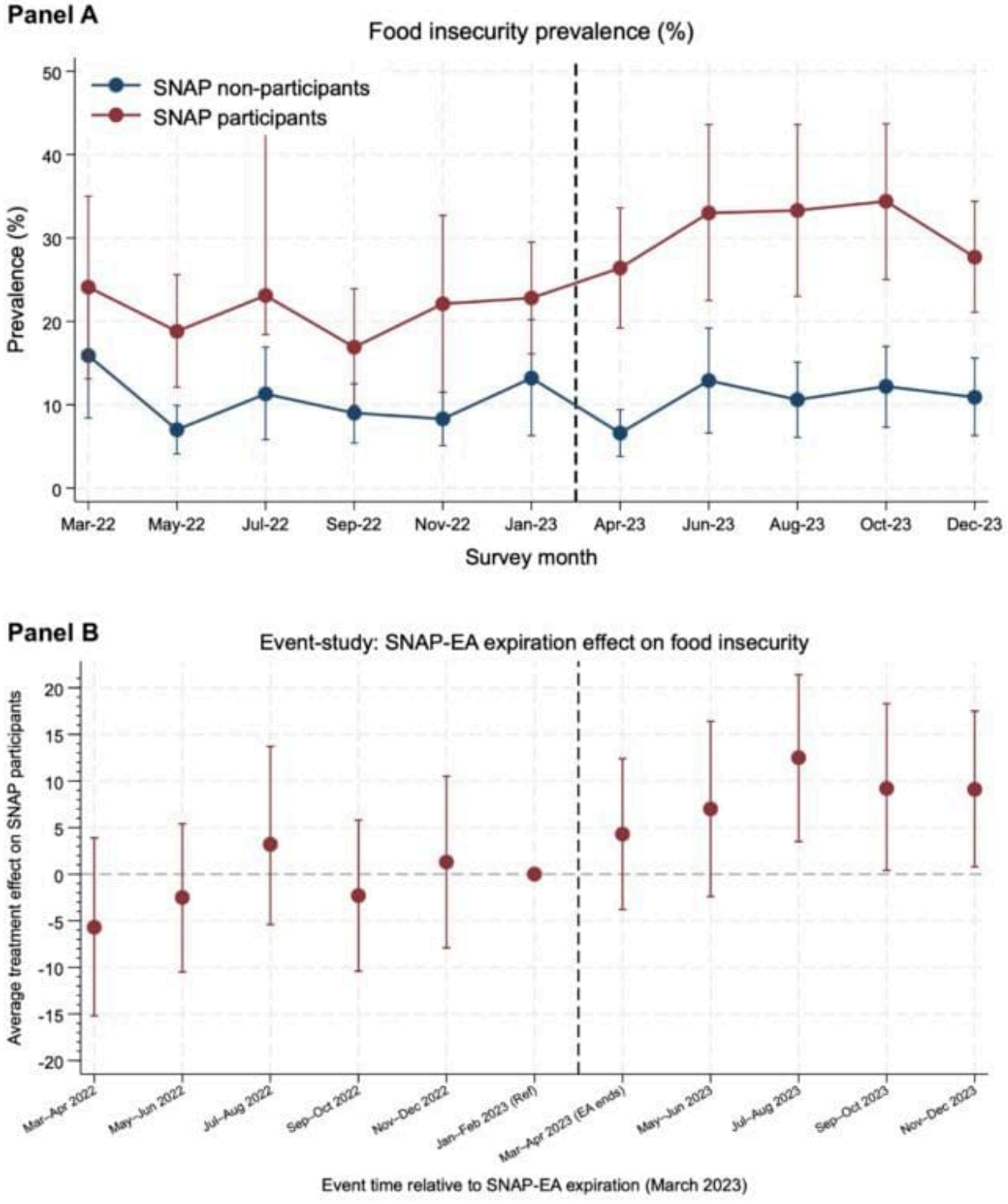
Methods
We conducted a serial cross-sectional study using Behavioral Risk Factor Surveillance System data from March 2022-December 2023. The analytic sample included 34,346 adults with disabilities residing in 22 states where SNAP-EA ended in March 2023 and who were eligible for SNAP based on state-specific income criteria. We compared SNAP participants with SNAP-eligible nonparticipants using survey-weighted difference-in-differences models adjusted for age, sex, race/ethnicity, education, marital status, income with state and survey month fixed effects. Event-study models assessed dynamic changes relative to EA expiration.

Results
Among adults with disabilities, 10,392 were SNAP participants (81.6% aged 18-64 years; 63.2% female) and 23,954 were SNAP-eligible nonparticipants (58.8% aged 18-64 years; 54.0% female). Food insecurity increased among SNAP participants after EA expiration, while remaining stable or declining among nonparticipants. Adjusted food insecurity increased by 6.2 percentage points among SNAP participants and decreased by 3.1 percentage points among nonparticipants, yielding an adjusted difference-in-differences of 9.3 percentage points (95%CI: 5.2-13.5; $p<0.001$). Event-study analyses showed no differential pre-trends and demonstrated an immediate and sustained post-expiration increase in food insecurity among SNAP participants through December 2023.

Conclusions
The expiration of SNAP emergency allotments was associated with a significant increase in food insecurity among adults with disabilities, highlighting disproportionate impact of benefit reductions on a medically and economically vulnerable population.

Figure. Changes in Food Insecurity Among Adults with Disabilities Before and After the Expiration of SNAP Emergency Allotments

Panel A shows survey-weighted prevalence of food insecurity among SNAP participants and SNAP-eligible nonparticipants from March 2022 through December 2023.
Panel B presents event-study estimates of the adjusted effect of SNAP emergency allotment expiration on food insecurity among SNAP participants, relative to January-February 2023. Points represent estimates and vertical bars indicate 95% confidence intervals. The vertical dashed line denotes the expiration of SNAP emergency allotments in March 2023.



Health Services/Policy

Comparison Group and Non-Random Selection Bias as Potential Modifiers on the Relationship between Supplemental Nutrition Assistance Program (SNAP) Participation and Obesity Risk: A Systematic Review and Meta-Analysis Arin A Balalian* Arin A Balalian Rachel C Thoerig Lauren E O'Connor Rupal Trivedi Shannon A Kugley Cassi N Leta Tanvi Reddy Aihui Li Trish Bosse Craig Gundersen Marlene Schwartz Elizabeth F Racine Angela Odoms-Young Margaret J Foster Kyle M Holland Amanda J MacFarlane Maureen K Spill

Background: Conclusions about SNAP participation and obesity in the U.S. are inconsistent, potentially due to several methodological factors, such as selecting an appropriate comparison group and controlling for non-random selection into SNAP (NRS). This systematic review assessed if these factors modify the relationship between SNAP participation and obesity risk.

Methods: We searched 9 databases for peer-reviewed studies and government reports from 1980 to Nov 2025. Randomized controlled trials, non-randomized interventions, and prospective and retrospective cohorts comparing obesity risk (adults: BMI ≥30.0 kg/m2; children: BMI-for-age and sex ≥95th percentile) between SNAP participants and non-participants (NP) with household income ≤200% of the federal poverty level were eligible. We assessed risk of bias (RoB) with ROBINS-I and certainty of evidence (CoE) with GRADE. Data were synthesized using multilevel-multivariate meta-analyses with robust variance estimation. Comparison group and NRS adjustment were assessed as potential modifiers.

Results: 10 articles from 3 prospective cohorts were eligible. SNAP participation was not associated with obesity risk (RD=0.01, 95%CI: -0.00, 0.02; CoE: very low). One article that could not be pooled reported higher but insignificant odds of obesity with SNAP (OR=1.58; 95%CI: 0.79, 3.19). Most articles had serious RoB due to confounding or misclassification. 9 articles used income-eligible NP and 2 used NP with unreported eligibility as the comparison group. 5 adjusted for NRS. Comparison group or adjusting for NRS did not modify the relationship ($p>0.05$).

Conclusions: Prospective cohorts suggest no association between SNAP participation and obesity risk. More studies are needed to increase precision of the modification analyses. More research is needed to investigate other sources of heterogeneity like population characteristics and statistical approach.

Nutrition/Obesity

Ultra-processed Foods and Nutrient Profiling Criteria for Front-of-Package Labeling: Identifying High-Risk Foods in NHANES 2021-2023 Anais Elena Fernandez Calzavara* Anais Elena Fernandez Calzavara Andrew O. Odegaard

Background. Ultra-processed foods (UPFs) are consistently associated with higher chronic disease risk, yet the overlap with foods high in nutrients of public health concern (saturated fat, sodium, and added sugar – HFSS) is unclear. The U.S. Food and Drug Administration has proposed front-of-package (FOP) labeling for HFSS foods. Clarifying the overlap may provide more nuanced public health guidance for distinguishing high-risk foods from other UPFs.

Objective. Estimate the proportion of UPFs that would qualify as HFSS and UPFs contributions to total energy intake.

Design/Methods. This was a cross-sectional descriptive analysis of dietary intake among 8,153 adults (≥18 y) in the NHANES 2021–2023 cycle using two 24-h recalls. Foods were classified as UPFs and evaluated for HFSS using absolute food-level nutrient thresholds. Participant-level percentages of energy from UPFs were averaged across recalls. The proportion of consumed UPFs high in each or ≥1 nutrient and their contribution to calories from HFSS were calculated. Unique UPF items were assessed for FOP labeling criteria.

Results. UPFs provided 39.1% (95% CI: 38.6-39.7) of daily energy. Of these, 50.2% (95% CI: 49.6-50.9) were high in saturated fat, 15.7% (95% CI: 15.2-16.1) in sodium, and 14.2% (95% CI: 13.7-14.7) in sugar. UPFs contributed 25.0% (95% CI: 24.5-25.5), 14.4% (95% CI: 14.0-14.8), and 9.3% (95% CI: 9.0-9.7) of daily calories from high saturated fat, sodium, and sugar, respectively. Among 1,450 unique UPFs, 57.7% (95% CI: 55-60) would require an FOP label for saturated fat, 28.4% (95% CI: 26-31) for sodium, and 14.3% (95% CI: 12-16) for sugar. Roughly a third (31%, 95% CI: 29-33) would require no label.

Conclusions. UPFs contributed substantially to saturated fat, sodium, and sugar intake, but not all UPFs were HFSS foods. These findings suggest that FOP labeling could help identify high-risk foods among UPFs, while UPF classification alone would be an imperfect indicator for nutrients of concern.

Nutrition/Obesity

Causal effect of ultra-processed food intake on incident obstructive sleep apnoea: TMLE and AIPW analyses in UK Biobank Yohannes Adama Melaku* Yohannes Adama Melaku Tefera Mekonnen Zegeye Abebe Abitew Anteneh Mengist Dessie Robert Adams

Background: Ultra-processed foods (UPF) are increasingly consumed and have been linked to obesity and cardiometabolic disease, but evidence on their causal role in obstructive sleep apnoea (OSA) is limited. We estimated the causal effect of UPF intake on incident OSA in UK Biobank.

Methods: We analysed 114,990 UK Biobank participants with dietary intake derived from the average of four 24-hour dietary recalls. UPF exposure was defined using the NOVA classification as the percentage contribution of UPF to total food intake (grams), evaluated at thresholds of ≥25%, ≥50%, and ≥75%. Incident OSA was ascertained via linkage to hospital admissions and primary care records. Causal risk ratios (RRs) were estimated using targeted maximum likelihood estimation (TMLE) and augmented inverse probability weighting (AIPW), adjusting for baseline sociodemographic, behavioural, and clinical confounders.

Results: During follow-up, 1,438 incident OSA cases were identified. Higher UPF consumption was associated with increased OSA risk in a graded manner. TMLE estimates were: UPF ≥25% RR 1.24 (95% CI 1.10–1.41), UPF ≥50% RR 1.54 (1.37–1.74), and UPF ≥75% RR 1.99 (1.57–2.53). AIPW results were highly consistent: UPF ≥25% RR 1.26 (1.12–1.40), UPF ≥50% RR 1.54 (1.38–1.73), and UPF ≥75% RR 1.96 (1.60–2.39).

Conclusions: Using two doubly robust causal estimators and repeated dietary assessment, higher UPF intake was associated with a dose–response increase in incident OSA risk. These findings support UPF reduction as a potential target for OSA prevention and motivate intervention and implementation research.

Nutrition/Obesity

Prevalence of U.S. adults eligible for FDA-approved obesity medications using bias-corrected BMI, BRFSS 2023 Lixia Zhao* Lixia Zhao Lyudmyla Kompaniyets Guixiang Zhao Samantha L. Pierce Kali Autrey Renee M. Porter Heidi M. Blanck Alyson B. Goodman

Background Obesity is a complex disease associated with multiple chronic conditions, including heart disease and some cancers, two leading causes of death. Several GLP-1 based medications are approved as adjuncts to diet and physical activity for weight management among individuals with obesity (BMI≥30 kg/m²) or BMI≥27 with a weight-related health condition. Little is known about the characteristics and prevalence of U.S. adults meeting these criteria.

Methods Using 2023 data from the Behavioral Risk Factor Surveillance System, we adjusted self-reported BMI using a validated bias-correction method and estimated the age-standardized prevalence of U.S. adults eligible (BMI≥30 or BMI≥27 with a weight-related, diagnosed health condition) for obesity medications (OMs). Estimates were calculated overall and stratified by sociodemographic characteristics. We used t-tests to compare prevalence estimates within subgroups.

Results Among 385,028 survey participants**,** 50.7% of adults were eligible for OMs in 2023. Eligibility varied significantly by age group, ranging from 38.8% (18–34 years) to 59.7% (50–64 years, P <0.01). The prevalence of eligibility decreased with higher education and household income. By employment status, self-employed adults had the lowest prevalence of eligibility (46.3%, 95% CI [45.1, 47.5]), while retired individuals had the highest (53.4% [48.1, 58.6]). Rural adults had a significantly higher prevalence of eligibility (55.6%) compared to urban adults (49.9%, P <0.01). Eligibility also differed by race/ethnicity, healthcare provider, payer type, and geographic region.

Conclusions Approximately half of U.S. adults were eligible for obesity medications, as an adjunct to lifestyle management, with substantial variations across subgroups. Awareness of these differences is important for decision makers and healthcare providers to allocate resources effectively and prioritize delivering interventions and treatments to high-risk populations.

Aging

Food Insecurity, the Supplemental Nutritional Assistance Program, and Physical Functioning in Older Adults Kelley Akiya* Kelley Akiya Amanda M Irish Suzanna M Martinez Anusha M Vable

Introduction: Food insecurity in older adults is associated with increased functional limitations, a significant barrier to healthy aging. Our study investigates whether the Supplemental Nutrition Assistance Program (SNAP), the largest anti-hunger program in the U.S., protects against the negative impact of food insecurity on aging adults' functional status. **Methods**: We used data from the Health and Retirement Study, a large population-based survey of older adults, and included participants ages 50 and older with at least three waves of outcome data (N= 5,507). SNAP receipt (yes/no) and food insecurity were collected in 2013 and functional status outcomes were collected biennially from 2014-2022. Food insecurity was measured with the Household Food Security Survey Module and participants were classified as having high, low, or very low food security. Functional status outcomes included counts of reported limitations with Activities of Daily Living (ADLs) and instrumental activities of daily living (IADLs). We used multilevel negative binomial models with a random intercept and interaction terms between level of food insecurity and SNAP receipt to estimate associations with ADLs and IADLs. Models were adjusted for demographic and socioeconomic confounders. **Results**: In our sample, 588 (10.7%) participants reported low food security, 454 (8.2%) reported very low food security, and 558 (10.1%) reported receiving SNAP. Very low food security was associated with subsequent ADLs among non-SNAP participants (Incident Rate Ratio [IRR] = 5.24, 95% CI = 3.73, 7.4), while the association was attenuated among SNAP participants (IRR of very low security * SNAP = 0.52, 95%CI = 0.29, 0.93). Results were similar for IADLs and those with low food security, though confidence intervals associated with the low food security * SNAP interaction terms included the null. **Conclusion**: SNAP participation may reduce functional limitations among food-insecure older adults.

Nutrition/Obesity

Examining the role of early pregnancy dietary intake on preterm birth using target trial emulations Kyle Busse* Kyle Busse Stefanie Hinkle Heather Burris Sara DeMauro Rana Chehab Sylvia Badon Enrique Schisterman Ellen Caniglia Yeyi Zhu Rita Strakovsky Alison Hipwell Dana Dabelea Lynn Yee Alison Gemmill Rui Ling Shalmali Bane Assiamira Ferrara Monique Hedderson Amanda Marma Perak Zhaozhong Zhu Nicole Spillane Anne Lang Dunlop Joseph Stanford Sunni Mumford

Introduction: Adhering to a healthy diet may reduce the risk of preterm birth, but it remains unclear which dietary strategies are most effective, as trials of dietary interventions in pregnancy are often infeasible. We estimated the observational analogs of the intention-to-treat effects of hypothetical interventions to meet 2015-2020 Dietary Guidelines for Americans (DGA) recommendations in pregnancy on the risk of preterm birth.

Methods: We used data from 10,095 pregnancies (10,069 people) in the Environmental influences on Child Health Outcomes (ECHO) Cohort with diet assessed before 20 weeks' gestation. Discrete interventions were defined as: 1) achieving a Healthy Eating Index-2015 (HEI) score ≥60th percentile; 2) meeting recommendations for ≥7 of 13 DGA components; 3) meeting recommendations for total fruits and vegetables; 4) meeting recommendations for all "moderation" components (sodium, refined grains, saturated fats, added sugars); 5) meeting recommendations for ≥2 moderation components. Modified Poisson regression with robust standard errors estimated risk ratios (RR) and 95% confidence intervals (CI) for preterm birth (<37 weeks'), adjusted for age, race, ethnicity, education, parity, pre-pregnancy BMI, household income, alcohol and tobacco use, and plurality. Multiple imputation (m=20) was used for missing covariate data.

Results: 1,044 deliveries (10%) were preterm. Achieving a HEI score ≥60th percentile (score of 67, RR=0.84 [95% CI 0.74-0.94]), meeting recommendations for ≥7 DGA components (17% of pregnancies, RR=0.86 [0.73-1.01]), and meeting recommendations for total fruits and vegetables (24%, RR=0.86 [0.75-0.98]) were associated with a lower risk of preterm birth. Meeting recommendations for all (1%) or ≥2 moderation components (20%) was not associated with preterm birth.

Conclusions: Identifying strategies to help pregnant people meet recommendations for overall diet quality and fruit and vegetable intake may reduce the risk of preterm birth.

Environment/Climate Change

Prenatal exposure to wildfire smoke and risk of ASD/ADHD in children among Medicaid recipients: a national cohort study Stefania Papatheodorou* Stefania Papatheodorou Krista Huybrechts Yang Liu Xinye Qiu Sonia Hernandez Diaz Wanyu Huang Matthew Shupler Hayon Michelle Choi Michael Leung Brent Coull Yaguang Wei Joel Schwartz Christopher J. McDougle Marc Weisskopf Antonella Zanobetti Danlu Zhang

Objective: Wildfires are an increasing threat to human health. While wildfire-attributed PM2.5 exposure has been linked to adverse birth outcomes, its potential impact on children's neurodevelopment remains poorly characterized. We examined associations between prenatal wildfire PM2.5 exposure and risk of autism spectrum disorder (ASD) and attention-deficit/hyperactivity disorder (ADHD) in a large, national cohort of Medicaid-enrolled children.

Methods: We constructed a longitudinal mother–child cohort using the Medicaid Analytic eXtract (MAX) from 2007–2014. Prenatal wildfire PM2.5 exposure was assigned as pregnancy-average concentrations at the maternal residential ZIP code using daily spatiotemporal wildfire smoke models. ASD and ADHD were identified using ICD-9 codes. Cox hazards models stratified by year and county, coupled with distributed lag models, were used to estimate associations, adjusting for ambient temperature, relative humidity, maternal age, race/ethnicity, behavioral risk factors (smoking, alcohol, drug use), area-level socioeconomic status, and season of conception. Effect modification by child sex was assessed.

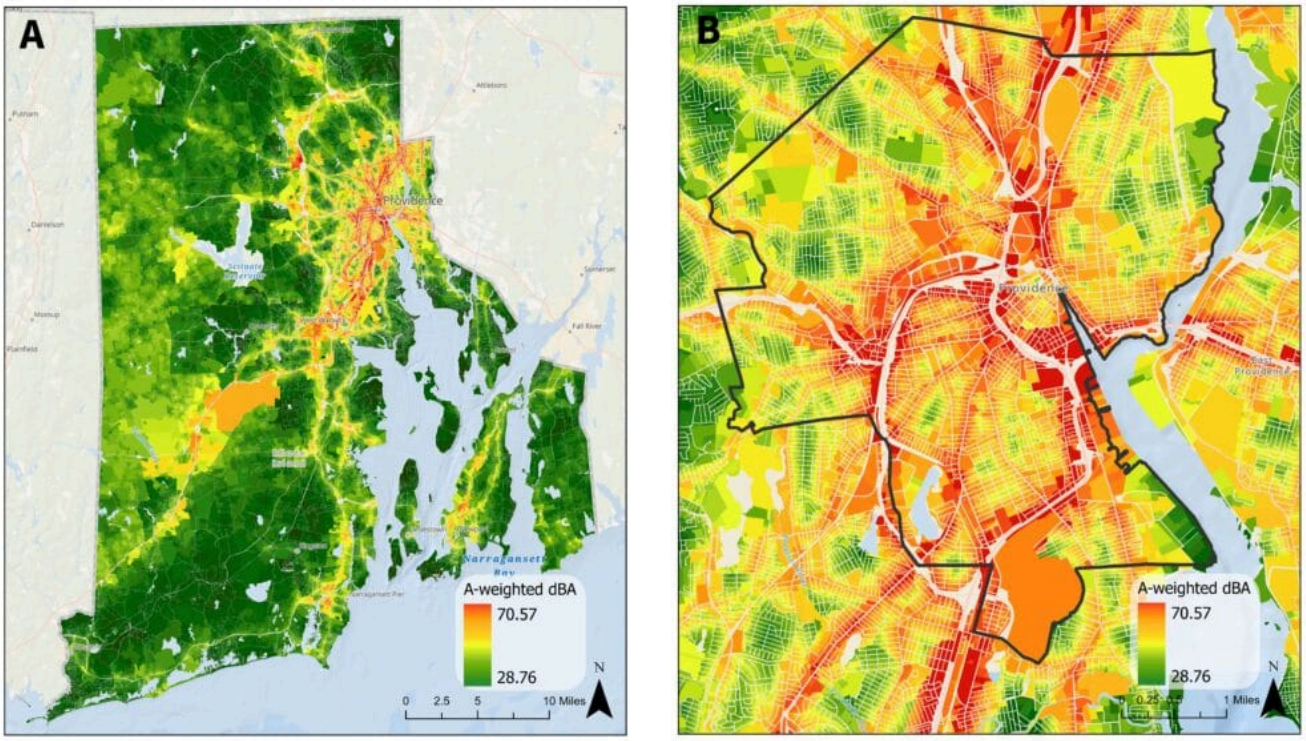
Results: The analysis included 1,010,197 births. A 1-μg/m^3 increase in average prenatal wildfire PM2.5 exposure was associated with increased risk of ASD (overall HR = 1.07; 95% CI: 1.01–1.15) and ADHD (overall HR = 1.13; 95% CI: 1.09–1.17). We observed windows of increased susceptibility in mid-pregnancy. Associations were observed in both sexes but were stronger among females (ASD HR = 1.12; 95% CI: 1.03–1.26; ADHD HR = 1.18; 95% CI: 1.13–1.23) than males (ASD HR = 1.01; 95% CI: 1.00–1.08; ADHD HR = 1.11; 95% CI: 1.07–1.15).

Conclusions: Prenatal exposure to wildfire smoke was associated with increased risk of ASD and ADHD among children in a low-income U.S. population. These findings underscore the neurodevelopmental risks of wildfire-related air pollution and highlight the need for targeted public health interventions to protect pregnant individuals and children. Further research is warranted to clarify underlying biological mechanisms, sex-specific susceptibility, and sensitive exposure windows.

Environment/Climate Change

High-resolution statewide spatial error sound models and unequal environmental burdens among local populations Nina Lee* Nina Lee Erica Walker William Goedel

Background: Environmental noise is a pervasive exposure with documented effects on human health, yet population-level assessments are often limited by sparse monitoring data, coarse spatial resolution, and a focus on A-weighted sound. These constraints hinder evaluation of fine-scale exposure variability and environmental justice implications. **Methods:** We conducted a monitoring campaign across Rhode Island, collecting over 29,000 hours of measurements from 340 locations. Six sound metrics were measured. Measurements were adjusted for temporal and meteorological variability. Statewide parcel-level noise exposure was predicted for ~420,000 land parcels using spatial error models incorporating land use, transportation, and built environment characteristics while accounting for residual spatial autocorrelation. Predicted noise metrics were linked to census block group characteristics from the American Community Survey and evaluated using univariate mixed-effects models with random intercepts for block group. **Results:** Predicted noise levels exhibited strong spatial patterning, with higher levels in urban areas and along major transportation corridors. Across all sound metrics, higher predicted noise levels were significantly associated with neighborhood characteristics indicative of structural disadvantage, including higher proportions of non-White residents, Black and Hispanic populations, lower income and educational attainment, renter-occupied housing, linguistic isolation, and disability. Parcels located within state-designated environmental justice focus areas experienced significantly higher predicted noise levels across all sound metrics. **Conclusions:** These state-wide, high-resolution noise models reveal significant social and spatial inequities in environmental noise exposure across an understudied state context. These well-defined exposure surfaces provide a framework for epidemiologic analyses requiring fine-scale exposure assessment.


A
Providence
Narragansett Bay
A-weighted dBA
70.57
28.76
0 2.5 5 10 Miles
N
B
Providence
A-weighted dBA
70.57
28.76
0 0.25 0.5 1 Miles
N

Environment/Climate Change

Residential street-view greenspace and cognitive decline in older adults in the Multi-Ethnic Study of Atherosclerosis (MESA) Tara E. Jenson* Tara Jenson Yingyan Wu Lilah Besser Brent Coull Ana V. Diez-Roux Matthew P. Fox Leidys Gutiérrez Martínez Jana A. Hirsch Timothy Hughes Peter James Joel Kaufman Jennifer Weuve Marcia Pescador Jimenez

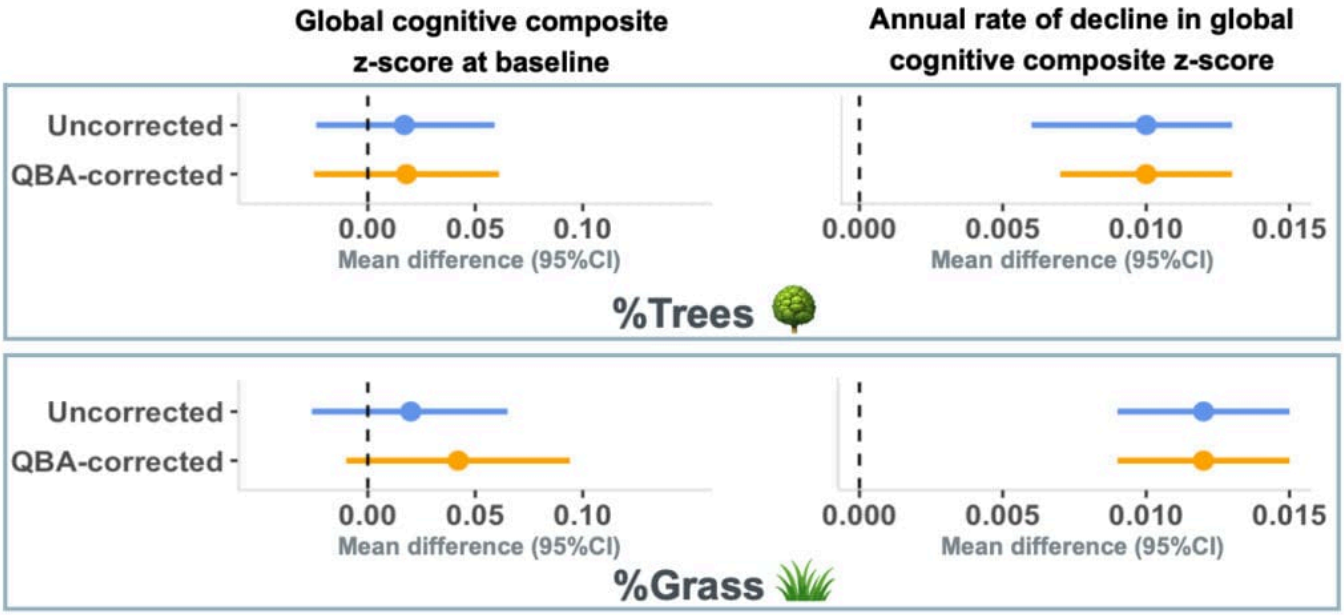
Background: Greenspace may protect against cognitive decline but it remains unclear if specific greenspace features drive protective associations. Street view (SV) based metrics (available since 2007), provide high resolution data on specific greenspace features (e.g. trees and grass) that may shed light on potential interventions. We aimed to assess associations between specific SV-based greenspace metrics and cognitive decline.

Methods: We used data from 4,160 participants enrolled in MESA 2000-02 (ages 45-84) with repeated global cognition composite (GCC) z-scores combining Cognitive Abilities Screening Instrument, Digit Symbol Coding, and Digit Span administered during follow-up exams 2010-12, 2016-18, and 2022-24. We linked participant addresses 2000-2020 with SV data within 500m. Addresses from 2000-2006 were assigned 2007 SV values. We conducted a quantitative bias analysis (QBA) to estimate direction and magnitude of potential mismeasurement error in 2000-2006 SV values using known satellite-based Normalized Difference Vegetation Index (NDVI). We then estimated fixed effects of cumulative average of %Trees and %Grass (uncorrected and QBA-corrected, separately) on baseline GCC and annual rate of GCC decline.

Results: Results are shown in Figure 1. Neither %Trees nor %Grass were associated with baseline GCC, for either uncorrected (mean difference z-score, %Trees 0.017 [-0.024, 0.059]; %Grass 0.020 [-0.026, 0.065]) or QBA-corrected measures (%Trees 0.018 [-0.025, 0.061]; %Grass 0.042 [-0.01, 0.094]). %Trees and %Grass were associated with slower annual rate of decline in GCC for both uncorrected (annual mean difference in z-score decline, %Trees: 0.010 [0.006, 0.013]; %Grass 0.012 [0.009, 0.015]) and QBA-corrected measures (%Trees: 0.010 [0.007, 0.013]; %Grass 0.012 [0.009, 0.015]).

Conclusion: Higher cumulative average trees and grass were associated with slower annual rate of cognitive decline. Our results were robust to QBA-corrected trees and grass measures.

Figure 1. Association per interquartile range of uncorrected and QBA-corrected street-view image tree and grass average percentages with baseline and annual rate of decline in global cognitive composite z-score in the Multi-Ethnic Study of Atherosclerosis (MESA) (2000-2024, N=4160).



Uncorrected: Estimates and 95% CIs from linear mixed models incorporating original, uncorrected 2000-2006 %Trees and %Grass measures

QBA-corrected: Estimates and 95% CIs from linear mixed models incorporating 2000-2006 %Trees and %Grass measures bias-corrected using modeled changes in greenspace based on 2000-2006 Normalized Difference Vegetation Index measures.

All models adjusted for age at baseline, time since baseline visit, sex, race/ethnicity, individual income, education, marital status, neighborhood socioecomonic status, MESA site, baseline fine particulate matter exposure.

Environment/Climate Change

Gestational Urinary Organophosphate Ether (OPE) Concentrations and Sleep Patterns in Children Kelli Williams* Kelli Williams Jagadeesh Puvvula John Holmes Wei Yang Sigrid Veasey Jianghong Liu Kimberly Yolton Kim M. Cecil Yingying Xu Joseph M. Braun Bruce P. Lanphear Clara Sears Ann M. Vuong Maria Ospina Antonia M. Calafat Aimin Chen

Organophosphate esters (OPEs) are widely used replacement flame retardants and plasticizers. These endocrine-disrupting chemicals are associated with adverse neurobehavioral outcomes in children; yet their effects on sleep remain unclear. OPEs are detected in nearly all U.S. adults, including women of reproductive age. We evaluated associations of gestational OPE concentrations with child sleep patterns in 277 mother–child dyads from the Health Outcomes and Measures of the Environment (HOME) Study. We calculated area under the curve (AUC) exposure metrics using specific-gravity urinary OPE biomarkers measured at 16 and 26 weeks' gestation and at birth, including BCEP (GM ± GSD: 0.77±3.18 µg/L), BDCIPP (0.85±2.55), DNBP (0.24±1.99), and DPHP (1.95±2.24). We assessed child sleep outcomes from ages 2 to 8 years using an adapted Children's Sleep Habits Questionnaire measuring sleep irregularity, hypersomnolence, sleep disruption, and sleep duration (minutes). Longitudinal associations between AUC urinary OPE concentrations and sleep outcomes were estimated using covariate-adjusted linear mixed-effects models. Visit-specific estimates were reported for OPE-by-visit interactions ($p<0.10$); otherwise, overall estimates were presented. A 10-fold increase in BCEP was associated with more sleep irregularity at age 8 years (β=0.24, 95% CI: 0.02, 0.46), while DNBP was associated with more sleep irregularity across all ages (0.19, 95% CI: -0.04, 0.42). A 10-fold increase in BDCIPP was associated with slightly longer sleep duration across all ages (14 m, 95% CI: -2.48, 30.66), and DPHP was associated with longer sleep duration at age 8 years (31 m, 95% CI: -1.24, 63.09). In contrast, BCEP was associated with shorter sleep duration across all ages (-15 m, 95% CI: -27.97, -1.20). No significant associations were observed for hypersomnolence or sleep disruption. These findings suggest that gestational OPE exposures are associated with important sleep disturbances in children.

Environment/Climate Change

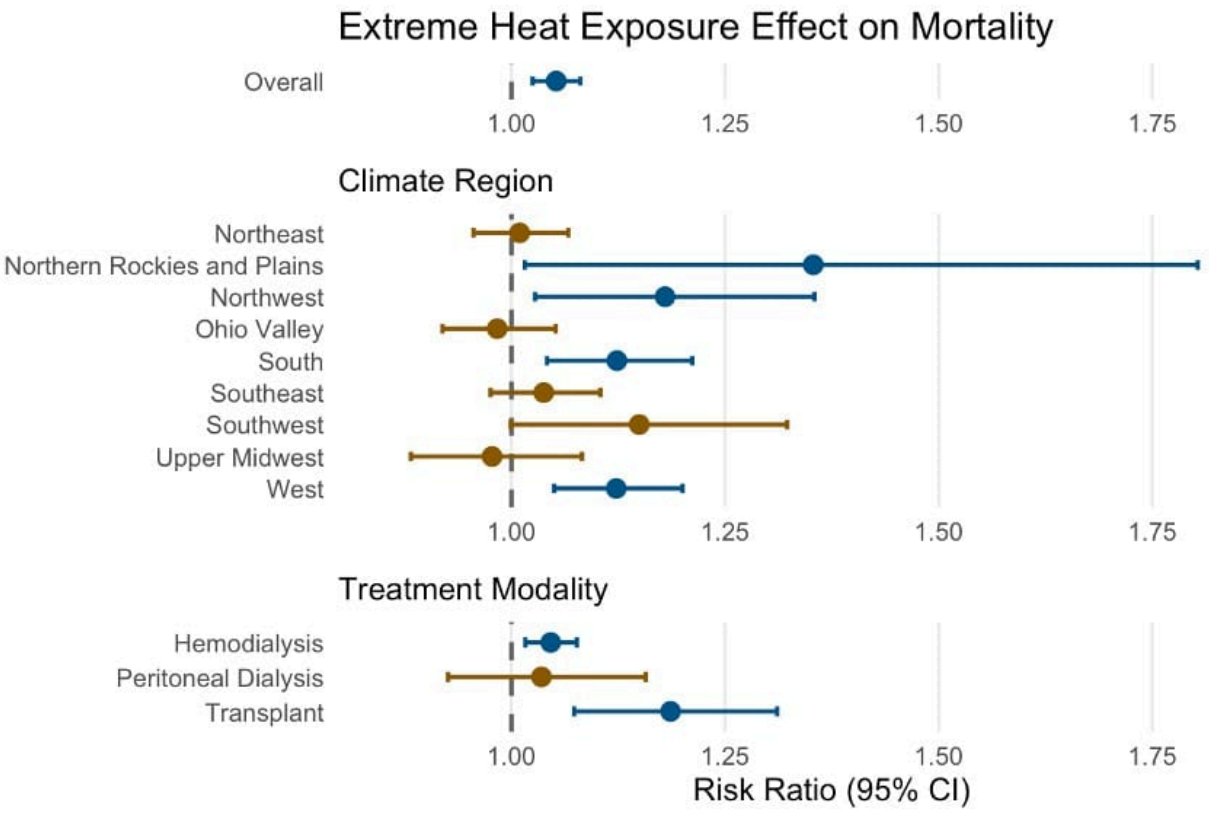
Increased Mortality Following Extreme Heat Events Among Patients with End-Stage Renal Disease: A National Study, 2010-2019 Rebecca Fillipo* Rebecca Fillipo Abhijit V Kshirsagar Ryan Salama M Alan Brookhart

Introduction: Extreme heat events (EHEs) secondary to climate change are a growing public health concern. Individuals with end-stage renal disease (ESRD), already a medically complex and vulnerable population, may be particularly susceptible to heat-related adverse events. We aimed to estimate the effect of EHE exposure on 14-day mortality in patients with ESRD using a quasi-experimental design.

Methods: We identified EHEs as ≥2 consecutive days at the 99th percentile of county-level heat index and matched each EHE to comparable non-EHE county-day periods within a 3-year window during warm months (2010-2019). Patient data were obtained from the United States Renal Data System. We used conditional logistic regression, using county-level EHE-control pairs as strata, to estimate the relative risk of mortality. We also examined risk stratified by climate region and treatment modality.

Results: We analyzed 2,761,746 observations from 715,328 individuals and 10,931 EHEs. Overall, exposure to EHEs increased the relative risk of 14-day mortality by 5% (RR = 1.05, 95% CI: 1.03, 1.08) compared to the matched non-EHE periods. Regional analyses revealed a greater risk increase in the West (RR 1.12, 95% CI: 1.05, 1.20), South (RR: 1.12, 95% CI: 1.04, 1.21), Northern Rockies and Plains (RR: 1.35, 95% CI: 1.02, 1.80), and Northwest (RR:1.18, 95% CI: 1.03, 1.35). Patients receiving hemodialysis (RR 1.05, 95% CI:1.02, 1.08) and those with kidney transplant (RR 1.19, 95% CI: 1.073, 1.31) also appeared to be at heightened risk.

Discussion: Patients with ESRD face increased risk mortality following EHE exposure. Substantial regional variation in heat vulnerability exists, and risk differs by treatment modality. As temperatures continue to rise, these findings underscore the urgent need for targeted, region-specific interventions to protect this high-risk population from heat-related mortality.


Extreme Heat Exposure Effect on Mortality
Overall
1.00
1.25
1.50
1.75
Climate Region
Northeast
Northern Rockies and Plains
Northwest
Ohio Valley
South
Southeast
Southwest
Upper Midwest
West
1.00
1.25
1.50
1.75
Treatment Modality
Hemodialysis
Peritoneal Dialysis
Transplant
1.00
1.25
1.50
1.75
Risk Ratio (95% CI)

Reproductive

Using cycle-timed air pollutant estimates to model fecundability Gabrielle S. Johnson* Gabrielle Johnson Kaniz Rabeya Timothy P. Canty Karen Schliep Rachael Hemmert Pauline Mendola Neil J. Perkins Akanksha Singh Allison M. Ring Sunni L. Mumford Carrie J. Nobles

Background: Accounting for sensitive windows of reproduction is crucial for understanding how timing of underlying biologic processes impacts the overall effect of environmental exposures, such as air pollution, on odds of pregnancy.

Methods: We included 1001 women from the Effects of Aspirin in Gestation and Reproduction (EAGeR) trial who lived in the Intermountain West and had residential georeferenced pollutant estimates. We abstracted pollutant data from the Air Quality Data for Health-Related Applications (AQDH) and Community Multiscale Air Quality Modeling System (CMAQ), including ozone (O3), particulate matter 2.5 (PM2.5), nitrogen dioxide (NO2), sulfur dioxide (SO2), and carbon monoxide (CO). We estimated biologically relevant sensitive windows to air pollution timed to cycle start date including pre-ovulation and implantation as well as the corresponding broader follicular and luteal phases, respectively. We constructed a multi-pollutant discrete-time Cox proportional hazards model to predict fecundability odds ratio (FOR) per inter-quartile range (IQR) increase in pollutants. Models adjusted for age, treatment status, income, education, and smoking.

Results: Multi-pollutant models using CMAQ data found that during pre-ovulation, O3 decreased odds of pregnancy by 20% (FOR 0.80, 95% CI 0.67, 0.96 per 15.6 ppb) and NO2 by 20% (FOR 0.8, 95% CI 0.56, 1.13 per 7.1 ppb). During implantation, O3, PM2.5, NO2, and SO2 were associated with trends of lower odds of pregnancy while CO increased odds of pregnancy by 43% (FOR 1.43, 95% CI 1.08, 1.91 per 80.6 ppb). Findings during pre-ovulation and implantation were consistent with follicular and luteal phases, respectively. AQDH data produced similar results.

Conclusion: Our findings account for sensitive windows of reproduction and suggest that air pollution may impact fecundability. Next steps include evaluating pollutant mixtures to further characterize pollutants associated with pregnancy.

Women’s Health

Clinical Preterm Delivery Phenotypes and Chronic Hypertension among Women in the Nurses’ Health Study II Karolina Edlund* Karolina Edlund Xiaoyu Che Holly Kathryn Janet

Preterm delivery (PTD) has been linked to elevated maternal cardiovascular disease. Yet mechanisms, such as chronic hypertension, underlying observed associations remain unclear due to limited investigation of clinical PTD phenotypes.

Leveraging data from 69,273 parous women in the Nurses’ Health Study II, we evaluated associations between lifetime PTD phenotype histories––spontaneous preterm labor (sPTL; n=1,775), preterm premature rupture of membranes (pPROM; n=1,037), medically indicated preterm delivery (miPTD; n=700), and/or nonphenotyped PTD (n=6,534)––and chronic hypertension up to 54 years since first birth. Cox proportional hazards models with time-varying exposures and covariates were used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs). We stratified estimates by time since first birth to identify potential periods of increased risk.

With a median follow-up of 29 years, we observed 27,376 (40%) cases of chronic hypertension. Lifetime histories of miPTD, sPTL, and nonphenotyped PTD were associated with 55% (HR 1.55; CI 1.39, 1.74), 12% (HR 1.12; CI 1.04, 1.21), and 13% (HR 1.13; CI 1.09, 1.18) increased rates of chronic hypertension, respectively, as compared to pregnancy histories uncomplicated by each phenotype. Adjustment for hypertensive disorders of pregnancy attenuated estimates for miPTD (HR 1.22; CI 1.09, 1.37), suggesting much of the risk associated with miPTD is driven by preeclampsia and gestational hypertension. Rates of chronic hypertension were highest in the first 10 years for miPTD (HR 2.33; CI 1.80, 3.01), sPTL (HR 1.61; CI 1.29, 2.01), and nonphenotyped PTD (HR 1.33; CI 1.18, 1.50). For pPROM, elevated risk of chronic hypertension emerged only after 40 years (HR 1.71; CI 1.09, 2.69).

Rates of chronic hypertension differed across clinical PTD phenotypes. Women with a lifetime history of miPTD were at greatest risk, especially during the first 10 years postpartum, indicating a critical window for screening and intervention.

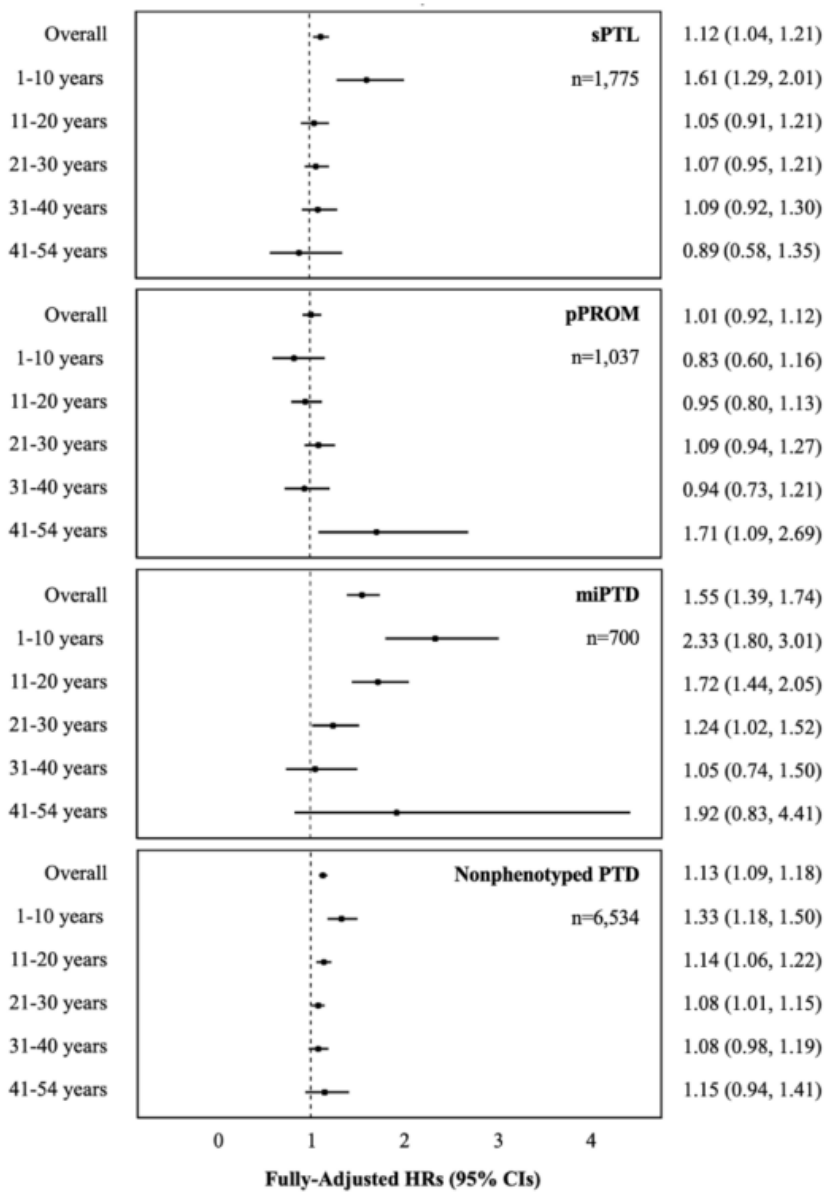


Figure 1. HRs and 95% CIs for the associations between lifetime PTD phenotype histories and chronic hypertension, across follow-up (Overall) and stratified in time-intervals since first birth (N=69,273). Models were adjusted for age at first birth, age at enrollment, race/ethnicity, parental education, and family history of hypertension, as well as pre-pregnancy BMI, smoking, Alternative Healthy Eating Index, alcohol intake, physical activity, oral contraceptive use, and parity.

Perinatal & Pediatric

Characterizing pregnancies with unobserved outcomes in administrative claims data Chase D. Latour* Chase Latour Baijun Zhou Elizabeth Simmons Oluwasolape Olawore Megan Delgado Jacob C. Kahrs Elizabeth A. Suarez Ellen C. Caniglia Mollie E. Wood

Introduction: Including pregnancies with unobserved outcomes (ie, lost to follow-up [LTFU]) may reduce selection bias but exacerbate measurement error in claims-based studies of prenatal exposures. Evidence is limited on how to best balance these concerns.

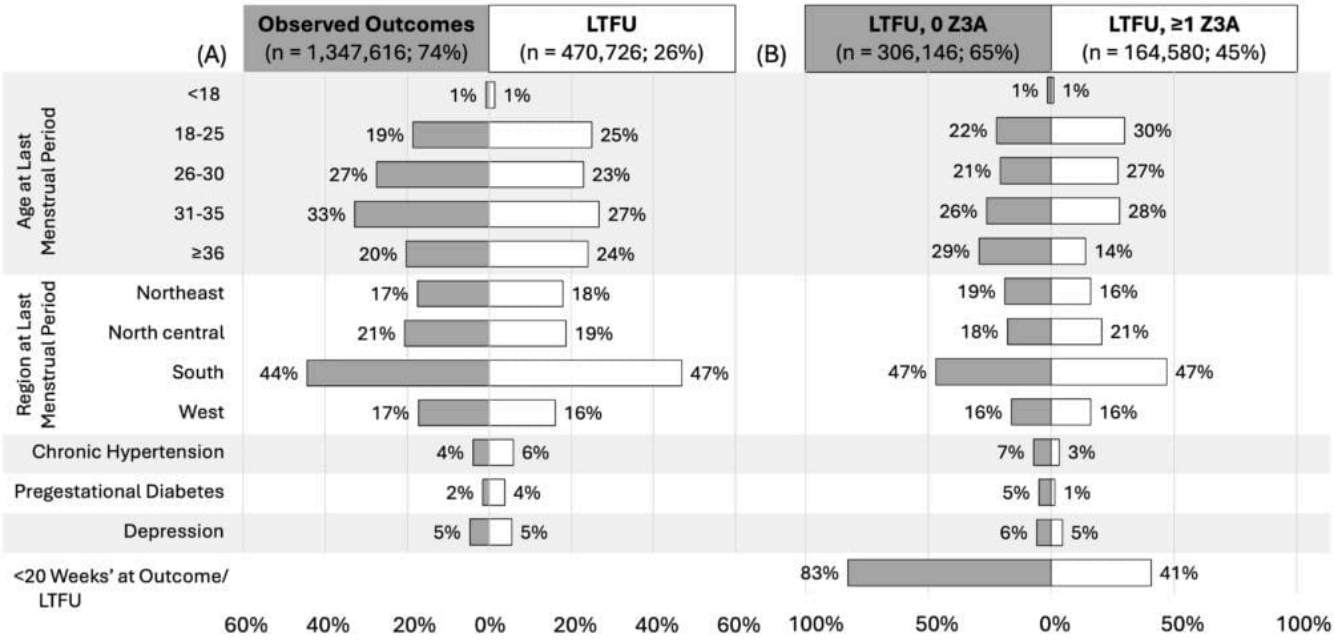
Objective: To characterize differences between pregnancies with observed versus unobserved outcomes.

Methods: We identified pregnancies using U.S. commercial insurance claims data based on pregnancy-related diagnosis and procedure codes. We included pregnancies with estimated last menstrual periods (LMPs) from 7/1/2016-2/1/2023 and ≥180 days pre-LMP continuous enrollment. Pregnancy outcomes were classified as observed versus LTFU, and among LTFU, by the presence of ≥1 gestational week-specific diagnosis code (Z3A.08–Z3A.42). We compared demographics, comorbidities, gestational age (GA) at end of pregnancy or LTFU, and timing of disenrollment for observed vs LTFU pregnancies and, among LTFU, by Z3A code presence.

Results: Of 1,818,342 pregnancies, 470,726 (26%) were LTFU. LTFU pregnancies had more comorbidities than observed pregnancies (chronic hypertension: 6% vs 4%). Among LTFU, only 35% had ≥1 Z3A code, and they had fewer comorbidities than those with 0 Z3A codes (chronic hypertension: 3% vs 7%). GA at LTFU differed by strata: 41% of those with ≥1 Z3A code were <20 weeks' gestation at LTFU, compared to 83% of those with 0 Z3A codes. Cumulative incidence of disenrollment within 30 days after LTFU differed: 60% for ≥1 Z3A code versus 24% for 0 Z3A codes.

Conclusions: Pregnancies LTFU differed from those with observed outcomes and by the presence of Z3A codes. Those with ≥1 Z3A code had fewer comorbidities and disenrolled quickly after LTFU, compared to those with none. Excluding pregnancies with such differing characteristics could result in meaningful selection bias in studies of prenatal exposures. Ongoing manual claim review will clarify LTFU pregnancy validity.

Figure. Characteristics of (A) pregnancies with observed outcomes versus lost to follow-up (LTFU) and (B) LTFU pregnancies with 0 versus ≥1 Z3A code.



Reproductive

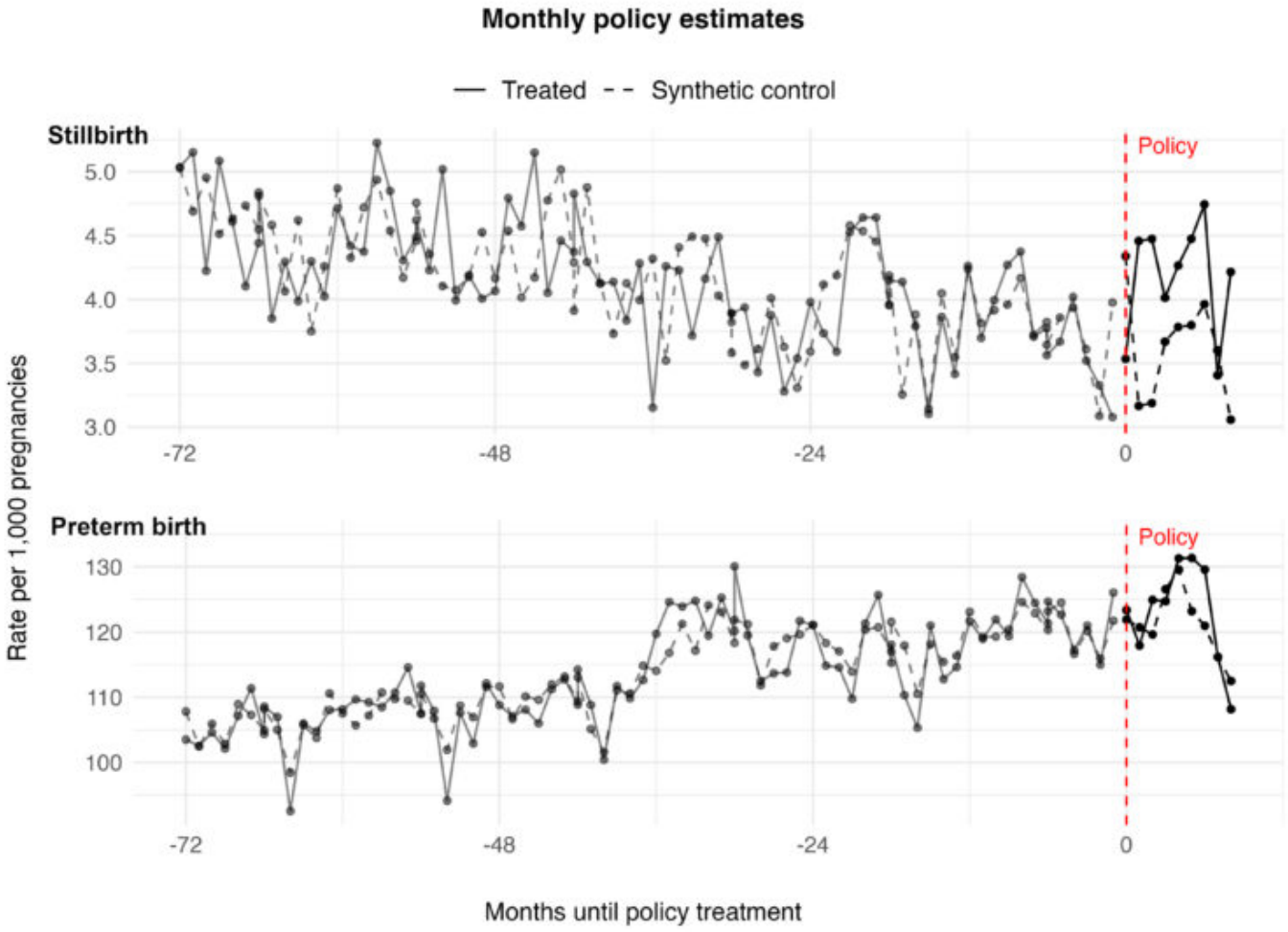
Fetal loss as a competing event in health policy studies: a case study using Texas' 6-week abortion ban Simone Wien* Simone Wien Elizabeth D. Wagner Timothy L. Lash Whitney S. Rice Melvin Livingston Hannah L.F. Cooper Michael R. Kramer

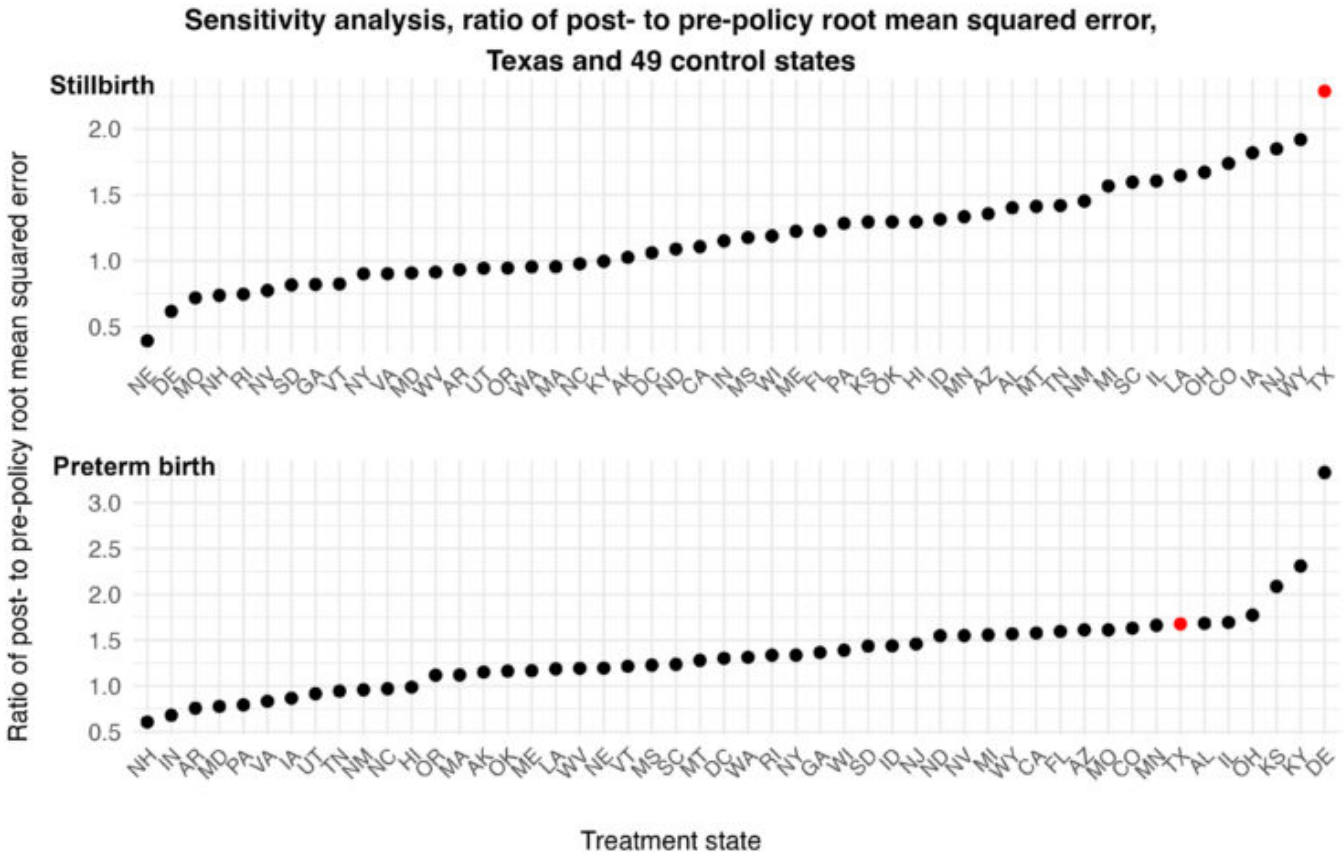
Policies may shift the burden of preterm birth towards fetal loss: as fetal loss increases, preterm birth (conditioned on surviving to delivery) decreases, making policies appear protective when they may be harmful. Collections of policy studies estimating effects on preterm birth may report heterogenous results due to differential susceptibility to this competing risk from fetal loss. Using Texas' (TX) 2021 abortion ban as a case study, we compare conclusions when estimating preterm birth alone versus including proxies for fetal loss to evaluate whether accounting for this competing risk alters study conclusions.

Using vital records from 2014-2022 and augmented synthetic controls, we estimated the policy's average treatment effect on the treated (ATT) for preterm birth and 3 proxies for fetal loss: stillbirth, live birth sex ratio, and live birth small-for-gestational-age sex ratio. Monthly estimates were calculated per 1,000 pregnancies or as ratios, adjusting for state- and time-varying policy and demographic factors. Sensitivity analyses considered states other than TX receiving the treatment during the same period and synthetic controls without augmentation.

Stillbirth and preterm birth increased in TX post-policy, but stillbirth results were more robust to sensitivity analyses. Stillbirths were higher than expected for months 2 (ATT 1.29, 95% CI 0.33, 1.89), and 8 (ATT 1.16, 95% CI 0.06, 1.83) post-policy; preterm births were higher than expected for months 6 (ATT 8.15, 95% CI 2.52, 16.11), and 7 (ATT 8.62, 95% CI 1.04, 16.19). No state diverged as much from the counterfactual in stillbirth as TX, but 6 states had larger divergences in preterm birth. Synthetic controls without augmentation had similar results; no change in sex ratios was observed.

Including stillbirth as a proxy for fetal loss may strengthen conclusions when studying preterm birth. Replication is needed to identify when this approach yields meaningful improvements in policy effect estimation.

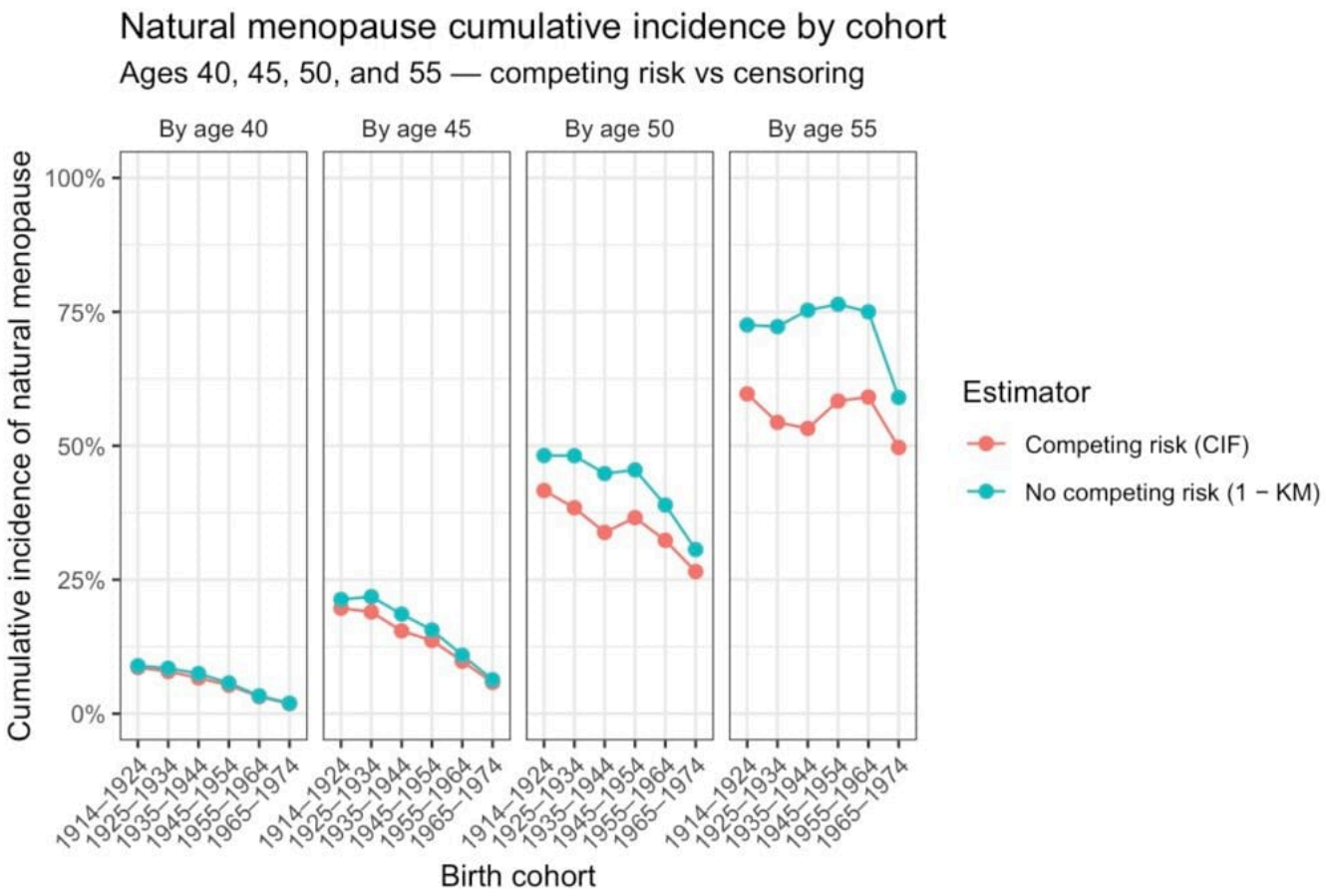

Monthly policy estimates
Treated
Synthetic control
Stillbirth
Policy
5.0
4.5
4.0
3.5
3.0
-72
-48
-24
0
Preterm birth
Policy
130
120
110
100
-72
-48
-24
0
Rate per 1,000 pregnancies
Months until policy treatment


Sensitivity analysis, ratio of post- to pre-policy root mean squared error,
Texas and 49 control states
Stillbirth
2.0
1.5
1.0
0.5
NE DE MO NH RI NV SD GA VT NY VA MD WV AR UT OR WA MA NC KY AK DC ND CA IN MS WI ME FL PA KS OK HI ID MN AZ AL MT TN NM MI SC IL LA OH CO IA NJ WY TX
Preterm birth
3.0
2.5
2.0
1.5
1.0
0.5
NH IN AR MD PA VA IA UT TN NM NC HI OR MA AK OK ME LA WV NE VT MS SC MT DC WA RI NY GA WI SD ID NJ ND NV MI WY CA FL AZ MO CO MN TX AL IL OH KS KY DE
Ratio of post- to pre-policy root mean squared error
Treatment state

Women’s Health

Cohort-based estimates of natural menopause timing in the US using competing risk models Alison Gemmill* Alison Gemmill Dana Sarnak

Menopause is a major but underexamined determinant of women’s health and population aging. Although prior studies suggest that the age at menopause has increased over time, recent US estimates rely largely on period-based prevalence measures that obscure birth cohort dynamics and do not account for competing reproductive endpoints, including bilateral oophorectomy and hysterectomy. Using repeated cross-sectional data from the National Health and Nutrition Examination Survey (NHANES) from 2000-2020, we estimated birth cohort differences in the timing of natural menopause using competing risk survival models and compared results to censoring-based estimates. By age 50, the cumulative incidence of natural menopause declined across birth cohorts, falling from 41.6% (95% CI: 36.6–46.6) in the 1914–1924 cohort to 26.5% (95% CI: 23.4–29.6) in the 1965–1974 cohort (Figure 1). The median age at natural menopause was 53 years (95% CI: 52–54) in the 1914–1924 cohort and occurred at older ages in more recent cohorts. The cumulative incidence of premature natural menopause (<40 years) fell from 8.6% (95% CI: 6.9–10.5) to 1.9% (95% CI: 1.4–2.3), and the cumulative incidence of early menopause (ages 40–44) declined from 11.1% (95% CI: 9.1–13.1) to 4.0% (95% CI: 3.1–5.0). In contrast, estimates that treated surgical menopause as censoring overstated cumulative incidence at older ages and implied earlier menopause timing. Together, these findings indicate that period-based approaches and censoring of surgical menopause underestimate the timing of natural menopause relative to cohort-based competing risk analyses. The population age at natural menopause in the US has increased more than previously recognized, with particularly large declines in early and premature menopause across successive birth cohorts.


Natural menopause cumulative incidence by cohort
Ages 40, 45, 50, and 55 — competing risk vs censoring
By age 40
By age 45
By age 50
By age 55
Cumulative incidence of natural menopause
100%
75%
50%
25%
0%
1914–1924
1925–1934
1935–1944
1945–1954
1955–1964
1965–1974
Birth cohort
Estimator
Competing risk (CIF)
No competing risk (1 − KM)

Environment/Climate Change

Per- and Polyfluoroalkyl Substances (PFAS), Perceived Stress, and Miscarriage in a Cohort of U.S. Black Women Samantha Schildroth* Samantha Schildroth Birgit Claus Henn Victoria Fruh Amelia K. Wesselink Anissa I. Vines Antonia M. Calafat Julianne Cook Botelho Alexander P. Keil Chandra L. Jackson Anne Marie Jukic Quaker E. Harmon Donna D. Baird Ganesa Wegienka Lauren A. Wise

Background: Per- and polyfluoroalkyl substances (PFAS) can dysregulate hormonal and metabolic processes supporting healthy pregnancies. PFAS exposure has been associated with miscarriage risk but less is known about co-exposure to multiple PFAS and psychosocial stressors, especially among Black women.

Methods: We used prospective data from 538 participants from the Study of Environment, Lifestyle, and Fibroids who self-identified as Black/African American. We measured concentrations of six PFAS in baseline plasma samples and participants completed the Perceived Stress Scale-4 (PSS-4) at baseline. Participants reported pregnancy outcomes (miscarriage, induced abortion, ectopic/tubal pregnancy, live birth, stillbirth) at follow-up study visits (~20, 40, and 60 months). We used Cox proportional hazards models, using gestational week as the time scale, to estimate hazard ratios (HRs) with 95% confidence intervals (CIs) characterizing miscarriage risk associated with PFAS concentrations and PSS-4 scores. We also used the survival extension of quantile-based g-computation to estimate associations of the mixture (PFAS and PSS-4 scores) with miscarriage risk.

Results: Ninety-five miscarriages were reported in the study. In Cox models, perfluorohexanesulfonic acid (PFHxS) was associated with 99% (95% CI=1.10, 3.58) and 52% (95% CI=0.73, 3.17) higher risk for miscarriage at the 50th-74th and ≥75th percentiles (vs. <50th percentile), respectively. Other PFAS were not strongly associated with miscarriage. PSS-4 scores (per 1-standard deviation increase) were associated with 23% (95% CI=0.98, 1.53) higher risk for miscarriage. The mixture (PFAS and PSS-4 scores) was non-linearly associated with higher miscarriage risk, but associations were imprecise.

Conclusions: PFHxS and experience of perceived stress were associated with higher risk of miscarriage in a cohort of Black women.

Mental Health

Chronic Pain, School Absenteeism, and Suicidal Behaviors in a Nationally-Representative Sample of US Adolescents. Chloe Child* Chloe Child Martie Thompson

Youth suicidality is a critical public health issue, reflected by suicide being the third leading cause of death among 13-18 year olds in 2023. An increasingly studied factor that contributes to worsened mental health in youth populations is chronic pain status. National data suggest that chronic pain among youth is prevalent, having been reported by over 20% of US adolescents. An additional dimension of chronic pain that can contribute to decreased youth mental health is its impact on school absenteeism. The purpose of our study is to add to this body of literature by investigating the mediating role of school absenteeism in the relationship between chronic pain and youth suicidality. We used nationally representative data from Waves 1-2 of the National Longitudinal Study of Adolescent and Adult Health to determine if chronic pain prospectively increased the risk for suicide ideation and attempts, and if school absenteeism partially accounted for this association. Chronic pain was measured at Wave 1 across four separate pain sites including: joint, headache, body aches, and stomach pain. School absenteeism and suicide ideation and attempts were measured at Wave 2. Logistic regression models, controlling for gender and race, indicated that both the presence and extent of chronic pain significantly increased the likelihood of both missing school (p: 1.4e-07) and suicidality (p: 2.04e-07). As hypothesized, the frequency of missing school mediated (accounted for) the increased risk of suicidal behaviors due to chronic pain (Proportion Mediated CI: 1.29e-03, 0.04, p: 0.028) Results will suggest future research directions as well as implications for intervening with health care providers, parents, and school personnel to educate them about the potential ramifications of chronic pain among youth.

Mental Health

Social cohesion, social support, and mental health diagnosis and care access: Findings from a community-based cohort of sex workers in Vancouver, Canada (2019-2024) Hannah Barca* Hannah Barca Kate Shannon Haoxuan Charlie Zhou Jennie Pearson Shira Goldenberg Andrea Krüsi

Background: Sex workers (SWs) experience disproportionate health inequities, including mental health challenges largely driven by criminalization. While social cohesion interventions effectively reduce HIV/STIs, mental health impacts of support across occupational and community contexts are understudied. Thus, we examined associations between social cohesion, social support, and anxiety and depression diagnoses and care access among SWs.

Methods: We analyzed semi-annual questionnaires collected with women SWs enrolled in the prospective An Evaluation of Sex Workers Health Access (AESHA) cohort from 2019-2024 (≥2 interviews). We used logistic regression with inverse probability of treatment weights to analyze associations between 6-month time-lagged 1. SW social cohesion and 2. social support (overall, affectionate, emotional/informational, positive social interaction, and tangible) and: depression and anxiety diagnosis and mental healthcare access.

Results: Between 2019-2024, the overall prevalence of recent anxiety diagnosis was 3.5% and depression 4.9%; 35.4% experienced barriers to mental healthcare, and most SWs had medium-high social support scores (65.9%). Higher social cohesion was associated with fewer recent diagnoses for depression (aOR = 0.69, 95%CI: 0.49, 0.96) and greater use of anxiety care (aOR= 1.26, 95%CI: 1.01, 1.56). Higher affectionate support was associated with fewer recent anxiety (aOR = 0.21, 95%CI: 0.08, 0.51) and depression diagnoses (aOR = 0.43, 95%CI: 0.22, 0.82), and more use of depression care (aOR = 1.72, 95%CI: 1.01, 2.92). Emotional/informational and overall social support were significantly protective against recent depression.

Conclusions: Social cohesion and support may protect against developing depression and anxiety and reduce barriers to care. Implementation and evaluation of community-based, sex worker-tailored interventions to strengthen social connections across occupational and community contexts is needed.

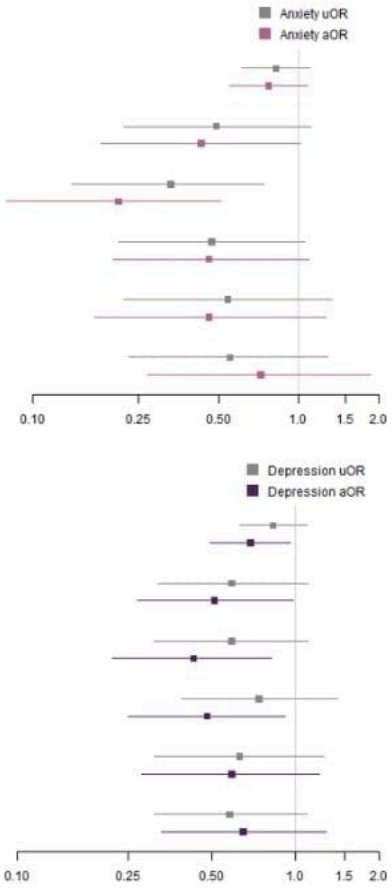
Figure 1. Unadjusted and adjusted odds ratios from GLMM models for the association between types of social support and mental health diagnosis, AESHA 2019-2024.

A. Recently diagnosed with anxiety

Exposure*	Anxiety uOR (95% CI)	Anxiety aOR (95% CI)
Social Cohesion,[a] 5-point increase	0.82 (0.61, 1.10)	0.77 (0.55, 1.08)
MOS Overall,[b] Average Score ≥ 3 vs < 3	0.49 (0.22, 1.11)	0.43 (0.18, 1.02)
MOS Affectionate,[b] Avg Score ≥ 3 vs < 3	0.33 (0.14, 0.74)	0.21 (0.08, 0.51)
MOS Emotional/Info,[b] Avg Score ≥ 3 vs < 3	0.47 (0.21, 1.05)	0.46 (0.20, 1.09)
MOS Pos Social,[b] Avg Score ≥ 3 vs < 3	0.54 (0.22, 1.33)	0.46 (0.17, 1.26)
MOS Tangible,[b] Avg Score ≥ 3 vs < 3	0.55 (0.23, 1.28)	0.72 (0.27, 1.87)

B. Recently diagnosed with depression

Exposure*	Depression uOR (95% CI)	Depression aOR (95% CI)
Social Cohesion,[a] 5-point increase	0.83 (0.63, 1.10)	0.69 (0.49, 0.96)
MOS Overall,[b] Avg Score ≥ 3 vs < 3	0.59 (0.32, 1.11)	0.51 (0.27, 0.98)
MOS Affectionate,[b] Avg Score ≥ 3 vs < 3	0.59 (0.31, 1.11)	0.43 (0.22, 0.82)
MOS Emotional/Info,[b] Avg Score ≥ 3 vs < 3	0.74 (0.39, 1.42)	0.48 (0.25, 0.92)
MOS Pos Social,[b] Avg Score ≥ 3 vs < 3	0.63 (0.31, 1.27)	0.59 (0.28, 1.22)
MOS Tangible,[b] Avg Score ≥ 3 vs < 3	0.58 (0.31, 1.10)	0.65 (0.33, 1.29)

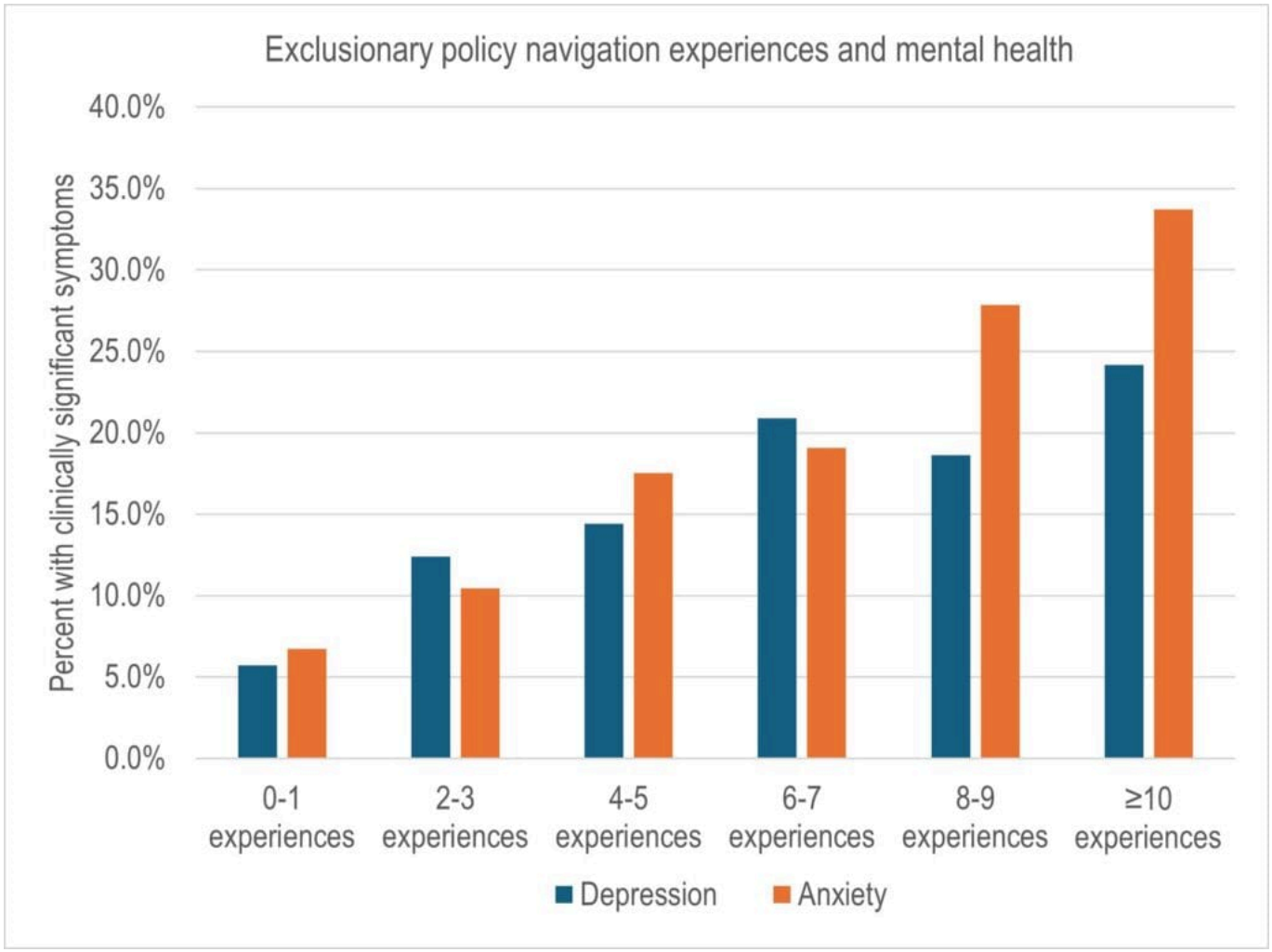


Note. Social cohesion adjusted models controlled for: year, age, any past 6-month drug use, living in Downtown Eastside Vancouver, im/migration status, any past intimate partner violence, LGBTQ2S+ identity, racialization, experiencing police harassment, and place of solicitation. MOS social support adjusted models controlled for: year, age, any past 6-month drug use, everyday discrimination, living in Downtown Eastside Vancouver, im/migration status, any past intimate partner violence, LGBTQ2S+ identity, racialization, and place of solicitation.
Abbreviations: aOR, adjusted odds ratio; CI, confidence interval; Emotion/Info, Emotional/Informational support; MOS, Medical Outcomes Study; Pos Social, Positive Social Interaction.
*All exposures and outcomes measured at each semi-annual study visit with a recall of the last six months
[a]restricted to survey years where mental health outcomes were disaggregated (by diagnosis and treatment) and among those who engaged in sex work in the last six months, n = 226, 2019-2024
[b]restricted to survey years where mental health outcomes were disaggregated (by diagnosis and treatment) and restricted to survey years where MOS social support scale was added, n = 277, 2020-2024

Mental Health

Exclusionary immigration policy experiences and mental health among Latino residents in rural California and Arizona: Findings from a population-based survey Sidra Goldman-Mellor*
Sidra Goldman-Mellor Nancy Burke Alec Chan-Golston Maria-Elena Young

Rural-dwelling foreign- and US-born Latinos experience worse mental health than urban Latinos. Exposure to exclusionary immigrant policies is a potentially important but understudied social determinant of their mental health. We conducted a population-based survey of adult Latinos in 14 rural counties in Arizona and California during May-Dec. 2024. Recruitment used address-based and prepaid cell phone list sampling in a multimode design with web- and phone-based interviewing. The survey assessed two aspects of respondents' exposure to exclusionary immigrant policy experiences: the navigation index summed 14 experiences asserting rights and obtaining resources from, or deciding to avoid, agencies/institutions (e.g., avoiding public benefits due to "public charge" concerns, relying on interpretation services); the encounters index included 16 instances in which policy resulted in Latinos being targeted by an agency/institution or in having a protected right denied (e.g., receiving immigration-related threats from an employer, citizenship verification by law enforcement, being deported). Clinically significant depression and anxiety symptoms were assessed using validated cutoff scores on the Patient Health Questionnaire-9 (PHQ-9) and Generalized Anxiety Disorder-7 (GAD-7). The survey had 3,148 respondents (50% male; 69% U.S.-born, 15% naturalized citizen, 16% non-citizen). Adjusted regression analyses showed that a one-unit increase in each experience index score was associated with 20% increased odds of current depression and 30%-40% increased odds of current anxiety. Results were consistent for both citizens and non-citizens, indicating shared burden among rural Latinos regardless of immigration status. Rural Latinos' exposure to exclusionary immigrant policies is associated with poor mental health in a dose-response manner. If causal, these findings suggest the need to change agency/institutional policies to reduce administrative burden and exclusionary encounters.


Exclusionary policy navigation experiences and mental health
Percent with clinically significant symptoms
40.0%
35.0%
30.0%
25.0%
20.0%
15.0%
10.0%
5.0%
0.0%
0-1 experiences
2-3 experiences
4-5 experiences
6-7 experiences
8-9 experiences
≥10 experiences
Depression
Anxiety

Mental health symptoms among adolescents experiencing suicide loss or non-suicide loss in the past year Rachel Slimovitch* Rachel Slimovitch Siddarth Seenivasa Jaimie Gradus AJ Rosellini

Introduction

Losing someone to suicide is a known risk factor for mental health outcomes, yet its impact during adolescence is underexplored. Research suggests that youth experiencing suicide loss are at increased risk for subsequent suicidal behavior compared to peers without suicide loss, but little is known about other outcomes.

Aim

To investigate differences in subsequent internalizing and externalizing symptoms among adolescents who experience past-year suicide loss, non-suicide loss (“general loss”), or no loss.

Methods

Using Adolescent Brain Cognitive Development Study data, we defined three exposure groups based on past-year bereavement at age 15: suicide loss, general loss, or no loss. Internalizing and externalizing symptoms at age 16 were assessed using the Youth Self Report (normed T-scores; mean=50, SD=10; >63 = clinical range). Linear regression models were run for each outcome separately, adjusting for sex, race/ethnicity, family income, and symptoms at age 14.

Results:

Among 3,259 adolescents, symptoms at age 16 were higher among those exposed to suicide loss (internalizing M = 54.5 [SD=11.4]; externalizing M = 50.7 [SD=9.2l]) compared to those exposed to general loss (internalizing M =51.6 [SD=11.3]; externalizing M=47.5 [SD=9.5]) or no loss (internalizing M = 51.4 [SD=11.0]; externalizing M 46.8 [SD=9.2]). In adjusted models, adolescents exposed to past-year suicide loss had more severe internalizing (b=1.37, 95% CI -0.89 to 3.63) and externalizing symptoms (b=2.53, 95% CI 0.63 to 4.43) than those not exposed to loss. In contrast, past-year general loss was not associated with higher internalizing (b=0.08, 95% CI -0.86 to 1.02) or externalizing symptoms (b=0.15, 95% CI -0.64 to 0.95).

Conclusion

Exposure to suicide loss during adolescence was associated with higher subsequent internalizing and externalizing symptoms relative to non-suicide loss or no loss, indicating that suicide loss has a distinct impact compared to general bereavement.

Mental Health

Social Support from Online Communities: A Protective Factor Against Suicidal Ideation in U.S. Veterans Julie Kittel* Julie Kittel Lindsey Monteith Ryan Holliday Claire Hoffmire

Veteran suicide prevention remains a critical public health concern as suicide rates have increased more than 60% since 2001 despite prevention efforts. Primary prevention strategies for veteran suicide may be bolstered by understanding protective factors for not only suicide, but also suicidal ideation (SI), a major risk factor for suicide. Perceived social support is a well-established protective factor for SI. However, limited research has evaluated the role of social support delivered by online communities, despite the ubiquity of such communities. We addressed this gap by evaluating the association of perceived social support from online platforms and past-month SI in a population-based, cross-sectional survey of 17,396 U.S. veterans. Overall online social support and specific subtypes (i.e., emotional-information, affectionate, and positive social interaction) were assessed, along with platform (e.g., Facebook, Instagram). Poisson regression models with robust standard errors were fit to compute prevalence ratios (PRs), adjusting for demographic and military service confounders. Analyses were stratified by platform, gender, age, and rurality to examine effect modification. Overall, online social support was associated with past-month SI: a 10-point increase in social support score (range 0-100) was associated with a 10% decrease in prevalence of past-month SI (PR=0.90; 95%CI=0.86-0.94) after adjustment. Similar findings were observed for all support subtypes and across most platforms examined, except LinkedIn and TikTok. No effect modification was observed by gender, age, or rurality; online social support remained protective for most subgroups examined. Findings indicate that online social support across many different platforms can potentially protect against SI within the heterogenous veteran population, regardless of type of support. Efforts to develop primary suicide prevention strategies focused on social support delivered virtually are warranted.

LATEBREAKER

Aging

Can Social Network Characteristics Predict Cognitive Resilience among Older Adults: Insights from the Framingham Heart Study Tianyu Liu* Tianyu Liu Huitong Ding Phillip H. Hwang

Background

Social engagement has been linked with preserved cognition in older adults, but it remains unclear whether social network measures can predict late-life cognitively resilience.

Methods

We included 148 dementia-free participants from the Framingham Heart Study Offspring cohort aged over 80 years at baseline (2005-2008). Social network was assessed with the Berkman-Syme Social Network Index questionnaire, including 11 indices. Individuals were cognitively resilient if they did not develop dementia by December 2024. Minimum Redundancy Maximum Relevance with five-fold cross-validation (CV), repeated 100 times, was used to rank feature relevance based on their selection frequencies. Eleven sequential classification and regression trees with CV were applied based on the base model, with each adding one social network feature in descending order of relevance. The base model included only sex, age, marital status, education, and APOE genotype. Model performance was evaluated by average Area Under the Curve (AUC), sensitivity, specificity, Positive Predictive Value (PPV), and Negative Predictive Value (NPV).

Results

The sample consisted of 83 females (57%) with a mean age of 82.6 years (SD=2.3). 115 participants were classified as cognitively resilient. The most frequently selected feature was “Feeling love and affection”, while the least selected feature was “Someone listens to you when you need to talk”. The AUC and sensitivity of the base CART model were 0.576 and 0.583, respectively (Figure 1). Adding social network features increased the sensitivity, peaking at 0.63 when the top 10 features were included. Other model performance measures showed minimal improvement.

Conclusion

Feeling loved emerged as the most important social factor associated with cognitive resilience in adults over 80. However, social network features did not substantially improve the predictive performance, underscoring the need for future studies using more refined measures and larger cohorts.

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LATEBREAKER

Aging

Trends and Associations between Food Insecurity, Metabolic Syndrome and Depression Among Older Adults RoiSan Nhpang* RoiSan Nhpang Shilpa Patil Suruthi Sundaramurugan Malinee Neelamegam

Background: Food insecurity is a critical public health issue and an important social determinant of health among older adults in the US. Food insecurity has increased in recent years, and similarly, the prevalence of related health conditions, including metabolic syndrome (MetS) and depression remains high. This study aimed to 1) examine trends in food insecurity, MetS, and depression from 2007-2018 and 2) determine the association between food insecurity and MetS, including whether this association differs by depression status among adults aged 60 years and older.

Method: Secondary data analysis of 2007 to 2018 waves of National Health and Nutrition Examination Survey was conducted. Food security was assessed using the USDA Food Security Survey Module, MetS based on ATP III criteria, and depression using PHQ-9. Chi-square tests and multivariable regression models were used to assess associations between food security, MetS, and depression. Interaction terms were included to evaluate whether depression modified the association between food insecurity and MetS.

Result: The prevalence of food insecurity exceeded 10% overall and increased to over 20% in the most recent cycle. More than half of older adults had MetS across all cycles, while depression prevalence ranged from 5% to 10%. In adjusted models, low food security was associated with higher odds of MetS compared to full food security (OR: 1.46, 95% CI: 1.06, 2.01). Food insecurity was also strongly associated with depression; individuals in the low food security had twice the odds of depression (OR: 2.03, 95% CI: 1.23, 3.35), and those with very low food security had over three times the odds of depression (OR: 3.1, 95% CI: 1.84, 5.24), compared to those with full food security. The interaction between food security status and depression was not statistically significant.

Discussion: Food insecurity remains highly prevalent among older U.S. adults and is associated with increased odds of both MetS and depression. Addressing food insecurity may be an important strategy for improving cardiometabolic and mental health outcomes in aging populations.

Aging

Sodium-Glucose Cotransporter-2 Inhibitor Use for Heart Failure Across Transitions between Community, Hospital, and Skilled Nursing Facility Settings Kelsey L Corcoran, DC* Kelsey Corcoran Parag Goyal, MD, MSc Derrick Lo, ScM Linda Resnik, PT, PhD Stefan Gravenstein, MD Ashkan Hashemi, MD Kira L Ryskina, MD, MSHP Andrew R Zullo, PharmD, PhD

Background

Sodium-Glucose Cotransporter-2 Inhibitors (SGLT2is) improve outcomes in heart failure (HF). The use of SGLT2d in skilled nursing facilities (SNFs), where nearly 25% of older adults are discharged following a HF hospitalization, is not well described.

Methods

This retrospective cohort study assessed SGLT2i exposure from June 28, 2017 to October 14, 2024 among older adults hospitalized for HF and discharged to SNFs contributing data to the Long-Term Care Data Cooperative. We examined SGLT2i exposure during the year prior to HF hospitalization and through 100 days after SNF admission. Medications were unobservable during hospitalizations. SGLT2is included were empagliflozin, dapagliflozin, and sotagliflozin, which are all FDA-approved for the management of HF. We defined inter-facility discontinuation as an SGLT2i dispensing in the pre-hospitalization setting that was not followed by an administration in the SNF. Intra-SNF discontinuation was defined as no SGLT2i administrations during the last 25% of SNF days for individuals with any administrations in the SNF.

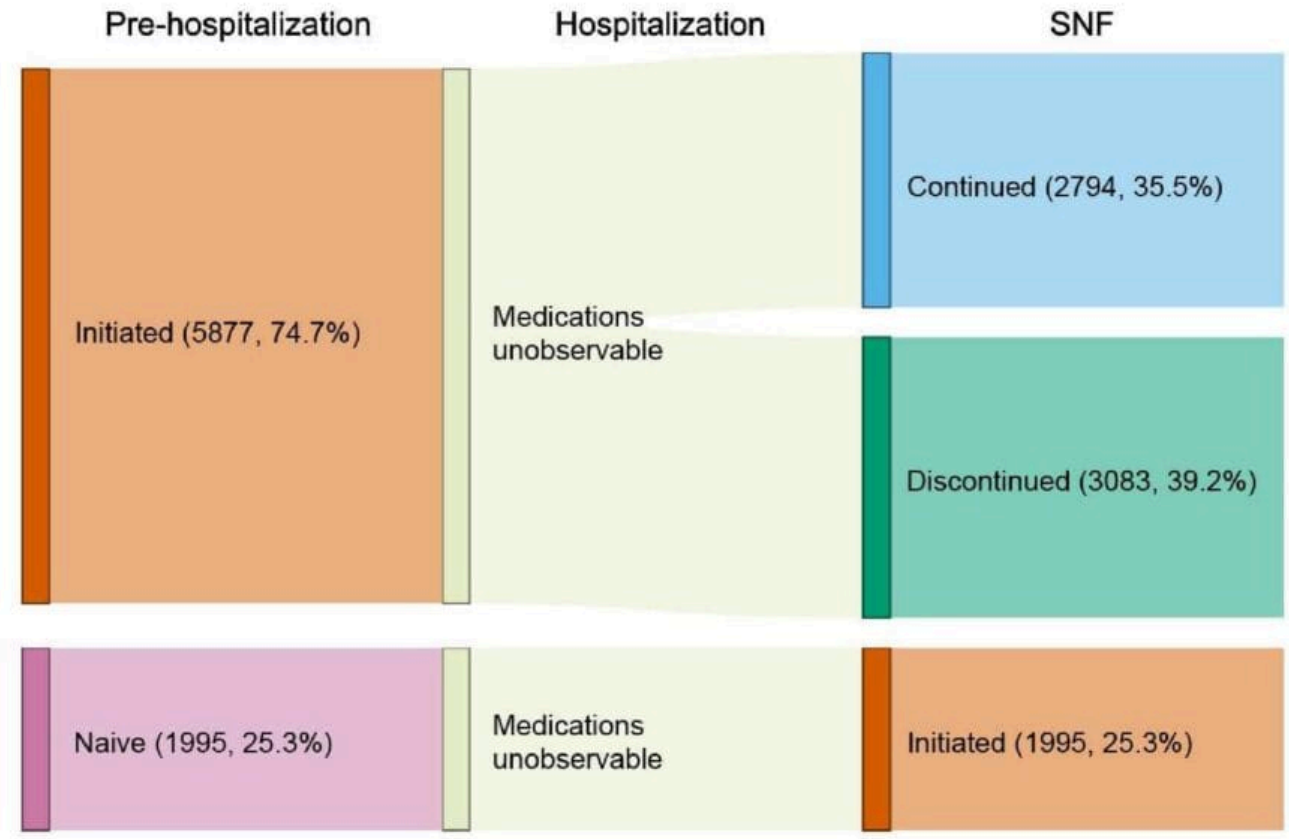
Results

There were 187,878 individuals hospitalized for HF and discharged to SNFs. The mean (SD) SNF length of stay was 27.7 (26.5) days. Only 7,872 (4.2%) of individuals received an SGLT2i at any point, with 4,789 (2.5%) administered the drug during SNF stay. Approximately 75% of SGLT2i initiations occurred in the pre-hospitalization setting and 25% occurred during SNF stays. Among those taking an SGLT2i in the pre-hospitalization period, 39.2% (3,083/5,877) had an inter-facility discontinuation (**Figure 1**). Intra-SNF discontinuations occurred among 4.8% (231/4,789) of individuals who had an SGLT2i administration in the SNF.

Conclusion

SGLT2i use is low among individuals discharged to SNF after a HF hospitalization. Inter-facility SGLT2i discontinuation occurs commonly. These patterns may reflect individualized prescribing in a high-risk population, missed opportunities to improve therapy, or both.

Figure 1. Sodium-glucose cotransporter 2 inhibitor (SGLT2i) exposure during transitions of care for older adults with a heart failure hospitalization who were discharged to a skilled nursing facility.



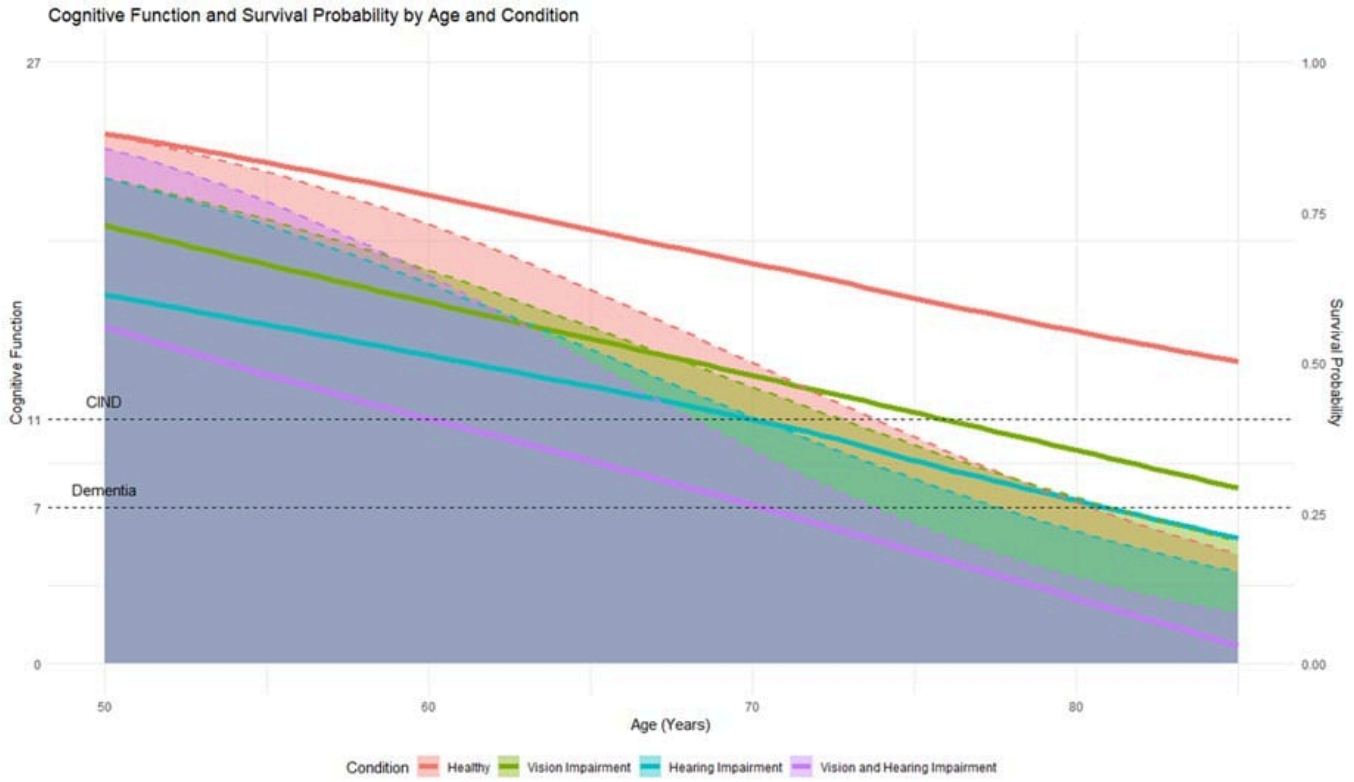
This Sankey graph depicts the flow of 7,872 participants on versus off SGLT2i across care settings. Naïve (pink) indicates no observed use in the current setting or any preceding period. Initiated (orange) indicates that the first observed use of SGLT2i began in the current setting. Continued (blue) indicates that the patient used the drug in a prior observable setting and current setting. Discontinued (green) indicates that the patient used the drug in the prior observable setting with no use in the current setting. Nodes represent the medication use state in each setting and flows represent patient counts (%) transitioning between states. Individuals who were SGLT2i naive in all observable settings are excluded.

Abbreviations: SGLT2i = Sodium-glucose cotransporter 2 inhibitor; SNF = skilled nursing facility.

Aging

Joint Associations Between Sensory Impairment, Cognition, and Mortality: A Population-Based Study Jordan Weiss* Jordan Weiss

Vision and hearing impairment are common in later life and have each been linked to adverse cognitive and survival outcomes. However, the joint associations of dual sensory impairment with cognitive decline and mortality, accounting for their interdependence, are not well characterized. We used 12 waves (2000–2022) of the Health and Retirement Study, a nationally representative longitudinal cohort of United States adults aged 50 years or older. The analytic sample included 16 234 adults aged 51 years or older who were dementia-free at baseline and followed biennially. Vision and hearing impairment were self-reported and classified as none, vision only, hearing only, or dual impairment. Cognitive function was assessed using a 27-point global cognitive score administered repeatedly over follow-up. Mortality was ascertained using national death records and exit interviews. Linear mixed-effects models estimated cognitive trajectories, Cox proportional hazards models estimated mortality risk, and joint longitudinal-survival models accounted for informative censoring due to death. Compared with participants without sensory impairment, those with dual sensory impairment had lower baseline cognitive scores and significantly faster cognitive decline over follow-up. Dual sensory impairment was also associated with substantially higher mortality risk than either vision or hearing impairment alone, independent of age, sex, race and ethnicity, and educational attainment. Joint models indicated that accelerated cognitive decline partially explained the excess mortality associated with dual sensory impairment. In this nationally representative cohort, dual sensory impairment was associated with both accelerated cognitive decline and increased mortality risk beyond single sensory impairments. These findings suggest that co-occurring vision and hearing loss may represent an important, potentially modifiable target for promoting cognitive health and longevity in aging populations.


Cognitive Function and Survival Probability by Age and Condition
27
11
7
0
CIND
Dementia
Cognitive Function
1.00
0.75
0.50
0.25
0.00
Survival Probability
50
60
70
80
Age (Years)
Condition
Healthy
Vision Impairment
Hearing Impairment
Vision and Hearing Impairment

Aging

Health-Related Quality of Life Association with Chronic Disease Burden in Missouri Sueny Paloma Lima dos Santos* Sueny Paloma Lima dos Santos Eduardo J. Simões, MD, MSc, MPH

Background:
Multimorbidity is increasingly common in primary care, yet population-based evidence on how chronic disease burden translates into health-related quality of life (HRQoL) remains limited at the state level. Identifying which HRQoL domains are most affected—and by which conditions—can inform prevention and care strategies, particularly in states with large rural populations such as Missouri.

Methods:
We analyzed cross-sectional data from the 2024 Center for Medical Epidemiology and Population Health Adult Health Survey (N = 547). HRQoL was measured using the SF-36 (eight domains) and Physical and Mental Component Summary scores (PCS, MCS). Chronic disease burden was defined by comorbidity count (0, 1, ≥2 conditions) and by specific conditions (CVD, arthritis, COPD/asthma, diabetes, depressive disorder, cancer, kidney disease). Multivariable linear regression estimated adjusted mean differences in HRQoL scores, controlling for age, sex, race/ethnicity, education, income, and rurality. False discovery rate (FDR) correction was applied across HRQoL outcomes for Aim 1.

Results:
Fifty-four percent of participants reported ≥2 chronic conditions. Compared with adults with no chronic conditions, those with ≥2 conditions had substantially lower physical HRQoL: Physical Functioning ($\beta = -21.6$, $p<0.001$), Role-Physical ($\beta = -30.7$, $p<0.001$), and General Health ($\beta = -10.6$, $p<0.001$), and worse Bodily Pain ($\beta = +23.0$, $p<0.001$). The PCS was lower among adults with ≥2 conditions ($\beta = -4.3$, $p < 0.001$), whereas differences in the mental and social domains were small and not statistically significant, including Mental Health ($\beta = -0.2$, $p = 0.846$) and MCS ($\beta = -0.1$, $p = 0.85$). Adults with one condition showed modest differences, including Bodily Pain ($\beta = 8.3$, $p = 0.007$). In condition-specific models, arthritis, CVD, and COPD/asthma were the largest drivers of physical HRQoL deficits, while depressive disorder showed the strongest associations with mental health and role-emotional functioning.

Conclusions:
Among Missouri adults, multimorbidity is associated primarily with declines in physical functioning, role performance, and pain, with comparatively limited differences in mental health by comorbidity count. Primary care approaches should prioritize functional status and pain management alongside chronic disease control, particularly in working-age and rural populations. Building on these results, future work will inform the development of a longitudinal, population-based cohort of Missouri adults to examine multimorbidity trajectories and their impact on functional and quality-of-life outcomes across the life course.

Aging

A Positive Outlook and the Aging Mind: Optimism and Cognitive Function in Older Women
Hayami Koga* Hayami Koga

Objectives: Optimism is associated with healthy aging, and cognitive health is a key component of healthy aging. Pathway studies of optimism and health suggest possible links between optimism and cognitive health, but few studies have examined this association. Here, we prospectively examine the association between optimism and global and domain-specific cognitive functioning.

Methods: Participants were 7,194 postmenopausal women from the Women's Health Initiative Memory Study (WHIMS) including 2,195 participants also enrolled in the Women's Health Initiative Study of Cognitive Aging (WHISCA). Baseline optimism was measured using the Life Orientation Test-Revised. Cognitive function was assessed using the Modified Mini-Mental (3MS) in WHIMS and 8 additional cognitive tests in WHISCA. We examined associations between optimism and cognition over up to 10 years of follow-up, using linear mixed-effects models.

Results: Adjusting for demographics and probable depression, each increment in optimism was associated with better baseline cognitive function using 3MS in WHIMS (mean difference=0.093; 95% CI, 0.076, 0.111) and a global composite combining all tests in WHISCA (mean difference=0.063; 95% CI, 0.041, 0.084). Each increment in optimism was not significantly associated with cognitive decline in either cohort; however, when considering the highest quartile of optimism, a significant association with a slower annual rate of decline in global cognitive function was observed in WHIMS, compared to the lowest optimism quartile (mean difference=0.014, 95% CI 0.000, 0.027). Stratified analyses showed similar patterns in strata of non-Hispanic White and Black women.

Discussion: Optimism was significantly associated with higher baseline cognitive function and with cognitive decline. Overall, our results may indicate that optimism could provide a novel target to test for possible interventions to promote healthy cognitive aging.

Aging

Differences in Global Cognition by Marijuana Use in Older Adults Participating in the Health and Retirement Study Nikhil Mullapudi* Nikhil Mullapudi

Background: With the growing rates of recreational marijuana use among older adults in the US, a deeper understanding of the impacts of marijuana use on the aging brain grows as well. Amid conflicting evidence regarding the cognitive effects of marijuana use, this study examines differences in later-life cognition by marijuana use in a nationally representative sample of older adults.

Methods: 1,309 respondents from the 2018 wave of the Health and Retirement Study (HRS) were included in this retrospective cross-sectional study. Respondent's marijuana use was categorized as never (65.9%), former (no use in past 5 years; 21%), or recent (use within 5 years; 13.1%). Global cognition was assessed using the HRS version of the Telephone Interview for Cognitive Status (TICS), which provides a score from 0 to 27, where higher scores indicate better cognitive function. A linear regression model was employed to investigate differences in total cognition by marijuana use category. Demographics, other comorbidities, and alcohol/tobacco use were included as covariates in the model.

Results: Study participants had a mean age of 67.1 (10.6) years, 58.7% were female, and 67% identified as white. Mean TICS scores were 1.21 points higher in former users (mean = 16.4), and 0.84 points higher in recent users (mean = 16.0), compared to never users (mean = 15.2). In fully adjusted models, former users had significantly higher TICS scores than never users (B = 1.67, p = 0.01, 95% CI [0.39, 2.96]), but did not differ for recent users (B = 0.05, p = 0.95, 95%CI [-1.60, 1.70]), compared to never users.

Conclusions: Among older adults in the 2018 HRS, former marijuana users had slightly better global cognitive function than never users, while recent and never users did not differ significantly. Although additional studies are needed to determine whether this association is causal, these findings suggest that past marijuana use may be associated with preserved later-life cognition.

Aging

Lifetime Earnings and Dual Functionality: Findings from Social Security Administration Earnings linked to the Health and Retirement Study Calvin Colvin* Calvin Colvin Katrina L. Kezios Xuexin Yu Allison E. Aiello Adina Zeki Al Hazzouri

Financial resources in older age are linked to better physical and cognitive health. Yet, financial resources accrue over the life course; assessments limited to older age, which are often self-reported, may obscure the contribution of earlier-life finances to healthy aging. We use US Social Security Administration (SSA) records linked to the Health and Retirement Study to examine how lifetime earnings influence healthy aging, measured by Dual Functionality (DF)—defined as the absence of physical or cognitive limitations.

Lifetime earnings were defined as participants' cumulative, inflation-adjusted earnings from all available SSA records through age 60 and categorized into gender and 5-year birth cohort-specific quintiles. DF, defined as having no limitations with activities of daily living and being dementia free, was assessed from 2000-2020, and participant's follow up for loss of DF began at the first interview they were ≥60 years of age within that period. We included participants born 1931-1956, with ≥2 measures of DF, and no history of DF loss at their first DF assessment. We analyzed men and women separately using generalized gamma accelerated failure time models with age as the time scale. Larger time ratios (TRs) indicate longer times to DF loss (i.e. prolonged physical and cognitive functioning).

Our sample included 4,914 men (mean age: 62.5) and 6,048 women (mean age: 62.3). In total, 32.3% of men and 34.7% of women lost DF over medians of 9 and 10 years of follow up. Compared to men in the bottom (1st) quintile, TRs (95% confidence intervals [CI]) were 1.05 (1.02-1.07), 1.09 (1.06-1.11), 1.09 (1.06-1.11), and 1.12 (1.09-1.15) for the 2nd, 3rd, 4th, and 5th quintiles, respectively. Compared to women in the 1st quintile, TRs (95% CIs) were 1.01 (0.99-1.03), 1.02 (1.00-1.14), 1.04 (1.02-1.07), and 1.05 (1.02-1.07) for the 2nd, 3rd, 4th, and 5th quintiles, respectively.

Higher lifetime earnings were associated with prolonged physical and cognitive functioning.

Aging

Systemic Inflammation and Its Interaction with Alzheimer's Disease Biomarkers in Cognitive Decline Diefei Chen* Diefei Chen Keenan A. Walker Marilyn S. Albert Jeremy D. Walston Jackie Langdon Alden L. Gross

Systemic inflammation may accelerate Alzheimer's disease (AD)–related cognitive decline, yet underlying mechanisms remain unclear. We examined whether markers of systemic inflammation are associated with cognitive change and whether they interact with AD biomarkers to accelerate decline. We analyzed 133 participants from the BIOCARD Study who were cognitively unimpaired at baseline and had their first biofluid collection at a mean age of 59.2 years (range: 50-75 years). Participants contributed 2-5 blood samples (median 3) over an average of 21.7 years of follow-up. Blood-based systemic inflammatory markers included IL-1β, IL-6, IL-8, TNFα, TNFR1, and CRP. Baseline biomarkers (Aβ42/40, p-Tau181, GFAP) were measured in both blood and cerebrospinal fluid (CSF). Linear mixed-effects models related (1) baseline systemic inflammation, (2) within-person change in systemic inflammation, and (3) interactions between baseline or change in systemic inflammation and AD biomarkers with longitudinal change in a general cognitive composite, adjusting for age, sex, education, and vascular risk. Higher baseline IL-8 (β=-0.014; 95% CI: -0.027, -0.001) and faster within-person increases in IL-8 (β=-0.006; 95% CI: -0.012, -0.0002) were associated with faster cognitive decline. Higher IL-1β and CRP were more strongly associated with cognitive decline among individuals with high Aβ42/40 (less cortical amyloid), whereas higher IL-1β was more strongly associated with cognitive decline among participants with higher p-tau181, and TNFα was more strongly associated with cognitive decline among participants with higher GFAP. Lower Aβ42/40 interacted with faster increases in CRP to accelerate cognitive decline. Results using CSF-based AD biomarkers were largely consistent with those from blood-based biomarkers. These findings support a conceptual model in which the relationship between systemic inflammation and cognition is disease-stage- and pathology-dependent.

Aging

Mediating Effects of DNA Methylation on the Association Between Health-Related Behaviors and Cognition Using Data From the Health and Retirement Study Junyub Lim* Junyub Lim Ross Andel Judith Rijnhart

[SER 2026 Poster Presentation Abstract]

Title: Mediating Effects of DNA Methylation on the Association Between Health-Related Behaviors and Cognition Using Data From the Health and Retirement Study

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Objectives: Biological mechanisms linking health-related behaviors to cognitive aging remain unclear. We examined whether DNA methylation–derived pace of biological aging, measured by the DunedinPoAm38, mediates associations between smoking, alcohol consumption, physical activity, sleep disturbance, and cognitive function in a nationally representative U.S. sample. **Methods:** Using Health and Retirement Study data (2014–2020), we analyzed data from 3,761 participants from the 2016 Venous Blood Study who were dementia-free at baseline (2014) and had complete data. Causal mediation analyses assessed whether the pace of biological aging mediated associations between health-related behaviors and cognition score, adjusting for sociodemographic factors. **Results:** Participants had a mean age of 67.2 years (SD = 9.6), and 58.5% were women. Current smoking and sleep disturbance were significantly associated with poorer cognition score (total effects = -0.148, 95% CI [-0.246, -0.055] and -0.073 [-0.099, -0.047], respectively), whereas vigorous physical activity and heavy alcohol consumption were significantly associated with better cognition score (total effects = 0.145 [0.086, 0.211] and 0.139 [0.030, 0.254], respectively). The pace of biological aging significantly mediated associations between four health-related behaviors and cognition score. Among current smokers, the pace of biological aging accounted for 45.2% of the association (indirect effect = -0.067 [-0.123, -0.012]); for vigorous physical activity, 11.4% (indirect effect = 0.016 [0.006, 0.028]); and for sleep disturbance, 2.8% (indirect effect = -0.002 [-0.004, 0.000]). Heavy alcohol consumption showed a significant negative indirect effect through the pace of biological aging (-0.014 [-0.028, -0.003]), indicating inconsistent mediation. **Discussion:** Findings suggest that the pace of biological aging mediated the associations between smoking, alcohol consumption, physical activity, sleep disturbance, and cognition.

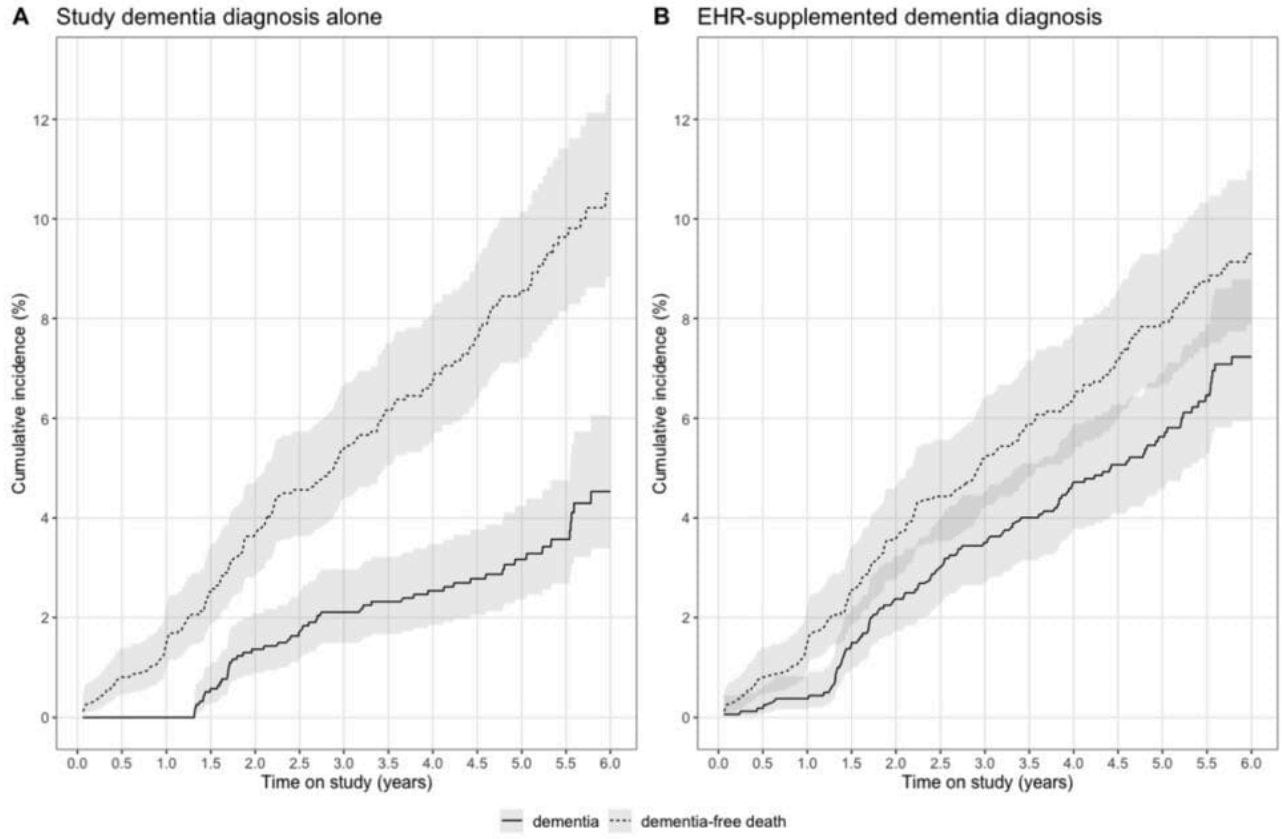
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Aging

Estimating dementia risk: leveraging electronic health records among study participants lost to follow-up Joseph Oliver Fong* Joseph Oliver Fong Yixuan Zhou L. Paloma Rojas-Saunero Ryo Ikesu Rachel A. Whitmer M. Maria Glymour Paola Gilsanz Dan Mungas Elizabeth Rose Mayeda

In cohort studies of aging, poor health, including incipient dementia, may influence continued study participation. The Kaiser Healthy Aging and Different Life Experiences (KHANDLE) study is a multi-ethnic cohort study of long-term Kaiser Permanente Northern California members that aims to examine lifecourse determinants of late-life brain health and cognitive decline. Participants were members of Kaiser at enrollment and completed 4 cognitive assessments (~18 months between each assessment) over 6 years of follow-up as part of the study. We evaluated dementia risk (i.e. cumulative incidence) using diagnosis information from study assessments alone ("study diagnosis alone") versus diagnosis information supplemented with diagnoses from electronic health records ("EHR-supplemented diagnosis") among those who dropped out. Dropout was defined as active/passive withdrawal from the study or missing >=2 visits. For "study diagnosis alone" analyses, participants were followed until study dementia diagnosis, death, dropout, or end of follow-up (4th assessment). Case ascertainment and censoring were similar in "EHR-supplemented" analyses; however, in these analyses those who dropped out were followed for incident EHR-supplemented dementia diagnosis from time to study dropout to time to last EHR contact time or 6 years, whichever came first. We used the Aalen-Johansen estimator to calculate dementia risk, with dementia-free death as a competing event (study time as timescale). In our analytic sample of 1609 participants, n=329 (20%) were lost to follow-up over 6 years. Dementia risk over 6 years was lower in study diagnosis alone analyses (n=53, 3%) versus EHR-supplemented analyses (n=101, 6%) (Figure). We captured additional incident dementia cases by supplementing with EHR data among participants who dropped out of the study; in future work, we will evaluate concordance of study-based and EHR-based diagnoses during follow-up.

Figure: Dementia risk and dementia free-mortality over 6 years of follow up comparing study dementia diagnosis alone and EHR-supplemented dementia diagnosis



Aging

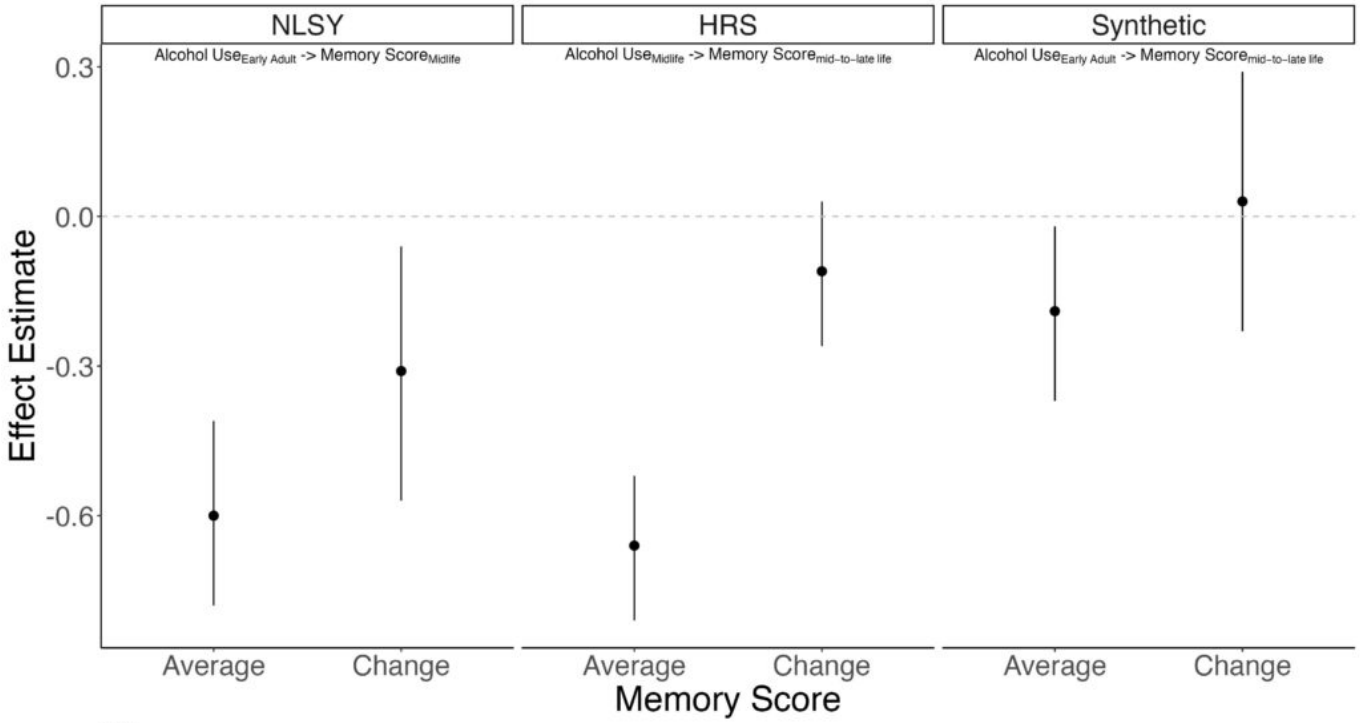
Association of heavy vs moderate alcohol use in early or middle adulthood with mid- and late-life memory: a pooled-cohort analysis Peter T. Buto* Peter Buto Scott C. Zimmerman Katrina Kezios Jillian Hebert Anusha M. Vable Laura Schmidt Kara Rudolph Adina Zeki Al Hazzouri M. Maria Glymour

Few cohorts have the follow-up time to estimate the association of early-adult heavy alcohol use with later life cognitive decline.

We pooled data from National Longitudinal Study of Youth 1979 study (NLSY, n=7540, ages 14-22 at enrollment) and Health and Retirement Study (HRS age 50-56 at enrollment 1998 on, n=13,090). Alcohol use was self-reported in early adulthood (ages 23-31 in NLSY) and at HRS enrollment (non-drinking, some drinking [≤7 drinks/week for women; ≤14 for men; no heavy episodic drinking], or heavy drinking). Memory was assessed up to twice in NLSY at age 48+ and up to 10 times in HRS at age 50+ as the sum of immediate and delayed word recall scores. We estimated associations between heavy drinking with average memory level and change within each cohort using covariate-adjusted linear mixed models. To leverage the advantages of both datasets, we then generated a synthetic life course cohort, matching 7,054 HRS participants to 4,908 NLSY participants based on 10 variables posited to confound/mediate the association between early adult alcohol use and late-life memory. We then estimated the association between early adult alcohol measures from NLSY with the repeated late life memory measures in the synthetic cohort.

In NLSY, heavy drinking at age 23-31 was associated with lower average memory scores (β=-0.60 [95% CI: -0.78,-0.41]) and faster declines in memory scores (-0.31 per decade [-0.57,-0.06]). In HRS, middle age heavy alcohol use (average age 53.1) was associated with lower average memory (-0.66 [-0.81,-0.52]) and slightly faster decline (-0.11 per decade [-0.26,0.03]). In the synthetic cohort, heavy alcohol use at age 23-27 was associated with lower memory score at age 50+ (-0.19 [-0.37,-0.02]) and with faster decline (0.03 per decade [-0.23,0.29]).

In the synthetic cohort, heavy alcohol consumption in early adulthood was associated with worse memory in later life while estimates for memory change were null.



Note:
NLSY alcohol measures were self-reported in 1988 (ages 23-31). Memory scores were obtained when participateds turned 48 and once again in 2020 (ages 55-63).
HRS alcohol measures were self-reported at enrollment (ages 50-56). Memory scores were obtained biennially thereafter.
Self reported alcohol use in the synthetic cohort was derived from NLSY participants. Similarly, longitudinal memory score trajectories in the synhtetic cohort were obtained from HRS participants. Matches shared at least 10* covariates suspected to mediate or confound the association between early adult alcohol use and late-life memory.
*Birth year, Sex, Race/ethnicity, US Nativity, Father's Education, Mother's Education, and Mid-Life: Age, Alcohol Use, Immediate Word Recall, Delayed Word Recall

Aging

Determinants of homecare use in old age: A meta-analysis of quantitative studies Afshin Vafaei* Afshin Vafaei Om Bhuva Maria Tavares Lauren Bal Marie Savundranayagam Susan Phillips

Background: Homecare services are essential for supporting older adults to age in place. A preceding systematic review revealed physical and social determinants influencing homecare utilization. This meta-analysis aimed to quantify the effect of those determinants, providing quantitative insight into barriers and safeguards pertaining to health service use in later life.

Methods: International data regarding homecare use and influencing determinants from 72 primary quantitative studies were imported onto review-managing software (RevMan). Pooled estimates of each factor and forest plots were generated for formal and informal homecare using DerSimonian-Laird random effect models and inverse-variance weighting in form or relative risks (RR) and corresponding 95% confidence interval (CI). I2 statistics were used to denote heterogeneity between studies.

Results: Effects of 17 identified homecare determinants in the systematic review evaluated in pooled meta-analyses. Overall, physical and social factors both significantly influenced formal homecare use, with physical factors exerting relatively stronger effects. Dementia was the strongest predictor (RR=2.77; 95% CI: 2.18-3.53), followed by older age (RR=1.78; 95% CI: 1.38-2.29), being unmarried (RR=1.78; 95% CI:1.42-2.22), and physical frailty (RR=1.74; 95% CI: 1.02-2.98). Social factors such as female sex and living alone were the only significant predictors of informal homecare.

Discussion: A complex interplay of physical conditions and social determinants of health influences homecare use patterns among older adults. Appreciating the protective or detrimental nature of these determinants is crucial for promoting healthier aging trajectories.

Aging

Subjective visuospatial cognition and dementia risk in adults over age 90: a comparison of time-to-event methods Alexander Ivan B. Posis* Alexander Ivan Posis Hilary L. Colbeth Aladdin H. Shadyab M. Maria Glymour Paola Gilsanz María M. Corrada Elizabeth Rose Mayeda Rachel A. Whitmer

Background: Visuospatial deficits are common in dementia. Yet, associations of visuospatial cognition and incident dementia are unknown in adults 90+. In this population with high mortality rates, it's unclear if dementia risk estimates are sensitive to underlying time-to-event model assumptions. We estimated associations of subjective visuospatial cognition and dementia risk in adults 90+ with 4 different time-to-event methods.

Methods: We included 778 LifeAfter90 participants (mean±SD age=92±2; 63% women; 36% ≥college education). Baseline subjective visuospatial cognition was assessed using a 7-item visuospatial Everyday Cognition scale (ECogVis) subscale. Scores were summed and averaged where greater scores suggest greater visuospatial impairment (range=1-4). Time-to-dementia was assessed every 6 months from baseline. Associations of ECogVis and dementia risk were estimated with 4 multivariable models: Cox proportional hazards (PH), Fine-Gray (FG), Aalen additive (AA), and Weibull accelerated failure time (AFT).

Results: Over 1983 person-years of follow-up, there were 101 dementia diagnoses (60/1000 person-years) and 272 deaths (137/1000 person-years). Worse baseline ECogVis scores yielded higher hazard of dementia in PH models, with similar estimates whether mortality was treated as a censoring event (HRCox PH=1.40, 95%CI 0.95,2.05) or competing risk (HRFG=1.37, 95%CI 0.96,1.96; Table 1). The AA model showed an absolute increase of 60 more dementia cases per 1000 person-years (AA SErobust=0.70 per 1000 person-years) for every 1 unit increase in the ECogVis score and the AFT model showed faster time-to-dementia (time ratio=-0.16; 95%CI -0.35,0.03).

Conclusions: While estimates were in the expected direction, low subjective visuospatial cognition was not associated with greater dementia risk in those with exceptional longevity. In this very high mortality population, findings from four time-to-event models were qualitatively similar in direction of estimates.

Table 1: Association of visuospatial Everyday Cognition scale (ECogVis) subscale with dementia by select time-to-event models in LifeAfter90

Model	Assumptions	Estimate for 1 unit increase in ECogVis score
Cox proportional hazards	- Proportional hazards - Non-informative censoring - Independence of observations - Correct model specification	$HR_{Cox\ PH}$ = 1.40 (95% CI 0.95, 2.05)
Fine-Gray	- Proportional subdistribution hazards - Non-informative censoring, with respect to censoring mechanisms other than competing events - Independence of observations - Correct model specification	$HR_{Fine\text{-}Gray}$ = 1.37 (95% CI 0.96, 1.96)
Aalen additive	- Linearity of relationship between covariates and hazard function - Allows for time-varying covariates - Non-informative censoring - Independence of observations - Correct model specification (including time-varying coefficients, if used)	Cumulative hazard difference = 0.06 (SE_{robust} = 0.0007)
Accelerated failure time, with Weibull distribution	- Acceleration factor on survival time - Specification of error distribution - Non-informative censoring - Independence of observations - Correct model specification	Time ratio = -0.16 (95% CI -0.35, 0.03)

Models adjust for baseline age, race/ethnicity, education, and gender.

Aging

Recent, cumulative depressive symptoms and memory in the Health and Retirement Study

Anna M. Pederson* Anna Pederson Scott C Zimmerman Peter Buto Catherine A Schaefer Ulrike Muench Yulin Yang M. Maria Glymour Cynthia I. Campbell Paola Gilsanz

Depressive symptoms are strongly associated with cognitive aging, yet the bidirectionality and time-varying nature complicate estimation of causal effects, especially when separating recent from cumulative exposure. These analyses follow 14,214 Health and Retirement Study participants enrolled 1996-2018 and born <1959. Elevated depressive symptoms were measured using 8 binary items from the Center for Epidemiologic Studies Depression scale (binary indicator, ≥ 3 items endorsed) for up to 12 biennial visits. Cumulative depressive burden was calculated as the proportion of prior waves with elevated symptoms. Cognition was assessed using the sum of immediate and delayed 10-word recall (range: 0-20). Stabilized inverse probability (IP) weights were estimated to account for baseline and time-varying confounding. Weighted and unweighted linear mixed effects models estimated associations of recent and cumulative depressive symptoms with memory, with adjustment for sociodemographics. At baseline, participants were mean [SD] age 57.9 [7.9] years. In unweighted models, prior wave depressive symptoms and cumulative exposure were both associated with worse memory (βprevious= -0.29; 95% CI: -0.35,-0.23 ; βcumulative= -0.67; 95% CI: -0.77, -0.57). In weighted models, estimates for both recent and cumulative symptoms were attenuated, but remained significant (βprevious= -0.13; 95% CI: -0.18, -0.08; βcumulative= -0.38; 95% CI: -0.48, -0.29). Our results suggest that both recent and cumulative exposure to depressive symptoms contribute to lower cognitive function. These results highlight the importance of early depression intervention to reduce adverse cognitive outcomes and suggests reverse causation from incipient dementia to depression is unlikely to account for the association.

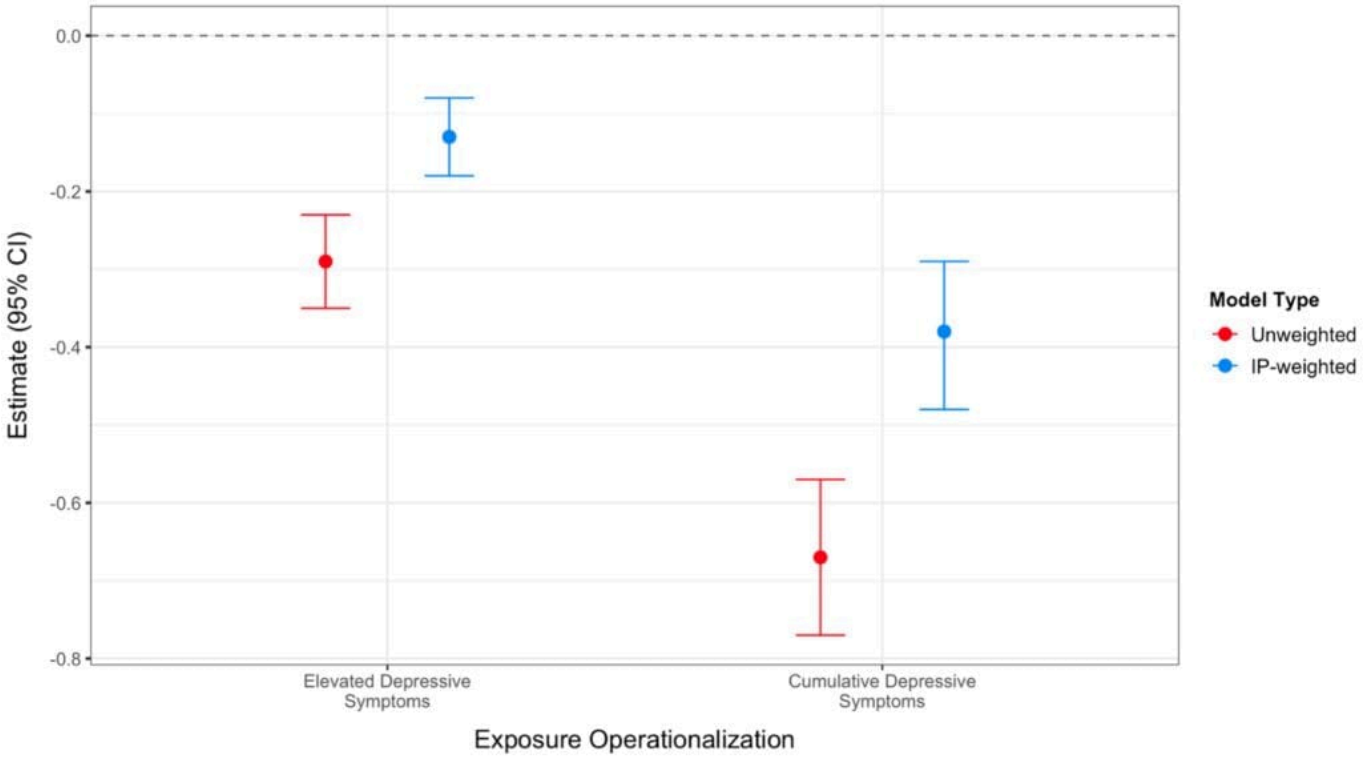


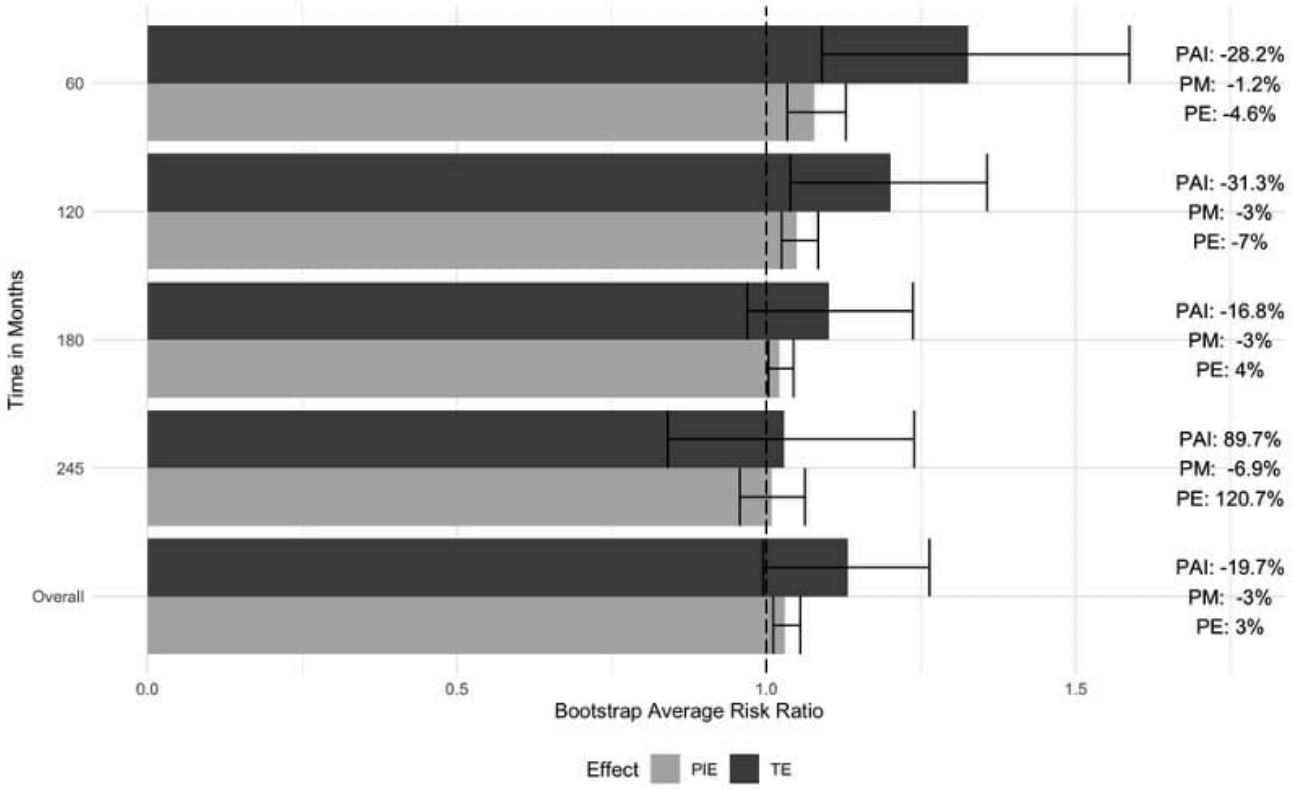
Figure. Estimates and 95% confidence intervals for linear mixed effects models of recent and cumulative depressive symptoms with memory. Red points show estimates from unweighted linear mixed effects models, adjusted for prior depressive symptoms, baseline age (centered at 65 and scaled per 10 years), prior age (centered at 65 and scaled per 10 years), race and ethnicity, sex, education (years), and wave. Blue points show estimates from weighted linear mixed effects models that account for time-varying confounding using stabilized inverse probability (IP) weights (product of exposure and censoring weights), with additional adjustment in the outcome model for prior depressive symptoms, baseline age (centered at 65 and scaled per 10 years), prior age (centered at 65 and scaled per 10 years), race and ethnicity, sex, education (years), and wave.

Aging

The Potential Role of Visual Acuity in the Effect of Age-Related Macular Degeneration on Dementia: A Discrete-Time Causal Mediation and Survival Analysis Mina Habib* Mina Habib Rod Walker Chloe Krakauer Yu-Ru Su Elizabeth Rose Mayeda Cecilia Lee Roch Nianogo

Alzheimer’s disease and related dementias remain a major public health challenge, with limited effective treatments. Prevention strategies are critical to addressing their increasing prevalence. We examined whether the association of age-related macular degeneration (AMD), a leading cause of vision loss, with incident dementia is mediated by visual acuity. We analyzed longitudinal study visit and electronic health record data (2003–2024) from 3,321 participants in the Adult Changes in Thought prospective cohort study. Parametric g-computation-based discrete-time causal mediation and survival analysis using pooled logistic regression estimated adjusted average, discrete-time (e.g. 5 years), and end-of-follow-up risk ratios (RRs) and differences (RDs, per 1,000) for the effect of AMD diagnosis on incident dementia (per DSM-IV criteria). We also estimated the proportions that are mediated and eliminated to quantify the role of visual acuity. Models were adjusted for sociodemographic and time-varying health-related variables. Inverse probability weights accounted for time-varying exposure, mediator, and attrition. Bootstrapping with 1000 resamples was used to obtain 95% CI. With an average baseline age of 75.9 and 8.4 years of follow-up, 23% (N = 766) developed dementia. On average over follow-up, AMD diagnosis was associated with increased dementia risk (RR: 1.13; 95% CI: 1.00,1.26; RD: 31.84; 95% CI: -1.30, 60.94). Five years post baseline, dementia risk was 1.33 times (95% CI: 1.09,1.59; RD: 33.57; 95% CI: 9.99, 56.97) among individuals diagnosed with AMD versus without. While mediation varied over time, -3% (pure indirect effect RR: 1.03, 95% CI: 1.01, 1.06) of the AMD–dementia relationship was mediated by visual acuity. If visual acuity were preserved in all with AMD, 3% of the total effect would be eliminated. Interventions to preserve visual acuity could offer a novel strategy to reduce dementia risk in individuals with AMD.

Figure: Total Effects (TE) of Age-Related Macular Degeneration on Dementia Risk, Pure Indirect Effects (PIE) via Visual Acuity, and 95% Confidence Intervals, with Proportions Attributable to Interaction (PAI), Mediation (PM), and Elimination (PE), Controlling for Visual Acuity by Follow-up Time.



Aging

Physiologic Aging and Longevity: The Association of 6 Blood Biomarkers with Age at Death in the Cardiovascular Health Study Lauren Q. Vuong* Lauren Vuong Mary Lou Biggs Cellas Hayes Alexis Reeves Bruce M. Psaty Anne B. Newman Michelle C. Odden

Ageing is accompanied by dysfunction in inflammation, kidney and cardiovascular function, and metabolism, which can lead to earlier mortality. Prior studies have observed relationships between biomarkers reflecting these pathways and health outcomes, but few have evaluated longevity. Among participants of the Cardiovascular Health Study (CHS), who were followed from enrollment in 1989 through death, we examined the association between 6 blood biomarkers—high-sensitivity C-reactive protein (hs-CRP), interleukin-6 (IL-6), cystatin C, B-type natriuretic peptide (BNP), insulin-like growth factor 1 (IGF-1), dehydroepiandrosterone sulfate (DHEAS)—and age at death.

This study included 5,795 Black and White participants from 4 sites in the U.S.: Pittsburgh, PA, Sacramento County, CA, Washington County, MD, and Forsyth County, MD. We used linear regressions of log-base-2 biomarkers taken near age 70 on age at death and adjusted for race, education, smoking, physical activity, body mass index (BMI), blood pressure, and estimated glomerular filtration rate (eGFR). In hs-CRP models, we stratified by sex to account for significant interaction, and a quadratic term was included for DHEAS and IGF-1 models to account for U-shaped relationships.

The median (IQR) age at biomarker measurement was 72.9 (70.0 – 77.0) years, and the median (IQR) age at death was 88.5 (83.0 – 93.1) years in females and 86.2 (80.8 – 91.0) in males. Unadjusted associations are shown in Figure 1. After adjusting for covariates, a 2-fold higher level of IL-6, cystatin C, and BNP was associated with significant 1.01-, 3.99-, and 1.02-year reductions in longevity (95% CIs: 0.80–1.22; 3.47–4.50; 0.75–0.99). A 2-fold higher level of hs-CRP was associated with a significant 0.30-year reduction longevity (95% CI: 0.14-0.46) among females and a significant 0.46-year reduction (95% CI: 0.29-0.64) among males. For DHEAS and IGF-1, significant U-shaped relationships between these biomarkers and age at death were observed, as indicated by $p < 0.001$ for coefficients of the quadratic terms in these models.

Higher levels of cystatin C, a biomarker reflecting worse kidney function, were most strongly associated with earlier death. Our results are consistent with prior literature and illustrate how these biomarkers relate to longevity outcomes.

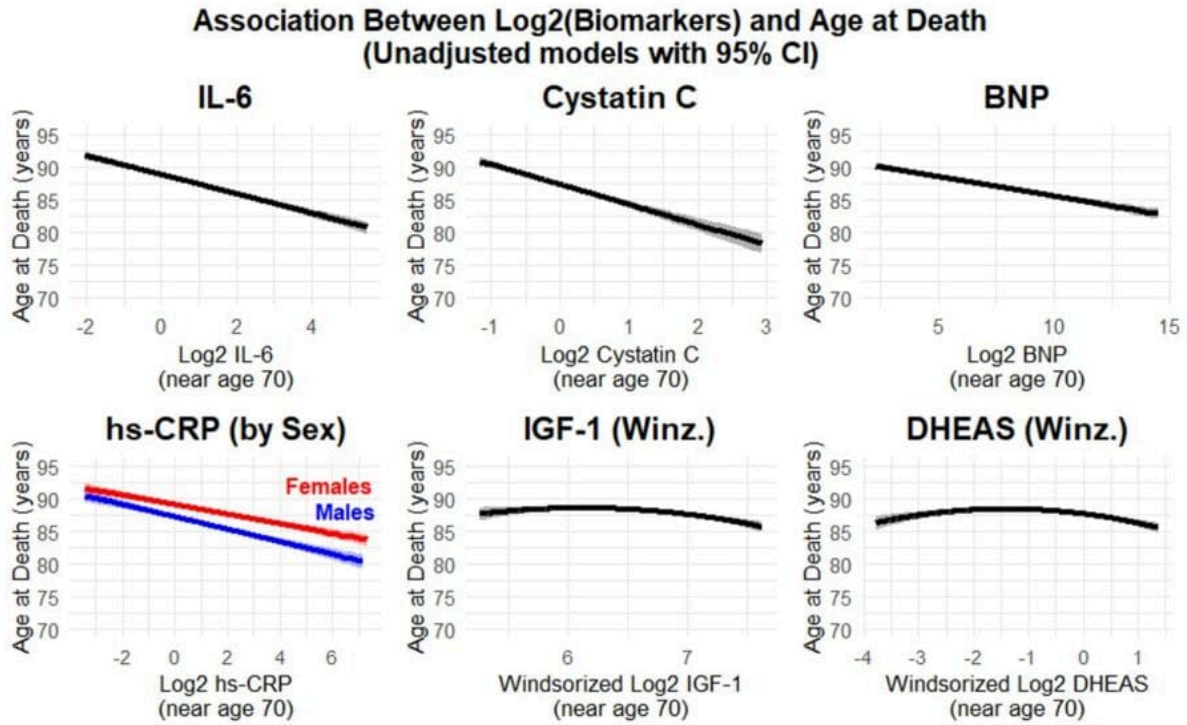


Figure 1. Association between six blood biomarkers measured near age 70 and age at death in the Cardiovascular Heart Study (CHS). This figure shows the relationships between six biomarkers (IL-6, Cystatin C, BNP, hs-CRP, IGF-1, and DHEAS) measured near age 70 and subsequent age at death. Linear regressions were run on the log-base-2 transformed biomarker measurements and age at death. Additionally, hs-CRP models were stratified by sex, and a quadratic term was included for DHEAS and IGF-1 models to account for U-shaped relationships between these biomarkers and longevity. Solid lines represent predicted values from the unadjusted models, and lighter shaded ribbons represent 95% confidence intervals. For hs-CRP, separate curves are shown for males (blue) and females (red). IGF-1 and DHEAS values were Winsorized to reduce the influence of extreme values.

Aging

Estimated effects of recent alcohol use on memory in the Health and Retirement Study: using marginal structural models to account for time-varying confounding and censoring

Scott C. Zimmerman* Scott C. Zimmerman Anna M. Pederson Rebecca E. Graff Laura A. Schmidt Jillian Hebert Shelli Vodovozov Yvette C. Cozier Suzanna M. Martinez Cynthia I. Campbell Catherine Schaefer Stacy A. Sterling M. Maria Glymour

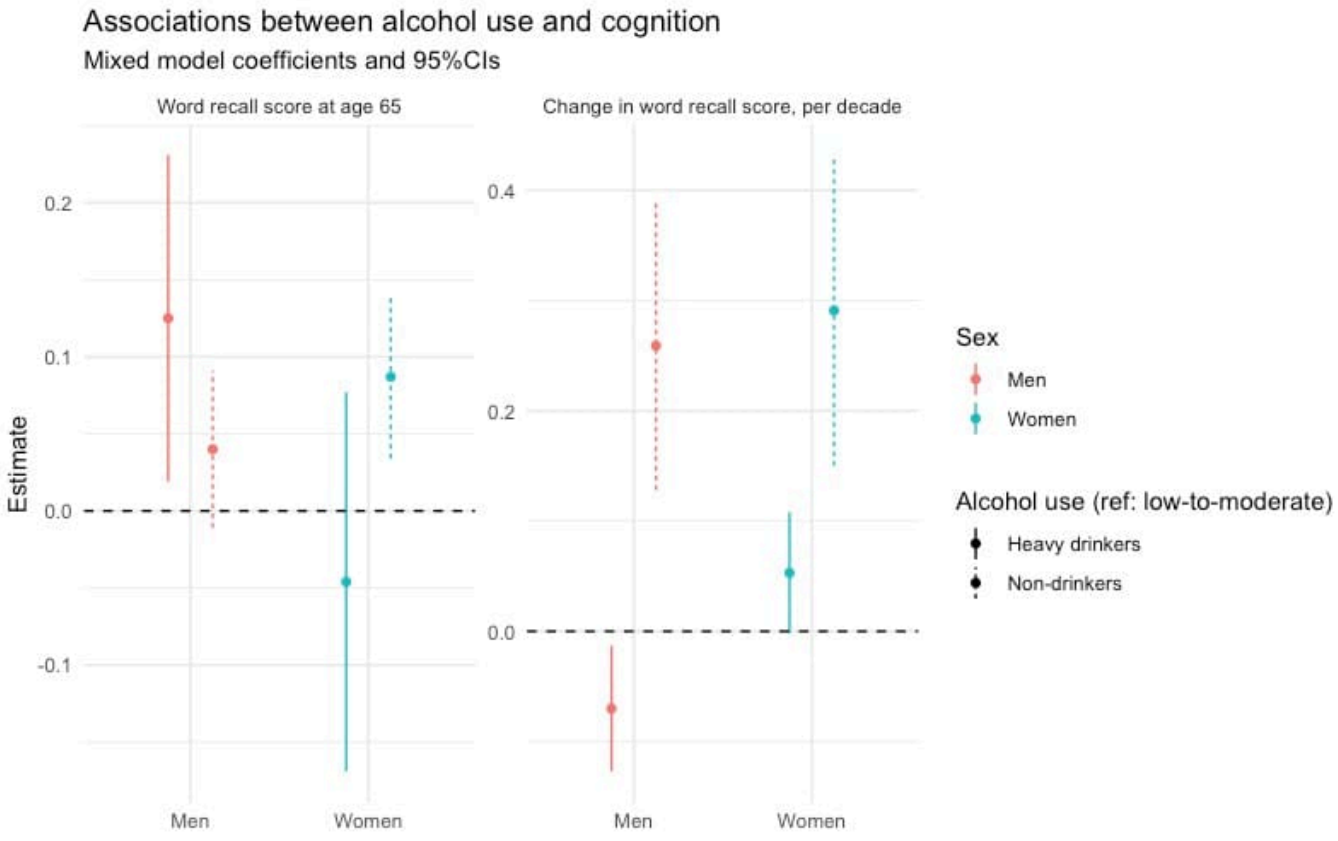
Estimating effects of current alcohol use on memory is difficult due to time-varying confounding (e.g. “sick quitting” effect) and informative censoring.

US Health and Retirement Study participants from waves 3–14 (1996-2018) born after 1957 were included (n=7,147 women, 6,332 men). We coded alcohol use in the last 30 days as: none; low-to-moderate (LtoM; women: ≤7, men: ≤14 weekly drinks and no heavy episodic drinking [HED; 6+ drinks/occasion]); or heavy (women: >7, men: >14 weekly drinks or any HED). Memory score was the sum of correctly recalled words from 10-item immediate and delayed word recall tests (range 0-20).

To account for time-varying confounding, we calculated stabilized exposure (multinomial regression) and censoring (logistic regression) weights, conditional on past cognitive, behavioral, health and sociodemographic predictors. We fit adjusted sex-stratified weighted linear mixed effects models of memory level and change on alcohol use reported at the prior wave.

A 1-point higher memory score in the previous wave was associated with lower odds of current abstinence compared to LtoM drinking (women: 0.970 [0.961,0.980]; men: 0.975 [0.964,0.986]), but similar odds of current heavy drinking. Among LtoM drinkers, average memory declined over time (women=0.8 & men=0.9 points/decade). In contrast, non-drinkers of both sexes had higher scores at age 65 (women: 0.087 points, 95%CI[0.034, 0.140], men: 0.04 [-0.011, 0.091]) and slower decline (women: 0.291 [0.150, 0.432], men: 0.259 [0.128, 0.390]). For heavy compared to LtoM drinkers, women had similar scores at 65 (-0.046 [-0.169, 0.077]) and similar decline (0.053 [-0.002, 0.108]), while men had higher scores at age 65 (0.125 [0.019, 0.231]), but faster decline (-0.07 [-0.127, -0.013]).

Abstinence may confer memory benefits relative to light-to-moderate drinking for both sexes, and heavy drinking may lead to faster memory decline for men. Sex differences may reflect different alcohol category definitions.


Associations between alcohol use and cognition
Mixed model coefficients and 95%CIs
Word recall score at age 65
Change in word recall score, per decade
Estimate
0.2
0.1
0.0
-0.1
0.4
0.2
0.0
Men
Women
Men
Women
Sex
Men
Women
Alcohol use (ref: low-to-moderate)
Heavy drinkers
Non-drinkers

Aging

Developing A Claims-Based Algorithm for Estimating State- and Local-level Dementia Prevalence Ruijia Chen* Ruijia Chen Jingxuan Wang Maria Glymour John Hsu

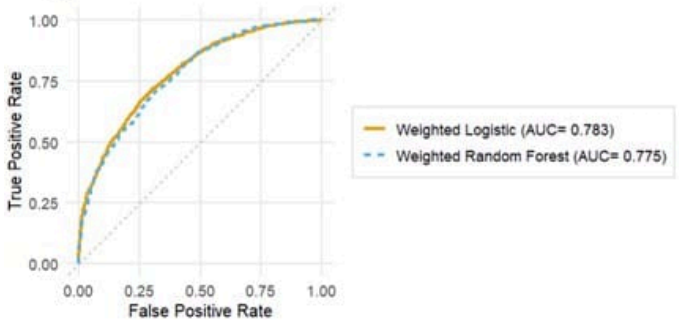
Background: Regional dementia prevention policy planning and monitoring requires reliable area-level estimates of dementia prevalence, which are currently lacking. The best sources of individual dementia status come from panel survey studies with systematic neuropsychological assessments, but these data are sparse at local area levels. Larger population-level datasets lack these measurements. Thus, using 2006–2020 Health and Retirement Study (HRS)–Medicare administrative-Medicare Current Beneficiary Survey (MCBS) linked data, this study developed and validated an individual-level dementia prediction algorithm.

Methods: Dementia status was defined using the Gianattasio-Power algorithm, an HRS-based approach validated against detailed neuropsychological assessments. Candidate algorithms included information on age, sex, race/ethnicity, dual Medicare/Medicaid eligibility, state of residence, Alzheimer's disease diagnosis, diabetes, hypertension, stroke, chronic obstructive pulmonary disease, obesity, and hearing impairment. The dataset was randomly split into training/testing (70/30%) samples. We fitted pooled logistic regression and random forest models using predictors measured at time t to predict dementia at time t + 1, with inverse probability attrition weights. Model performance was then evaluated using the testing sample.

Results: Among 3,643 beneficiaries with dementia status information, the mean baseline age was 81 years (SD=7). Both models demonstrated good discrimination (AUC ~0.78), with high specificity (79–82%) and moderate sensitivity (56%) (Figure). The discrimination slope for the random forest model was 0.84 and calibration-in-the-large=-0.005.

Conclusion: A simple prediction model using available Medicare administrative data performs well with respect to a well-validated dementia algorithm using experimentally ascertained survey data. These individual-level assessments could improve area-based estimates to inform future resource allocation decisions.

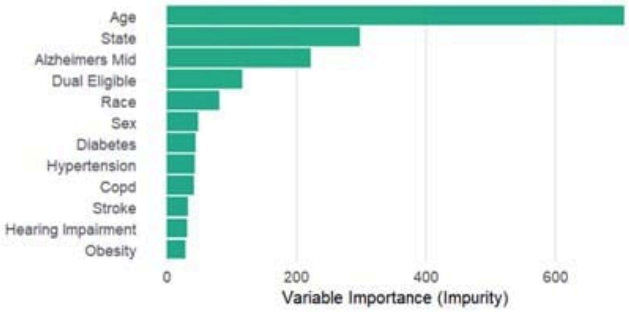
A



B

Model	AUC	Sensitivity	Specificity	PPV	NPV
Logistics	0.783	0.568	0.816	0.684	0.730
Random Forest	0.775	0.563	0.792	0.655	0.721

C



Aging

Assessing oral health status and disparities among LGBTQ+ older adults in the United States Amanda J Llaneza* Amanda Llaneza Danielle H Llaneza Janis E Campbell

Background: Adults 65+ are the fastest growing demographic in the US, and experience dental health disparities. This may be exacerbated by the intersection of older age and LGBTQ+ identity that requires further attention to increase quality of life.

Objective: To analyze the relationship between older adult sexual and gender minority identity and oral health status nationwide, utilizing the 2022 Behavioral Risk Factor Surveillance System (BRFSS).

Methods: This analysis investigated sexual orientation and gender identity (LGBTQ+ Identity versus Cis/Heterosexual Identity) and oral health among adults 65+ years. Outcomes of interest were tooth removal and time of most recent dental visit. Frequencies, percentages, and weighted chi-square statistics were estimated. Weighted logistic regression was conducted to estimate ORs and 95% CIs, controlling for sex, race/ethnicity, education, income, insurance status, general health, depression, and diabetes.

Results: 70,429 older adults were included, where 2,333 (3.1%) self-identified as LGBTQ+. Most were females (52%), non-Hispanic White (85%), with Medicare or similar insurance (84%). About 65% of older adults experienced tooth loss, and 69% visited a dentist in the past year. No statistically significant differences were found between older adults who experienced tooth loss by LGBTQ+ identity vs. cis/heterosexual identity. There was a significant association between LGBTQ+ identity and no dental visit in the past year ($p < 0.001$). Unadjusted OR showed a 37% higher odds of no dental visit in the past year among those with a LGBTQ+ identity compared to those with a cis/heterosexual identity (OR: 1.37, 95% CI: 1.14-1.64, $p=0.001$). After adjustment for covariates, there was a 12% higher odds of no dental visit in the past year among those with an LGBTQ+ identity compared to those with a cis/heterosexual identity, though not statistically significant (OR: 1.12, 95% CI: 0.92-1.35, $p=0.25$).

Conclusions: Gender identity and sexual orientation is a significant factor in managing dental health care among older adults. Consideration of patients' demographics is important in tailoring dental healthcare visits for older adults.

Aging

Sex differences in cognitive predictors of functional independence in an oldest-old cohort: A multi-group structural equation modeling approach Natalie Pandher* Natalie Pandher Yi Lor Alexander Ivan B Posis Batool Rizvi Maria M Corrada Paola Gilsanz Rachel A Whitmer

Independent living, a critical aspect of healthy aging, can be measured by Instrumental Activities of Daily Living (IADLs). IADL impairments are prevalent in older adults, women, and individuals with dementia/MCI, but sex differences in cognition-IADL pathways are unclear. We assessed if sex moderates associations of cognitive function with functional independence in the oldest-old from cross-sectional data on IADLs and cognition collected in wave 2 of the LifeAfter90 Study. Using confirmatory factor analysis, IADLs of money management, meal preparation, and chores were weighted by factor loadings to create a functional independence latent factor (higher scores = less independence). Z-scored semantic memory (SM), working memory (WM), verbal episodic memory (VEM), and executive function (EF) were measured with the Spanish and English Neuropsychological Assessments Scale. After testing for scalar measurement invariance to account for baseline sex differences in the sample, we employed multi-group structural equation modeling with a weighted least squares estimator and created regression models of cognition and functional independence for each sex while adjusting for age, education, race/ethnicity, and marital status (Fig 1). Sex differences were assessed by the Wald test. The sample (N=475; 62% female) had mean age of 93 (SD= 2.2; range: 90-103 yrs) with 75% college educated, 28% married/partnered, and a race/ethnicity breakdown of 30% White, 26% Black, 21% Asian, 15% Latino/Hispanic, and 8% other. The model revealed sex differences in associations of VEM (βdiff= 0.23; 95%CI: 0.02, 0.44) and EF (βdiff= -0.36; 95%CI: -0.70, -0.02) with functional independence. WM was predictive of functional independence in females only. Our findings suggest memory may play a larger role in independence for females, while executive control is more critical in males. Thus, tailoring independent living support systems to be sex-specific may help promote aging-in-place in the oldest-old.

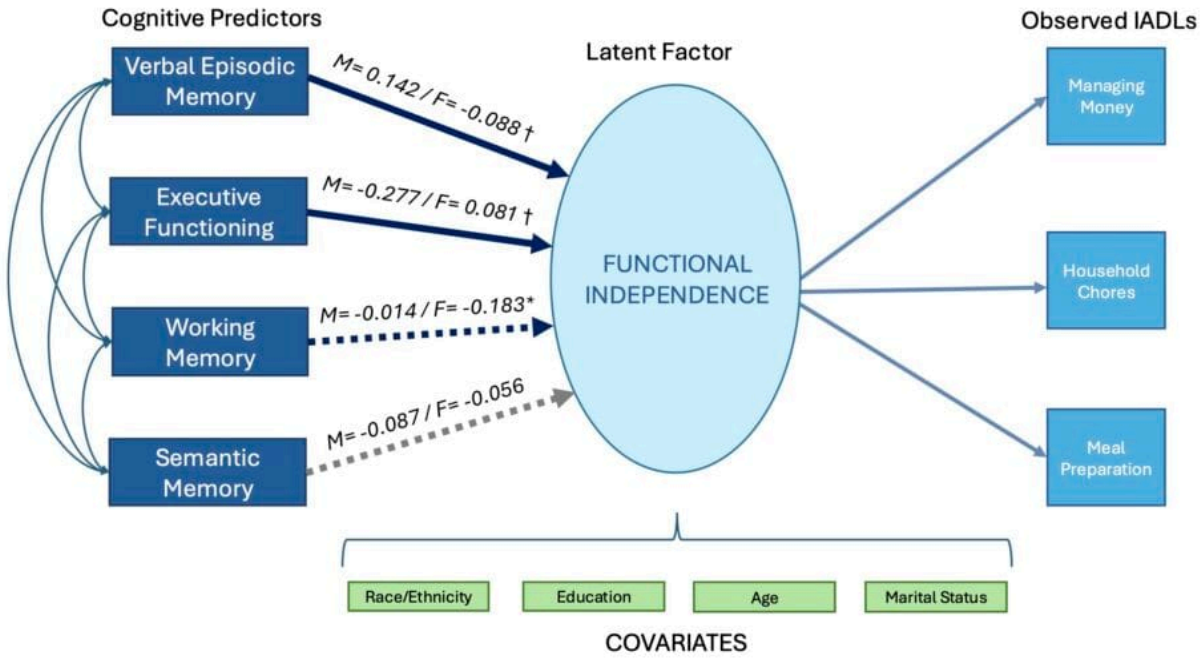


Figure 1. Path diagram for a multi-group Structural Equation Model for cognitive predictors of functional independence. Regression coefficients are presented for males and females with significant sex-specific associations (* = p<.05) and sex differences calculated by the Wald test († = p<.05). Pathways that are significantly different for males and females are depicted by solid lines, while the non-significant pathways are dashed lines. The latent factor construction using the observed IADLs is highlighted on the right. SEM fits the data well with a Comparative Fit Index and Tucker-Lewis Index of 1, Root Mean Square Error of 0, and Standardized Root Mean Square Residual of 0.007.

Aging

Association between gait speed and incident dementia among those aged 90 and older: findings from LifeAfter90 Study Rifat Alam* Rifat Alam Hilary L. Colbeth Nancy X. Chen Alexander Ivan B. Posis Kristen M. George Paola Gilsanz Maria M. Corrada Rachel A. Whitmer

Background: Slower gait speed has been linked to higher risk of dementia, but evidence is limited among adults aged 90+ years, the oldest-old. We examined the association between gait speed and incident dementia in an ethnoracially diverse cohort of the oldest-old.

Methods: We analyzed 421 LifeAfter90 participants with baseline gait speed measured using the 4-Meter Walk Test (meters/second); z-scored average of two attempts. Incident dementia was identified through clinical assessments occurring every 6 months for up to 11 visits between 2018 and 2025. Follow-up time was defined as years from baseline to dementia, death, or the end of follow-up, whichever occurred first. We used cause-specific Cox proportional hazards models to estimate dementia risk and Fine-Gray models to account for the competing risk of death. Hazard ratios (HR) are reported per 1 SD increase in gait speed, adjusted for age, sex, race/ethnicity, and education.

Results: Participants' mean±SD baseline age was 92.8±2.3, 63% were women, and 20% self-identified as Asian, 21% as Black, 11% as Latine, 9% as Multiracial/Other, and 38% as White. Over an average±SD follow-up of 2.7±2.1 years, 136 participants developed dementia and 156 died. Faster gait speed was associated with a lower risk of dementia in the cause-specific Cox model (HR=0.67,95%CI=0.55,0.81), and the Fine-Gray model (sHR=0.74,95%CI=0.62,0.90) (Figure 1).

Discussion: Faster baseline gait speed was associated with lower risk of dementia among this diverse cohort of adults aged 90 and older. Our findings remained after accounting for death as a competing event. These results support gait speed as a simple, measurable marker of future dementia risk in the oldest-old.

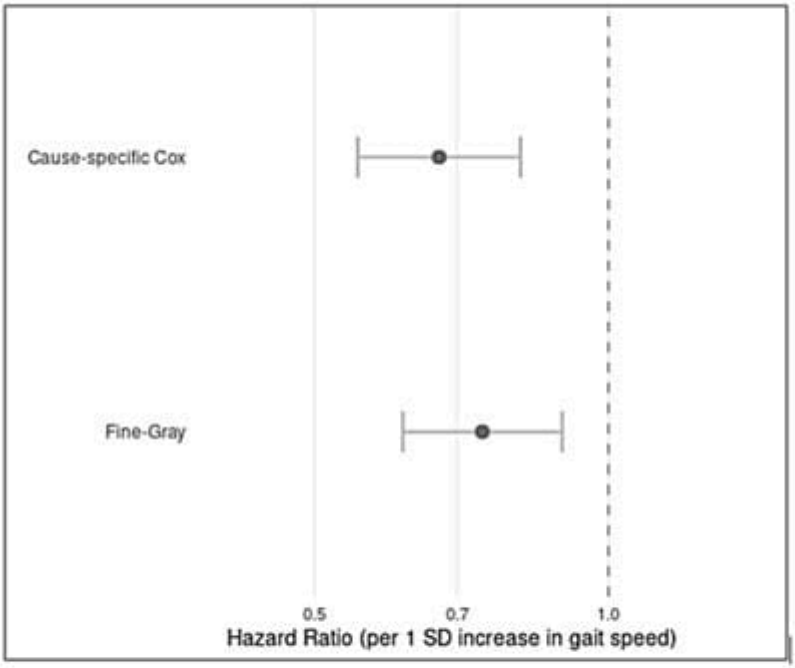


Figure 1: Hazard Ratios and 95% confidence intervals for the association between gait speed and incident dementia among 90+ years old adjusted for age, sex, race/ethnicity, and education: the *LifeAfter90* Study

LATEBREAKER

Autoimmune diseases

Latent Early Disease Trajectories in Systemic Autoimmune Rheumatic Diseases and the Association with Subsequent Mortality Choa Yun* Choa Yun May A. Beydoun Minkyo Song

Background: Post-diagnosis progression in systemic autoimmune rheumatic diseases (SARDs) is not well characterized across domains. Prior studies often evaluate domains separately or use composite indices, which can miss co-occurring changes. We assessed whether jointly modeling early post-diagnosis trajectories of healthcare utilization, overlapping autoimmune conditions, and comorbidity burden identifies progression patterns associated with mortality.

Methods: In UK Biobank, SARD participants and 1:4 age-, sex-, and landmark date–matched controls (n=16,576; 72% females) were followed for up to six years. Multivariable latent class trajectory modeling jointly characterized longitudinal patterns of SARDs-related healthcare revisits, non-SARD comorbidity accumulation, and comorbidity burden, classifying individuals to trajectory classes. Associations between trajectory classes and all-cause mortality were evaluated using landmark Cox regression. To predict high risk class, we developed prediction models using one and two years post-diagnosis data (elastic net, random forest, XGBoost).

Results: Three trajectory classes were identified. The high-progression class showed steep increases in healthcare revisits and comorbidity burden. Compared with healthy controls, mortality increased stepwise across trajectory classes (HR 1.90 [95% CI 1.51–2.39] for low; 2.51 [1.11–5.67] for moderate; and 4.92 [3.07–7.88] for high). Prediction models yielded moderate discrimination for identifying high-risk trajectory, with XGBoost performing best (AUC up to 0.75 using two-year data). Top predictors included co-occurring SARDs, age at diagnosis, biological age, C-reactive protein, Charlson comorbidity index and socioeconomic deprivation.

Conclusion: Early post-diagnosis disease trajectories among patients with SARDs were strongly associated with mortality. Joint trajectory modeling combined with early prediction may support risk stratification and inform targeted monitoring.

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Behavior

Intergenerational Transmission of Parenting Practices: The Role of Childhood Exposures to Stimulations and Disciplines as Predictors of the Variety of Current Parenting Practices in Mwanza, Tanzania Yi-Tien Hsu* Yi-Tien Hsu

Background: Parenting practices are critical determinants of early child development, yet the intergenerational transmission of parenting behaviors in Tanzanian context remain under-explored. This study examines how frequent childhood parenting experiences predicts the number of different parenting practices caregivers use, specifically focusing on the moderating role of the caregiver's gender.

Methods: Data from 794 participants in the Familia Bora Study was analysed. The primary exposures included caregivers' early-life experiences of parental physical discipline and play, and the outcomes were the past month use of 7 stimulation and 9 discipline types. Linear regression models were adjusted for caregiver gender, socioeconomic status, and coresidency.

Results: Adjusted analyses showed frequent childhood exposures to maternal play had higher variety of current stimulation types (β=0.62; 95% CI: 0.37-0.86) and frequent childhood paternal play predicted a broader range of current stimulation (β=0.79; 95% CI: 0.45-1.13). No gender interaction was found for stimulation variety. Conversely, frequent childhood experience with maternal physical discipline was associated with a higher number of current discipline behaviors (β=0.44; 95% CI: 0.17-0.70) , a significant interaction was observed between maternal discipline and caregiver gender (p=0.019). Paternal physical discipline in childhood also showed a significant interaction with caregiver gender (p=0.004) regarding the types of current discipline methods used.

Conclusions: Positive and negative parenting experiences in childhood predict the variety of recent strategies caregivers use, whereas the transmission of negative disciplines varies by caregiver's gender, indicating the transmission of diversed discipline repertoire is gender-dependent.

Key words: intergenerational transmission of parenting behaviors, stimulation and discipline, and gender

LATEBREAKER

Big Data/Machine Learning/AI

Predicting Mortality in Alzheimer's Disease and Related Dementias: A Machine Learning Comparison Using the South Carolina Alzheimer's Disease Registry Data Daniel A Amoatika* Daniel A Amoatika Stella Self Matthew Lohman Bryan Love Maggi C Miller Monique J Brown

Background: Older adults living with Alzheimer's Disease and Related Dementias (ADRD) have an increased risk of mortality compared to those without an ADRD diagnosis. Various statistical methods have been used to predict mortality in the ADRD population. However, they face several limitations when applied to high-dimensional data. We compared the predictive performance of three machine learning models using the South Carolina Alzheimer's Disease Registry (SCADR).

Method: Data from the South Carolina Alzheimer's Disease Registry (2007–2018) were analyzed. Three machine learning models, LASSO regression, Random Forest, and Support Vector Machines, were developed in R using the glmnet, ranger, and kernlab packages. Data were split into training (70%) and testing (30%) sets, with normalization and stratification by mortality status. Class imbalance was addressed using the Synthetic Minority Over-sampling Technique (SMOTE). Five-fold cross-validation was used to tune model hyperparameters. Optimal classification thresholds were determined using Youden's Index. Model performance was compared using the area under the receiver operating characteristic curve (ROC-AUC).

Results: A total of 13,620 participants from the SCADR were included (mean age = 77 years), with an overall mortality rate of 71%. Twenty-five predictors were evaluated across models. The LASSO model demonstrated strong discrimination for mortality prediction (ROC-AUC = 0.81). The Support Vector Machine model achieved the highest overall accuracy (74%), outperforming both LASSO and Random Forest models. Nine predictors, including year of diagnosis, race, sex, and disease-specific conditions, were consistently identified as influential across all three machine learning approaches.

Conclusion: Machine learning models demonstrated moderate to very good discrimination and good overall accuracy in predicting mortality within the Registry. These approaches may be extended to predict other clinically relevant outcomes and support risk stratification, informing tailored interventions and resource allocation in the Registry.

Keywords: Alzheimer's Disease and Related Dementias, Machine Learning, Mortality, Prediction, Outcomes

Big Data/Machine Learning/AI

Evaluation of Research Credibility in Alzheimer's Disease: A Comparative Analysis of Amyloid and Tau Sarah Ackley* Sarah Ackley Michael Flanders Kendra D. Sims Audrey R. Murchland Michelle Caunca Carlos Morales Valentin Lon S. Schneider

Amyloid and tau are implicated in Alzheimer's disease (AD). Scientific and popular sources have raised concerns that amyloid has received disproportionate attention relative to tau and that fraud has occurred in the amyloid literature—conditions that may increase incentives for biased statistical practices. However, systematic evidence on these subtler threats to research credibility remains limited. Advances in large language models (LLMs) and variable-power p-curve methods enable formal evaluation of bias. We analyzed PubMed-indexed abstracts referencing amyloid or tau published 1992-2024. P-values were extracted using validated LLM-based tools and analyzed. We first quantified the magnitude of the discontinuity at 0.05 using a model-free "cliff" statistic defined as the difference in probability mass between 0.04-0.05 and 0.05-0.06. We then estimated excess probability mass from 0.01 to 0.05 using variable-power p-curve models fit while excluding this interval, under the assumption that analysis manipulation operates primarily within this region. Both p-value distributions have a cliff at 0.05 (Figure). Amyloid exhibited a larger discontinuity at the 0.05 threshold than tau, with an estimated cliff-size difference of 0.015, 95% CI: (0.008, 0.023); this difference was smaller and not statistically distinguishable from zero when restricting to a later time period [difference=0.008, 95% CI: (-0.005, 0.020)]. Excess probability mass from 0.01 to 0.05 ranged from 0.18 to 0.38 depending on model, biomarker, and time period. Amyloid-tau differences ranged from 0.046-0.049; this difference was substantially attenuated when restricting to a later time period (difference range: 0.020-0.026). Differences between amyloid and tau likely reflect publication timing and evolving norms in statistical reporting, as bias signatures are comparable recently. Strong signatures of bias for both biomarkers underscore the need for rigorous evaluations of research credibility.

Cancer

Neighborhood-Level Vulnerability and Pediatric Cancer Survival in the United States: An Analysis of SEER Data from 2000-2021 Amelia Nichols* Amelia Nichols Emma Hymel Shinobu Watanabe-Galloway

Background: It is established that geography impacts health and wellbeing; the Social Vulnerability Index (SVI) is a validated, regularly updated tool summarizing county-level vulnerabilities. Cancer is the leading cause of death by disease in children and adolescents; there are variabilities in survival which may be partially explained by neighborhood-level vulnerability. The objective of this study was to explore the differences in pediatric cancer survival among levels of vulnerability.

Methods: A specialized data set from Surveillance Epidemiology, and End Results (SEER) program with county FIPS codes was matched with SVI 2010 data. Selection criteria included children aged ≤ 19 years with first primary malignancy not identified from death certificate or autopsy. Demographics, cancer type, diagnosis year, and rurality were compared by SVI quartile. A Kaplan Meier curve assessed survival by SVI quartile and multivariable cox proportional hazards modelling assessed the hazards of mortality by SVI and other demographic and clinical factors.

Results: There were 85,768 records that met inclusion criteria. Median overall SVI was 0.66 (IQR: 0.47-0.85). Increasing SVI quartile from lowest to highest vulnerability was associated with worsening survival ($p < 0.0001$). Adjusting for covariates, increased hazards of mortality were seen for males, earlier diagnosis year, non-White race, non-hematologic malignancies, rural residence, and increasing SVI quartile. Compared to the lowest SVI quartile, the adjusted hazard of mortality in the highest quartile is 1.19 (95% CI: 1.13-1.25; $p < 0.0001$).

Conclusions: Despite reductions in pediatric cancer mortality, disparities remain. Increasing SVI is associated with worse survival, even after adjusting for covariates. These findings highlight the importance of incorporating neighborhood-level vulnerabilities into future research to understand the underlying factors impacting survival disparities in increasingly vulnerable geographies

Cancer

The Association between Prostate Cancer and PFAS- Associated Pesticides in the Multiethnic Cohort Jazmine Chism* Jazmine Chism Christopher Haiman Jesse Goodrich Myles Cockburn

Prostate cancer has few established environmental risk factors, yet ambient pesticide exposure may contribute to risk even in peri-urban regions like Los Angeles County. Prior evidence largely focuses on occupational and self-reported pesticide use, which increases exposure misclassification and biases toward the null. California's Pesticide Use Reporting (PUR) system enables an objective assessment of residential pesticide exposure, including PFAS-associated pesticides, which may bioaccumulate and increase prostate cancer risk.

We conducted a nested case–control study within the Multiethnic Cohort, including 4977 prostate cancer cases and 4 non-repeated cancer-free controls (16653), using cumulative density sampling to address left truncation. The case diagnosis year served as the exposure reference year. Ambient residential pesticide exposure from 1990–2020 was estimated by linking geocoded residential histories to PUR data and GIS layers capturing pesticide applications within 500-meter buffers. Exposure was summarized cumulatively and within 10, 15, and 20 years prior to diagnosis, as well as 10–15, 15–20, and 10–20 year latency windows. We evaluated 782 pesticides, including 68 PFAS-associated pesticides identified by active ingredient.

Conditional logistic regression estimated odds ratios (ORs) and 95% confidence intervals (CIs), adjusting for age at exposure index and race/ethnicity. No associations were observed across the full exposure period. However, within the 15–20 year window, PFAS-associated pesticide exposure demonstrated a dose–response relationship. High exposure was associated with increased prostate cancer risk (OR = 1.66; 95% CI: 1.26–2.20), while low exposure showed a suggestive inverse association (OR = 0.71; 95% CI: 0.49–1.03).

These findings suggest a latency-dependent association between PFAS-associated pesticide exposure and prostate cancer risk and may represent an underappreciated route of exposure to these chemicals.

Cancer

Knowledge, Attitude, and Perceived Barriers to Breast Cancer Screening Among African Immigrant Women Working in Beauty Salons Rexford Anson-Dwamena* Hadiza Galadima
Rexford Anson-Dwamena

Background: Women employed in beauty salons are at increased risk of breast cancer due to chronic exposure to chemical agents found in hair dyes, bleaches, relaxers, and other salon products. Despite this potential occupational vulnerability, little is known about breast cancer screening (BCS) beliefs and behaviors among African immigrant beauty salon workers. This study assesses knowledge, attitudes, and perceived barriers toward BCS and examines how subscale scores from the Breast Cancer Screening Beliefs Questionnaire (BCSBQ) relate to self-examination practices among African immigrant women in the Washington, D.C., Maryland, and Virginia (DMV) region.

Methods: Convenience sampling and snowball recruitment were used to recruit African immigrant women aged ≥18 years who work in beauty salons across malls, plazas, and independent establishments in the DMV area. Recruitment was supported by partnerships with African community leaders and salon owners, who granted access to workplaces and community spaces for study outreach. Participants completed the validated BCSBQ, which measures three subscales (knowledge, attitudes, and perceived barriers) rated on a 5-point Likert scale (1 = completely agree to 5 = completely disagree). Descriptive analyses summarize demographic characteristics and screening behaviors. Further analyses will assess associations between BCSBQ subscores and breast self-examination practices.

Results: Among early respondents (n=27), 66.7% were≥35 years old, 55.5% were married, 50% reported having health insurance, and 94% had lived in the United States for more than 1 year. Although 82.4% indicated that they obtain health information from a personal doctor or healthcare provider, 52.6% had never undergone a breast cancer screening test. Remarkably, about 77.8% reported performing a breast self-examination at least once.

Conclusion: Participant recruitment has been challenging, largely driven by fear of identification and heightened concerns related to current immigration policies. This study fills a critical gap by characterizing screening beliefs and barriers in a high-risk, underserved population.

Cancer

Pooled analysis of cell-free DNA derived 5-hydroxymethylcytosine signatures and risk of multiple myeloma using Bayesian machine learning Saurabh Bhandari* Saurabh Bhandari Yuan Ji Brian C.-H. Chiu

Background: Epigenetic changes play a critical role in the development of multiple myeloma (MM), but most studies use surrogate tissues (e.g., peripheral blood lymphocytes because obtaining tumor cells from the bone marrow in controls is not feasible) and do not distinguish 5-hydroxymethylcytosine (5hmC), a distinct epigenetic mark involved in gene activation, from the common-studied 5-methylcytosine due to technical constraints.

Methods: To elucidate novel 5hmC contributions to the risk of MM, we conducted a pooled case-control analysis of cell-free DNA (cfDNA) derived genome-wide 5hmC profiles from 575 MM cases and 294 controls across two independent studies. We applied semi-parametric Bayesian Additive Regression Trees integrating high-dimensional genomic features with confounders, using Bayesian false discovery rate control for variable selection. Model performance was evaluated in a held-out validation set (n=369) using area under the receiver operating characteristic curve (AUC) and Brier score.

Results: We identified eight genes (IL1RAP, ST5, HERC6, KL, MYO1E, ELK3, CAPN2, UBR4) associated with risk of MM, all with posterior inclusion probability of 1.00. The model achieved excellent discrimination in validation (AUC: 0.96; 95% credible interval: 0.95-0.97) with good calibration (Brier score: 0.085). Seven genes were independently confirmed by Elastic Net regularization. The identified genes implicate established MM pathogenic pathways, including interleukin-1 inflammatory signaling, fibroblast growth factor 23/Klotho-mediated bone destruction, and ubiquitin-proteasome dysregulation.

Conclusions: Using a Bayesian machine learning approach, we identified eight 5hmC-modified genes in cfDNA that are associated with risk of MM. These findings not only improve our understanding of epigenetic mechanisms that underlie MM risk but may also provide novel approaches for individualized prevention of this incurable malignancy.

Cancer

Occupational exposure to asbestos and risk of bladder cancer Sarina D. Murray* Sarina Murray Stella Koutros Melissa C. Friesen Dalsu Baris Alison Johnson Margaret R. Karagas Debra T. Silverman

Bladder cancer is the 10th most common cancer worldwide, occurring mainly in men over 65 and in white populations. About half of the cases are attributable to tobacco smoking, with occupational exposures accounting for ~20-25% of cases among men. Evidence on asbestos-related bladder cancer risk remains inconclusive, largely due to limited individual-level data and insufficient adjustment for smoking and other high-risk occupations. We assessed occupational asbestos exposure and bladder cancer risk among 1182 cases and 1408 controls in the New England Bladder Cancer Study, adjusting for age, race, sex, smoking, and high-risk occupations. Exposure was estimated from lifetime job histories using a job-exposure matrix. Participants were classified as ever exposed if they held any job with ≥25% exposure probability. Cumulative exposure was calculated as the sum of intensity of exposure (1–5–25 scale) multiplied by job duration, with jobs below the probability threshold assigned zero. Adjusted OR and 95% CIs were estimated using logistic regression models. Ever exposure to chrysotile asbestos (270 cases (22.8%) and 241 controls (17.1%) was associated with increased bladder cancer risk (OR = 2.10, 95% CI: 1.56–2.82). Cumulative exposure showed a significant exposure–response trend across quartiles (ORQ1vsUnexposed = 1.96, 95% CI: 1.27-3.04; ORQ2vsUnexposed = 1.93, 95% CI: 1.29-3.07; ORQ3vsUnexposed = 2.02, 95% CI: 1.31-3.12; and ORQ4vsUnexposed = 2.4, 95% CI: 1.58-3.65, p-trend=0.0001). Amphibole asbestos metrics were highly correlated with chrysotile asbestos, as all amphibole-exposed participants were also exposed to chrysotile asbestos. Adjusting for other bladder cancer–related occupational exposures (metalworking fluids, diesel exhaust, solvents) did not materially alter risk estimates. Although evidence remains limited, our findings suggest an independent exposure–response relationship between asbestos and bladder cancer, improving understanding of its etiology.

Cancer

Duration of depressive symptoms prior to a cancer diagnosis and post-cancer memory function and decline Ashly C. Westrick* Ashly Westrick

Background. Depressive symptoms are associated with increased risk for cognitive decline in the general population, but less is known about how depressive symptoms might influence cognitive aging after a cancer diagnosis in mid-to-later life. We aimed to determine if the duration of depressive symptoms before a cancer diagnosis was associated with post-cancer diagnosis memory function and decline.

Methods: Data were from 425 adults aged ≥50 with an incident cancer diagnosis (2004-2020) and three waves of depression data prior to their diagnosis (1998-2020) in the US Health and Retirement Study. Depressive symptoms were measured biennially using the Center for Epidemiologic Studies Depression Scale (CES-D; range 0 to 8); a score of ≥3 was considered clinically relevant depressive symptoms. Duration of clinically relevant depressive symptoms was categorized as never, 1 time point, or ≥2 time points. Episodic memory was assessed from the time of cancer diagnosis as a composite of immediate and delayed recall. Multivariable adjusted linear mixed-effects models estimated the association between pre-diagnosis depression duration and post-diagnosis memory function.

Results: The mean age was 68.9 years (SD: 8.55) and 52.7% were male. In the three waves (~9 years) prior to diagnosis, 23.3% of participants (99/425) had depressive symptoms at ≥2 time points, 20.0% (85/425) had depressive symptoms at 1 time point, and 56.7 (241/425) had no depressive symptoms. The mean follow-up time after cancer diagnosis was 8 years (SD=5.03). A longer duration of depression was associated with worse memory at the time of diagnosis (-0.45 SD units, 95% CI: -0.72, -0.18) and a faster rate of memory decline post-diagnosis (-0.17 SD units/year, 95% CI: -0.68, 0.34), although imprecisely estimated.

Discussion: Increased duration of depressive symptoms was associated with worse memory function at the time of cancer diagnosis and may be associated with faster memory decline.

Cancer

Comparison of area and volumetric radiologically assessed body composition metrics with survival among colorectal cancer patients in the ColoCare Study Stephanie R. Hogue* Stephanie Hogue Daniel Jeong Maria F. Gomez Mahmoud Abdalah Olya Stringfield Adetunji T. Toriola Christopher I. Li Jane C. Figueiredo Biljana Gigic Bettina K. Budai David Shibata Cornelia M. Ulrich Sheetal Hardikar Caroline Himbert Matthew T. Rondina Mmadili N. Ilozumba Patricia Erickson Jeffrey Yap Jennifer Ose Alicia R. Richards Erin M. Siegel Jacob K. Kresovich Doratha A. Byrd

Body composition has been associated with colorectal cancer (CRC) survival but was largely characterized from CT scans with single slice area metrics. Multi-slice volumetric measures may better characterize total abdominal fat and muscle. We compared associations of area and volumetric measures with survival among CRC patients. We used Data Analysis Facilitation Suite to segment diagnostic CT scans and generate cross-sectional area at the axial mid-L3 vertebral level (cm2) and volume from the axial T12 vertebrae to the sacrum (cm3) metrics among 264 Moffitt CRC patients in the ColoCare cohort. All metrics [intermuscular (IMAT), visceral (VAT), and subcutaneous adipose tissue (SAT), plus skeletal muscle (SKM)] were indexed by dividing by height in m2. Proportional metrics were calculated (e.g., for VAT: VAT/[SAT+VAT+IMAT+SKM]) and transformed into sex-specific z-scores. We used multivariable Cox proportional hazards models to estimate associations of area and volumetric measures with overall [OS] and recurrence-free survival [RFS]. Participants were mostly men (56%) and had stage III CRC (50%). VAT was most strongly associated with survival versus IMAT, SAT, or SKM. Compared to VAT area at L3 (HR: 1.13, 95% CI:0.79-1.61), total VAT volumes from T12-Sacrum, T12-L3, and L3-Sacrum were more strongly associated with worse OS (HR: 1.25, 95% CI: 0.89, 1.77; HR: 1.21,95% CI:0.84, 1.74; and HR: 1.22, 95% CI:0.87, 1.72, respectively). A similar trend was observed for RFS (HR: 1.34, 95% CI: 0.95, 1.91 for L3; HR: 1.50, 95% CI: 1.08, 2.08; HR: 1.42, 95% CI: 1.01, 2.02; and HR: 1.49, 95% CI: 1.09, 2.03, respectively, for T12-Sacrum, T12-L3, and L3-Sacrum). Both single slice and volumetric VAT were associated with worse survival, though effect sizes were larger for volumetric measures, likely better reflecting inter-individual variability in adiposity across the abdominal cavity. Preliminary results will be expanded to include data from ColoCare sites across the US and Germany.

LATEBREAKER

Cancer

Synergistic effect of cancer and sexual minority status on overall mortality May Baydoun*
Sri Banerjee Jagdish Khubchandani

Individuals that are considered sexual minority continue facing stigma and discrimination by healthcare professionals and society alike. Often due to mistrust, people belonging to sexual minority communities have low cancer screening. In this study, we explored the relationship between sexual minority, history of cancer, and overall mortality to gain improved understanding of health equity. Data from the National Health and Nutrition Examination Survey (1999–2018) individuals aged 20-59 were used with mortality follow-up through through December 31, 2019. Multiple cox regression models were used to compare history of cancer between sexual minority (gay/lesbian, bisexual) and heterosexual participants, adjusted for predetermined covariates. We found that individuals that people with a history of cancer (15.9%) were slightly higher to be sexual minority than those without cancer (15.8%). For overall mortality, the crude hazard ratio (HR) for cancer was 2.41 (95% confidence interval [CI], 1.84-3.14 p< 0.01). The adjusted HR was elevated, 4.46 (CI 2.62-7.59, p< 0.001), among individuals with history of cancer who were sexual minorities but close to 1.0 (1.44 CI 1.01-2.05, p< 05) among individuals with cancer who were not sexual minorities, after adjusting for medical (obesity, hypertension, diabetes, and cardiovascular disease) and demographic variables (age, gender, ethnicity, education level, and poverty).The main finding in this research was that people with cancer and sexual minority individuals were 4 times more likely to experience mortality as individuals without cancer and belonging to the sexual minority community. This demonstrates the need to improve cancer screening by addressing stigma related to sexual minority status.

Cancer

Machine learning classification of HER2 mutations and treatment response using gene expression in breast cancer Muyiwa Ategbole* Muyiwa Ategbole Kesheng Wang Swann Adams

Background:
HER2 hotspot mutations are actionable targets in breast cancer, yet transcriptomic signatures that reliably distinguish clinically relevant variants, including V777L, and predict treatment-related phenotypes are not well characterized.

Methods:
We analyzed RNA sequencing data from recount3 (SRP166112), comprising 864 breast cancer cell samples representing multiple HER2 genotypes and drug exposures. After variance-stabilizing transformation and filtering, we used LASSO regularization to identify a sparse panel of 29 informative genes. Machine learning models (random forest, LASSO, elastic net, support vector machine, and gradient boosting) were trained to classify treated versus control samples using a 70/30 stratified train–test split. Model performance was evaluated on an independent test set using accuracy, sensitivity, specificity, and area under the receiver operating characteristic curve (AUC).

Results:
All models demonstrated strong discrimination between treated and control samples. Test-set accuracy ranged from 98.1% to 99.6% across models, with AUC values near 1.00. The LASSO model achieved the highest accuracy (99.6%), sensitivity (97.6%), and specificity (100%). Random forest, elastic net, support vector machine, and gradient boosting models showed similarly high performance (AUC 0.995–1.000). The LASSO-selected gene panel included biologically relevant predictors such as **CYP1A1**, **SERPINA6**, **CISH**, and **CYP1B1**, which were strongly associated with treatment exposure.

Conclusions:
A sparse set of gene expression markers enables highly accurate classification of treatment exposure in HER2-mutant breast cancer cell models. These transcriptomic signatures provide a foundation for biomarker discovery and future translational studies aimed at stratifying HER2-mutant tumors by therapeutic response.

Cancer

Evaluation of Colorectal Cancer Screening of Minority Populations at Community Safety Net Clinics: A Retrospective Chart Review Willie Rajvong* Willie Rajvong Soham Datar Melkon Harutunian Evan Burchfiel Jeff Huynh Jacqueline Hirth Roger Zoorob Malvika Juneja

Introduction: The fecal immunochemical test is used to screen for colorectal cancer. However, patients must navigate multiple steps from test ordering to colonoscopy after a positive result. Disruptions during this process may delay cancer diagnosis and exacerbate existing disparities in high-risk, predominantly minority populations. This study aimed to evaluate FIT testing and colonoscopy uptake in a predominantly minority population.

Methods: This study is a retrospective chart review focused on 837 patients aged 50-75 who visited a primary care physician at community safety net clinics in Houston, Texas, for an annual wellness visit between January 1, 2021, and December 31, 2022, and had a follow-up visit within the subsequent 12 months. Relevant patient characteristics, FIT results, referrals, and colonoscopy results were extracted from medical records to evaluate referrals and follow-up related to FIT testing.

Results: Among patients, the majority were female (61.41%), Hispanic (71.41%), and had a mean age of 56.4 years. Among these patients, 97.61% had FIT tests ordered, and 97.80% of those were returned. In total, there were 129 (16.15%) FIT tests that were positive. Among positive FIT tests, 94.57% were referred for colonoscopies, 42.97% had colonoscopies performed, and 88.52% of colonoscopies performed had abnormal findings. Of these abnormal findings, 55.56% reported polyps, 35.19% reported hemorrhoids, and 22.22% reported other abnormalities, including diverticulosis.

Conclusion: Nearly all eligible patients had FIT tests ordered, and nearly all were returned. However, while the majority of positive FIT tests were referred for colonoscopies, less than half had colonoscopies performed. Further investigations are needed into potential barriers to having colonoscopies performed in this predominantly minority population.

LATEBREAKER

Cancer

Parental HPV Vaccine Misperceptions and Childhood Vaccination: Effect Modification by Child Sex Among Parents in San Diego County, California Kayla Saadeh* Kayla Saadeh Shira Goldenberg Humberto Parada Jr Maria Elena Martinez Corinne McDaniels-Davidson

Background: In the US, the HPV vaccine has been recommended for cancer prevention for girls since 2006 and boys since 2011; uptake has been consistently lower among boys. We evaluated if the established effect of parent/guardian HPV vaccine misperceptions on child HPV vaccination differed by child sex.

Methods: We conducted a cancer-focused population health assessment in San Diego County in 2019. Data were weighted to the county adult population. Prevalence ratios (PRs) and 95% confidence intervals (CIs) for the association between parent HPV vaccine misperceptions, assessed using the HPV Vaccine Misperceptions Scale (per standard deviation [SD]; higher scores indicate greater misperceptions), and their child not receiving the HPV vaccine were modeled using survey-weighted modified Poisson regression by child sex. Effect measure modification (EMM) was assessed using relative excess risk due to interaction (additive scale) and ratio of PRs (multiplicative scale) from a single model with joint indicators for child sex and HPV vaccine misperception scores.

Results: Our study sample (n=239) represented a weighted sample of 893,364 parents with HPV vaccine age-eligible children. Median parental scores (range: 0-36) were 11.0 (IQR=5-16) for parents of boys and 13.0 (IQR=8-19) for parents of girls; 64.3% of boys and 56.1% of girls were ever vaccinated. After adjustment, a one SD increase in parental misperception score was associated with a 75% prevalence increase of not vaccinating daughters (PR=1.75; 95% CI: 1.41, 2.10) and a 51% prevalence increase of not vaccinating sons (PR=1.51; 95% CI: 1.05, 1.97; Figure 1); however, EMM by child sex was not statistically significant (Ps≥0.05).

Conclusions: Higher parental HPV vaccine misperceptions were associated with not vaccinating both daughters and sons, with a stronger, but not significantly different association for daughters. Misperceptions measured by our scale do not appear to impact parents differentially based on child sex.


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Cardiovascular

Evaluating the Impact of Mechanical CPR in OHCA Patients in a Large Urban EMS System

Madeline Cannon* Madeline Cannon Pamela Lai Rachel Zeig-Owens Elizabeth Lancet

Background: While use of a mechanical chest compression device for cardiopulmonary resuscitation (CPR) enhances crew safety, it is unclear whether it results in better survival outcomes for out-of-hospital cardiac arrest (OHCA) patients. In 2023, the Fire Department of the City of New York Emergency Medical Services (FDNY-EMS) implemented a citywide phased rollout of a mechanical CPR device (Stryker LUCAS® 3 chest compression system) onto Basic Life Support (BLS) ambulances, creating a natural experiment which emulated a stepped wedge cluster randomized trial.

Methods: Mechanical CPR devices were installed sequentially onto municipal BLS ambulances in each of New York City's nine EMS divisions over seventeen weeks. The device was used during transport only. To estimate the effect of mechanical CPR on sustained return of spontaneous circulation (S-ROSC) at emergency department arrival, we used multilevel mixed-effects logistic regression models clustered by EMS division and adjusted for time and other potential confounders. We additionally used two-stage residual inclusion (2SRI) to estimate the local causal effect among "compliers" (those who would be treated with mechanical CPR if assigned to the mechanical CPR group).

Results: Our study included 1,317 non-traumatic OHCA patients at least 15 years of age who were treated and transported by FDNY-EMS municipal BLS ambulances between 8/6/2023 and 12/30/2023. Compliance with protocol was 80% in the mechanical CPR group and 99% in the manual CPR group. S-ROSC was achieved in 275 (35%) patients in the mechanical CPR group and 188 (36%) patients in the manual CPR group (AOR=0.83, 95% CI 0.59-1.16). In the 2SRI analysis, mechanical CPR was associated with lower odds of S-ROSC, though the association was not statistically significant (OR=0.61, 95% CI 0.34-1.09).

Conclusions: We did not observe a significant difference in S-ROSC to emergency department arrival among patients treated with mechanical CPR vs. manual CPR.

LATEBREAKER

Cardiovascular

Simpson´s Paradox in a Clinical Trial: Myth or Reality?. Controversy Over Systolic Blood Pressure Sustainability in The SPRINT Trial. Oscar Leonel Rueda-Ochoa* Oscar Leonel Rueda-Ochoa Catalina Maria Alejandra Reyes Ronnie Celis-Amaya Dimitris Rizopoulos

Introduction
The SPRINT study demonstrated that intensive systolic blood pressure (SBP) treatment consistently and significantly reduces the primary outcome by 25%. However, a recent secondary analysis by the SPRINT Group evaluated whether this protective effect persists post-trial. By applying a linear mixed-effects model to repeated SBP measurements, they found the intervention lost its effect, citing a loss of SBP control during the post-trial period. Our group previously showed that this protection vanishes at different follow-up stages depending on the subgroup analyzed. This study explores why results diverge when using the Cox proportional hazards model versus Joint Model Analysis (cJM) within the trial. We propose that Simpson's paradox explains these divergent findings.
Materials and methods
We analyzed 9,068 participants with 128,139 repeated SBP measurements, randomized to either intensive treatment (SBP <120 mmHg) or standard treatment (SBP 130–139 mmHg). We employed a cJM to integrate longitudinal SBP data with the Cox model. Additionally, we evaluated the causal association of Serious Adverse Events (SAEs), blood pressure variability (BPV), and cumulative SBP with a composite outcome of myocardial infarction, acute coronary syndromes, heart failure, stroke, and cardiovascular mortality. We performed all analyses using R Studio v.12.0 and STATA v.19
Results
The intensive treatment's protective effect lost significance during the intra-trial follow-up across all groups: the total population (3.4 years), women (1.1 years), and patients with cardiovascular disease (1.3 years), chronic kidney disease (1.3 years), Black race (1.8 years), or age under 75 (2.1 years). Participants experiencing SAEs lost the protective effect earlier (3.4 years) than those without SAEs (4.2 years). Intensive treatment significantly increased systolic BPV. Furthermore, SAEs in the intensive group tripled the risk of the primary outcome compared to the standard group.
Conclusion

In the context of survival analysis, we postulate that the SPRINT trial suffers from a **Longitudinal Simpson's Paradox**, where temporal aggregation and the omission of endogenous time-varying mediators (SAEs, BPV) generate a marginal Hazard Ratio (HR) that is highly misleading regarding the true causal effect at the individual level.

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LATEBREAKER

Cardiovascular

Secondary prevention targets and guideline-directed medical therapy utilization following hospitalizations for myocardial infarction Lily G Bessette* Lily Bessette Bridget M Mayrer Timothy S Anderson

Background

Despite clear guideline recommendations for secondary prevention after a myocardial infarction (MI), blood pressure, cholesterol, and medication utilization may remain suboptimal after hospitalizations.

Methods

Observational cohort study of adults hospitalized for MI and discharged home between 2018-2022 with electronic health records in a US hospital system. Secondary prevention goals included low-density lipoprotein (LDL) < 70 mg/dL, systolic blood pressure (SBP) < 130 mmHg, and use of beta-blockers (BBs), statins, P2Y12 inhibitors, and renin-angiotensin-system inhibitors (RAS) measured during 12-months prior to admission, at discharge, and 12-months post-discharge. We tested changes before and 12-months after hospitalization in median LDL and SBP with Wilcoxon Signed-Rank tests and in use of medications with McNemar's test.

Results

The cohort included 5265 patients hospitalized for an MI (age 68 [IQR 77-60] years, 39% female, 91% White, 7% Black). Prior to admission, 30% had an LDL at goal (median [IQR] 88 mg/dL [64-116]), 41% had an SBP at goal (133 mmHg [123-145]), and use of BBs was 31%, statins 19%, P2Y12 inhibitors 15%, and RAS 39% (**Figure**). At discharge, 36% met goal LDL and 61% met goal SBP, and use of BBs increased by 24 percentage points (pp), statins 21 pp, P2Y12 inhibitors 25 pp, and RAS 9 pp.

At 12 months post-discharge, median [IQR] LDL decreased to 63 mg/dL [46-83] and SBP decreased to 128 mmHg [118-140] and use of BBs was 54%, statins was 45%, P2Y12 inhibitors was 47%, and RAS was 38%. Compared to prior to admission, significant improvements in median LDL, median SBP, and use of BBs, statins, and P2Y12s, but not RAS, were observed at 12 months post-discharge ($p<0.001$). Thus, targets for LDL, SBP, and use of all four evidence-based medications were achieved at 12-months post-discharge for only 60%, 54%, and 16%, respectively.

Conclusions

One year following an MI hospitalization, many patients do not meet critical secondary prevention targets.

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Cardiovascular

The Association Between Major Life Stressors and Cardiovascular Disease: Findings from the Jackson Heart Study Shuqi Zhang* Shuqi Zhang Sara Jones Berkeley Brian W. Pence Shakia Hardy Arnita F. Norwood Bryce Rowland Wayne Rosamond

Background: Major life stressors, defined as dramatic and severely taxing situations, may have traumatic and cumulative impacts on cardiovascular disease (CVD), yet evidence remains limited in Black adults. This study investigated the associations between major life stressors and coronary heart disease (CHD), stroke and heart failure (HF) in the Jackson Heart Study (JHS), a cohort of Black adults.

Methods: Major life events (MLEs) were assessed at the first annual follow up call after exam 1 (2000-2004) where participants reported the occurrence of 11 major life stressors in the past year. Another stressor, bereavement (i.e., death of a family member) was assessed annually. CVD events were monitored from the first-year post baseline, except HF which was ascertained from 2005, through 2016. Cox proportional hazard models estimated the HRs and 95% CIs of incident CVD subtypes. Marginal structure models estimated the associations between time-dependent bereavement and CVD.

Results: Among the 4,424 included Black participants (age 54 ± 13 years; 65% female), 71% reported at least one MLE at the first annual follow-up. During a median follow-up of 12 years, 210 CHD events, 146 stroke events and 282 HF events occurred. Serious illness or injury (HR = 1.57, 95% CI: 1.07, 2.28) and unwilling retirement (HR = 2.14, 95% CI: 1.17, 3.91) were associated with higher hazard of CHD. Both dichotomized MLEs (≥1 vs. 0, HR = 1.76, 95% CI: 1.03, 3.01) and continuous MLEs (HR = 1.20, 95% CI: 1.01, 1.42) were associated with higher risk of CHD among males. We also observed an association between bereavement and CHD within one year following the loss, but not thereafter (**Figure 1**). Additionally, bereavement was consistently associated with a higher risk of HF over time, particularly among males within one year following the loss.

Conclusion: Some major life stressors are associated with higher hazard of CHD and HF among Black adults, with associations varying by stressors, sex, and timing.

Figure 1. Hazard ratios between time-dependent bereavement and cardiovascular disease

Time following bereavement	CHD	Stroke	HF
Overall			
1 year	**1.73 (1.09, 2.75)**	1.01 (0.58, 1.77)	**1.74 (1.17, 1.93)**
2 years	1.14 (0.72, 1.80)	0.65 (0.37, 1.14)	1.13 (0.77, 1.67)
3 years	1.11 (0.74, 1.66)	0.76 (0.46, 1.24)	1.26 (0.91, 1.75)
5 years	1.00 (0.68, 1.45)	0.72 (0.46, 1.13)	**1.38 (1.03, 1.85)**
10 years	1.25 (0.91, 1.73)	1.04 (0.70, 1.55)	**1.57 (1.18, 2.10)**
Remaining follow-up	1.19 (0.86, 1.64)	1.06 (0.71, 1.58)	**1.55 (1.16, 2.08)**
Male			
1 year	**2.01 (1.02, 4.19)**	1.25 (0.53, 2.97)	**2.85 (1.59, 5.12)**
2 years	1.40 (0.69, 2.83)	0.83 (0.35, 1.96)	**1.92 (1.15, 3.24)**
3 years	1.05 (0.52, 2.11)	0.89 (0.41, 1.94)	**1.94 (1.07, 3.46)**
5 years	1.15 (0.64, 2.01)	0.77 (0.37, 1.59)	**2.07 (1.29, 3.31)**
10 years	1.43 (0.87, 2.34)	0.68 (0.34, 1.36)	**1.88 (1.16, 3.02)**
Remaining follow-up	1.33 (0.81, 2.18)	0.74 (0.38, 1.47)	**1.83 (1.13, 2.96)**
Female			
1 year	1.47 (0.83, 2.58)	0.86 (0.42, 1.77)	1.16 (0.70, 1.92)
2 years	0.94 (0.54, 1.66)	0.54 (0.26, 1.23)	0.74 (0.45, 1.13)
3 years	1.19 (0.74, 1.93)	0.68 (0.37, 1.27)	0.93 (0.62, 1.40)
5 years	0.91 (0.57, 1.46)	0.71 (0.40, 1.24)	1.06 (0.73, 1.54)
10 years	1.15 (0.76, 1.72)	1.46 (0.93, 2.30)	**1.41 (1.13, 2.09)**
Remaining follow-up	1.10 (0.73, 1.66)	1.44 (0.92, 2.25)	**1.50 (1.10, 2.06)**

Note: Hazard ratios and 95% confidence intervals were estimated using marginal structural models with inverse probability of treatment weights and inverse probability of censoring weights, adjusting for demographic, socioeconomic, and clinical characteristics, health behaviors, and perceived stress.

Cardiovascular

Social Risk Factors Associated with Coronary Heart Disease and Stroke Among US Adults Aged ≥18 Years Guixiang Zhao* Guixiang Zhao Machell Town Jing Fang Fatima Coronado Paul Eke

Background: Social risk factors are non-medical factors that influence people's health and exacerbate existing chronic conditions. This study examined the associations between social risk factors and coronary heart disease (CHD) and stroke among US adults.

Methods: The 2022 Behavioral Risk Factor Surveillance System collected data on a series of social risk factors including life satisfaction; social and emotional support; social isolation/loneliness; employment stability; food, housing, and utilities security; transportation access; mental stress; and health care access. Weighted prevalences for CHD and stroke were estimated by individual or cumulative social risk factors, and the associations were assessed by conducting log-linear regression analyses with adjustment for potential confounders.

Results: The prevalences of CHD and stroke were significantly higher among adults with most social risk factors (except for employment instability and no health insurance coverage) compared to those without. After adjustment for demographic characteristics and traditional CVD risk factors, the adjusted prevalences for CHD and stroke remained significantly higher for adults with most social risk factors (except for no health insurance coverage) compared to those without. The relative increases ranged from 13% for CHD and 14% for stroke among those lacking social and emotional support, to 64% and 78%, respectively, for those lacking reliable transportation. Increasing number of social risk factors were linearly and positively associated with higher adjusted prevalences of CHD and stroke

Conclusions: The findings of this study highlight strong associations between various social and economic factors and increased prevalences of CHD and stroke. Because the temporality and causality cannot be inferred from this study, future research may focus on whether addressing social risk factors along with medical therapy and lifestyle modifications could help improve cardiovascular health.

Cardiovascular

Eleven-year counterfactual risk of cardiovascular hospitalization under hypothetical sustained reductions in post-traumatic stress disorder symptom severity: the WTC-Heart Cohort, New York State, 2012–2023 Sean Andrew MacAllister* ALFREDO MORABIA Sean Andrew MacAllister Leia Y Saltzman Maurizio Trevisan Paola Angel Janine Flory Sonja Swanson Alfredo Morabia

Sustained reductions of post-traumatic stress disorder (PTSD) symptom severity may reduce the risk of cardiovascular disease (CVD). Randomized controlled trials are not well suited to assess the long-term effects of PTSD symptom duration (“load”) on risk for myocardial infarction (MI) and stroke, given the prolonged follow-up and large sample sizes required. To address this gap, we use longitudinal observational data to emulate key features of an hypothetical trial of sustained PTSD symptom reduction.

The WTC-Heart study is a prospective cohort initially comprising 6,481 first responders involved in World Trade Center debris cleanup. The cohort was assembled in 2012–2013 and followed through July 2025, with 85% retention. PTSD symptoms and conventional CVD risk factors were assessed repeatedly over follow-up. Incident CVD events were self-reported and validated through medical record review or, through 2023, ascertained via linkage to the New York Statewide Planning and Research Cooperative System (SPARCS). Dates and causes of death were confirmed through linkage with the National Death Index.

Among 5,446 New York State residents, we will estimate the 11-year counterfactual risk of hospitalization for MI (n=342), stroke (n=80), or both CVD events under hypothetical sustained reductions in PTSD severity, using repeated assessments of PTSD symptoms (PTSD Checklist; PCL). We will apply the parametric g-formula to estimate: (1) the counterfactual CVD risk under sustained reductions in PTSD severity of 10%, 20%, and 100%, compared with the natural course; and (2) the causal effect of reducing cumulative PTSD exposure by one PTSD-year (severity-time units) on CVD risk. Analyses will adjust for baseline and time-varying sociodemographic, cardiometabolic, trauma-related, and mental health confounders. We will report absolute risk differences and risk ratios at 11 years and present standardized cumulative incidence curves comparing counterfactual risks with the observed natural course.

Under standard assumptions, including no unmeasured confounding, correct model specification, and missing at random covariate data, the parametric g-formula will provide estimates of CVD risk under full adherence to sustained hypothetical reductions in PTSD severity. These findings have potentially major public health implications, given the high prevalence of PTSD among first responders to an increasing number of human-made or climate-related disasters.

Cardiovascular

Associations between heart rate variability from wearable devices and cardiovascular risk factors Yi-Hsuan Wu* Yi-Hsuan Wu Han-Ping Huang Chang Francis Hsu Andrew C. Ahn Po-Kai Huang Chi Chang Eunhye Lee Ziv Lautman Clete A. Kushida Ann W. Hsing

Heart rate variability (HRV) is a noninvasive marker of autonomic nervous system (ANS) function and cardiovascular disease (CVD) risk but is typically assessed using electrocardiography in clinical settings. Wearable devices enable continuous monitoring of HRV outside clinics and may support early detection of changes in cardiovascular function. This longitudinal study examined whether wearable-derived HRV is associated with established CVD risk factors. We analyzed data from 69 U.S. participants (aged 24-77 years; 78.3% female) in the Stanford WELL Wearable Pilot Study who wore photoplethysmography (PPG)-based smartwatches continuously for up to 60 days between July 26 and September 23, 2021. Pulse-to-pulse intervals were derived from PPG signals collected under free-living conditions, and frequency-domain HRV metrics were calculated. Analyses focused on the LF/HF ratio during sleep for the first seven weeks of monitoring, when motion effects were minimized and data completeness was highest. The LF/HF ratio was used as an indicator of autonomic modulation in this context. Hypertension, hyperlipidemia, sleep quality (Pittsburgh Sleep Quality Index), and covariates were assessed by baseline survey. Participants were classified into low, medium, and high sleep LF/HF ratio groups based on the median of weekly mean values. Compared with the low LF/HF group, higher LF/HF groups were less likely to have hypertension, hyperlipidemia, and poor sleep quality, although differences were not statistically significant. After adjustment for age, sex, body mass index, physical activity, and history of clinical depression, the medium (OR = 0.07; 95% CI: 0.01-0.58) and high LF/HF groups (OR = 0.01; 95% CI: 0.00-0.15) had lower odds of hypertension. These findings suggest that higher sleep HRV-derived LF/HF ratios, reflecting more preserved ANS regulation during sleep, are relevant to blood pressure-related CVD risk.

Causal Inference

Handling Missing Data in Cluster Randomized Trials: A Comparison of Multiple Imputation and Two-Stage TMLE Joy Zora Nakato* Joy Zora Nakato Laura B. Balzer

Missing data are ubiquitous in research studies and pose particular challenges in cluster randomized trials (CRTs), which randomize groups (e.g., communities or clinics) to the intervention versus control. CRTs often have complex dependence structures and are prone to missing data due to their pragmatic nature. A range of methods have been proposed to handle missing data in CRTs. Here, we compare multiple imputation (MI), a model-based method relying on strong assumptions about the data generating process (DGP), and Two-Stage TMLE, a machine learning method facilitating flexible estimation of both outcome and missingness processes. Although MI and TMLE have been compared in other settings, their relative performance in CRTs remains underexplored. To address this gap, we conducted a simulation study reflecting OPAL, the motivating CRT designed to improve use of HIV prevention in rural East Africa. Specifically, we simulated 1000 CRTs each with 100 clusters of size ~100 under two scenarios: a simple DGP where the outcome and missingness processes were linear and a complex DGP where these processes were highly non-linear. In the simple scenario, both methods achieved low bias and nominal 95% confidence interval coverage. However, in the complex scenario, MI was meaningfully biased, resulting in poor coverage (89.2%), whereas Two-Stage TMLE retained robust performance with negligible bias and near-nominal coverage (93.4%). Our findings demonstrate that while MI performs adequately when models are correctly specified its performance deteriorates under more realistic settings. In contrast, Two-Stage TMLE maintains robust performance under complex missingness and outcome mechanisms, highlighting its potential as a flexible approach for handling missing data in CRTs.

Causal Inference

A Novel Two-Step Framework for Estimating Dynamic Treatment Effects Using Longitudinal Covariate Information and Outcome Follow-up Io Murayama* Io Murayama Yoshimitsu Shimomura Kosuke Inoue Tomohiro Shinozaki Takahiro Kinoshita Tetsuhisa Kitamura

Routinely collected healthcare data often present heterogeneous measurement granularity over follow-up: a short period of intensive longitudinal observation with frequent measurements of treatments, outcomes, and covariates, followed by longer follow-up in which only outcomes can be ascertained. In our intensive care unit (ICU) electronic health record database, high-frequency patient status and treatment information is recorded during the ICU stay, but only mortality is observed after ICU discharge. In such settings, standard causal approaches for time-varying treatments restrict analysis to the period of intensive observation, leaving subsequent outcome information underutilized.

We propose a novel estimand and its inference framework for dynamic regimes defined during an initial period of intensive longitudinal observation. The framework is implemented using the parametric g-formula with two distinct modelling components: (1) an in-period model for time-varying covariates, treatment decisions, and outcomes during longitudinal observation, and (2) a post-observation outcome model for outcome occurrence conditional on covariates and treatment history at the end of longitudinal covariate observation. These components are connected through sequential simulation, enabling estimation of causal effects beyond the period in which longitudinal covariates are observed.

We applied this framework to an observational study comparing dynamic blood transfusion strategies defined by hemoglobin thresholds in ICU patients, with 28-day mortality as the outcome. The median length of ICU stay was only 4.9 days, substantially shorter than the 28-day follow-up period. Applying the proposed framework, the estimated 28-day mortality was 16.8% under a restrictive strategy and 15.4% under a liberal strategy (RD −1.3%, 95% CI −3.2% to 0.5%). This example illustrates how causal effects of policy-relevant dynamic treatment strategies defined during intensive longitudinal observation can be efficiently evaluated over longer follow-up.

Causal Inference

Evaluating the effects of New Jersey's extreme risk protection order law on firearm violence among men and women Aayush Chitransh* Aayush Chitransh Roni Barak Ventura

Statement of purpose:

In 2019, New Jersey implemented an Extreme Risk Protection Order (ERPO) law to reduce firearm-related violence. Evidence suggests that ERPO laws may affect firearm homicide rates differently for men and women. It is also plausible that those effects can be attributed to cities' violence burden and law implementation practices. In New Jersey in particular, Camden, Elizabeth, Jersey City, Newark, Paterson and Trenton comprise approximately 12% percent of the state's population yet account for 53% of fatal and non-fatal shootings. This study evaluated the causal effect of ERPO law on firearm homicide between men and women across six counties that housed these cities: Camden, Union, Hudson, Essex, Passaic, and Mercer, respectively.

Method:

We used the Augmented Synthetic Control Method to evaluate the effectiveness of the ERPO law on men and women in the six counties. First, we considered the impact of the law at the county level and then we applied the same framework separately for men and women. Control units included all counties from the eight most geographically proximate states that had not implemented an ERPO law: Kentucky, Maine, New Hampshire, North Carolina, Ohio, Pennsylvania, Tennessee, and West Virginia.

Result and conclusion:

When considering the entire population, the law was observed to reduce firearm homicides in Camden, Essex, Hudson and Union counties, but not in Mercer and Passaic. Among men, similar reduction in firearm homicide rates was observed in the four aforementioned counties. Only in Union did firearm homicide rates decline for women.

Significance:

Results suggest that the ERPO law had a significant impact in four of the six counties, with stronger effects observed among male subgroups. Further analysis could consider city-level comparisons between high- and low-crime areas to better understand local variation in policy outcomes by gender.

LATEBREAKER

COVID-19 Pandemic

Abstract Unavailable Jee Won Park* Jee Won Park Andrew Fenelon Andrew R. Zullo Jaquelyn L. Jahn Whitney N.L. Pirtle Tariz D. Viera-Rojas Alexandra Skinner John W. Jackson Chanelle J. Howe

Abstract unavailable

COVID-19 Pandemic

Prevalence and characteristics of post-acute sequelae of COVID-19 in recovered patients
Zuri Dale* Zuri Dale

Long COVID, also known as post-acute sequelae of SARS-CoV-2 infection, has emerged as a major public health concern following the COVID-19 pandemic. Although initially perceived as a respiratory illness, growing biomedical evidence confirms that COVID-19 affects multiple organ systems. This study aimed to explore the clinical manifestations, risk factors, and long-term outcomes associated with long COVID and to identify patients at highest risk. The research also contributes to the ongoing discourse on establishing a unified definition of long COVID.

A secondary analysis of a cross-sectional, community-based study was conducted using data from 168 households, representing a weighted total of 14,769 households in Third Ward, Houston, Texas. Data were collected via interviewer-administered surveys and included variables on demographics, pre-existing comorbidities, COVID-19 symptom severity, and post-acute symptom persistence. Symptom variables were recoded as binary indicators, and weighted logistic regression models were applied to identify associations between acute phase characteristics and the development of long COVID.

Risk factors significantly associated with long COVID included symptom severity during acute infection (OR = 29.58, 95% CI [1.38, 632.53]), heart disease (OR = 6.00, 95% CI [1.15, 31.28]), asthma (OR = 3.49, 95% CI [1.05, 11.59]), and poor physical health (OR = 4.20, 95% CI [1.12, 15.75]). Acute symptoms predictive of long COVID included anxiety (OR = 22.94, 95% CI [2.01, 262.31]), chest pain (OR = 7.15, 95% CI [1.13, 45.23]), constipation (OR = 16.81, 95% CI [1.33, 213.23]), heart palpitations (OR = 6.59, 95% CI [1.08, 40.18]), and shortness of breath (OR = 4.97, 95% CI [1.16, 21.36]). No statistically significant associations were found between long COVID and race, education, or income.

The findings underscore the multisystemic nature of long COVID, characterized by a diverse range of symptoms including fatigue, cognitive impairment, shortness of breath, and neuropsychiatric issues such as depression. While clinical factors are critical in understanding long COVID, the results also suggest that addressing associated health outcomes requires broader consideration of social determinants of health.

COVID-19 Pandemic

Covid-19 Survival Analysis in elderly patients, Rio de Janeiro Brazil Renan MVR Almeida* Renan Moritz VR Almeida Daniella Manhães Nogueira Núbia Karla de Oliveira Almeida

Objective: To evaluate the survival of elderly patients (≥60 y.o.) hospitalized for COVID-19 in the state of Rio de Janeiro, Brazil, February 2020 to December 2021.

Methods: This was a retrospective cohort study with COVID-19 hospitalization data provided by OpenDataSUS (a data repository maintained by the country's Ministry of Health). Individuals aged 60 years or older, hospitalized in the state of Rio de Janeiro, Brazil, were included. The variables analyzed were sex, age group, race/color (white x non-white), municipality of residence (Rio de Janeiro city x others), ICU admission, peregrination (travel between cities for health care), delay in admission, and year of occurrence (2020 x 2021). Survival estimates were obtained using the Kaplan–Meier method, and factors associated with risk of death were evaluated with the Cox proportional hazards model, α=5%. Goodness of fit was assessed by Harrel's C-index, and the R software (v.4.3) was used for all data analysis.

Results: Of the 1,473,182 hospital admissions during the period, 33,485 eligible cases were selected, and after missing or inconsistent data exclusion, 20,382 could be analyzed, with 11,939 deaths. Harrel's C-index was 0.563, and the model was statistically significant ($p<0.001$). A higher risk of death was observed for males (HR=1.05; 95% CI: 1.02–1.09), non-whites (HR=1.10; 95% CI: 1.07–1.15), those admitted to ICU (HR=1.26; 95% CI: 1.21–1.31), those in the older age group (HR=1.32; 95% CI: 1.27–1.37) and those with delayed admission (HR=0.86; 95% CI: 0.83–0.89). No significant associations were observed for municipality of residence, peregrination or year of admission.

Conclusion: The analysis identified clinical and sociodemographic factors associated with the risk of death in elderly patients hospitalized for COVID-19, with emphasis on advanced age and ICU admission. The findings reinforce the importance of using large databases to support planning and response to future public health emergencies.

COVID-19 Pandemic

Time to Death as an Indicator of Pandemic Preparedness During COVID-19 in South Korea

Suyoung Jo* Suyoung Jo Hyun-Kyung Kim Kyung-Duk Min Sung-il Cho

Background: Although COVID-19 mortality has been extensively studied, little is known about how long health systems were able to sustain individuals after diagnosis during pandemic surges. Time to death after diagnosis may reflect acute health system performance and resilience.

Objective: To quantify host vulnerability, immune burden, and structural health system-mediated factors associated with time to death within 90 days after COVID-19 diagnosis in South Korea.

Methods: We analyzed nationwide linked insurance claims and confirmed case records including 4,971,772 individuals diagnosed between October 2020 and June 2023. Follow-up was administratively censored at 90 days after the most recent diagnosis. Time to death was modeled using an accelerated failure time approach assuming a Weibull distribution. Covariates included age, recent vaccination within six months prior to diagnosis, insurance type, and pandemic period.

Results: A total of 24,326 deaths occurred within 90 days. Increasing age showed a strong graded association; individuals aged 80 years or older had survival times 92% shorter than those aged 20–34 years (95% CI 91%–92%). Marked structural inequities were observed, with medical aid beneficiaries showing survival times 22% shorter than employed insurance holders (95% CI 21%–22%). Individuals without recent vaccination had survival times 15% shorter than those vaccinated within six months (95% CI 14%–15%). Compared with the Omicron period, survival time was 25% longer during the pre-Delta period (95% CI 22%–27%) and 7% longer during the Delta period (95% CI 6%–9%).

Conclusions: Time to death after diagnosis revealed substantial disparities in acute health system performance by baseline host vulnerability, structural health system–mediated inequities, and immune burden. Modeling survival time provides a framework for identifying system-level vulnerabilities relevant to future pandemic preparedness.

COVID-19 Pandemic

Post-COVID-19 Cognitive Impairment: A systematic Review of Prevalence, Affected Domains and Underlying Mechanisms Snigdha Sahai* Snigdha Sahai Snigdha Sahai

Long-term cognitive consequences of COVID-19 have emerged as a critical public health concern in recent times. An increasing body of evidence indicates that individuals recovering from the SARS-CoV-2 infection frequently experience “brain fog” scientifically referred as cognitive impairments. These impairments consequently affect memory, attention, execution of decisions and processing speed, significantly affecting the quality of life and functional outcomes (Gwenaëlle Douaud et al., 2022). Therefore, understanding the prevalence, persistence and underlying mechanisms of post-COVID-19 cognitive deficits is crucial for developing targeted interventions and informing healthcare policies.

Objectives:
This study aims to systematically review and synthesize current evidence regarding post-COVID-19 cognitive impairments, focusing on their prevalence, affected cognitive domains, persistence over time and potential neuropathological mechanisms.

COVID-19 Pandemic

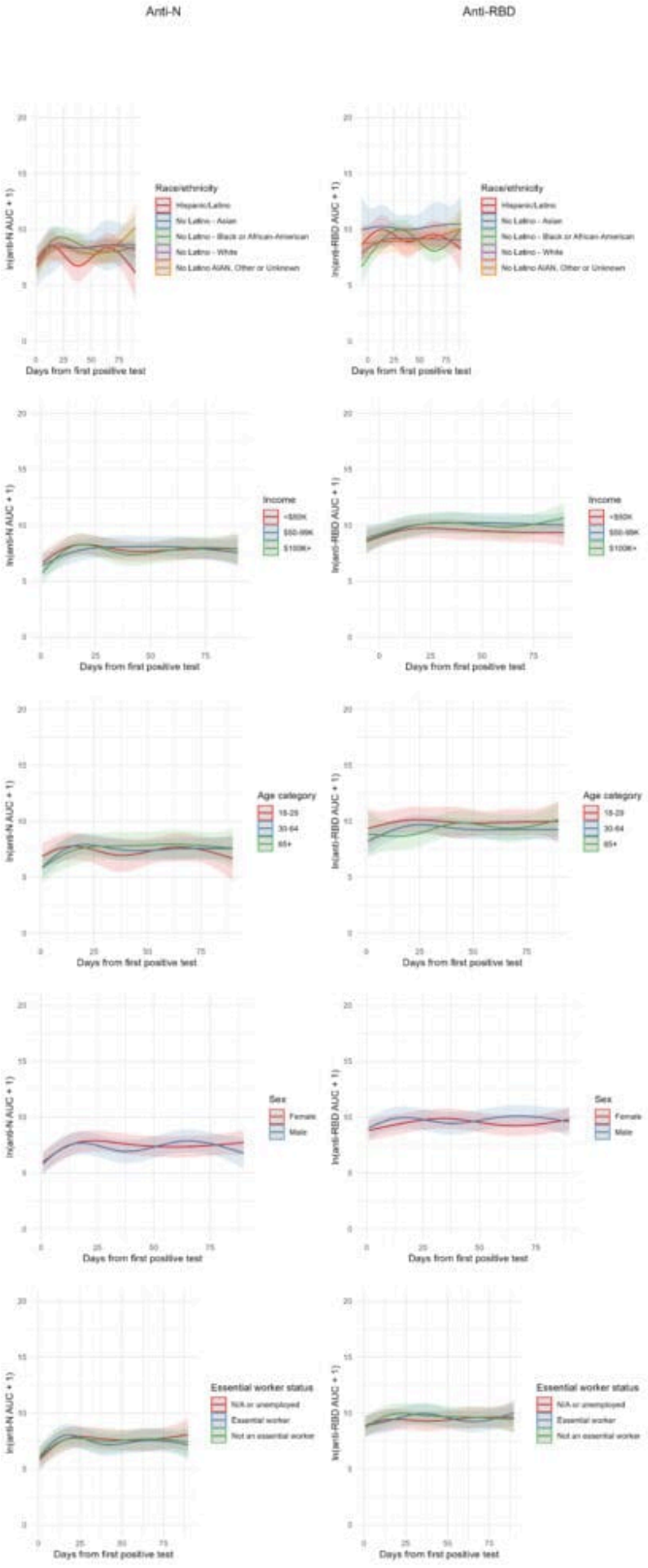
Demographic characteristics associated with SARS-CoV-2 antibody trajectories, February 2021 to January 2023 Ashley Judge* Ashley Judge David B Allison Stephanie Dickinson Anna LM Macagno Jon Macy Molly Rosenberg Christina Ludema

Background: Antibody trajectories after SARS-CoV-2 infection provide information on immune response to natural infection [i.e. Anti-Nucleocapsid proteins (Anti-N)] and both natural infection and vaccination [i.e. Anti-Receptor Binding Domain proteins (Anti-RBD)]. Information on differences in antibody trajectories after incident SARS-CoV-2 infection among demographic subgroups may inform potential targets for future public health interventions.

Methods: We used data from a prospective cohort study of ~2,100 US adults collected between February 2021 to January 2023 to compare trajectories of anti-N antibodies (measured in ln(1+ AUC) values) after incident infection by age group, sex, race/ethnicity, income, and essential worker status. For each demographic factor, we employed separate linear mixed-effect models with random subject-specific intercepts and an interaction term between the factor and time after infection, modelled with a natural cubic spline with four degrees of freedom. We estimated peaks in trajectories by locating the maximum estimated marginal mean of antibody values during the first 90 days after infection. We performed unadjusted pairwise comparisons of the predicted peak values for each demographic group. We restricted analyses to individuals vaccinated and without prior infection to assess whether these factors influenced conclusions.

Results: Among 430 individuals with an incident infection and complete data and among correctly identified peaks, there were no statistically significant differences in the magnitude of anti-N peaks by demographic factors. Among 402 vaccinated and among 324 without prior infection, conclusions remained consistent.

Conclusion: Initial immune response to natural infection appears to be robust in magnitude across a range of social and biological factors. Future work will refine methods to identify and model anti-RBD peaks and may assess whether there exist differences in peak timing.


Anti-N
Anti-RBD
ln(anti-N AUC + 1)
ln(anti-RBD AUC + 1)
Days from first positive test
Race/ethnicity
Hispanic/Latino
No Latino - Asian
No Latino - Black or African American
No Latino - White
No Latino AIAN, Other or Unknown
Income
<$50K
$50-99K
$100K+
Age category
18-29
30-64
65+
Sex
Female
Male
Essential worker status
N/A or unemployed
Essential worker
Not an essential worker

LATEBREAKER

Diabetes

Real-world Evidence of GLP-1 receptor agonists and Cardiovascular Outcomes among Diabetes: A Target Trial Emulation Motohiko Adomi* Motohiko Adomi Atsushi Goto Shinichi Goto Tomohiro Shinozaki Daisuke Yabe Kosuke Inoue

Background: Cardiovascular benefits of glucagon-like peptide-1 receptor agonists (GLP-1 RAs) have been established in randomized trials among patients with type 2 diabetes; however, evidence about whether benefits translate comparably across individual agents in routine clinical practice remains limited.

Objectives: To compare GLP-1 RA initiation versus DPP-4 inhibitor initiation on the risk of cardiovascular events and all-cause death.

Methods: Using the DeSC nationwide claims database in Japan (April 2014–March 2025), we applied an active comparator new-user design among adults with type 2 diabetes actively treated with ≥1 antidiabetic medication and without contraindications. The primary outcome was a composite of hospitalization for myocardial infarction, stroke, or heart failure, and all-cause death. Propensity score overlap weights and inverse probability of censoring weights were applied to address confounding and differential censoring, respectively. Cumulative risks at 24 months were estimated via pooled logistic regression, with RRs, RDs, and 95% CIs obtained using robust variance.

Results: A total of 114,282 patients (12,787 GLP-1 RA initiators, 101,495 DPP-4 inhibitors initiators) were included in the analysis. Mean age was 69.0 and 73.6 years, and 47.6% and 48.0% were female, in GLP-1 RA and DPP-4 inhibitor initiators, respectively. The weighted 24-month risk of the composite outcome was 15.5% (95% CI: 14.7–16.3) in GLP-1 RA initiators and 17.8% (95% CI: 17.4–18.3) in DPP-4 inhibitor initiators (reference), corresponding to RD of -2.3 percentage points (95% CI: -3.2, -1.5) and RR of 0.87 (95% CI: 0.82, 0.92).

Conclusions: In this nationwide cohort study in Japan, GLP-1 RA initiation was associated with a lower 24-month risk of cardiovascular events and all-cause death compared with DPP-4 inhibitor initiation. Agent-specific comparisons of liraglutide, dulaglutide, and semaglutide against DPP-4 inhibitors using a consistent design will also be presented.


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Diabetes

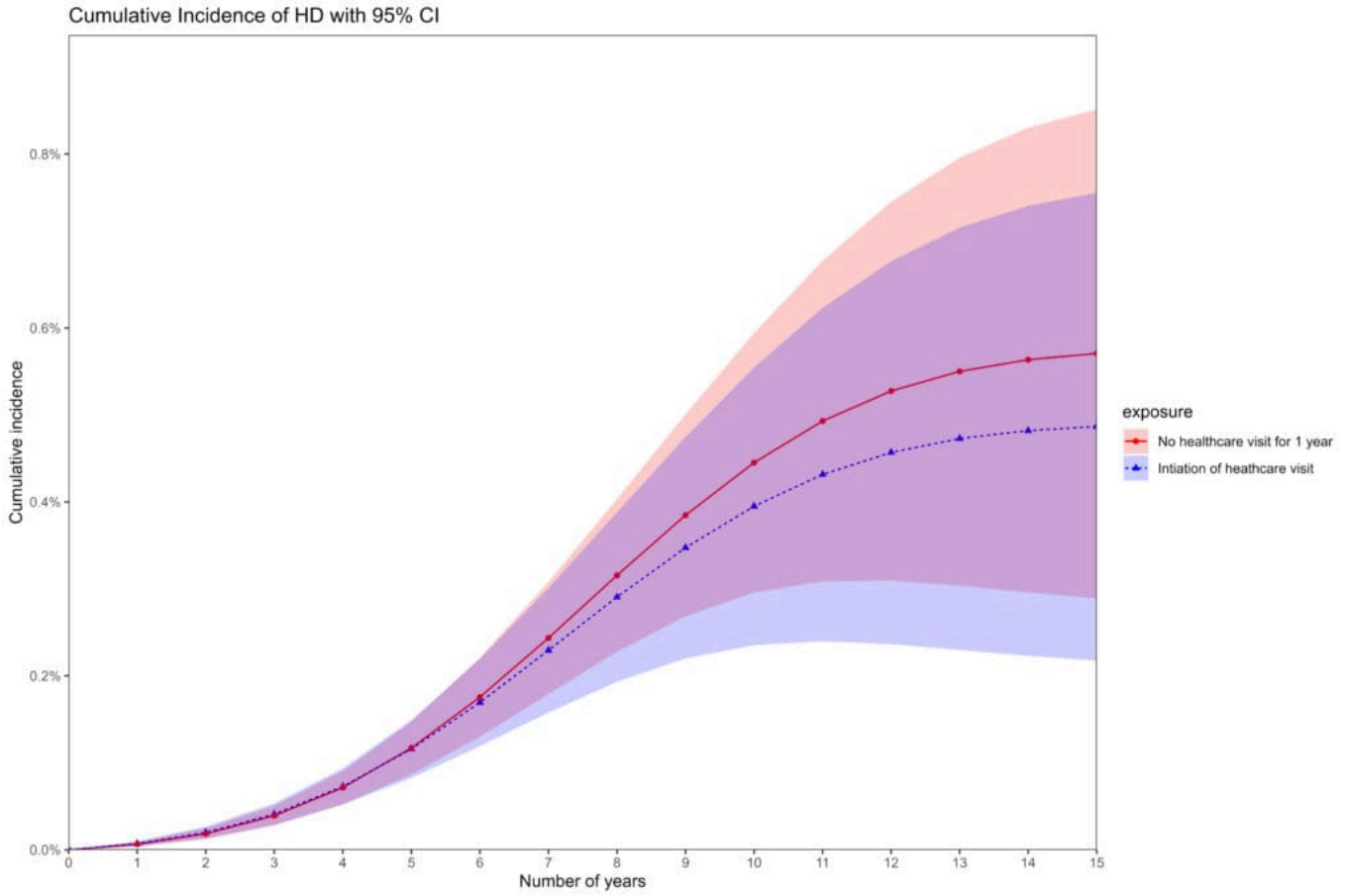
Early post-screening diabetes care and 10-year risk of hemodialysis initiation: a target trial emulation Kiyomitsu Fukaguchi* Kiyomitsu Fukaguchi Tomohiro Shinozaki Zui C. Narita Atsushi Goto

Background: Early engagement in diabetes care after screening could prevent kidney failure, but evidence on hard renal endpoints such as hemodialysis is limited.

Methods: We emulated a target trial using the nationwide JMDC Claims Database (>12 million beneficiaries) in Japan (2005–2021). Adults aged 40–74 years with newly screen-detected diabetes (HbA1c ≥6.5% or fasting glucose ≥126 mg/dL) and no history of renal failure or dialysis were eligible. Participants were assigned to: (1) initiating ≥1 diabetes-related visit <1 year after detection (Strategy 1), or (2) no diabetes-related visit <1 year (Strategy 2). To address immortal time bias and selection bias due to censoring, we used a clone–censor–weight approach. Stabilized inverse-probability weights were estimated using >30 baseline confounders (demographics, lifestyle, metabolic parameters including eGFR and proteinuria, and health-seeking behaviors) and time-varying confounders (cumulative healthcare visits, medications). Follow-up started at diabetes detection. Outcome was maintenance hemodialysis initiation. Weighted pooled logistic regression estimated 10-year risk differences (RD) and risk ratios (RR).

Results: Among 153,455 participants (mean age 53 years; 78% men), 54,278 initiated care <1 year and 71,659 did not; the remainder were censored. Hemodialysis occurred in 74 (Strategy 1) and 54 (Strategy 2) participants (total=128). Early care was associated with RD −0.12 percentage points (95% CI −0.74 to 0.32) and RR 0.94 (95% CI 0.51 to 1.51) at 10 years. Risk curves showed slight separation after approximately 7 years, but confidence intervals substantially overlapped throughout the follow-up.

Conclusions: Among adults with screen-detected diabetes, initiating care <1 year showed no clear association with 10-year hemodialysis risk. Given renal failure’s latency and slight later divergence, longer follow-up is warranted to clarify early engagement’s impact on hard renal outcomes.


Cumulative Incidence of HD with 95% CI
Cumulative incidence
0.0%
0.2%
0.4%
0.6%
0.8%
0
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
Number of years
exposure
No healthcare visit for 1 year
Intiation of heathcare visit

Diabetes

Associations Between Mental Health and Type 2 Diabetes Among Adolescents and Young Adults: The PAPAYA Study Cindy J Huang* Cindy Huang Shylaja Srinivasan Jennifer Y. Liu Julianna Deardorff Sonya Negriff Alka M. Kanaya Julia Acker Saher Daredia Andrew J. Karter Ai Kubo

Introduction: Adolescents and young adults (AYAs) with type 2 diabetes (T2D) face elevated mental health risks, but existing studies lack statistical power for subgroup analyses. We examined associations between T2D diagnosis and mental health outcomes among diverse AYAs within an integrated healthcare system and tested for effect modification by age, sex, and race/ethnicity.

Methods: This cross-sectional study used data from the Predictors of Adverse Cardiometabolic Problems in Adolescents and Young Adults (PAPAYA) cohort at Kaiser Permanente Northern California (KPNC) and included AYAs (adolescents: ages 10-19, young adults: ages 20-30), identified as of 1/1/2022. T2D was defined using a validated algorithm. Depression and anxiety were defined using ICD-10 diagnosis codes and screening tools (depression: PHQ-2 ≥ 3 and PHQ-9 ≥ 10; anxiety: GAD-7 ≥ 10). Logistic regression models estimated prevalence odds ratios (PORs) for associations between T2D diagnosis and each mental health outcome, adjusting for and testing effect measure modification (EMM) by age, sex, and race/ethnicity.

Results: Among 789,363 AYAs (50.3% female; race/ethnicity: 31.9% White, 25.7% Hispanic, 20.5% Asian, 7.2% multiracial, 6.9% Black, 7.8% other/unknown), 3,392 (0.43%) had a T2D diagnosis. AYAs with T2D had higher odds of depression (POR = 1.81, 95% CI: 1.68-1.95) and anxiety (POR = 1.60, 95% CI: 1.49-1.73), compared to AYAs without diabetes. EMM by age demonstrated that adolescents with T2D had higher odds of depression (POR = 2.73, 95% CI: 2.26-3.29) and anxiety (POR = 2.16, 95% CI: 1.78-2.62), with stronger associations compared with young adults (depression: p_int < 0.0001; anxiety: p_int = 0.003). EMM by race/ethnicity showed significant associations between all major racial/ethnic groups and depression (POR range: 1.62-2.53, p_int = 0.02). There was no evidence of effect modification by sex.

Conclusion: AYAs with T2D are at higher risk for depression and anxiety than their peers without diabetes. Adolescents with T2D experience particularly high mental health burden, underscoring the need for targeted interventions to support this high-risk subgroup.

Environment/Climate Change

Serum Perfluoroalkyl substances (PFASs) concentrations and associations with Mammographic Density in postmenopausal women Sabiha Nasrin* Sabiha Nasrin Katherine W. Reeves Youssef Oulhote Philippe Grandjean Jennifer Hadro

Perfluoroalkyl substances (PFAS) are possible carcinogens with widespread population exposure. Mammographic density (MD) is a strong, established biomarker of breast cancer risk and may provide insight into biological mechanisms linking PFAS exposure to breast carcinogenesis. However, evidence on associations between PFAS and MD remains limited.

Data were analyzed from 196 postmenopausal, cancer-free women not using hormone therapy from the Susan G. Komen Tissue Bank. Percent mammographic density (PMD) and dense breast area (DBA) were measured from digital mammography images taken near the time of blood donation. Serum PFAS concentrations were measured using online solid-phase extraction followed by high-pressure liquid chromatography with tandem mass spectrometry (HPLC-MS/MS). Associations were examined using multivariable linear regression, Bayesian Kernel Machine Regression (BKMR), and Quantile g-computation.

Participants had a mean age of 58.4 years and mean BMI of 29.6 kg/m^2, and most were White (71.4%). When evaluating individual PFASs through both traditional and mixtures approaches, only PFOA was significantly negatively associated with both PMD and DBA. There was some evidence of a positive association between PFUnDA concentration, categorized as quartiles, and PMD in the linear regression model, however this association was not supported by the mixtures analysis. No statistically significant associations were observed with other individual PFASs. BKMR analyses suggested a negative relationship between the total PFAS mixture and PMD, which was especially noted among parous women who had never breastfed. Quantile G-computation analyses, however, did not identify a statistically significant effect of the PFAS mixture on either measure of MD when exploring within the full study population or when stratifying on breastfeeding history.

This study adds to the limited literature by jointly evaluating individual and mixture PFAS effects on mammographic density.

LATEBREAKER

Environment/Climate Change

Associations of Neighborhood Built Environment Typologies and Mental Health in Children: Longitudinal Results from the All Our Families Cohort Tona Pitt* Tona Pitt Gavin McCormack Maria Ospina Suzanne Tough Sheila McDonald

Neighborhood built environment is associated with health outcomes, including mental health symptoms. Existing evidence is largely based on adult populations and mental health associations have primarily focused on neighborhood greenness. However, children may interact differently with their neighborhoods, and neighborhood environments are complex interactions of multiple built features beyond greenness.

This study aims to estimate the association of neighborhood typologies and mental health symptoms in children aged 5 to 12 years.

The All Our Families birth cohort (Calgary, Canada) measured parent-reported symptoms of anxiety, depression, hyperactivity, and inattention using the Behaviour Assessment System for Children at ages 5, 8, and 12. Clinical cut point of at-risk or higher was defined as outcome. Neighborhood was defined as 500m buffers from the participants dissemination area (the smallest census area, 400-700 people) representative point. Neighborhood typologies were developed using principal component analysis and k-means cluster analysis.

Generalized estimating equations adjusted on household characteristics, maternal characteristics, and neighborhood deprivation, were used to estimate adjusted risk ratios (aRRs) for the full cohort and sex-stratified analyses.

Five neighborhood typologies in Calgary were identified (Figure 1).

The study sample is 1,467 children (52% male) and 3,059 observations. Preliminary results suggest that compared with males who have the most access to useable parkland (Cluster 1), males living in low-density suburban neighborhoods (Cluster 2) and those with a higher proportion major roads (Cluster 5), have higher aRRs for anxiety (1.59 [95% CI: 1.02,2.51] and 1.82 [95%CI: 1.12,2.96], respectively). No significant associations for depression, inattention, hyperactivity or in females are observed.

Neighborhood typology is associated with elevated RRs in neighborhoods with low-density suburban form and major transportation corridors.

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LATEBREAKER

Environment/Climate Change

Higher exposure to environmental toxicants during pregnancy is associated with preterm hypertensive disorders of pregnancy in a prospective cohort of Black women. Gary Joseph* Gary Joseph Chelsea A. DeBolt Michal A. Elovitz Lauren Petrick

Background

Emerging evidence suggests that increased exposure to environmental toxins during pregnancy is associated with an increased risk of hypertensive disorders of pregnancy (HDP). Exposure to toxins is ubiquitous, and a better understanding of its effects on pregnancy health outcomes is needed. We evaluated the environmental determinants of preterm HDP in a prospective cohort of Black women in Philadelphia.

Methods

In a subset of 68 participants enrolled in a prospective cohort of Black pregnant women, we measured plasma environmental chemicals collected between 16- and 24-weeks' gestation via untargeted metabolomics. Cases of preterm HDP included women with gestational hypertension or preeclampsia who delivered before 37 weeks' gestation, while controls included those who delivered at term (≥ 37 weeks' gestation) without medical or obstetric comorbidities. Cases and controls (n=19 cases and 49 controls) were frequency matched by pre-pregnancy obesity (body mass index ≥30kg/m2), parity, insurance, education, and fetal sex. The association between $\log_2$-transformed individual's chemicals (n=32), dichotomized around the median (low/high), and HDP risk was assessed using logistic regression, while Weighted Quantile Sum regression (constrained in the positive direction) assessed the mixture effect, adjusted for the covariates.

Results

Higher exposure to 2-(phenyl methylene) octanal and carbofuran during pregnancy was associated with over 3-fold increase in the odds of HDP (OR: 3.28; 95%CI: 1.04- 10.27, and OR: 3.63, 95%CI: 1.06, 12.39, respectively). However, several environmental toxicants were significantly associated with a decreased risk of HDP. The mixture of chemicals was not significantly associated with the risk of HDP.

Conclusion

Our findings indicate a possible association between higher exposure to some environmental toxicants during pregnancy and increased risk of HDP in Black women. Larger prospective analyses are needed to strengthen this association.

LATEBREAKER

Environment/Climate Change

Prenatal air pollution exposure and placental vascular development in Pittsburgh, Pennsylvania Fariha Hoque Rimu* Fariha Hoque Rimu Shivram Kumar Carolyn M. Salafia Theresa Girardi Richard Miller Sally W. Thurston Donald Harrington Pathik D. Wadhwa Claudia Buss Jill Tarr Yihui Ge Albert Presto Philip K. Hopke Hyagriv Simhan Thomas G. O'Connor Junfeng Zhang David Q. Rich

Background: Air pollution exposure has been associated with reduced fetal growth and birth-size with changes in placental vascular structure proposed as mediators of this association. Previously, we reported that early-pregnancy NO2 exposure was associated with altered chorionic surface arterial vasculature in pregnant Rochester, NY residents.

Objective: We examined associations between gestational-week residential PM2.5 and NO2 concentrations and increases/decreases in placental chorionic surface vasculature in pregnancies of Pittsburgh, PA residents.

Methods: Using placenta photographs from term deliveries of 51 pregnant women in the Magee-Women's Research Institute cohort, we estimated 17 chorionic plate surface vessel outcomes. We used distributed lag models to determine if/when gestational week (0–37) PM2.5 and NO2 concentrations were associated with each outcome.

Results: Each 4-ppb increase in PM2.5 during weeks 8–22 and 6-19 was associated with decreased mean arc length (-0.30 cm; 95% CI = -0.57, -0.04) and decreased standard deviation of arc length (-0.26 cm; 95% CI = -0.50, -0.03) respectively. $PM_{2.5}$ during weeks 16-28 was associated with decreased mean tortuosity (-0.02; 95% CI = -0.03, 0.00). During weeks 4-16 and 14-24 weeks, PM2.5 was associated with decreased arterial-end to venous-end distance (-0.01 cm; 95% CI = -0.02, 0.00) and mean artery-vein distance (-0.10 cm; 95% CI= -0.18, -0.02), respectively. Each 4-ppb increase in NO2 during weeks 0-10 was associated with increased mean distance from arterial endpoint to venous endpoint (0.07 cm; 95% CI: 0.04, 0.10).

Conclusion: Although we had limited sample size, we found associations between early- and mid-pregnancy PM2.5 and NO2 and changes in arterial length, variability in length, and arterial branching in the placenta. These findings suggest altered placental angiogenesis and vascular development is associated with increased residential air pollution exposure during pregnancy.

LATEBREAKER

Environment/Climate Change

Air Pollution, Incident Stroke, and Mortality in the REasons for Geographic and Racial Differences in Stroke Physical Activity Ancillary Study Yingyan Wu* Yingyan Wu Leidys Gutierrez Martinez Elizabeth Rose Mayeda Marcia Pescador Jimenez

Higher ambient air pollution, such as particulate matter 2.5 (PM2.5), has been linked to increased stroke risk and mortality in prior research. It may also lead individuals to decrease physical activity, creating an indirect behavioral path linking PM2.5 to stroke. Our overall objective was to evaluate whether physical activity mediates the path between PM2.5 and stroke. As an initial step in mediation analysis, we estimated the total effect of PM2.5 on incident stroke and mortality. We included participants from the REasons for Geographic and Racial Differences in Stroke (REGARDS) Physical Activity Accelerometer Ancillary Study (2009–2013; n=7,663; mean age 57.6 years; 57% women, 31% Black) followed through 2022. Residential exposure to annual PM2.5 was dichotomized as upper quartile vs. lower three quartiles. We fit pooled logistic regression models adjusted for baseline covariates: age, sex, race, education, household income, marital status, urbanicity, neighborhood SES, smoking, and health conditions (diabetes, hypertension, left ventricular hypertrophy, atrial fibrillation, history of heart disease). We estimated adjusted cumulative incidence curves and derived risk ratios (RR) and risk differences (RD) at 5 and 10 years for stroke and mortality separately; 95% confidence intervals (CIs) were obtained via bootstrapping. We observed 350 cases of stroke and 1,881 deaths over 13 years of follow-up. Adjusted models unexpectedly suggested an inverse association between PM2.5 and incident stroke at 10 years of follow-up (RR=0.65, 95% CI: 0.49, 0.84). Participants residing in areas with PM2.5 concentrations in the highest quartile had a 1.11 (95% CI: 1.02, 1.22) times the risk of all-cause mortality over 10 years compared with those in the lower three quartiles (Figure). Ongoing analyses will address competing risks between stroke and death, investigate potential uncontrolled confounding, and conduct mediation analysis to formally assess the role of physical activity.

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LATEBREAKER

Environment/Climate Change

Associations Between Ambient Exposure to Styrene, Benzene, Toluene, Ethylbenzene, and Xylenes and Hospitalizations in the US Gulf Region Yongsoo Choi* Yongsoo Choi Chi-Tsan Wang Joshua L. Warren Jung-Hun Woo Lawrence S. Engel Bok Haeng Baek Michelle L. Bell

Styrene, benzene, toluene, ethylbenzene, and xylenes (SBTEX) are hazardous air pollutants studied primarily in occupational settings, where high exposures are linked to adverse health outcomes and subject to strict regulation. In contrast, the health impacts of ambient SBTEX exposure, which occurs at lower concentrations, remain poorly characterized.
The study population comprised Medicare beneficiaries aged 65 years and older in the US Gulf region during 2011–2016. Outcomes were hospitalizations for cardiovascular and respiratory diseases. Ambient SBTEX exposures were derived from validated prediction models with high spatial (4 × 4 km) and temporal (daily) resolution. A time-stratified case-crossover design with conditional logistic regression was applied.
We observed significant associations between ambient concentrations of benzene, toluene, ethylbenzene, and xylenes (BTEX) and cardiovascular and respiratory hospitalizations, but not for styrene. An interquartile range increase in daily mean benzene concentration (0.087 ppb) was associated with a 0.38% (95% CI: 0.08, 0.68) increase in cardiovascular hospitalizations at lag 0 and a 1.00% (95% CI: 0.60, 1.41) increase over lags 0–7. The corresponding increases in respiratory hospitalizations were 0.88% (95% CI: 0.50, 1.25) at lag 0 and 2.74% (95% CI: 2.29, 3.19) over lags 0–7. Similar associations were observed for toluene, ethylbenzene, and xylenes. An interquartile range increase in total BTEX (0.297 ppb) was associated with increases of 0.85% (95% CI: 0.44, 1.27) and 1.87% (95% CI: 1.41, 2.32) in cardiovascular and respiratory hospitalizations over lags 0–7, respectively.
Even at low ambient concentrations, BTEX exposures may increase the risk of cardiovascular and respiratory hospitalization among older adults. These findings support greater public health attention to ambient BTEX, extending beyond traditional concerns focused on occupational and industrial settings.

LATEBREAKER

Environment/Climate Change

Particulate Matter Waves and Mortality: Evidence from 37 Countries and 340 Cities Garam Byun* Garam Byun Haidong Kan Masahiro Hashizume Ho Kim Yasushi Honda Satbyul Estella Kim Ben Armstrong Antonio Gasparrini Michelle L. Bell MCC Collaborative Research Network

Background: The association between daily particulate matter (PM) and mortality is well documented. However, the health effects of sustained exposure to high PM levels over several consecutive days (PM wave) are less understood, and evidence across diverse regions is limited. We evaluated short-term associations between PM waves and mortality across multiple countries and cities.

Methods: We collected data for daily all-cause mortality and PM10 and/or PM2.5 concentrations from 37 countries and 340 cities from 1995 to 2019. PM wavs were defined using different combinations of concentration thresholds (relative or absolute) and duration. City-specific effects of PM waves over lag 0-1 were estimated using two approaches: (1) time-series analysis and (2) a matched design that matched each PM wave day to non-wave days within the same city, year, month, and day of week. The overall effect compared PM wave versus non-wave days, and the added effect further controlled for daily PM. City-specific estimates were pooled using multilevel random-effects meta-analysis.

Results: Preliminary results indicated that PM10 waves were associated with increased mortality. Using the city-specific 90th percentile threshold for ≥3 days, PM10 waves were associated with a 0.96% increase in mortality (95% CI 0.44, 1.47%) for the overall effect and a 0.50% increase (95% CI 0.06, 0.94%) for the added effect in time-series analyses. Using an absolute threshold (PM10 ≥ 75 µg/m3 for ≥3 days) yielded 1.19% (95% CI 0.71, 1.68%) for the overall effect and 0.59% (95% CI 0.24, 0.95%) for the added effect. Results were consistent in the matched design. PM2.5 wave estimates were positive but not statistically significant.

Conclusions: Multi-day high PM10 episodes were associated with elevated mortality beyond the effect of high daily concentrations alone, suggesting additional risk during persistent pollution periods. PM wave indicators may complement daily PM metrics in early warning and response systems.

Environment/Climate Change

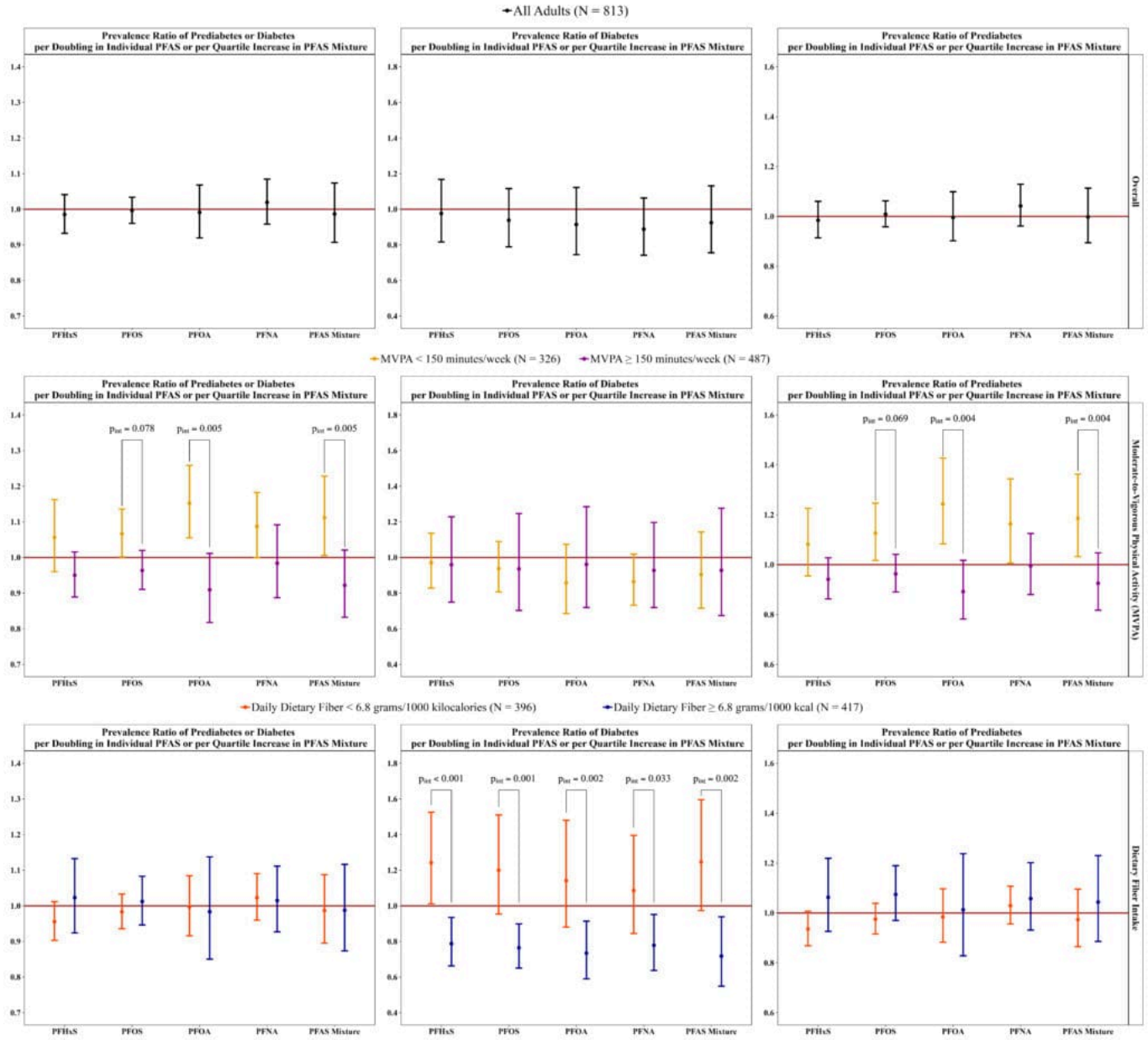
Association of PFAS Exposure with Prevalent Prediabetes or Diabetes among Adults in the United States: Effect Modification by Physical Activity and Dietary Fiber Intake Jennifer Arzu* Jennifer Arzu Joseph Braun

Per- and polyfluoroalkyl substances (PFAS) exposure have been linked to type 2 diabetes. However, few studies have investigated lifestyle behaviors that may modify these associations. We explored whether the associations of PFAS with prevalent prediabetes or diabetes differ by moderate-to-vigorous physical activity (MVPA) and dietary fiber intake.

This study analyzed data from 813 non-pregnant adults ages ≥20 years in the 2017–2020 U.S. National Health and Nutrition Examination Survey. Using survey-weighted modified Poisson regression models, we estimated the covariate-adjusted prevalence ratios of prediabetes/diabetes (i.e., self-report, fasting plasma glucose≥100 mg/dL, or HbA1c≥5.7%), diabetes only (i.e., self-report, fasting plasma glucose≥126 mg/dL, or HbA1c≥6.5%), and prediabetes only (i.e., self-report, fasting plasma glucose≥100 and <126 mg/dL, or HbA1c≥5.7% and <6.5%, excluding diabetes) per doubling in serum perfluorohexane sulfonic acid (PFHxS), perfluorooctane sulfonic acid (PFOS), perfluorooctanoic acid (PFOA), perfluorononanoic acid (PFNA) concentrations. We used quantile g-computation models to estimate these associations per 1-quartile increase in PFAS mixture.

We observed no overall associations of PFAS with prevalent prediabetes or diabetes. Among adults who were less physically active (MVPA<150 minutes/week), higher PFOS, PFOA, and PFAS mixture were associated with 7% [PR:1.07 (95% CI:1.00,1.14)], 15% [PR:1.15 (95% CI:1.06,1.26)], 11% [PR:1.11 (95% CI:1.00,1.22)] higher prediabetes/diabetes prevalence, but with 4% [PR:0.96 (95% CI:0.91,1.02); pinteraction=0.078], 9% [PR: 0.91 (95% CI:0.82,1.01); pinteraction=0.005], and 8% [PR:0.92 (95% CI:0.83,1.02); pinteraction=0.005] lower prevalence among adults meeting the MVPA guidelines (≥150 minutes/week). We found similar patterns of associations between PFAS and prevalent prediabetes across physical activity levels. The associations of PFHxS, PFOS, PFOA, PFNA, and PFAS mixture with prevalent diabetes were consistently positive among adults with lower fiber intake (≤median of 6.8 gram/1000 kcal) and inverse among adults with higher fiber intake (>median of 6.8 gram/1000 kcal) [pinteraction=0.0001, 0.001, 0.002, 0.033, and 0.002 respectively]. For example, each doubling in PFHxS was associated with 24% [PR:1.24 (95% CI:1.01,1.53)] higher diabetes prevalence in adults with lower fiber intake, but 21% [PR:0.79 (95% CI: 0.66,0.94)] lower prevalence in adults with higher fiber intake.

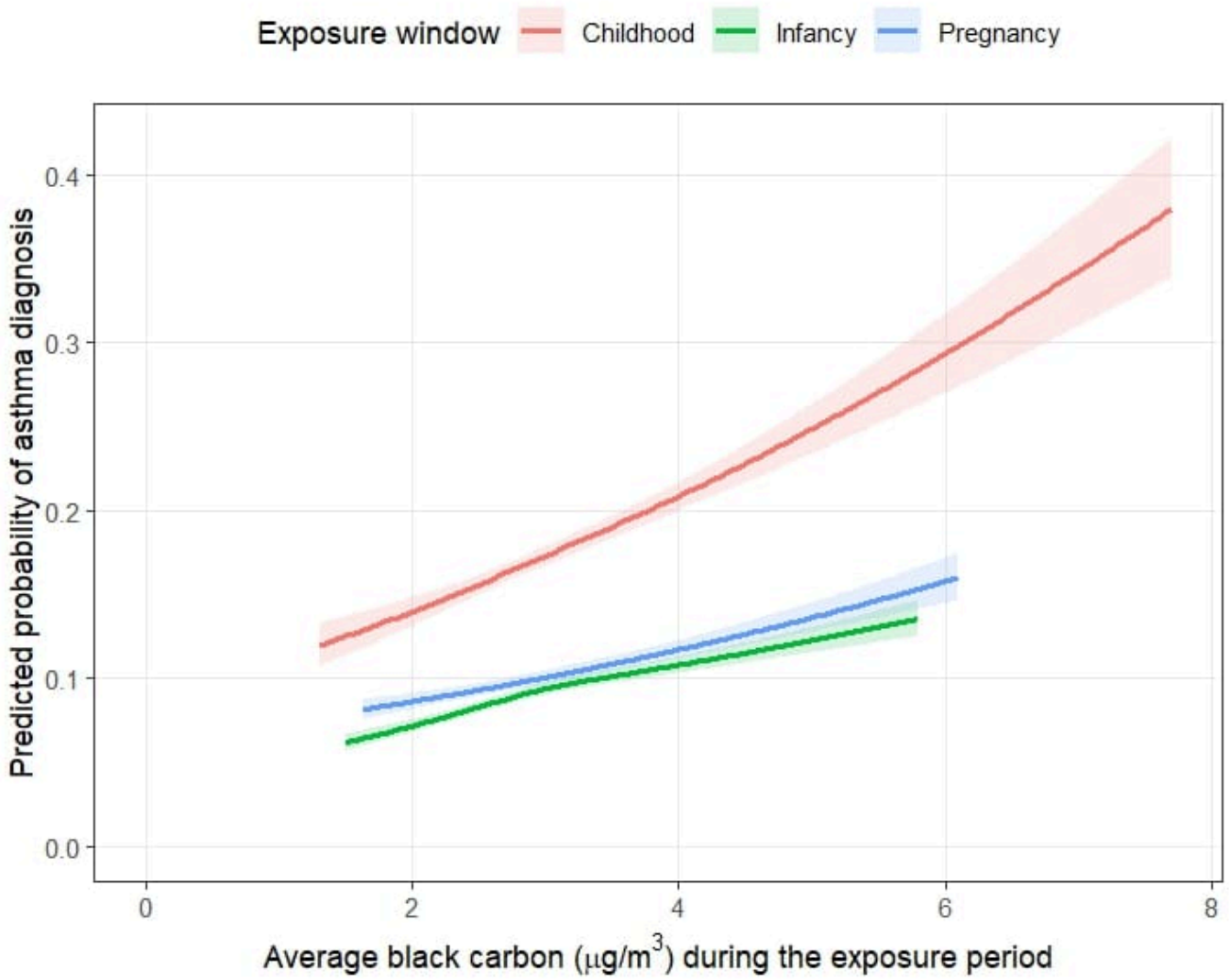
Physical activity levels and dietary fiber intake modified the associations of individual PFAS and their mixture with prediabetes or diabetes prevalence.


All Adults (N = 813)
Prevalence Ratio of Prediabetes or Diabetes per Doubling in Individual PFAS or per Quartile Increase in PFAS Mixture
Prevalence Ratio of Diabetes per Doubling in Individual PFAS or per Quartile Increase in PFAS Mixture
Prevalence Ratio of Prediabetes per Doubling in Individual PFAS or per Quartile Increase in PFAS Mixture
Overall
PFHxS
PFOS
PFOA
PFNA
PFAS Mixture
MVPA < 150 minutes/week (N = 326)
MVPA ≥ 150 minutes/week (N = 487)
p_int = 0.078
p_int = 0.005
p_int = 0.005
p_int = 0.069
p_int = 0.004
p_int = 0.004
Moderate-to-Vigorous Physical Activity (MVPA)
Daily Dietary Fiber < 6.8 grams/1000 kilocalories (N = 396)
Daily Dietary Fiber ≥ 6.8 grams/1000 kcal (N = 417)
p_int < 0.001
p_int = 0.001
p_int = 0.002
p_int = 0.033
p_int = 0.002
Dietary Fiber Intake

Environment/Climate Change

Association between early life traffic-related exposures and subsequent childhood asthma development in the Tennessee Medicaid population: A retrospective cohort study Akihiro Shiroshita* Akihiro Shiroshita Pingsheng Wu Tebeb Gebretsadik Kai Zhang Brittney Snider Alexandra Sundermann Tan Ding Tina Hartert

Traffic-related exposures during early life are associated with increased risk of childhood asthma. However, most studies have not accounted for residential relocation, and were conducted primarily in urban settings and in highly selected populations. In this study, we evaluated eight measures of traffic-related exposure among children enrolled in the Tennessee Medicaid program (TennCare), a vulnerable low-income population. We constructed three cohorts based on exposure windows: a dyad cohort (exposure during pregnancy), an infant cohort (exposure during the first year of life), and a childhood cohort (exposure during the first four years of life). Traffic-related exposures included road proximity, traffic density and road length within a 500-m buffer, and nitrogen dioxide and black carbon levels estimated using previously validated machine learning models. To account for residential relocation during the exposure window, exposures were weighted by the number of months each child resided at each address. The outcome was childhood asthma, defined using ICD-9/10 diagnosis codes and medication prescriptions between ages 4 and 6 years. Logistic regression models were fitted, adjusting for clinically meaningful covariates, and exposures were modeled using restricted cubic splines. A total of 455,116 (dyad), 552,080 (infant), and 489,360 (child) children were included in each cohort. About 10–15% of children had an asthma diagnosis across cohorts. Across all exposure windows, higher average black carbon levels during the exposure period were consistently associated with an increased risk of childhood asthma (Figure). In contrast, other traffic-related indicators did not capture biologically plausible dose-response relationships with asthma. These findings suggest that reducing black carbon exposure among pregnant women and children may be an effective strategy for mitigating childhood asthma risk.


Exposure window
Childhood
Infancy
Pregnancy
Predicted probability of asthma diagnosis
0.0
0.1
0.2
0.3
0.4
0
2
4
6
8
Average black carbon (μg/m3) during the exposure period

Environment/Climate Change

Community Health Impacts of the Tijuana River Pollution Crisis: Results from the Healthy Water Healthy Air Study Baseline Community Health Survey Yu Ni* Yu Ni Elizabeth Mikita Christine T Loftus Jamie Moody Savannah Shifflett Penelope J.E. Quintana Paula Stigler Granados

Background: Untreated sewage and industrial waste carried by the Tijuana River has created a longstanding transboundary environmental crisis. This pollution has significantly intensified since July 2024, with border community members reporting noxious odor and major health symptoms. In response to these escalating community concerns, we launched the Healthy Water Healthy Air Study.

Methods: A bilingual online survey was conducted to establish a comprehensive community profile characterizing members' environmental perceptions, health symptoms, and precautionary behaviors as indicator of resilience. We performed descriptive analyses and further Poisson regressions to estimate the associations of environmental perceptions with health symptoms and precautionary behaviors, controlling for sociodemographic characteristics.

Results: By October 2025, 409 community members (primarily women, White, and of relatively high socioeconomic status) completed the survey. Most participants expressed high concern regarding local air and water quality, with frequent malodor exposure. A wide range of health symptoms were reported, most notably upper respiratory symptoms (74%), certain gastrointestinal symptoms such as nausea (50%) and bloating (52%), and psychological distress. Perceptions of poorer air quality, more frequent exposure to malodor, and occurrence of boil water notices were associated with a 28-80% higher prevalence of any upper respiratory symptoms, a 1.41-3.51-fold increase in expected counts of gastrointestinal symptom scores, a 1.70-2.19-fold increase in psychological distress symptoms and high-risk behaviors, and a 1.31-4.16-fold increase in precautionary behaviors.

Conclusion: This study is among the very few to understand the health and behavioral impacts of border communities during the Tijuana River pollution crisis. The findings support current and future public health interventions and binational policy changes aimed at mitigating transboundary sewage pollution.

Environment/Climate Change

Residential mobility and exposure misclassification of $PM_{2.5}$ among pregnant Medicaid enrollees from 2001-2014 Stefania Papatheodorou* Stefania Papatheodorou Yinying Qian Krista Huybrechts Sonia Hernandez Diaz Matthew Shupler Wanyu Huang Xinye Qiu Michael Leung Michele Hayon Choi Yaguang Wei Joel Schwartz Brent Coull Christopher J. McDougle Antonella Zanobetti Marc Weisskopf

Background:
Residential mobility during pregnancy can introduce exposure misclassification in environmental epidemiology and is socially patterned. However, large-scale evidence on prenatal mobility and the direction and magnitude of associated changes in $PM_{2.5}$ exposure remains limited.

Methods:
We analyzed 1,548,303 Medicaid-covered pregnancies in the United States (2001–2014). Residential mobility was defined as a change in ZIP code between the last menstrual period (LMP) and delivery. Movers were classified by directional change in ambient $PM_{2.5}$ exposure between LMP and delivery (High→High, High→Low, Low→High, Low→Low), based on the median annual ZIP code $PM_{2.5}$ (10.8 $\mu g/m^3$). Maternal sociodemographic, neighborhood, and clinical characteristics were compared using standardized mean differences (SMDs).

Results:
Overall, 259,918 pregnancies (16.8%) involved residential mobility. Movers were younger (mean age 23.4 vs. 24.8 years; SMD −0.23), more likely to be Black (37.0% vs. 31.6%), and had a median (IQR) move distance of 12.4 (6.5–23.8) km. Most moves were from high-to-high (32.7%) or low-to-low (31.9%) $PM_{2.5}$ areas. The overall mean $PM_{2.5}$ difference was -0.55 $\mu g/m^3$ (SD 4.12), masking substantial heterogeneity, as indicated by the movement from low to high $PM_{2.5.5}$ areas (13%) were associated with a mean increase of 3.9 $\mu g/m^3$, while moves from high- to low-$PM_{2.5}$ areas (18%) showed a mean decrease of -4.7 $\mu g/m^3$. Moves into higher-exposure areas were associated with greater neighborhood disadvantage, whereas moves into lower-exposure areas were associated with higher household income, homeownership, and lower neighborhood poverty. Movers also had modestly higher prevalence of selected comorbidities (all SMDs <0.20).

Conclusions:
Approximately one in six Medicaid-covered pregnancies involved residential mobility, often over short distances but frequently accompanied by meaningful changes in $PM_{2.5}$ exposure and neighborhood context. These findings underscore residential mobility as an important source of differential exposure misclassification in perinatal environmental health studies.

Environment/Climate Change

Radon exposure and cognitive impairment Yijia Zhang* Yijia Zhang Shai Bejerano Meghan Angley Longxiang Li Ka Kahe

Background Ionizing radiation exposure may contribute to cognitive impairment. Radon is a ubiquitous radioactive gas that can expose the brain to low-dose radiation, but evidence linking radon exposure to cognitive outcomes remains limited.

Methods We included 24,652 participants from the Reasons for Geographic and Racial Differences in Stroke (REGARDS) Study who were free of baseline cognitive impairment and stroke and had complete exposure and outcome data. Radon exposure was assigned using monthly ZIP Code–level estimates generated via machine learning, with radon level at enrollment used as the exposure. Radon was analyzed as a binary variable using a cutoff of 2 pCi/L, corresponding to the US Environmental Protection Agency–recommended level at which mitigation should be considered. Global cognitive status was assessed using the Six-Item Screener (SIS). Cognitive impairment was defined as either a SIS score <4 on the most recent assessment or in a sensitivity analysis SIS scores <4 on the 2 most recent assessments. Associations were estimated using ORs with 95% CIs.

Results Approximately 9.3% of participants resided in ZIP codes with radon levels ≥2 pCi/L. After adjustment for demographic, socioeconomic, lifestyle, and health factors, radon exposure was not associated with cognitive impairment overall in this predominantly low-radon cohort. However, smoking status modified the association. Among never smokers, radon exposure ≥2 pCi/L was associated with increased odds of cognitive impairment defined by the most recent SIS <4 (OR, 1.26; 95% CI, 1.05–1.50) and by SIS <4 on the 2 most recent assessments (OR, 1.35; 95% CI, 1.05–1.75). No associations were observed among ever smokers.

Conclusion In a large population predominantly residing in low-radon regions, radon exposure ≥ 2 pCi/L was associated with cognitive impairment among never smokers but not ever smokers. Further studies are needed to clarify potential confounding, particularly from competing risks.

Environment/Climate Change

Country-level associations of climate related disasters and anxiety disorder Anna Krasnova*
Anna Krasnova Michaeline Bresnahan Inge van Balkom Keely Cheslack-Postava

Background: Climate-related natural disasters have lasting biological and psychological consequences, yet evidence on their association with anxiety disorders is limited. We examined country-level association between climate-related disasters and estimated incidence of anxiety disorders across 68 countries from 1990-2019, assessing potential heterogeneity by age and time period.

Methods: Data on climate-related disasters, including extreme temperature, wildfire, storm, flood, and drought, was from the International Disaster Database. Estimated incidence of anxiety disorder by country was obtained from the Global Burden of Disease Collaborative Network. We utilized generalized linear mixed models to estimate the within-country association of annual exposure to climate-related disaster with anxiety disorder incidence, reporting exponentiated regression coefficients (β). Models adjusted for the calendar year, lagged effects of total disaster count, region, proportion of females, number of physicians per 1,000 people, unemployment rate, population density, gross domestic product per capita, life expectancy at birth.

Results: We found heterogeneity by age and time-period in the association between country-level exposure to climate-related disasters and estimated incidence of anxiety disorder. Exposure to 2 or more disasters was associated with a greater incidence of age-standardized anxiety (β = 1.009, 95% CI 1.003, 1.016) in 1990-2004, but not in 2005-2019. In 1990-2004, but not in 2005-2019, exposure to extreme temperature, wildfires, droughts, and 2 or more floods was associated with greater incidence of age-standardized anxiety. Among children age ≤14, exposure to 1 (β = 1.012, 95% CI 1.003, 1.021) and 2 or more (β = 1.015, 95% CI 1.005, 1.025) disasters, respectively, was associated with greater incidence of anxiety in 2005-2019 but not in 1990-2004.

Conclusions: Approaches to address anxiety related to climate change among children and adolescents may be warranted.

LATEBREAKER

Environment/Climate Change

Drinking Water Lithium Exposure and Risk of All-Cause and Cause-Specific Dementia in the United States: A Cohort Analysis of the All of Us Research Program Se-Hyun Hwang* Se-Hyun Hwang Hyeong-Moo Shin

Background: Lithium is a naturally occurring trace element in food and drinking water and is widely used therapeutically for bipolar disorder. Experimental and clinical evidence suggests potential neuroprotective effects, but epidemiologic findings on lithium and dementia remain inconsistent. We examined the association between drinking water lithium exposure and incident dementia in the U.S.

Methods: Drinking water lithium concentrations were obtained from the U.S. EPA's Fifth Unregulated Contaminant Monitoring Rule (UCMR 5). Regression kriging was applied to estimate nationwide lithium concentrations using UCMR 5 data, U.S. Geological Survey's groundwater levels and primary water sources. Concentrations were averaged at the 3-digit ZIP code level and linked to participants in the All of Us Research Program by residential location. Dementia outcomes (all-cause dementia, Alzheimer's disease [AD], and vascular dementia [VD]) were ascertained from electronic health records. Lithium exposure was categorized into four groups. Cox proportional hazards models estimated hazard ratios (HRs), with stratified analyses by sex, age, APOE ε4 carrier status, obesity status, and insurance status.

Results: Among participants residing in the same ZIP code for >5 years, the highest lithium exposure category was associated with a lower hazard of AD (HR = 0.287, 95% CI: 0.097–0.855). Within this group, inverse associations were stronger among APOE ε4 carriers (HR = 0.097, 95% CI: 0.017–0.557) and those with obesity (HR = 0.070, 95% CI: 0.007–0.689). For VD, higher lithium exposure was associated with lower risk among participants living in areas where ≥80% of drinking water was supplied by community water systems (p-trend = 0.027).

Conclusion: Higher estimated drinking water lithium exposure was associated with lower hazards of select dementia outcomes, with stronger inverse associations in specific subgroups. Replication with improved individual-level exposure assessment is warranted.

Genetics

Associations of hematological traits-related polygenic risk scores with liver function Kyeezu Kim* Hye-Young PARK Yoosoo Chang Seungho Ryu

Emerging evidence supports a hematological–hepatic axis linking liver function and blood cell traits. We examined associations between blood cell polygenic risk scores (PRSs) and liver-related phenotypes. We calculated PRSs for 13 hematological traits–red blood cell count (RBC), hemoglobin (Hb), hematocrit (Hct), platelet, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), white blood cell count (WBC), basophil, eosinophil, lymphocyte, neutrophil, and monocyte–in 6,671 adults. Liver phenotypes included serum alanine aminotransferase (ALT), aspartate aminotransferase (AST) levels, and fibrosis-4 (FIB-4) index. We examined associations between hematological PRSs and liver-related phenotypes using multivariable linear and logistic regression, adjusting for sociodemographic, behavioral, and clinical factors and stratifying by sex.

Compared with the lowest tertile, the middle tertile of platelet PRS was inversely associated with ALT and AST (ALT: $\beta = -1.37$ AST: $\beta = -0.36$, both $p = 0.01$), whereas the highest tertiles of MCV, MCHC, and eosinophil PRSs were associated with higher ALT ($\beta = 1.02$-1.17) and AST levels ($\beta = 0.87$-0.99; all $p < 0.05$). The highest tertiles of platelet and neutrophil PRSs were associated with lower FIB-4 scores (platelet: $\beta = -0.08$, neutrophil: $\beta = -0.02$; all $p \leq 0.01$) and reduced fibrosis severity (platelet PRS: OR = 0.49, $p = 0.002$) while higher tertiles of Hct, MCH, and MCHC were associated with higher FIB-4 scores ($\beta = 0.015$-0.019, $p < 0.05$). Sex-specific associations were observed, with stronger effects of platelet, eosinophil, and MCH PRSs in men; monocyte PRS was associated only in men, whereas RBC, Hct, Hb, neutrophil, and lymphocyte PRSs were associated only in women. MCV and MCHC showed opposite associations with ALT by sex (both p-interaction < 0.01).

Together, our findings support a trait- and sex-specific genetic link between blood cell traits and liver function.

Genetics

Integration of functional genomics in variant-to-gene annotation for Alzheimer's Disease pathway-specific polygenic risk score construction Katrina Bazemore* Katrina Bazemore Taha Iqbal Jin Sha Joseph Manuel Jacob Haut Wan-Ping Lee Yi Zhao Otto Valladares Li-San Wang Gerard D. Schellenberg Jin Jin Adam C. Naj

Pathway-specific polygenic risk scores (pathway PRS) measure aggregated genetic liability to disease within biological pathways, better representing the heterogeneity of individual-level genetic risk composition than global PRS. Pathway PRS measure liability across single nucleotide variants annotated to genes in the pathway of interest. In application, most variant-to-gene annotation is based on variant position with respect to gene boundaries. This is error-prone for intergenic and intronic variants, which can regulate gene expression at long distances and are a large proportion of risk variants for Alzheimer's Disease (AD). We hypothesized that integrating chromatin interaction and expression quantitative trait locus (eQTL; variants associated with gene expression) data derived from adult brain tissue (nbrains=3 and 1,387) will improve AD pathway PRS performance. We trained 20 AD pathway PRS with clumping and thresholding on positional and integrative variant-to-gene annotation using ten repeated 80:20 holdouts in the UK Biobank. AD cases had validated ICD9/10 codes indicating AD (true cases) or reported parental AD/dementia (proxy cases) (ncases=41,632; ncontrols=286,904); a sensitivity analysis used only true cases (ncases=2,917; ncontrols=256,179). The integrative strategy annotated fewer variants to pathways than positional, though the linkage disequilibrium-independent variant count was similar across strategies (median differences: -46% and 5%). Most pathway PRS had greater incremental R2 under integrative annotation for both outcome definitions (**Figure 1**). The top pathway PRS included genes from 4 Gene Ontology (GO) amyloid-related biological processes (GO:0034249, GO:1902991, GO:1902430, GO:1902992). Integrative variant-to-gene annotation improved AD pathway PRS performance with fewer variants overall. This strategy uses publicly available data and can be implemented to improve power and precision in pathway PRS applications across outcomes.

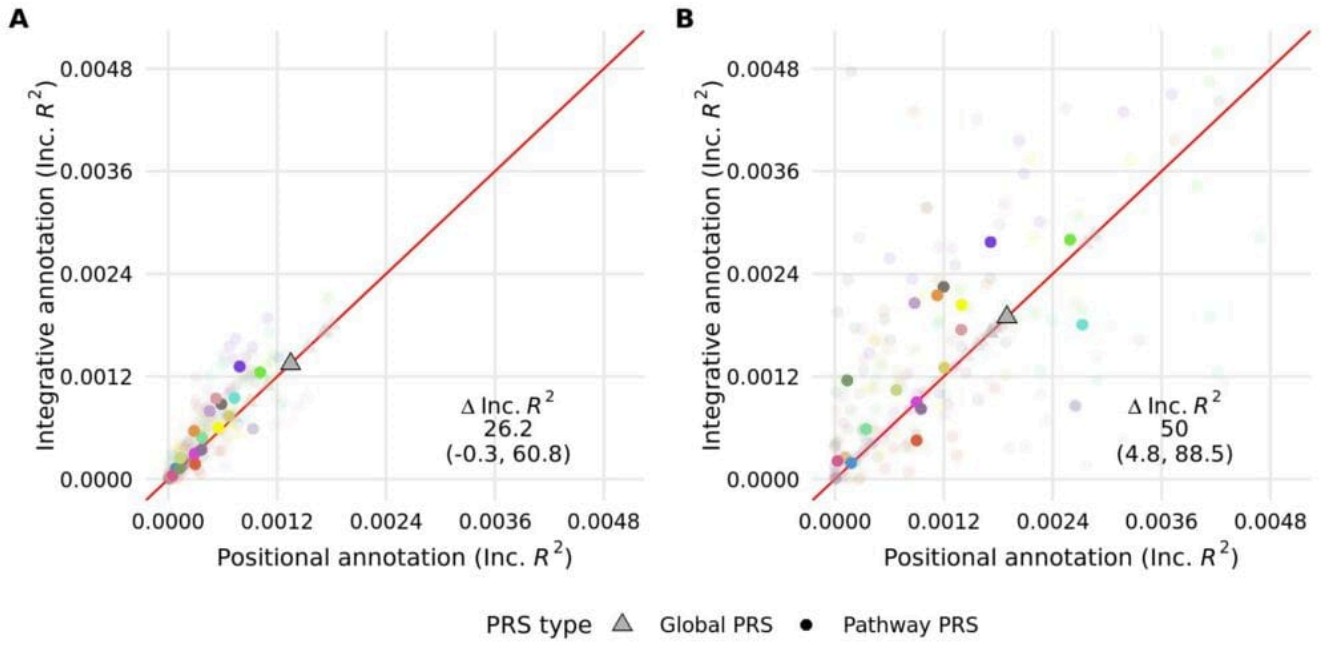


Figure 1 | PRS performance as single repeat incremental R2 (transparent points) and average incremental R2 over 10 repeats (solid points) under the positional and integrative annotation strategies in the A) combined true & proxy case analysis and B) true case only analysis. Incremental R2 (Inc. R2) calculated as 1-((1-Full.R2)/(1-Cov.R2)) where Full.R2 is estimated from the model including the pathway PRS and covariates and Cov.R2 is estimated from the covariate-only model including age, sex*, number of APOE ε4 alleles, and the top 5 principal components; Δ Inc. R2, percent change in Inc. R2 from positional to integrative as median (IQR); Point color corresponds to pathway PRS for different pathways. *Age and sex in proxy cases are age and sex of the affected parent or the average of affected parents.*

Global Health

Are Wastewater Treatment Plants Representative of Off-Sewer Communities? Edem Fiatsonu* EDEM FIATSONU Dustin Hills Chrsitopher Dunham

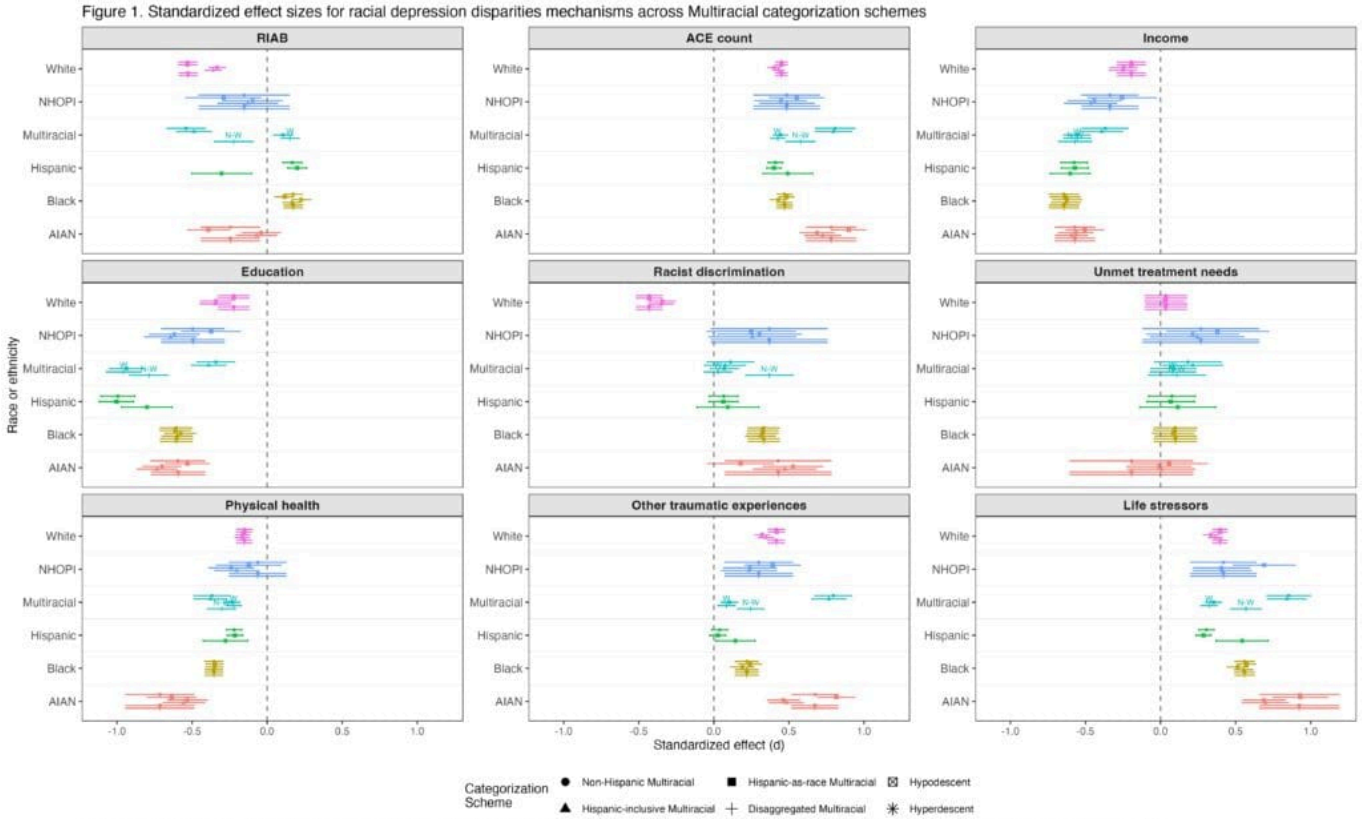
Wastewater-based epidemiology (WBE) is widely used to monitor respiratory pathogens, but it remains unclear whether wastewater treatment plants (WWTPs) represent disease dynamics in nearby off-sewer communities. For respiratory transmission, representativeness depends on human mobility linking sewered and non-sewered populations.
Using SARS-CoV-2 surveillance data from New York State (excluding New York City), we quantified epidemiologic alignment between on-sewer and off-sewer communities using weekly incidence (per 100,000) and test positivity. We estimated statewide and county-level in–off correlations and modeled heterogeneity using weighted regression. To identify structural drivers of alignment, we constructed tract-level mobility networks from anonymized Advan data and applied a random-walk–based community detection algorithm (Walktrap) to identify routinely connected areas. We conducted spatial diagnostics to quantify (i) tracts without community assignment, (ii) unstable tracts, (iii) isolated tracts, and (iv) tracts differing from ≥75% of neighbors. Mobility communities were overlaid with WWTP sewersheds and county boundaries.
On-sewer and off-sewer communities showed strong statewide alignment (incidence $r \approx 0.76$; positivity $r \approx 0.99$), with substantial county-level variation. Higher population density was associated with stronger in–off correlation, while transportation access and vulnerability explained additional heterogeneity. Mobility communities were spatially coherent and often crossed WWTP and county boundaries. Isolated or weakly connected tracts, concentrated in rural areas, showed weaker alignment.
Epidemiologic alignment between sewered and non-sewered populations is primarily structured by human mobility rather than sewer infrastructure alone. Integrating mobility-based spatial methods improves interpretation of WBE and supports more equitable infectious disease surveillance across rural–urban gradients.

Health Disparities

Empirical support for a mechanism-driven approach to categorizing Multiracial participants in depression disparities research Sarah Forthal* Sarah Forthal Katherine Keyes

Studies suggest that Multiracial American adults may have higher depression rates than those identifying with any single racial group. Approaches to categorizing Multiracial participants in racial disparities research may affect the detection and interpretation of this finding, yet these decisions often lack theoretical grounding. We (1) developed an approach to categorization that varies by hypothesized depression disparity-driving mechanisms and (2) tested statistical relationships between categorization schemes and hypothesized mechanisms to provide empirical evidence that supplements theory in guiding researchers' choices. We used the National Epidemiologic Survey on Alcohol and Related Conditions-III, a nationally representative cross-sectional study of US adults conducted 2012-2013 (N=36,309). We compared standardized effect sizes representing the relationship between race and 9 depression disparity-driving mechanisms identified in the literature to assess sensitivity to scheme and compared R^2, AIC, BIC, and 95% CI widths to assess statistical performance. Figure 1 demonstrates the sensitivity of estimates to Multiracial categorization. Estimates for nearly all mechanisms varied by scheme, particularly for the Multiracial, Hispanic, and American Indian or Alaska Native groups, demonstrating the significance of Multiracial categorization for estimating disparities. Grouping all Multiracial participants into one "non-Hispanic Multiracial" group performed best for the mechanisms of racial identity affirmation and belonging, income, education, and traumatic experiences; disaggregating the Multiracial group ("disaggregated Multiracial") performed best for discrimination; and grouping Multiracial participants with their lowest-income single race group ("hypodescent") performed best for adverse childhood experiences, physical health, and life stressors. Aligning categorization schemes with underlying mechanisms may improve the validity of disparities research.

Figure 1. Standardized effect sizes for racial depression disparities mechanisms across Multiracial categorization schemes



Reference group = Asian. AIAN = American Indian or Alaska Native; NHOPI = Native Hawaiian or Other Pacific Islander; RIAB = racial identity affirmation and belonging, ACEs = adverse childhood experiences; W = Multiracial White; N-W = Multiracial non-White. Error bars represent the 95% confidence interval.

Health Disparities

Associations between the Social Determinants of Health and Preterm Birth in the Diverse Hispanic Community Health Study/Study of Latinos (HCHS/SOL) Faizah Alshehri* Faizah Alshehri Brooke C. Mattern Michelle A Kominiarek Carmen R Isasi Linda C Gallo Krista M Perreira Sheila F Castañeda Danielle S. Downs Harold H. Lee Lindsay Fernández-Rhodes

Social determinants of health (SDoH), such as acculturation (language, social and ethnic relations), discrimination, educational attainment, familism, and religiosity, are associated with adverse maternal and infant outcomes, with higher rates among U.S. Hispanic/Latina women compared to non-Hispanic White women. Most studies examine SDoH in isolation rather than their collective influence, which may provide a more accurate estimate of their association with outcomes. We leveraged a diverse community-based cohort—the Hispanic Community Health Study/Study of Latinos—to gather information about pregnancies in the ~6 years between visits 1-2 (2008-11 and 2014-17), resulting in 489 singleton live births with complete information on six pre-pregnancy SDoH and a total of 42 PTBs (<37 weeks, 11.2%). The top two principal components (PCs) of the six SDoH measures explained >50% of variation and had loadings indicative of both acculturation (PC1) and discrimination/education (PC2) related processes. We ran a generalized estimating equation to account for familial clustering with PCs as predictors of PTB, adjusting for seven indicators of Hispanic/Latina background, center, time since visit 1, maternal age at birth, and time in the US/nativity categories. Most births were to women of Mexican (51%) and Puerto Rican (10%) backgrounds. Neither PC was associated with PTB in our logistic regression; however, Puerto Rican background was a significant risk factor for PTB (Odds Ratio=3.56, 95% Confidence Interval= 1.05-12.13). Prior studies have shown persistent disparities in birth outcomes among Puerto Rican women, particularly for PTB. Our results provide a strong foundation for further latent modeling of multiple SDoH and the investigation of bio-psychosocial underpinnings of the observed background-specific effects. Improved understanding of disparities in PTB faced by Hispanic/Latinas, a large and growing demographic group in the US, is important for population precision health

Health Disparities

Disparities in hospital length of stay among inpatient surgical patients by sex, race, ethnicity, and language spoken Bridget Lally* Bridget Lally Kelly McQueen Jeremy Sullivan

Objective: The purpose of this study is to determine if there are disparities in hospital length of stay (LOS) among inpatient surgical patients by sex, race and ethnicity and evaluate language as an effect modifier of that relationship.

Method: The dataset included 39,503 inpatient surgical patients over the age of 18 from a single health system that underwent any surgical procedure between 2017 and 2023. An inverse gaussian generalized linear model estimated the relationship between LOS and race, ethnicity, sex, and language spoken (English or not English). The model controlled for BMI, age, anesthesia type, surgical specialty, and comorbid mental health and substance use disorders. Interactions between language spoken and sex, ethnicity and race were tested and stratified analyses were conducted for English and non-English speaking males and females and for each racial and ethnic group.

Results: Patients were an average age of 57.7 (SD: 16.8), 50.7% were male, 92.2% were white, 3.3% Hispanic and 1.9% spoke a language other than English. There were statistically significant interactions between language and patient sex (p=.003) as well as language and white/non-white patient race (p=.024). Patients with Hispanic/Latino ethnicity, males, and males speaking a language other than English experienced longer LOS. Stratified analyses revealed that male patients who spoke a language other than English experienced the longest LOS (mean ratio 1.57, 95% CI 1.31,1.89, reference: English-speaking females), and 3 of the 4 non-English speaking racial and ethnic subgroups experienced approximately 40% longer LOS. English-speaking, white, Hispanic individuals and non-white, non-Hispanic individuals experienced a 25.5% and 21.1% longer LOS, respectively, relative to White, Non-Hispanic, English-Speaking individuals.

Conclusion: Disparities in LOS are evident between sex, racial, ethnic, and language groups. Results support language as an effect modifier in the relationship between sex, race, ethnicity and LOS. Additional support for patients speaking languages other than English should be considered to ensure timely release from the hospital following surgery.

Health Disparities

Racial and ethnic variation in rates of injury and death from violent victimization among boys and men in California from 2005-2022 Caitlin S. Chan* Caitlin Chan Emily F. Liu Tracy Lam-Hine Jennifer Ahern

Background:

Violent victimization of boys and men is a major public health concern. A majority of victims of violent assault are male, including three-quarters of homicide victims in the United States, with evidence of variation by race and ethnicity. Enumeration of long-term population trends in male violent victimization sheds light on shifting patterns and provides context for further examination of structural processes.

Methods:

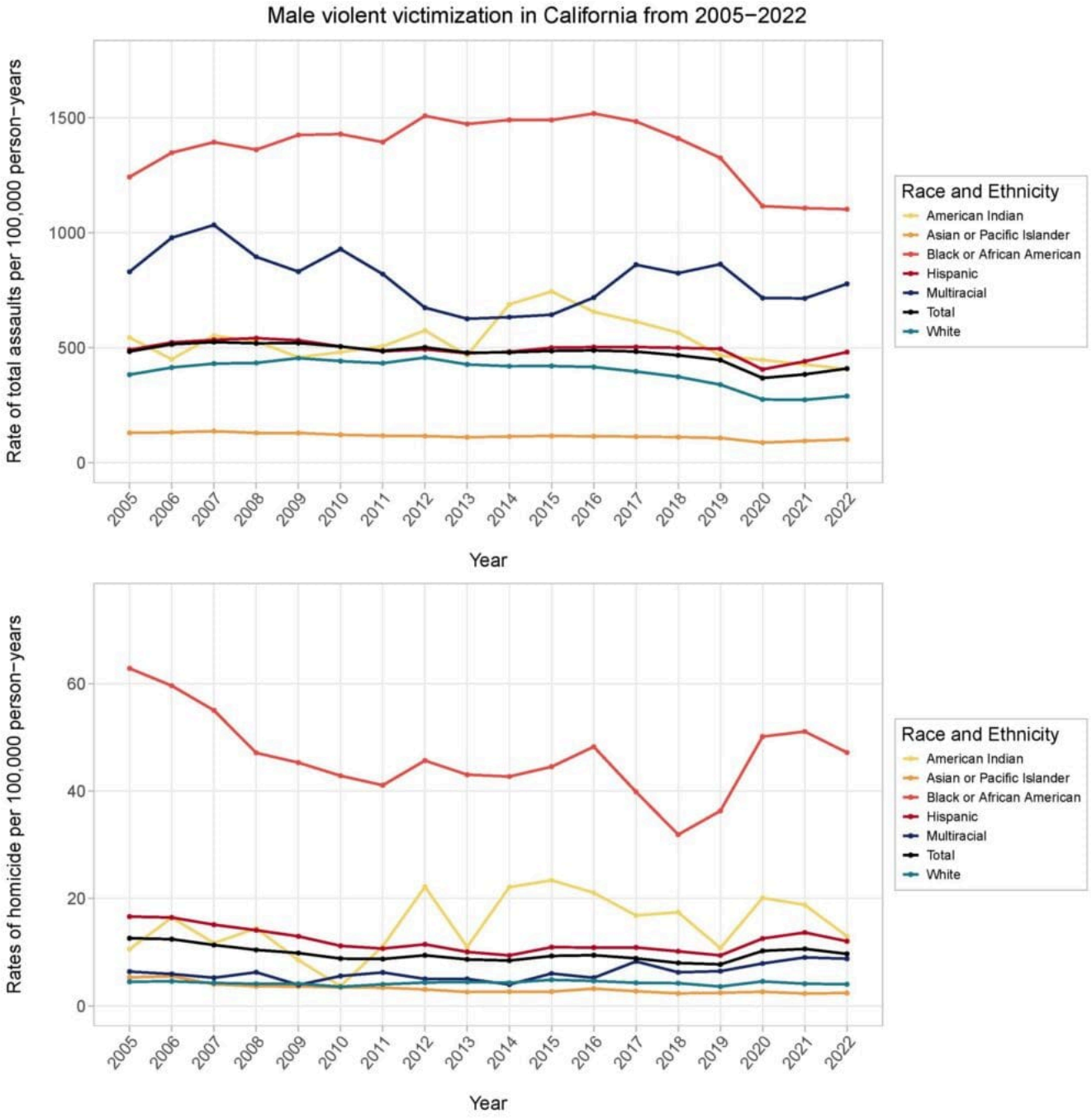
We conducted a retrospective cohort study to examine changes in rates of violent victimization of boys and men across California from 2005 to 2022, stratified by race and ethnicity. We calculated age-adjusted rates of fatal and total (fatal and non-fatal) assault injuries using hospital and death records of California residents recorded as male. We calculated rates as cases per 100,000 person-years using Census population estimates.

Results:

State-wide rates of total male violent victimization were highest in 2007 at 524.91 and lowest in 2020 at 368.46, with 2018 marking a clear sustained drop in rates, and heterogeneity between the groups defined by race and ethnicity. Homicide rates were lowest in 2005 at 12.6 and highest in 2019 at 7.73, and did not follow the same time trend as total violent victimization. Rates of total violent victimization dropped during the COVID-19 pandemic, but homicide rates increased. Subgroup analyses revealed substantially elevated rates of total violent victimization of Black and Multiracial residents (1370.04 & 795.16) and elevated homicide rates of Black residents (46.42).

Conclusion:

Violent victimization of men and boys in California declined slightly over two decades, but racial inequities have not declined over time, indicating structural patterning and a lack of sustained improvement in violence prevention at the population level. Stable inequities in violent victimization by race and ethnicity may reflect structural influences and the institutional priorities of California’s political economy.


Male violent victimization in California from 2005–2022
Rate of total assaults per 100,000 person−years
1500
1000
500
0
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017
2018
2019
2020
2021
2022
Year
Race and Ethnicity
American Indian
Asian or Pacific Islander
Black or African American
Hispanic
Multiracial
Total
White
Rates of homicide per 100,000 person−years
60
40
20
0
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017
2018
2019
2020
2021
2022
Year
Race and Ethnicity
American Indian
Asian or Pacific Islander
Black or African American
Hispanic
Multiracial
Total
White

Health Disparities

The forgotten middle at work: examining labor sector-specific declines in health and well-being across middle income strata Agata Foryciarz* Agata Foryciarz Christian Jackson John W. Rowe David Rehkopf

Despite overall increases of life expectancy in the United States, many health metrics and health disparities continue worsening. US middle-aged adults in the lower middle class, known as the "forgotten middle," are experiencing particularly steep declines in physical, mental and functional health, compared to those in other income groups. These declines have been observed concurrently with a number of changes in the US labor market, including declining union density and the rise of precarious employment. We hypothesize that health declines experienced by the lower middle class may be concentrated in a subset of sectors and occupations most affected by those labor market shifts, such as manufacturing, food and service sectors, and less pronounced in the public sector, where union density is declining less rapidly. In this study, we will examine sector-specific declines in health and well-being of the middle-aged population across the income distribution over the last decade. While prior work has examined how health metrics vary by industry and occupation, to our knowledge the trends across time for middle income groups have not previously been characterized.

We leverage the Behavioral Risk Factor Surveillance System dataset, a cross-sectional, state-level, nationally representative survey of health and health behaviors, which includes data on occupation and industry. We focus on individuals aged 40-74, observed in the period 2013-2024 in the 8 states which collected data for each year (MT, IL, NH, MS, MN, MA, LA and ND) (n=444,109, 32,966-45,693 in any given year). Using linear regression, we estimate changes in measures of physical, mental and functional well-being by industry category, stratified by household-size adjusted income and age groups, in line with prior work. We will characterize the identified trends in the context of sector-specific changes. These results will support work that identifies causal drivers of declining health among the forgotten middle.

Health Disparities

Has Accessibility to Healthcare Institutions for People with Disabilities Improved? A Comparative Study of All 213 Healthcare Facilities in Jongno District, Seoul (2003–2025)

Jaechan Yoon* Jin Yong Lee Hoyun Lee Jungun Lee

Introduction:
Equal access to healthcare is a fundamental human right, yet people with disabilities continue to face substantial mobility barriers. In Korea, national legislation has mandated accessibility standards for healthcare facilities since 1997. However, the extent to which this long-standing policy intervention has translated into population-level improvements in functional accessibility, beyond mere installation, remains unclear. This study evaluated long-term changes in healthcare facility accessibility by comparing installation and adequacy rates of legally mandated accessibility features between 2003 and 2025.

Methods:
An on-site assessment was conducted between December 22 and December 31, 2025, across all 213 healthcare institutions in Jongno district, Seoul. Trained assessors evaluated ten accessibility criteria specified by law, including access routes, parking, entrances, vertical circulation, restrooms, tactile paving blocks, and reception counters. Installation and adequacy rates—defined as full compliance with legal standards—were calculated at the population level and compared with 2003 baseline data.

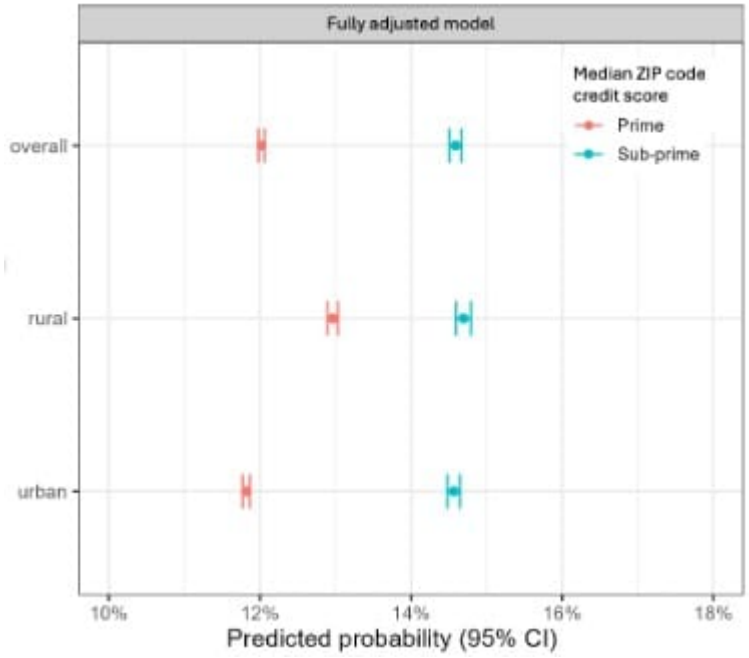
Results:
Overall installation rates increased substantially from 70.0% in 2003 to 93.1% in 2025, whereas adequacy rates improved only modestly (31.2% to 37.8%). Installation increased markedly for tactile paving blocks (3.8% to 100%), elevators (28.4% to 85.0%), and main entrance access routes (31.3% to 85.9%). In contrast, adequacy improvements were uneven: accessible parking, elevators, and restrooms improved, while adequacy declined for stairs and entrances and remained consistently low for reception counters. Several features were widely installed but did not meet legal specifications.

Conclusions:
Korea has achieved substantial and measurable progress in expanding the installation of accessibility features in healthcare institutions. However, limited gains in adequacy indicate that current legislation has been more effective in promoting coverage than ensuring functional usability. Building on these achievements, future policies should strengthen adequacy standards aligned with universal design principles to ensure meaningful and equitable access to healthcare.

Health Disparities

Credit deserts and depression in the U.S.: neighborhood credit scores, rurality, and mental health in a large national sample Catherine Ettman* Catherine Ettman Kyungeun Jeon Elena Badillo Goicoechea Elizabeth A. Stuart Mudia Uzzi Elizabeth A. Stuart

Given close links between economic context and mental health, we sought to understand how area-level credit scores are related to depression in the U.S. and whether the relationship varies across urban and rural areas. Using data from the Facebook COVID-19 Trends and Impact Surveys (CTIS; N=12,378,999 responses from November 2020-June 2022), we estimated the association of median area-level credit scores from TransUnion (sub-prime: 660; prime or above >660) with cross-sectional daily individual level frequent feelings of depression. We used multilevel logistic regression models with ZIP code random effects to estimate the association between area-level credit scores and depression. Fully adjusted models included individual-level demographics (race and ethnicity, sex, education, employment and age) and area-level covariates (median household income in the ZIP code, rurality), and a 6-month calendar-time indicator. We then ran a fully adjusted model with an interaction between credit score and urban versus rural areas. First, we found that living in a sub-prime ZIP-code was associated with higher odds of depressive feelings in the U.S. Overall, the predicted probability of frequent feelings of depression was 12.03% (95% CI 11.98%, 12.07%) compared with 14.57% (95% CI 14.49%, 14.65%) among those living in prime versus sub-prime ZIP codes. When we examined predicted probabilities from a model including an interaction between rurality and prime vs. sub-prime area, we found that the association between credit scores and depression varied across rurality, with sub-prime being more strongly related to depression in rural vs. urban areas. The highest predicted probability of depression was observed among adults living in sub-prime ZIP codes in rural areas (14.82%, 95% CI 14.68%, 14.95%). Living in a sub-prime ZIP code was associated with worse mental health in both rural and urban areas, with the greatest risk for depression in rural areas with sub-prime credit.



LATEBREAKER

Health Disparities

Investigating Social Support as an Effect Measure Modifier in the Relationship Between Race and Hypertensive Disorders of Pregnancy Autumn Clemons* Autumn Clemons Lisa Bates Pam Factor-Litvak Tian Wang

Background: Non-Hispanic (NH) Black pregnant individuals experience disproportionately higher rates and more severe complications of hypertensive disorders of pregnancy (HDPs) compared to their NH White counterparts. Limited research has explored whether factors such as social support modify these disparities. This study examined whether social support modified the relationship between race and HDP.

Methods: Included were 6,289 nulliparous individuals with singleton pregnancies who self-identified as NH Black or NH White. Race (a proxy for racism) was the primary exposure. Self-reported perceived social support (Multidimensional Scale of Perceived Social Support at visit 1 (first trimester) was the effect measure modifier of interest and dichotomized at the 75th percentile (reference: high). Outcomes, preeclampsia (PE) and new-onset gestational hypertension (GHTN), were analyzed separately. Effect modification on the multiplicative scale was assessed using multivariable logistic regression.

Results: NH Black participants had higher rates of PE (12.3% vs. 8.7%; $p < 0.001$) and were more likely to report low perceived social support (77.4% vs. 67.9%; $p < 0.001$) than NH White participants. In adjusted models, the joint effects of NH Black race and low perceived social support were associated with nearly twice the odds of PE compared with NH White participants with high social support (OR = 1.81; 95% CI: 1.30–2.52). No effect modification was observed for GHTN.

Conclusion: The joint effects of NH Black race and low perceived social support were associated with increased odds of PE, but not GHTN. These findings suggest that interventions incorporating social support during pregnancy may help reduce the risk of PE in this high-risk group.

Health Disparities

Assessing mediation of sexual orientation disparities in miscarriage by age at pregnancy

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

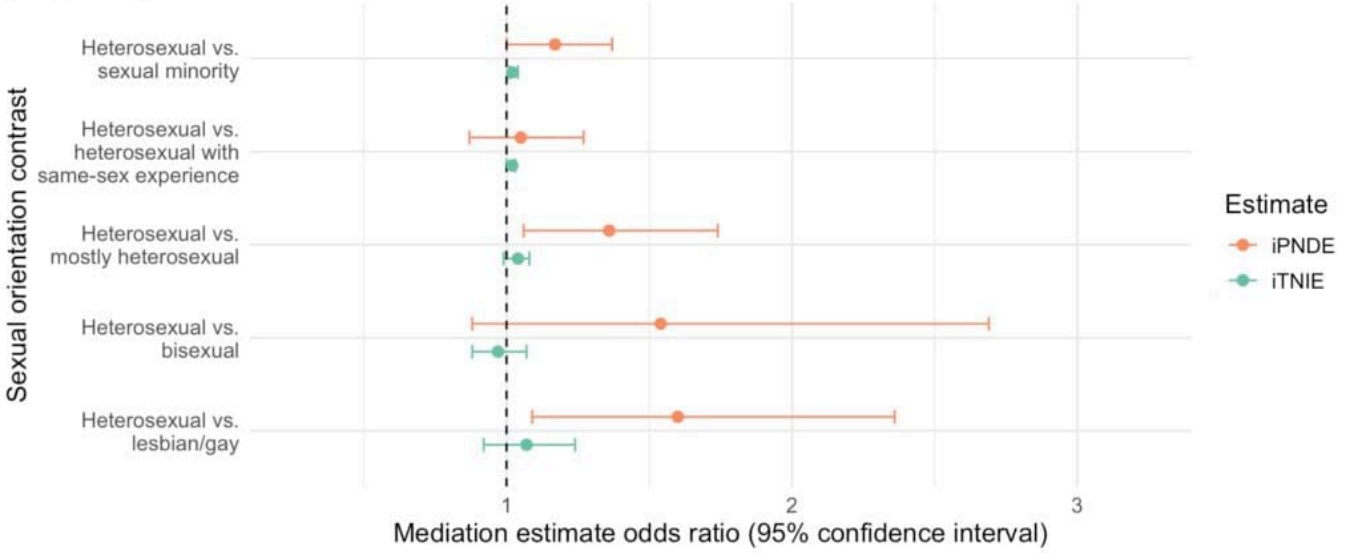
Background: Existing studies show sexual orientation-related disparities in miscarriage. Because age is strongly associated with miscarriage and may lie on the causal pathway (e.g., higher rates of both teen and later-life pregnancies among sexual minority people), conventional age adjustment fails to produce direct effect estimates. To address this, we used formal mediation methods to evaluate the role of age at pregnancy in sexual orientation disparities in miscarriage.

Methods: We used pregnancy data from the Nurses' Health Study 2, randomly selecting one pregnancy per person as pregnancy outcomes within a person are correlated. Because exposure induced mediator-outcome confounding was likely present, we estimated interventional mediated effects (interventional pure natural direct effect [iPNDE] and total natural indirect effect [iTNIE]). Our outcome was miscarriage (yes vs. no). We treated age as multinomial (pregnancies at age <20 or ≥35 vs. 20–34 years). We examined sexual orientation dichotomously (sexual minority vs. heterosexual) and with sexual minority groups disaggregated (heterosexual with same-sex experience, mostly heterosexual, bisexual, and lesbian/gay). Baseline covariates included measures of social origin and mediator-outcome confounders included a variety of demographic and health factors.

Results: Among 64,713 participants, 12% had a miscarriage. About 3% of pregnancies occurred at age <20 and 16% at age ≥35 years. We found some evidence of mediation by age comparing sexual minority groups combined to heterosexual participants (iPNDE: 1.17; 95% CI: 1.00–1.37; iTNIE: 1.02; 95% CI: 1.01–1.04; proportion mediated: 12%). Results varied for sexual orientation subgroups (Figure).

Conclusions: Age at pregnancy may contribute to a small portion of sexual orientation disparities in miscarriage. Analyses of other clinically relevant pregnancy characteristics, such as use of medically assisted reproduction, are ongoing.

Figure. Assessing mediation of sexual orientation disparities in miscarriage by age at pregnancy*



*We examined interventional mediated effects (interventional pure natural direct effect [iPNDE] and total natural indirect effect [iTNIE]) via marginal structural models. Sexual orientation (exposure) was modeled using logistic regression (binary) and multinomial logistic regression (disaggregated), miscarriage (outcome) was modeled using logistic regression, and age (mediator) was modeled using multinomial logistic regression. We allowed for exposure-mediator interaction. Our outcome was whether the pregnancy ended in miscarriage (yes vs. no). We treated age as multinomial (pregnancies at age <20 or ≥35 vs. 20–34). Baseline confounders included year of birth and race/ethnicity. Post-exposure confounders included PCOS, endometriosis, prior miscarriage, gravidity, partner status, SES, healthcare use, hormonal condition, autoimmune condition, cancer, and depression/anxiety. We used multiple imputation to account for missing data on confounders.

Health Disparities

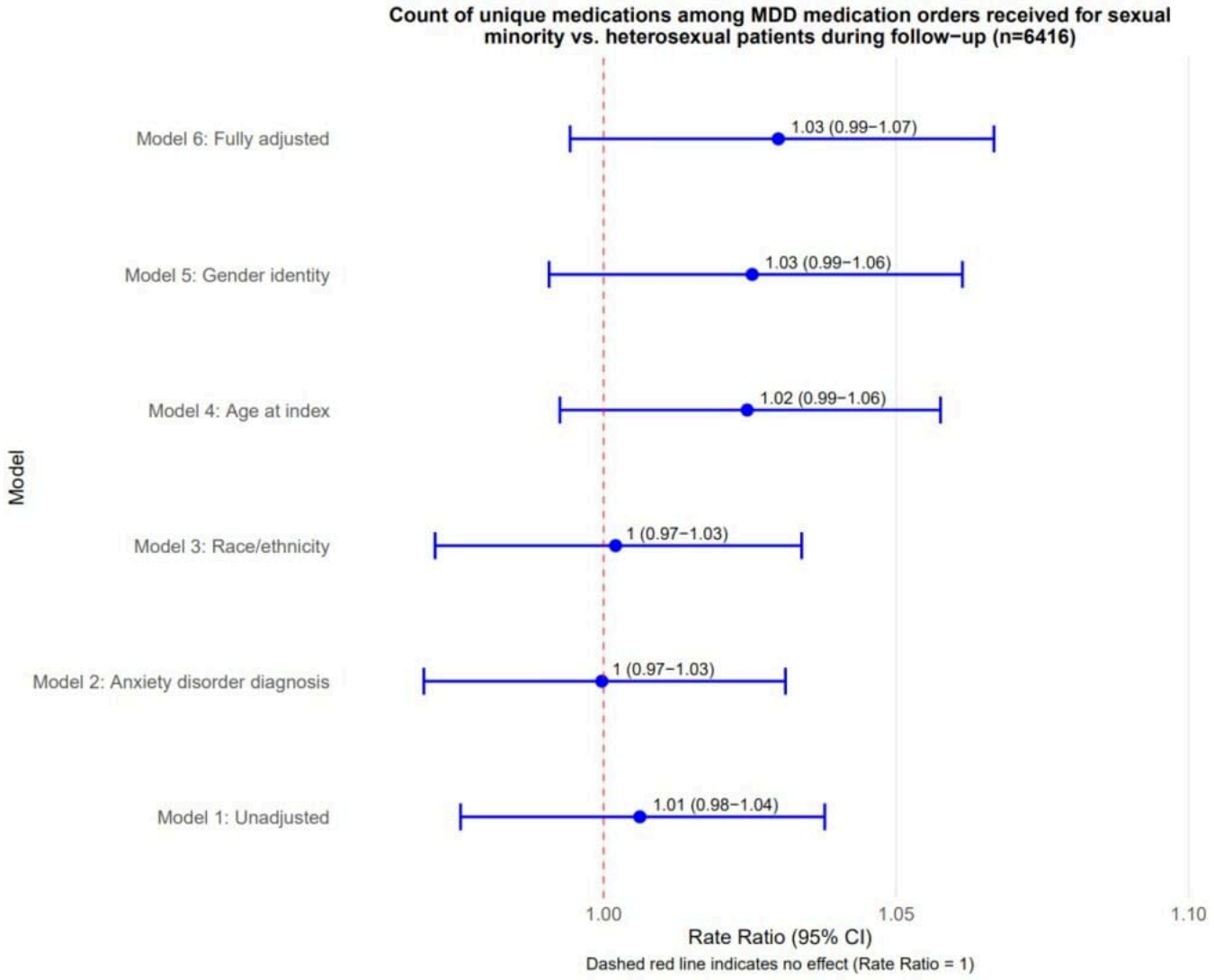
Differences in initial clinical prescription of antidepressant mediations among sexual minority and heterosexual populations with major depressive disorder Frank M. Wolf* Frank Wolf William Brown III Yulin Hswen Ann Lazar Shivani Mehta Jack Turban

Introduction: Major depressive disorder (MDD) is more prevalent among sexual minority individuals (SM), likely due to the stigma and discrimination they experience per the minority stress model. Scarce literature on the utilization and effectiveness of pharmacotherapy treatments for MDD among SM exists to inform care delivery.

Methods: De-identified clinical records for patients with MDD (F32 or F33 ICD-9 or ICD-10) who initiated MDD-directed pharmacotherapy at UCSF Health between January 1, 2018 and December 31, 2023 (index date: date of first pharmacotherapy) were analyzed. Patients with ≥1 UCSF encounter 12 months prior to index and complete sexual orientation data were eligible for inclusion. Frequency of antidepressant medication orders at index were described for SM and heterosexual patients. Mixed-effect Poisson regression models were fit to compare the count of unique medications among MDD medication orders received for SM vs. heterosexual patients during follow-up (1 year).

Results: 6,416 patients were eligible. SM (1,291 [20.1%]) were more likely to identify as Latinx, multi-race/ethnicity, White, and gender minority than heterosexual patients. The three most prescribed first-line antidepressants for SM and heterosexual patients were escitalopram (Lexapro; SM: 21%; Heterosexual: 23%), sertraline (Zoloft; SM: 19%; Heterosexual: 20%), and bupropion (Wellbutrin; SM: 17%; Heterosexual: 12%). Models adjusted for age at index and gender identity indicated an increased count of unique antidepressant medications ordered for SM vs. heterosexual populations. The fully adjusted model indicated a 3% increase (RR 1.03; 95% CI 0.99-1.07) and was of borderline statistical significance.

Discussion: Similar initial medication utilization and 3% greater medication diversity during follow-up may indicate reduced effectiveness or less tolerable side effect profiles of guideline-concordant MDD treatment among SM. Investigation of antidepressant effectiveness among SM is merited.


Count of unique medications among MDD medication orders received for sexual minority vs. heterosexual patients during follow−up (n=6416)
Model 6: Fully adjusted
1.03 (0.99−1.07)
Model 5: Gender identity
1.03 (0.99−1.06)
Model 4: Age at index
1.02 (0.99−1.06)
Model
Model 3: Race/ethnicity
1 (0.97−1.03)
Model 2: Anxiety disorder diagnosis
1 (0.97−1.03)
Model 1: Unadjusted
1.01 (0.98−1.04)
1.00
1.05
1.10
Rate Ratio (95% CI)
Dashed red line indicates no effect (Rate Ratio = 1)

Health Disparities

Implementing teledentistry in rural and underserved communities: A review of barriers, facilitators, and implementation outcomes Edmond Kubi Appiah* Edmond Appiah Joseph Nimako-Boateng

Teledentistry has emerged as a promising strategy to improve access to oral healthcare, particularly in rural and underserved communities. While its clinical effectiveness is increasingly documented, less is known about the practical challenges and success factors for its real-world implementation. This scoping review aimed to map the literature on the implementation of synchronous and asynchronous teledentistry programs, focusing on contextual barriers, facilitators, and reported implementation outcomes. We followed the PRISMA-ScR extension and systematically searched PubMed, CINAHL, Dentistry & Oral Sciences Source, and ProQuest Dissertations for studies (2015-2025) describing teledentistry implementation. From 1,250 citations, 98 studies were included. Data were charted using the Consolidated Framework for Implementation Research (CFIR) to categorize barriers and facilitators, and the RE-AIM framework to assess outcomes (Reach, Effectiveness, Adoption, Implementation, Maintenance). Key barriers included restrictive state licensure laws, inadequate reimbursement structures, limited patient/provider digital literacy, and technological inequities (e.g., broadband access). Facilitators included cross-state licensure compacts, institutional champions, and workflow integration. Most studies reported on Reach and Adoption; fewer measured Implementation fidelity or long-term Maintenance. This review identifies critical policy and practice gaps that must be addressed to translate teledentistry from pilot projects to sustainable, equitable components of the oral healthcare system.

Health Services/Policy

Primary care follow-up visits after discharge from hospital among older adults with dementia Derek Manis* Derek Manis Andrew Costa David Kirkwood Jennifer Watt Chantal Backman Colleen Webber Wenshan Li Stacey Fisher

Older adults with dementia have fragmented health service use, particularly after discharge from hospital. This population-based, retrospective cohort study used linked, individual-level health system administrative data in Ontario, Canada to examine the time to a primary care physician (PCP) follow-up visit among older adults (≥ 66 years) with a previous physician-diagnosed dementia billing claim who were discharged from the emergency department and/or a hospital admission between July 1, 2018 and June 30, 2023; these older adults were followed until March 31, 2024. Older adults who were residents of licensed assisted living facilities were compared to community-dwelling home care recipients. Stabilized inverse probability (IP) weighted pooled logistic regression models were used to graph marginal cumulative incidence curves that were standardized by each exposure status at each day of follow-up from the hospital discharge date. There were 3,144 older adults from licensed assisted living facilities (Mean [SD] age = 88.0 [6.4] years, 72% female) and 25,046 home care recipients (Mean [SD] age = 84.5 [7.4] years, 60% female) who were discharged from hospital (N = 29,190; 1,538,936 person-days). The mean of the stabilized IP weights was 0.99. There were 44 (95% CI [11, 77]), 47 (95% CI [13, 81]), and 26 (95% CI [-5, 58]) additional visits with a PCP per 1,000 older adults if all older adults were residents of assisted living facilities at the 7-, 14-, and 30-days of follow-up after discharge from hospital. The risk of a visit with a PCP was 1.13 (95% CI [1.03, 1.24]), 1.10 (95% CI [1.03, 1.17]), and 1.04 (95% CI [0.99, 1.09]) times higher if all older adults were residents of assisted living facilities at the 7-, 14-, and 30-days of follow-up after discharge from hospital. These population-level findings of follow-up PCP visits likely signal that residency in a licensed assisted living facility can better support the health service needs of older adults with dementia.

Health Services/Policy

Multilevel factors associated with on-site childcare availability within substance use disorder treatment settings, US, 2024 George Pro* George Pro Mofan Gu Sarah “Alex” Marshall Brooke Montgomery Alison Oliveto

Background

Childcare is a major barrier to parents and caregivers in need of substance use disorder (SUD) treatment. Childcare services located within SUD treatment settings are increasing and offer a promising solution to a longstanding problem, but availability is limited. Epidemiologic and health services research are needed to identify multilevel factors related to childcare access in order to direct resource allocation and strengthen treatment systems.

Methods

We used the Mental Health and Addiction Treatment Tracking Repository to identify characteristics and the location of all known outpatient SUD treatment facilities in the US (N=7,796). The outcome of on-site childcare was modeled using multilevel regression, with a range of facility-, census tract-, county-, and state policy-level independent variables. First we estimated main effects, then added interactions between each state policy and the percentage of a census tract that was rural, Black, and Hispanic. Clustering was defined at the state level.

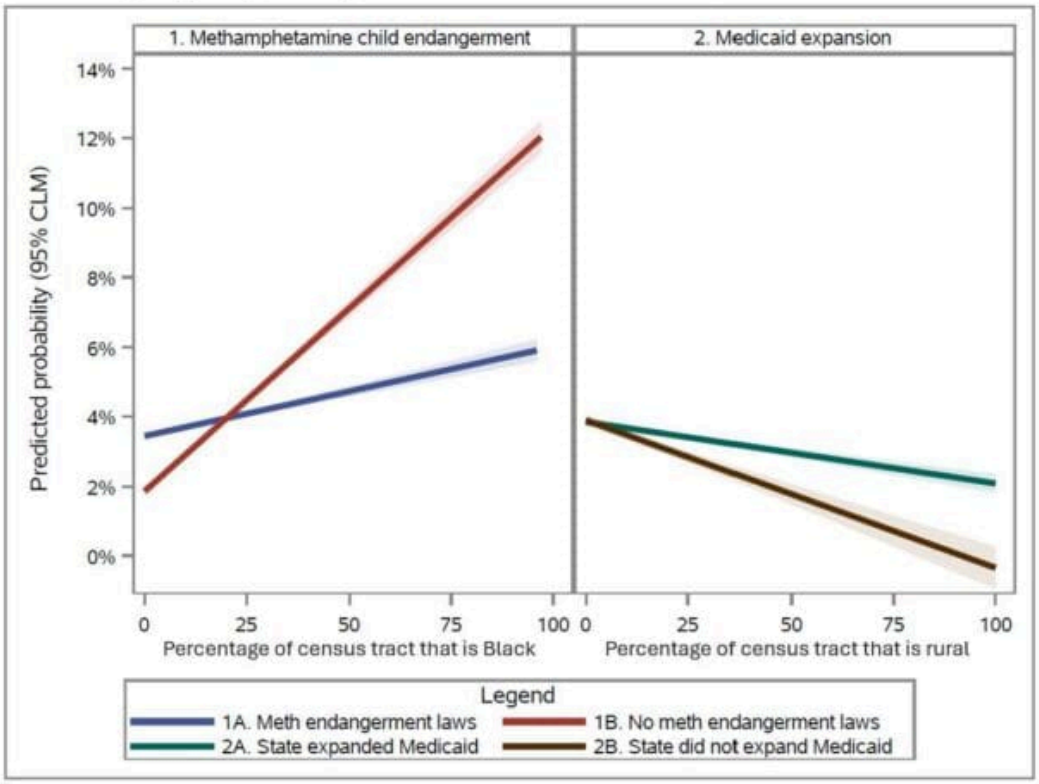
Results

Four percent of treatment facilities offered childcare (n=323). The model-based probability of childcare availability was highest (12%) in facilities located in communities with large Black populations in states that did not specifically mention methamphetamine in child endangerment laws (interaction p=0.01). Childcare availability was lowest (0%) in facilities located in rural communities in states that did not expand Medicaid (interaction p=0.06) (Fig. 1). 17% of the variation in childcare availability was attributable to unmeasured state characteristics ($p<0.01$).

Conclusion

Access to childcare in SUD treatment settings remains very low. Several state health and child abuse laws influenced access to childcare differently for various populations within states. The absence of methamphetamine language in laws defining child endangerment and Medicaid expansion showed the strongest effects in communities that were predominately Black and rural, respectively.

Figure 1: Model-based predicted probability of SUD treatment facilities providing childcare, by state health policy and percentage of census tract that is Black and rural



HIV / STI

Prescribing patterns of dementia-specific medication in US persons with HIV and clinically recognized dementia, 2016-2022 Madeline Brooks* Madeline Brooks Alden L. Gross Catherine R. Lesko Leah H. Rubin Jennifer O. Lam Sonia Napravnik Damani Piggott Maile Karris Kathleen Akgun Michael Horberg Keri N. Althoff

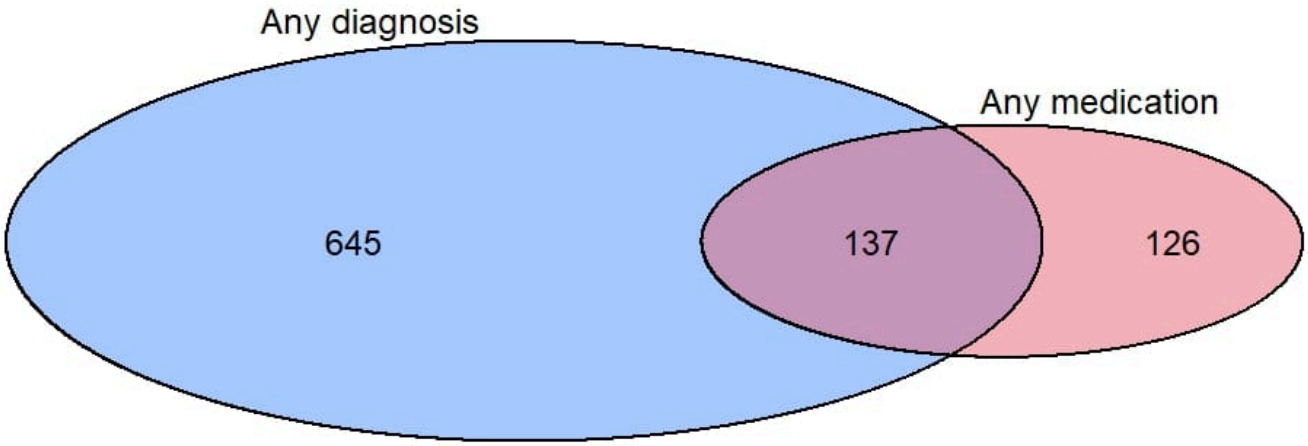
Dementia is a growing concern for aging persons with HIV (PWH). While there is no cure for dementia, drugs to manage symptoms offer modest benefits. Given the history of disparities in HIV treatment prescription among PWH, we characterized dementia-specific medication prescribing patterns in US PWH in the last decade.

Participants included PWH aged ≥50 years with clinically recognized incident dementia between 2016-2022, defined as the first occurrence of an ICD-9/10 diagnosis code or prescription of donepezil, rivastigmine, galantamine, or memantine. Poisson regression with robust variance was used to estimate crude and adjusted prevalence ratios (aPR) and 95% confidence intervals ([,]) for factors associated with receipt of medication, either before receipt of a diagnosis code or at any time over follow-up.

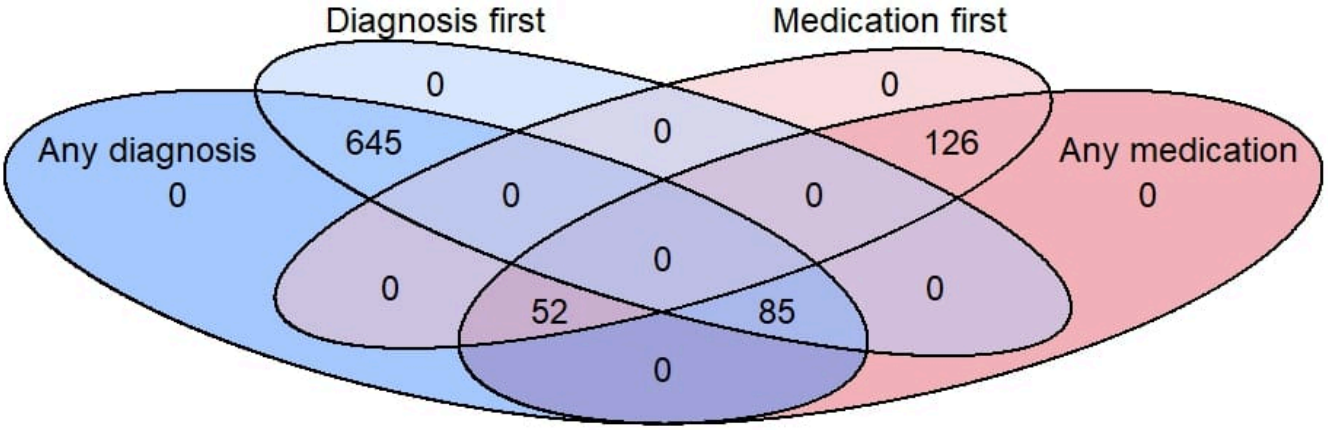
Among 908 PWH with clinically recognized dementia from 2016-2022, most were classified by first dementia diagnosis code (n=730, 80%) and the remaining by first dementia-specific medication (n=178, 20%) (Figure 1). Nearly one-third (n=263, 29%) received a medication during the study period, primarily donepezil. Eighty-five received medication following a diagnosis code (median: 3.4 months, IQR: 5 days, 10.6 months). Those who received a dementia-specific medication (regardless of diagnosis code) were less likely to have low CD4 count (<200 vs. ≥500 cells/μL, aPR=0.46 [0.26, 0.80]), virologic failure (aPR=0.67 [0.49, 0.92]), and cardiovascular disease (aPR=0.71 [0.56, 0.89]) and more likely to be female (aPR=1.36 [1.03, 1.81]) or obese (vs. normal weight, aPR=1.37 [1.06, 1.77]).

PWH who receive dementia-specific medication tend to have better measures of HIV control, which may reflect greater care engagement, medication adherence, or clinical determination that the dementia was unlikely to be HIV-associated, all of which may make medication prescription more appropriate. Sex may also influence the receipt of dementia-specific medications in PWH.

1a) Receipt of dementia diagnoses and medications



1b) Timing of dementia diagnoses and medications



HIV / STI

What happened to people with HIV after they did not show up at a scheduled HIV primary care appointment in 2021-2023? A descriptive analysis of subsequent visit and viremia Sita Lujintanon* Sita Lujintanon Michael Mugavero Joyce L. Jones Lauren C. Zalla Katerina Christopoulos Heidi M. Crane Joseph A. C. Delaney Mari M. Kitahata Thomas C.S. Martin Kenneth H. Mayer Sonia Napravnik George Yendewa Keri N. Althoff Peter F. Rebeiro Catherine R. Lesko

Background

People with HIV (PWH) who miss a scheduled routine HIV care visit may risk adverse outcomes. We describe events after no-show visits among PWH in care at 8 clinics of the CFAR Network of Integrated Clinical System clinical cohort who had ≥1 no-show in-person/telemedicine visit in 2021-2023.

Methods

We examined visit patterns of PWH who (A) attended a subsequent visit, (B) no-showed a subsequent visit, or (C) had no subsequent visit scheduled within 6 months of index no-show visits, stratified by last prior viral load (VL; viral suppression (VS), <200 copies/mL, or viremia, ≥200 copies/mL). We described the proportions of subsequent viremia (≥1 VL ≥200 copies/mL) or no VL test during 1 year after index no-show visits. We weighted each no-show by 1/number of no-shows for each person to draw inference at person level and bootstrapped 95% CI.

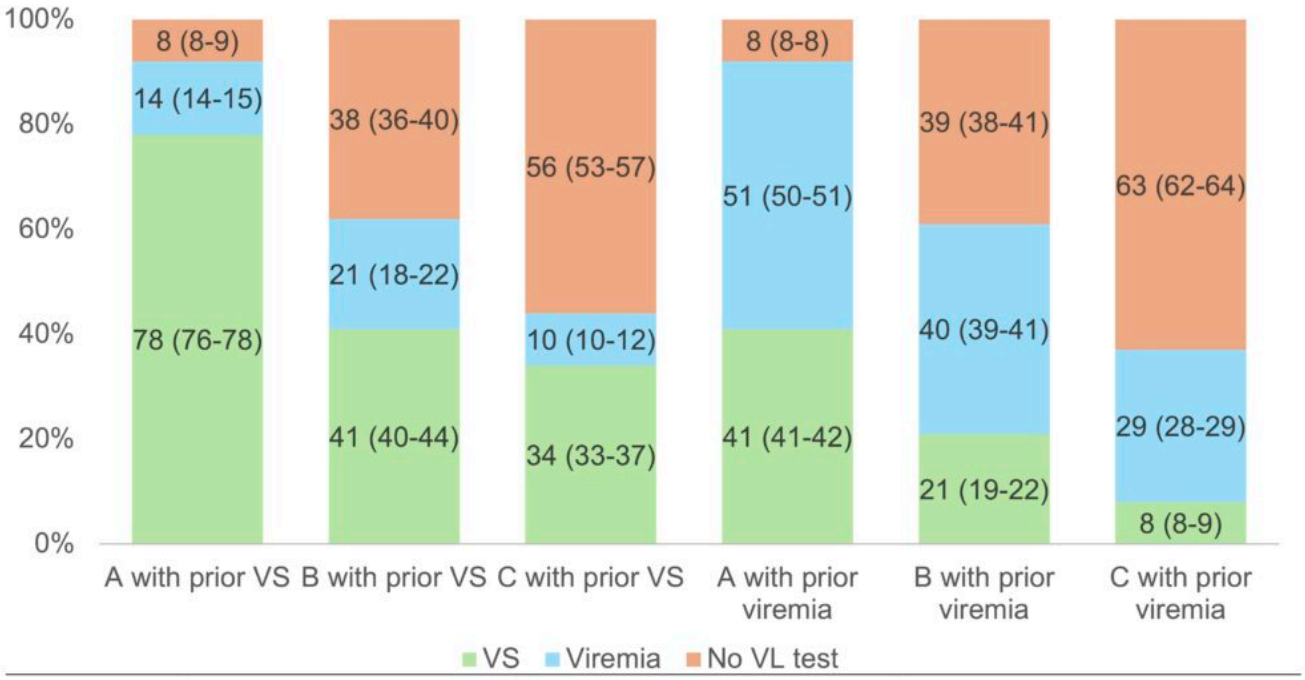
Results

There were 23,035 no-show visits from 8,067 PWH (median no-shows/PWH: 2, range: 1-25; median age: 48 (IQR: 37-57); 77% cis-men; 48% non-Hispanic Black; 17% Hispanic; 16% acquired HIV via injection drug use). Most no-show visits were followed by attended visit: 79% (14,714/18,664) with prior VS and 70% (3,044/4,371) with prior viremia. Repeated no-show visits was higher for PWH with prior viremia at 17% (745/4,371) vs. 11% (2,031/18,664) with prior VS as was no subsequent visits scheduled at 13% (582/4,371) vs. 10% (1,919/18,664), respectively. For PWH and prior VS, subsequent viremia was highest among PWH in pattern B (21%; 95% CI: 18-22%), followed by patterns A (14%; 14-15%) and C (10%; 10-12%). For PWH and prior viremia, 51% (95%CI: 50-51%) in A, 40% (39-41%) in B, and 29% (28-29%) in C stayed viremic, but many PWH in B and C had no subsequent VL test (Figure).

Conclusions

PWH who repeatedly no-show regardless of prior VL face higher viremia risk and may require re-engagement and social support (e.g., treatment for substance use) to achieve VS. PWH with no rescheduled visits may have transferred care or died, and warrant further investigation.

Figure. Proportions of people with HIV with subsequent viral suppression, viremia, or no viral load test (95% confidence interval) during 1 year after index no-show visits by visit patterns.



Visit patterns: (A) Attended a subsequent visit, (B) No-showed a subsequent visit, (C) Had no subsequent visit scheduled.
Note: Subsequent viral suppression (VS) was defined as all viral load (VL) <200 copies/mL; subsequent viremia was defined as ≥1 VL ≥200 copies/mL.

HIV / STI

Hidden Over Time: Rising “No Risk Reported” in State HIV Surveillance and Its Treatment in CDC Data Cindy Tran* Angel Algarin Cindy Tran Jeffrey Sneed Danielle deMontigny Avila Alyssa Robillard

Background:

Accurate HIV transmission risk classification is central to U.S. surveillance and prevention planning. Yet a substantial proportion of new HIV diagnoses are reported with no reported risk (NRR). To address missingness, the Centers for Disease Control and Prevention (CDC) applies multiple imputation (MI) to reassign cases to existing transmission categories. However, the accuracy of MI depends on both the extent of missing data and the strength of associations between missing and observed data. How CDC-imputed classifications compare with state-reported data over time remains poorly characterized.

Methods:

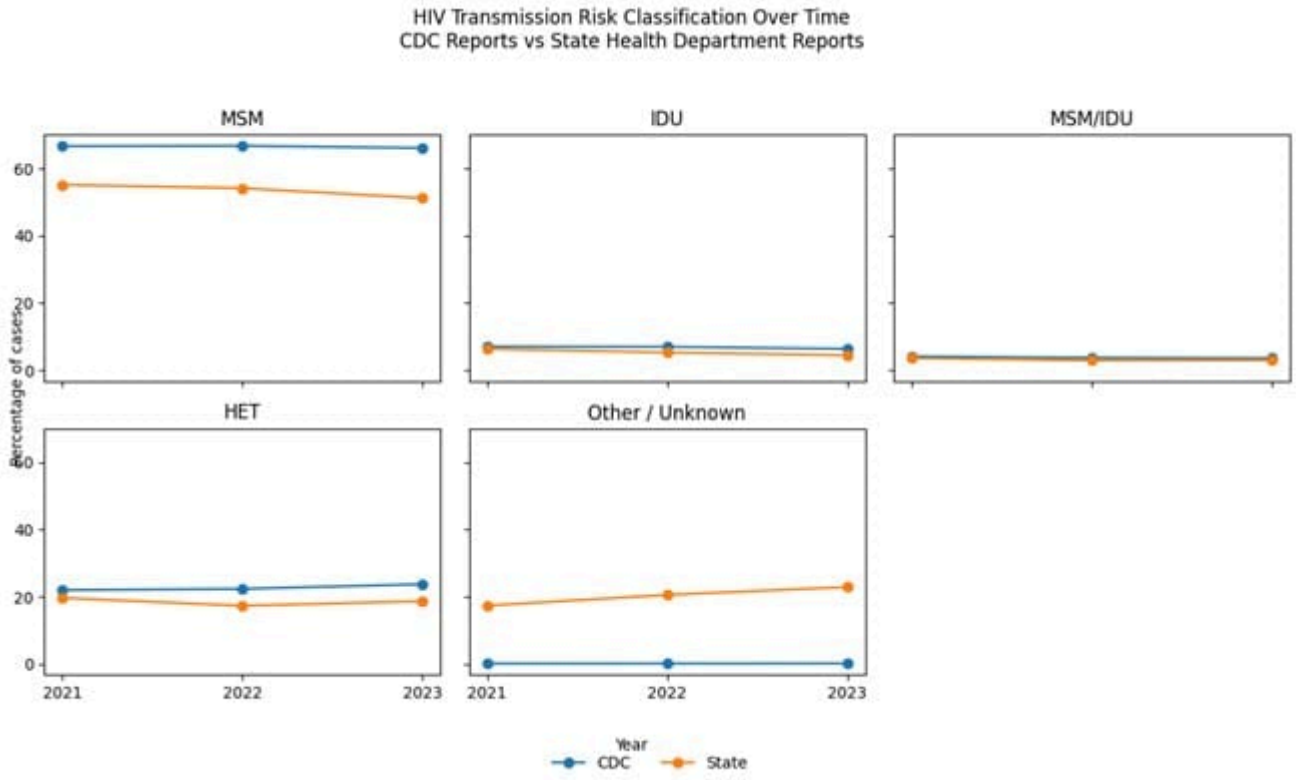
We compared state-reported HIV transmission data abstracted from publicly available surveillance reports and direct health department requests against CDC-imputed data abstracted from AIDSVu for 2021–2023. Analysis was limited to 42 states and jurisdictions with usable data across all years. Transmission categories were harmonized into five groups: men who have sex with men (MSM), injection drug use (IDU), MSM/IDU, heterosexual contact (HET), and NRR/Other/Unknown. These distributions were visualized using multiple-line plots.

Results:

From 2021–2023, the proportion of new HIV diagnoses classified as NRR differed greatly between state-reported and CDC data. In state reports, the proportion of cases classified as NRR increased steadily from 17.4% in 2021 to 22.9% in 2023. In contrast, CDC classified less than 0.2% of cases as NRR in all three years. Visual comparisons indicate that this divergence reflects a growing share of cases classified as NRR in state data rather than single-year fluctuations.

Conclusions:

Systematic differences exist between state-reported and CDC-imputed HIV transmission data. While MI addresses missing data, reliance on MI without data transparency may obscure accurate interpretation. Upstream interventions improving transmission data collection may reduce missingness and enhance the accuracy of HIV surveillance data.


HIV Transmission Risk Classification Over Time
CDC Reports vs State Health Department Reports
MSM
IDU
MSM/IDU
HET
Other / Unknown
Percentage of cases
0
20
40
60
2021
2022
2023
Year
CDC
State

HIV / STI

Understanding Care Gaps in the HIV Care Continuum Post-Incarceration for People with HIV and Criminal Legal Involvement in San Francisco, CA: Insights from Multistate Modeling Paul Wesson* Paul Wesson Edwin Charlebois Graham Hinchcliffe Emily Dauria Janet Myers Aaloke Mody Shelley Facente Angelo Clemenzi-Allen

Introduction

One in seven people living with HIV (PWH) pass through a carceral setting each year. PWH with criminal legal involvement (CLI) often achieve viral suppression (VS) while incarcerated due to a consistent antiretroviral treatment (ART) regimen, but VS and ART adherence usually lapse upon community re-entry. We modeled the HIV care continuum (linkage to care, retention in care, VS) for PWH-CLI in San Francisco, to understand where, and for whom, gaps occur.

Methods

We constructed a retrospective cohort of PWH-CLI receiving HIV care at jail entry in San Francisco from 1/1/18 to 12/31/22. PWH-CLI were matched to records from an integrated data repository of electronic health records, social services utilization, and mortality from county agencies receiving public health funding. We linked cohort data with HIV viral load data from the Department of Public Health's HIV Surveillance. We used multistate modeling to model transition probabilities for the HIV care continuum, accounting for re-incarceration, disengagement from HIV care, disengagement from all care, and death as competing events. Multivariate Cox Proportional hazards models examined demographic correlates with state transitions.

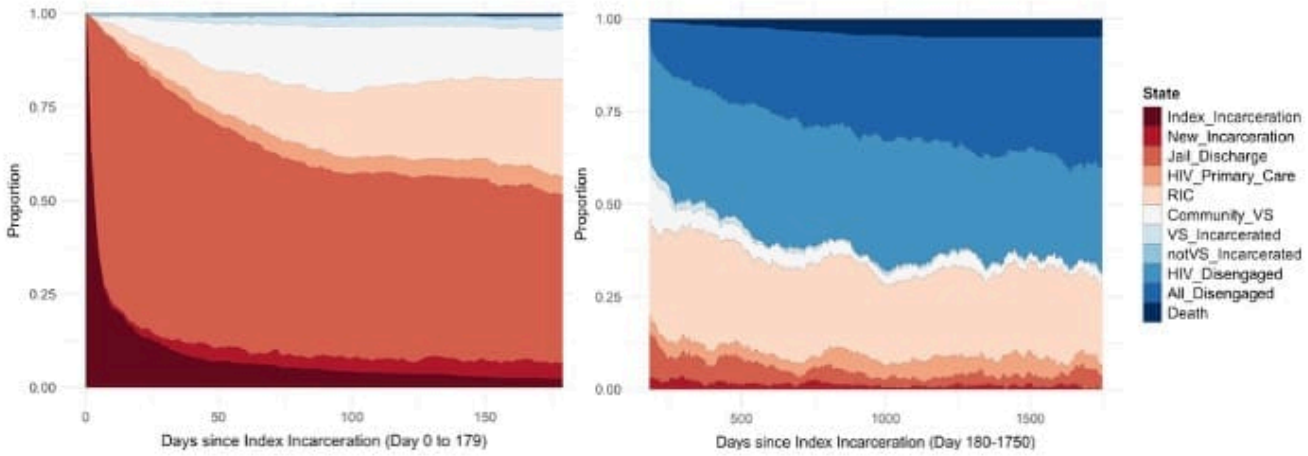
Results

Our analytic cohort included 725 PWH-CLI (mean age 42; IQR: 36, 53). Compared to White PWH-CLI, Asian PWH-CLI were less likely to be retained in HIV care (aHR 0.51; 95% CI: 0.27, 0.96). Both Asian (aHR 2.01; 95% CI: 1.25, 3.23) and Hispanic PWH-CLI (aHR 1.35; 95% CI: 1.00, 1,83) were more likely to disengage from all health care services compared to White PWH-CLI. Roughly half of the cohort disengaged from either HIV care or all care services within two years of release from their index incarceration (Figure).

Conclusion

Maintenance of HIV VS and disengagement from care services are persistent challenges for PWH-CLI. As one intervention target, re-engagement strategies should study why PWH-CLI are accessing other care services while disengaging from HIV care services.

Stacked transition probabilities of occupying each state of the HIV care continuum and competing events; San Francisco, CA, 2018-2022



HIV / STI

Interventions Targeting Loneliness in Aging Populations with HIV: A Scoping Review Lien Quach* Lien Quach Christine Ritchie Aniyah Travis Melis Lydston

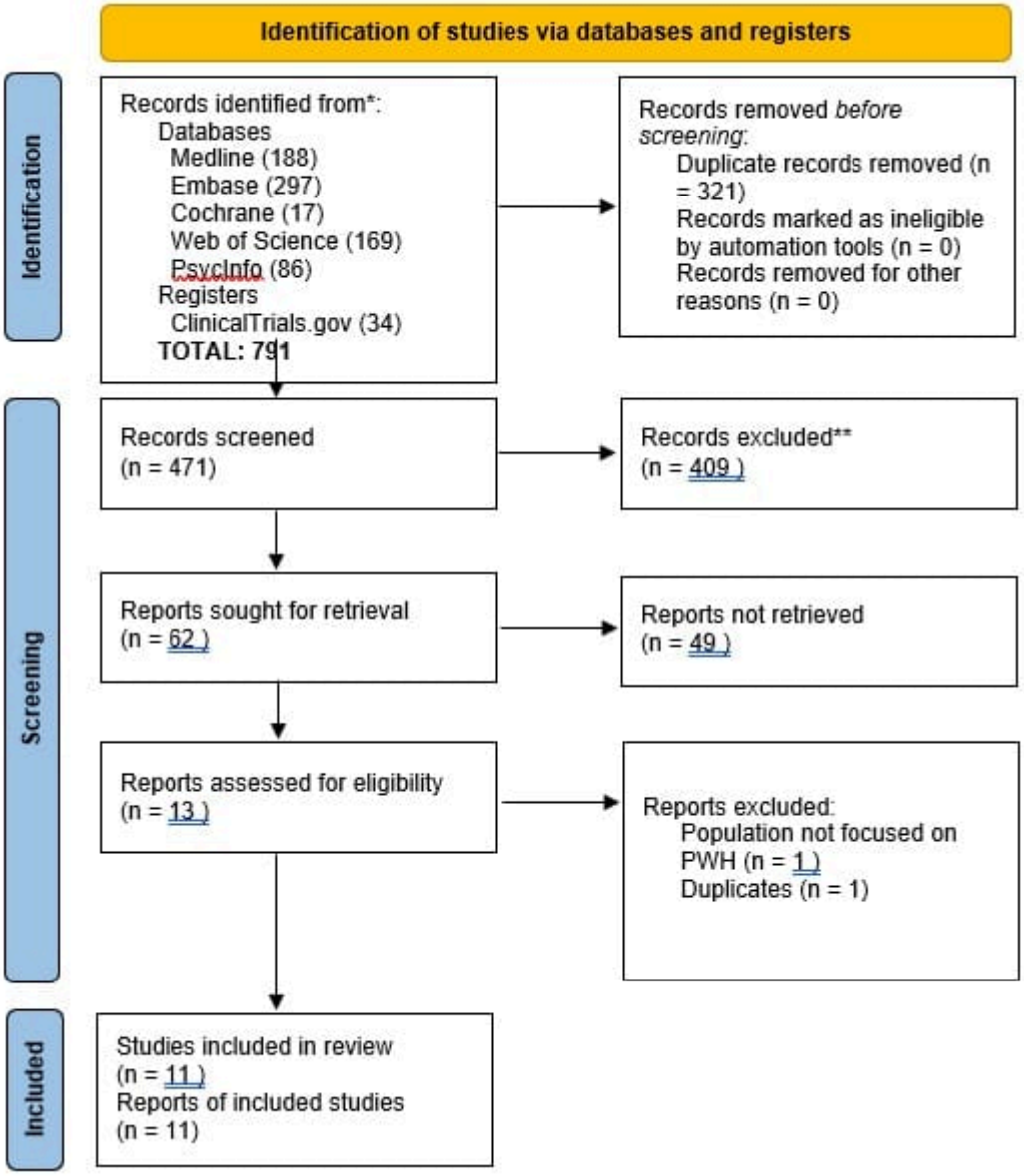
Interventions Targeting Loneliness in Aging Populations with HIV: A Scoping Review

Background: Loneliness is a critical public health concern linked to adverse cognitive and physical outcomes, disability, and premature mortality. Although loneliness is highly prevalent among older people with HIV (PWH), evidence guiding effective interventions remains limited. We conducted a scoping review to synthesize studies evaluating interventions to reduce loneliness among older adults living with HIV.

Methods: Using a prespecified protocol and PRISMA guidelines, we conducted a scoping review of English-language studies identified through searches of Ovid MEDLINE, Embase, Web of Science, Cochrane CENTRAL, ClinicalTrials.gov, and PsycINFO. Records were de-duplicated and screened using Covidence.

Results: Of 471 screened articles, 11 studies met inclusion criteria. Study designs included randomized controlled trials (n=7), a quasi-experimental study (n=1), and longitudinal qualitative studies (n=3) evaluating community-based navigator interventions. All studies examined non-pharmacologic interventions, including cognitive-behavioral therapy (CBT), mindfulness-based stress reduction, peer support, and community-based programs. Interventions were delivered through in-person formats and technology-based platforms such as telephone, social media, and digital human interactions. Mindfulness-based and peer-support interventions particularly those delivered via technology showed promising reductions in loneliness despite persistent stigma and discrimination. Evidence for CBT-based interventions was mixed. Digital human interventions demonstrated potential benefits but lacked evaluation in larger, diverse populations. Community-based programs improved quality of life and reduced stigma but did not explicitly assess mechanisms for strengthening social ties.

Conclusions: Non-pharmacologic interventions, especially mindfulness-based and peer-support approaches, show promise for reducing loneliness among older adults living with HIV. However, evidence remains limited and heterogeneous, underscoring the need for theory-driven interventions that address mechanisms of loneliness and structural stigma. Further evaluation of digital human interventions in larger and more diverse populations is warranted.


Identification of studies via databases and registers
Identification
Records identified from*:
Databases
Medline (188)
Embase (297)
Cochrane (17)
Web of Science (169)
PsycInfo (86)
Registers
ClinicalTrials.gov (34)
TOTAL: 791
Records removed *before screening*:
Duplicate records removed (n = 321)
Records marked as ineligible by automation tools (n = 0)
Records removed for other reasons (n = 0)
Screening
Records screened
(n = 471)
Records excluded**
(n = 409)
Reports sought for retrieval
(n = 62)
Reports not retrieved
(n = 49)
Reports assessed for eligibility
(n = 13)
Reports excluded:
Population not focused on PWH (n = 1)
Duplicates (n = 1)
Included
Studies included in review
(n = 11)
Reports of included studies
(n = 11)

LATEBREAKER

HIV / STI

Who benefits from cash-incentivized HIV adherence counseling? Heterogeneity in a machine learning-targeted HIV trial in Tanzania Huiyu (Joyce) Hu* Huiyu (Joyce) Hu Matilda Mlowe Babuu Joseph Anna Nachbor Amon Sabasaba Jingshen Wang

Background: Retention and viral suppression remain uneven among adults living with HIV (PLHIV) in Tanzania. To proactively identify individuals at high risk of disengagement from care, a machine-learning (ML) algorithm was previously developed using routine electronic health record data to predict disengagement risk. Cash transfer-enhanced adherence counseling (EAC) may improve viral suppression among people living with HIV (PLHIV) at high risk of disengagement, but benefits may be heterogeneous. Identifying which subgroups benefit most is important for equitable and cost-effective program targeting in resource-limited settings.

Methods: In the RKPK Objective 2 trial (four facilities in Geita, Tanzania), 692 machine-learning–flagged high-risk PLHIV were randomized 1:1 to EAC alone versus EAC plus cash. The primary outcome was viral suppression (<50 copies/mL) within 9-16 months. We used honest causal forests with cross-fitting to estimate conditional average treatment effects (CATEs) across baseline demographic, clinical, and ML-risk covariates. Because global heterogeneity diagnostics suggested limited precision for individual-level ranking, primary inference emphasized pre-specified subgroup effects with multiplicity control and facility-clustered bootstrap confidence intervals.

Results: Overall, 12-month viral suppression was 86.5% in the incentive arm versus 81.3% in standard EAC (risk difference +5.3%; 95% CI -0.3, +10.9). Global heterogeneity tests did not support reliable individual-level ranking. Variable-importance measures identified ML risk score, ART duration, sex, and enrollment period as the strongest candidate effect modifiers. Subgroup analyses identified larger effects among men with 3-7 years on ART (+27.9%; 95% CI +6.9, +49.0) and among participants in ML risk quintile 4 (60th-80th percentile; +18.5%; 95% CI +5.5, +31.5).

Conclusion: In this ML-targeted trial population, cash incentives layered onto EAC yielded modest overall benefit, with greater effects among men with intermediate ART duration and individuals at intermediate ML-predicted risk. These findings provide actionable guidance for equity-focused, precision implementation of EAC programs in sub-Saharan Africa.

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LATEBREAKER

HIV / STI

Sociodemographic and Structural Correlates of Past-Year HIV Testing in a Statewide Sample: Analysis of the 2024 California BRFSS Roxana Rezai* Roxana Rezai Wilson H. Hammett

Background

Factors such as healthcare access, stigma, socioeconomic factors, and perceived risk are associated with HIV testing behaviors. In recent years, California has aimed to improve HIV testing by reducing barriers to screening, yet awareness of HIV status remains low, indicating potentially persistent gaps in testing.

Methods

Data from the 2024 Behavioral Risk Factor Surveillance System (BRFSS) were used to examine prevalence and correlates of past-year HIV testing among California adults. Past-year testing was defined using self-reported test dates. Independent variables included age, race/ethnicity, sex, education, insurance coverage, marital status, self-reported general health, and HIV risk behaviors (e.g. injection drug use, sex work, or recent STI diagnosis). Survey weights using iterative proportional fitting were applied. Multivariable logistic regression models estimated adjusted association with past-year testing

Results

Thirteen percent of respondents reported receiving an HIV test in the past year. In survey-weighted models (N=5,799), those reporting HIV risk behaviors had higher odds of past-year testing (OR=2.75, 95% CI: 2.04–3.71). Adults aged 18–34 (OR=3.59, 95% CI: 2.56, 5.02) and 35–54 (OR=2.66, 95% CI: 1.88, 3.76) were more likely to test than those ≥55. Black (OR=2.90, 95% CI: 1.93, 4.34) and Hispanic (OR=1.42, 95% CI: 1.10, 1.83) respondents had greater odds of recent testing compared to White respondents. Being single (OR=1.63, 95% CI: 1.29, 2.05) and insured (OR=2.21, 95% CI: 1.43, 3.40) and in fair/poor health (OR=1.37, 95% CI: 1.04, 1.81) were also associated with past-year testing.

Conclusions

HIV risk was strongly associated with past-year HIV testing and structural factors–such as insurance coverage and demographic differences–were found to be significantly associated with testing. Findings highlight disparities and a need to expand routine HIV testing beyond younger and high-risk populations to identify and/or prevent new infections.

LATEBREAKER

HIV / STI

Going the Distance: HIV Testing Site Access is a Determinant of Both New HIV Diagnoses and Late Presentation in Tennessee Jesse J. Carlson* Jesse Carlson Elisa Yazdani Justin Z. Amarin Amber J. Hackstadt Robb Garman Riley Gulbronson Samantha Mathieson David K. Fields April C. Pettit Robertson Nash Peter F. Rebeiro

HIV test-and-treat strategies depend on structural conditions, including proximity to testing. We evaluated associations between access measures with new HIV diagnoses and late presentations in Tennessee (TN). We used statewide surveillance data among adults diagnosed with HIV between 2018–2023 across TN's 95 counties. Outcomes were annual county counts of new diagnoses and late presentations (AIDS-defining event or CD4<200 cells/µL ≤90 days after diagnosis). Exposures were population-weighted mean drive time to nearest test site and site density (effective sites per 100,000 residents down-weighted by distance-decay; γ=10 minutes), using sites from the CDC's National Prevention Information Network. We constructed census tract population-weighted centroids, estimated drive times using an origin-destination matrix, and aggregated to county means. Spatial GAMs included year and a county adjacency smoother: log-link Poisson with population offsets for new diagnoses (IRR) and binomial-logit for late presentations (OR). County z-scores for model-based outcomes were averaged separately for drive-time and effective sites. In 2018–2023, 4,715 people were diagnosed; 18.69% (n=881) presented late. There were 234 sites, with a mean drive time of 14.75 minutes (range 3.15–31.23). Per 10-minute decrease in drive time, the rate of new diagnoses was 51.06% higher (IRR=1.51, 95%CI: 1.10–2.07) and the odds of late presentation were 26.56% lower (OR=0.734, 95%CI: 0.498–1.082). Each 5-site increase per 100,000 residents was associated with 5.14% higher rate of new diagnoses (IRR=1.05, 95%CI: 1.03–1.07) and 1.75% lower odds of late presentation (OR=0.982, 95%CI: 0.968–0.997). Priority scores identified high-priority clusters in northeast and south-central TN (**Figure**). Geographic access to testing sites is an important determinant of disease progression, and expanding access in high-priority areas could improve timely diagnosis. Findings may be affected by unmeasured service differences.

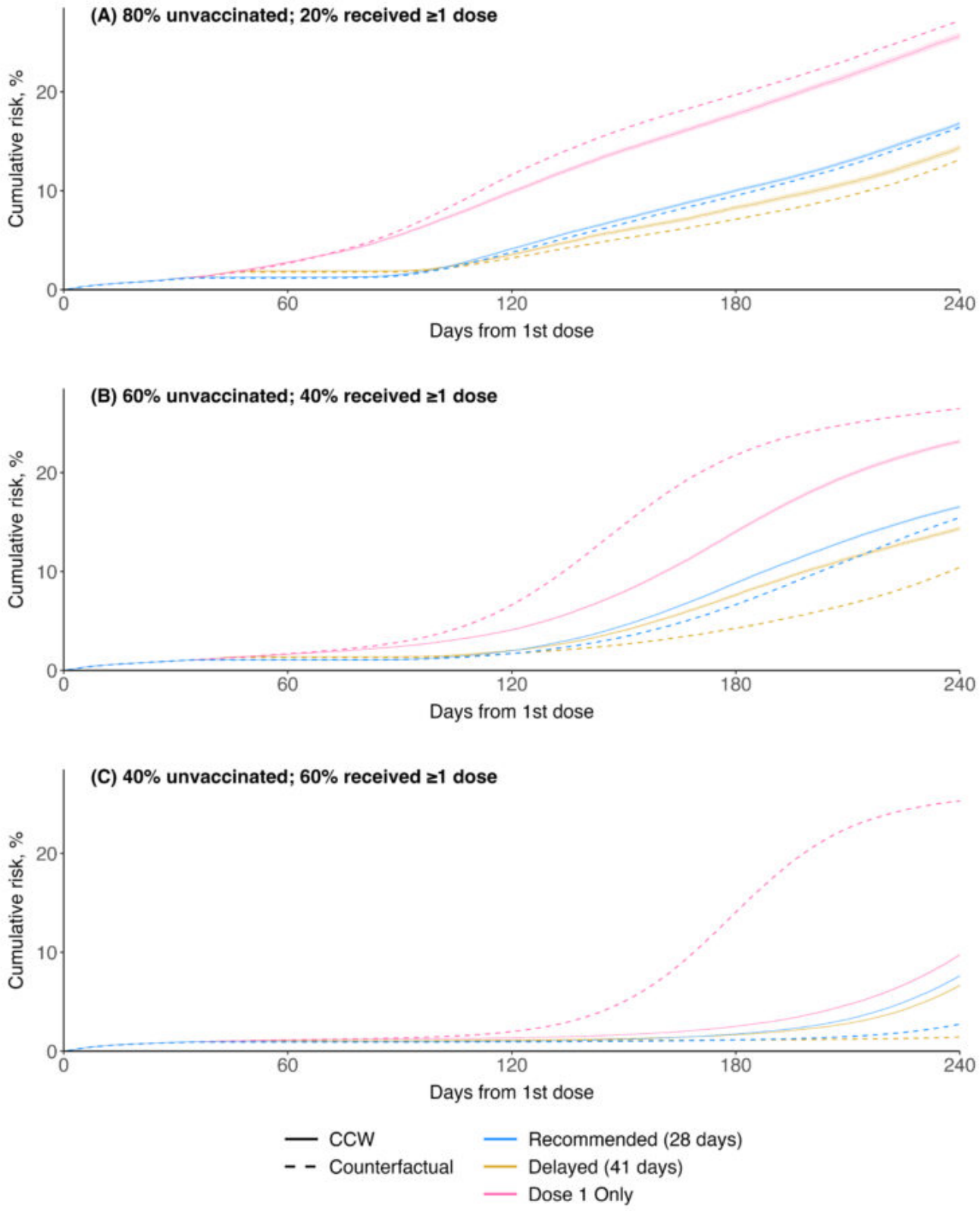
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Infectious Disease

Target Trial Emulation in Vaccine Evaluation: Challenges and Opportunities Kanako Fuyama* Kanako Fuyama Kanako Fuyama Margaret Lind Kayoko Shioda

Target trial emulation (TTE) is a causal inference framework that emulates a randomized trial using observational data. Although TTE has been increasingly applied in vaccine evaluations, infectious disease outcomes often violate a key causal inference assumption: no interference. The purpose of this simulation study is to assess the performance of conventional TTE using the clone-censor-weight (CCW) approach in the presence of interference. We compared three dosing schedules: a single-dose protocol; a two-dose protocol administered at the recommended interval (second dose given 28 days after the first); and a delayed two-dose protocol (41 days), assuming that the delayed protocol produced the highest protection. Using an agent-based transmission model, we simulated transmission in a population of 1 million individuals with mixed vaccination protocols and estimated cumulative infection risks using CCW, while true counterfactual risks were derived from simulations in which all vaccinated individuals followed the same vaccination schedule. We considered scenarios with varying levels of vaccine coverage, adherence to dosing schedules, and timing of the first dose. Although discrepancies were observed in cumulative risks and risk ratios between the simulated counterfactuals and CCW estimates, both indicated that the delayed protocol yielded the lowest cumulative risk of infection. However, in scenarios where adherence to the dosing protocols varied over time, CCW using Cox proportional hazards regression for inverse probability of censoring weighting did not capture this trend, whereas the Kaplan-Meier method and stratified Cox regression did. This discrepancy may be explained by violations of the proportional hazards assumption induced by time-varying adherence. Overall, our analysis suggests that CCW may be able to identify the superior dosing schedule; however, caution is warranted when interpreting the estimated cumulative infection risks under each dosing schedule.

Fig. Cumulative risk of infection since dose 1 (dose 1 on day 250)



CCW: estimated from a mixed dataset of dose-1 recipients (50% dose 2 at the recommended interval; 20% dose 2 delayed; 30% dose 1 only)

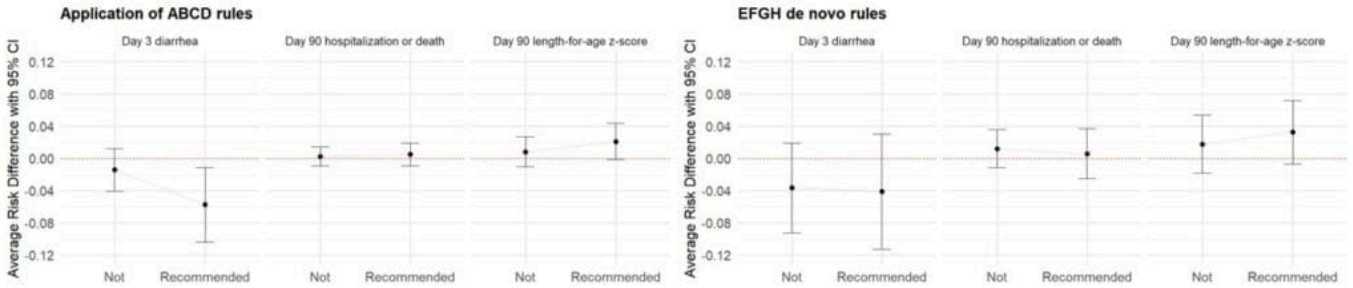
Counterfactual: three separate datasets of dose-1 recipients were generated (dose 2 at the recommended interval, dose 2 delayed, or dose 1 only)

Infectious Disease

Generalizability of machine-learned antibiotic treatment rules for children with watery diarrhea in low-resource settings Allison Olmsted* Allison Olmsted Sara Kim Allison Codi Patricia Pavlinac James Platts-Mills David Benkeser Elizabeth Rogawski McQuade

Some children with watery diarrhea could benefit from antibiotic therapy not indicated by current guidelines. Data from the AntiBiotics for Children with severe Diarrhea (ABCD) randomized trial was used to develop personalized rules based on expected child-level benefits of azithromycin treatment with respect to diarrhea duration, re-hospitalization or death, and linear growth. To evaluate generalizability to a more representative population, we applied ABCD-learned rules for antibiotic treatment to the Enterics for Global Health (EFGH) study, a seven-site diarrhea surveillance study, and compared these to novel rules developed using EFGH data. Rules were developed using a robust ensemble machine learning-based procedure validated across 10 folds. Treatment was recommended if the child-level benefit exceeded a 7% reduction in day 3 diarrhea, 2% reduction in 90-day hospitalization or death, and 0.06 increase in length-for-age z-score (LAZ). We estimated the proportion recommended treatment by each rule and compared expected benefit by treatment recommendation. Overall treatment effects were 2.4% reduction (95% CI 0.2, 4.6) in day 3 diarrhea, 0.3% increase (95% CI -0.6, 1.2) in 90-day hospitalization or death, and a 0.01 increase (95%CI 0.0, 0.03) in 90-day LAZ. Comparing the ABCD to EFGH rule, the difference in the antibiotic effect among those recommended for treatment compared to not in terms of reduction in day 3 diarrhea was 4.3% (95%CI 1.0, 9.7) and 0.04% (95%CI -9.5, 8.6), respectively. The ABCD rule more often recommended treatment for children with bacterial etiology (59.7% vs. 40.3%) and acute malnutrition (median weight-for-age z-score -1.42 vs. -1.07). Neither rule identified heterogeneity in treatment effects for other outcomes. The ABCD rule successfully identified children in EFGH who would benefit from antibiotic treatment and better-identified heterogeneity in treatment effects against diarrhea duration compared to the EFGH rule.

Figure 1. Performance of machine-learned antibiotic treatment rules in among children with watery diarrhea in low-resource settings



Infectious Disease

Investigating heterogeneity of effect of albendazole treatment on neurocysticercosis parasite death by host sex, age and immune function indicators Zachary Zuchowski* Zachary Zuchowski Arturo Carpio W. Allen Hauser Karina Quinde-Herrera Elizabeth A. Kelvin

Albendazole treatment for neurocysticercosis (NC) resolves all active cysts in only 31% of patients. Host immune response appears to vary by patient characteristics, including sex and age, and it impacts parasite lifespan, but whether it modifies the impact of albendazole treatment is unclear. We used data on 99 participants of a randomized controlled trial (RCT) of albendazole treatment for NC to investigate if the effect of albendazole treatment on active cysts was modified by patient sex, age and pretreatment immunological lab measures (white blood cell, basophil, lymphocyte, eosinophil and monocyte counts). We used log-binomial models to look at resolution of all active cysts and linear regression to look at change in the number of active cysts by one month post treatment, adding interaction terms between treatment and each hypothesized effect modifier. We also ran stratified models to look at the direction of effect modification. We found that the impact of albendazole in resolving all active cysts was higher among males than females (RR=12.19 versus 2.74), younger than older patients (RR=8.69 versus 4.32), those with lower basophile count (RR=8.36 versus RR=1.5) and lower eosinophil count (RR=7.27 versus RR=3.82), but none of the interaction terms were statistically significant. When looking at change in the number of active cysts, the interaction between treatment and eosinophil count was significant and there was a reduction in the number of active cysts associated with treatment among those with low eosinophil counts but not those with high counts (β=-4.69 versus β=0.38). The impact of albendazole on NC parasites appears to be stronger among those with a weaker immune response, although most of the associations were not statistically significant, perhaps due to low power given the small sample size. Understanding how the host-immune system impacts the effectiveness of albendazole is key to developing improved treatment.

Infectious Disease

Forecasting Human West Nile Virus Incidence Using Mosquito Pool Infection Data in High-Risk Land Use Categories Jordan Robinson* Jordan Robinson Kacey Ernst

West Nile Virus (WNV) is one of the most prevalent vector-borne diseases in the United States. As the scale and distribution of WNV and its vector, the Culex mosquito, changes, there is a growing need to predict when and where WNV outbreaks will occur. Arizona suffers from above average WNV incidence. Previous work has highlighted an association between viral presence in mosquito pools and a higher number of reported human cases for the season. While previous forecasting has focused on peak mosquito activity, there has been little evaluation of early season activity and its use in predicting seasonal case burden. This project aims to measure if early season disease rates in mosquito pools can predict total human WNV cases for the season. Further, this work aims to determine if efficiency in forecasting can be developed by narrowing input data to mosquito pool information from specific land-use categories. Mosquito surveillance data from Maricopa County Vector Control was used to calculate average abundance and vector index at different intervals, which were then tested using negative binomial regression to identify the earliest seasonal interval at which mosquito indicators were associated with human WNV incidence. Surveillance data were further stratified by land-use categories, according to land-use composition within trap flight-range buffers, to determine which land-use categories were most impactful for predicting human cases. Results from the forecast model will inform WNV spread and relevant mapping can be used to focus vector surveillance and control efforts, and shape priorities in public education.

Infectious Disease

HIV and the detectability of within-host minor variants in Mycobacterium tuberculosis whole-genome sequencing data Marie Nancy Séraphin* Marie Nancy Séraphin Jane Afriyie-Mensah Julia Chariker Patrick Valois Michael Amo Omari Matt D.T. Hitchings Lori Johnston Marco Salemi

Background: Within-host minor variants in Mycobacterium tuberculosis (intra-host single nucleotide variants; iSNVs) may improve transmission inference, but detectability depends on sequencing quality. Human immunodeficiency virus (HIV) can alter tuberculosis (TB) biology and specimen characteristics, providing a setting to study when iSNVs are observed.

Methods: We analyzed culture-confirmed TB isolates sequenced by whole-genome sequencing (WGS) from Florida statewide surveillance (n = 342) and a hospital-based cohort in Ghana (n = 97). Using biological replicates from Ghana, we calibrated iSNV-calling thresholds and defined iSNV detectability as ³ 1 iSNV outside repetitive regions. We compared detectability by HIV status overall and in a high-quality subset defined by high read depth and high callable genome. We tested robustness to alternative thresholds and to analyses restricted by sequencing run and quality metrics (read depth and callable genome).

Results: In Florida, iSNV detectability was higher among HIV-positive than HIV-negative isolates [Prevalence Ratio (PR) = 1.43(95% CI:1.25 – 1.63)]. In Ghana, detectability was also higher among HIV-positive isolates [PR = 1.63 (95% CI:0.78 – 3.38)], with greater imprecision due to smaller numbers. Restricting to high-quality samples produced similar or slightly stronger contrasts in both settings. Sensitivity analyses varying thresholds, filters, and outcome definitions did not eliminate the association.

Conclusions: HIV coinfection was associated with higher iSNV detectability in two settings and persisted after restricting to high-quality sequencing. Studies that assume equal minor-variant detectability across host groups may have differential sensitivity by HIV status. Calibrated thresholds, standardized quality criteria, and host-stratified reporting can improve interpretation of iSNV-based within-host diversity measures from M. tuberculosis WGS.

Infectious Disease

Association of Chronic Diseases with Herpes Zoster in China: A Nationwide Population-based Survey Wenhui Zhu* Wenhui Zhu

Background: The global burden of herpes zoster (HZ) is rising, posing a major public health challenge, especially among aging populations with high chronic disease prevalence. Although chronic conditions are known risk factors, population-based evidence from China remains scarce.

Objective: To examine the association between chronic diseases and HZ using nationally representative data from China, considering demographic and lifestyle factors.

Methods: We conducted a national population-based survey using the 2024 China Family Panel Survey (CFPS). A probability proportional to size sampling method was employed, covering 25 provinces and regions and representing 95% of the population in mainland China. A structured questionnaire collected data on HZ diagnosis, chronic disease status, and demographics. Incidence rates were calculated, and multivariable logistic regression was used to estimate adjusted odds ratio (aOR).

Results: Among 27868 participants (21496 adults; 6372 minors), 809 adult HZ cases were identified, with 64.40% (n=521) having at least one chronic condition. Female adults with chronic diseases had a higher incidence (12.94/1000 PY; 95% CI: 11.45-14.56) than males (8.78/1000 PY; 95% CI: 7.55-10.12). Incidence increased with age, from 8.07/1000 PY (95% CI: 4.45-13.10) in those aged 18-29 to 13.36/1000 PY (95% CI: 11.08-15.96) in those ≥70. Chronic disease was associated with elevated HZ risk (aOR=1.84; 95% CI: 1.51-2.24). Among 14 chronic conditions, heart disease showed the strongest association (aOR=2.91; 95% CI: 2.07-4.10), followed by diabetes (aOR=2.04; 95% CI: 1.48-2.80) and hypertension (aOR=1.89; 95% CI: 1.47-2.42).

Conclusions: Chronic diseases, particularly cardiovascular and metabolic conditions, are significantly associated with increased HZ risk. These findings highlight the need for targeted HZ prevention strategies, including vaccination, among high-risk groups in China.

Infectious Disease

Predictors of future Lyme disease vaccine acceptability among healthcare professionals in 2025: a cross-sectional survey Courtney Olson* Courtney Olson Aaron Scherer Natoshia Askelson Courtney Gidengil Andrew Parker Amber Gedlinske Christine Petersen

Introduction: Lyme disease (LD) is one of the most common tick-borne diseases in the US with over 400,000 estimated diagnoses annually. Several candidate LD vaccines are currently in clinical trials and may be available soon. It is important to understand factors that may influence healthcare professionals (HCP) LD vaccine recommendations once a vaccine becomes available. In this study, we explored how LD symptom knowledge and local incidence might influence HCP LD vaccine recommendations.

Methods: We surveyed 750 primary care physicians who practice in US states with high or emerging LD incidence in July 2025. Participants indicated if ten symptoms (randomized display order) were associated with LD or not, with “Unsure” as a third response option. A “symptom knowledge” score was created based on total correct responses, with “Unsure” classified as incorrect. Mean knowledge scores were compared between high and emerging incidence areas using Independent Samples t- tests. We conducted an adjusted logistic regression controlling for demographic factors to determine the association of symptom knowledge and local LD incidence with likelihood to recommend LD vaccination to eligible patients.

Results: 739 completed all survey items included in the analyses. HCPs in emerging incidence areas had significantly lower symptom knowledge scores (7.96, SD=1.44) compared to HCPs in high incidence areas (8.24, SD=1.50; p=.01). Symptom knowledge score was not statistically associated with a future vaccination recommendation (aOR=1.06, 95% CI=0.92-1.22), while practicing in high incidence areas (aOR=2.32, 95% CI=1.53-3.53) was significantly associated with future vaccine recommendation compared to emerging incidence areas while holding all else constant.

Conclusions: Local LD incidence level may have a greater influence on HCP LD vaccine recommendations than symptom knowledge, indicating more efforts may need to be made in emerging LD incidence areas during future LD vaccine rollouts.

Infectious Disease

Increases in blastomycosis incidence in humans and dogs by ecoregion in Minnesota, 1999-2023 Vanessa M. Slack* Vanessa M. Slack Malia Ireland Jennifer R. Head

Blastomycosis, an emerging infectious disease caused by inhalation of Blastomyces fungal spores, often presents as a respiratory infection but can disseminate, causing severe disease with a mortality rate of 8-10%. Examining incidence changes across ecological regions may yield insights into climate or environmental profiles associated with endemicity and emergence. We analyzed surveillance data reported to Minnesota Department of Health (1999-2023) to assess trends in blastomycosis incidence rates (IRs) in humans and dogs across 7 EPA-defined ecological regions spanning wetlands, plains, and forests. Between 1999-2023, 1,111 human and 2,825 dog cases were reported; statewide incidence increased 1.6 times for humans and 3.1 times for dogs. The 2 forest regions (N. Central Hardwood Forests and N. Lakes and Forests) comprised 80% of human cases (n=447 and n=443) and 88% of dog cases (n=900 and n=1589). IRs and ratios (IRRs) in both humans and dogs were highest in 2019-2023 compared to previous years, except N. Glaciated Plains, which has not reported a human case since 2004. Human IRRs (2019-2023 vs. 1999-2003) ranged from 1.7 (95%CI: 1.2-2.0) in N. Lakes and Forests to 9.4 in Lake Agassiz Plain (95%CI: 0.54-164), while dog IRRs ranged from 2.9 in N. Glaciated Plains to 21.0 in N. MN Wetlands. Compared to 2014-2018, recent incidence increased most rapidly for humans in W. Corn Belt Plains and N. Central Hardwood Forests (IRRs 2.7, 95%CI: 1.2-6.0 and 2.4, 95%CI: 1.6-3.0); dog incidence increased most rapidly in N. MN Wetlands (IRR: 2.7) and doubled in 4 regions: N. Central Hardwood Forests, N. Lakes and Forests, Lake Agassiz Plain, and W. Corn Belt Plains (IRRs: 1.9, 2.0, 2.2 and 2.2). These findings show that rising cases are a statewide concern for humans and dogs. While the 2 forest regions dominate the epidemiology of blastomycosis in the state, increases in all ecoregions should motivate statewide control measures such as awareness messaging for earlier diagnoses.

Infectious Disease

The Association Between Long-COVID Symptom Incidence in COVID-19 Patients and COVID-19 Vaccination David Olatunji* David Olatunji Angie Bowman

Introduction:

Millions globally experience Long-COVID-19. Evidence shows higher risk of among women, smokers, the obese, and those with pre-existing conditions. COVID-19 vaccination is associated with reduced risk of persistent symptoms. This study examines the relationship between Long-COVID symptom incidence in COVID-19 patients and COVID-19 vaccination

Methodology

A cross-sectional study was conducted using secondary data from the 2023 Behavioral Risk Factor Surveillance System (BRFSS), including non-institutionalized adults ≥ 18 years across all U.S. states and territories. The outcome variable was Long-COVID status, and the primary exposure variable was COVID-19 vaccination status. Statistical analysis was performed using IBM SPSS Statistics Version 29, including descriptive and bivariate analyses.

Results:

A total of 433,323 participants were included. Among respondents, 52.2% reported prior COVID-19 infection, and 13.8% of these developed Long COVID. Vaccinated individuals reported slightly lower Long COVID prevalence (13.5%) than unvaccinated individuals (14.7%) (OR=0.90, CI:0.81–1.01). Among asthmatics, vaccinated individuals had higher Long COVID prevalence (22.7%) than unvaccinated (20.8%) (OR=1.12, CI:0.86–1.45). Vaccinated individuals with COPD also reported higher prevalence (28.1%) compared with unvaccinated (24.6%) (OR=1.20, CI:0.83–1.73). Pregnant individuals showed similar Long COVID prevalence whether vaccinated (8.9%) or unvaccinated (7.1%). Pregnant females had lower prevalence overall (7.1–8.9%) compared to non-pregnant females (16.1–17.4%), with vaccination showing minimal effect in this group

Conclusion: COVID-19 vaccination was associated with a modest reduction in Long COVID in the general population. This effect was less evident among individuals with asthma, COPD, and those who were pregnant. These findings highlight the need for targeted prevention efforts and further research in high-risk subgroups.

Infectious Disease

Key Informant Interviews to Inform Community-Driven Vector-Borne Disease Education in Arizona Skyler Finucane* Skyler Finucane Kacey Ernst Mary Hayden Jordan Robinson

Background: Vector-borne diseases (VBDs) pose a persistent and preventable threat to human health in Arizona and across the United States. Despite the availability of effective prevention strategies, continued transmission highlights gaps in public awareness and engagement. Novel, community-centered educational approaches are needed to improve prevention behaviors. Partnering with key informants, trusted community leaders with direct public engagement experience, offers an opportunity to develop education strategies that are locally relevant, feasible, and aligned with community needs. This study aims to assess interest, capacity, and perceived barriers among Arizona community leaders to collaborating on VBD education and outreach efforts.

Methods: We are conducting qualitative key informant interviews with leaders of local organizations and businesses across Pima County (urban) and Santa Cruz County (rural). Participants include individuals working in hardware stores, community gardens, nurseries, and feed stores which are settings where community members frequently seek guidance and advice regarding outdoor activities and pests such as mosquitoes. Approximately 20-30 participants are being recruited through publicly available professional channels and community organizations. Interviews are conducted in person, by phone, or virtually depending on participant preference and range from 10 to 60 minutes in length. Semi-structured interview guides explore participants' roles within their organizations, experiences with mosquito and tick-related questions from the public, current education practices, and interest in potential collaboration. Interviews are audio-recorded with consent and will be analyzed using a thematic analysis.

Results (preliminary): Current interviews with hardware store and community garden participants indicate that community leaders frequently receive questions related to mosquitoes and how to control them, but no one has received questions related to ticks. Many hardware store participants expressed interest in receiving or helping to develop brochures and posters that could be displayed near insect repellent products. Some commonly identified barriers to participation include time constraints and limited staffing capacity.

Conclusion: This ongoing study is building partnerships with local organizations and identifying opportunities for community-driven VBD education in southern Arizona. Findings will inform the development of new VBD educational materials and outreach strategies that incorporate advice and suggestions from trusted community leaders.

LATEBREAKER

Infectious Disease

The Role of Flooding in Pediatric Malaria Hospitalization in Rural Ugandan Communities

Annika K Gunderson* Annika Gunderson Ashley Wade Raphael Mbusa Abel Bwambale Huipeng Liao Dana A Giandomenico Emmanuel Baguma Bonnie Shook-Sa Moses Ntaro Edgar M Mulogo Ross M Boyce

Across sub-Saharan Africa, delayed care-seeking is a driver of severe malaria. Climate change is intensifying the frequency and severity of rainfall events, often resulting in flooding which can disrupt access to healthcare. Yet the effects of flooding on hospitalizations attributable to malaria has not been examined.

This study is a secondary analysis of cross-sectional data collected during a cluster randomized trial in rural western Uganda (NCT06870344). All households in selected villages along three flood-prone rivers were eligible. Surveys documenting household characteristics, resident demographics, exposure to flooding, and child health history were administered. Analyses were conducted using a mixed-effects logistic regression with random effects for household assessing indirect flooding exposure, defined as no flooding of the household or property but reported disruptions in daily life including work, school, and access to healthcare and markets, and direct flooding exposure, defines as flooding of the household or property.

The analysis included 10,948 children from 3,754 households. Indirect flooding exposure increased the odds of pediatric malaria hospitalization by 1.75 times (95% CI: 1.06–2.90), while direct exposure increased the odds by 2.45 times (95% CI: 1.54–3.91), compared with no exposure. Among exposed households, work disruptions were associated with nearly fourfold higher odds of hospitalization (OR = 3.94; 95% CI: 2.17–7.14), and disruptions in care-seeking with nearly twofold higher odds (OR = 1.89; 95% CI: 1.01–3.40). No association was found between the number of flooding events and hospitalization.

These findings suggest that indirect consequences of flooding, particularly financial and livelihood disruptions, may delay care-seeking and increase malaria hospitalization risk. Interventions addressing post-flood economic and access barriers could reduce severe malaria outcomes in flood-prone regions.

LATEBREAKER

Infectious Disease

Accounting for individual-level social contact heterogeneity in transmission modeling

Kayoko Shioda* Jessica Ibiebele Anne Shapiro Dehao Chen Judy Donald Mark A. Schmidt Samuel Jenness Benjamin A. Lopman Kayoko Shioda

Background

Human behavior is a key factor in the spread of infectious diseases, with age as a particularly important predictor of social mixing behavior. Existing data on contact mixing patterns typically involve healthy individuals or those whose health status is unknown; thus, the use of contact matrices derived from data on healthy individuals to evaluate public health interventions may paint an inaccurate picture of their effectiveness. This study evaluated how social contact patterns over the course of acute infection may affect the estimated impact of interventions.

Methods

SickMix is a longitudinal study of social mixing patterns among individuals in Portland, OR, experiencing acute respiratory illness or acute gastroenteritis. Using contact matrices from SickMix, we developed two age-structured susceptible-infectious-recovered (SIR)-type models with acute and late infectious compartments: a behavior-dynamic model accounts for reductions in social contacts during acute and late infectious phases, while a behavior-naive model does not. Simulating the spread of a generic respiratory pathogen among the U.S. population, we compared cumulative cases, differences in the basic reproductive number (R0), and outcomes of public health interventions for the dynamic and naive models.

Results

The behavior-naive model yielded 37% more cases compared to the dynamic model, with an R0 ratio of 1.35 (2.37/1.76). Age-specific and total attack rates were lower for the dynamic model (Figure). Failing to account for reduced social mixing associated with illness resulted in an overestimation of the reduction in total cases for daycare closures (5.6% vs. 4.9%) and nursing home isolation (2% vs. 0.8%) and similar reductions for K-12 school closures (99.9% vs. 99.9%).

Conclusion

Our results demonstrate the importance of accounting for changes in social behavior during illness when modeling infectious disease transmission and evaluating the effectiveness of public health interventions.

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Injuries/Violence

Iowa Rural and Urban Parents: Beliefs & Prevention of Violence Efforts Abby Schueller* Abby Schueller Karisa Harland

To create effective prevention approaches in rural communities, we must understand violence's physical, social, and emotional impact. Though reported occurrences of violence provide valuable insights, they often fail to capture the full context of safety and how rural communities undertake the safety of their children.

To address this gap, Iowa conducted a statewide survey from 2019 to 2021, focusing on adult perceptions of safety and violence. The primary aim of the survey was to understand how prevention education, in the areas of preventing harm (perpetration) and avoiding harm (victimization), was implemented at the family level. Additionally, researchers conducted stratified analyses by parent-reported gender and residence in rural areas of the state.

Among parents completing the survey (N=268), 41.7% were male, 35.7 lived in rural Iowa counties, 88.1% were White, 73.5% married, and 80.7% had some college education. Bullying was the top safety concern for parents (63.3%). When asked about preventative conversations with their children, parents reported they discussed topics of being harmed (85.1%) and causing harm (84.7%). Conversations varied based on the respondent's gender, rural location, and the violence experienced. Compared to female parents in urban counties, female parents in rural counties had 2.39 (95% CI: 1.04-5.52) times the odds of speaking with a child about causing sexual harm and 2.68 (95% CI: 1.02-7.05) times the odds of having a conversation about being harmed. Male parents in rural counties reported significantly lower odds of talking to their child about preventing sexual assault than female parents in urban counties (OR [95% CI]: 0.25 [0.11-0.84]), but there was no significant difference in conversations about being sexually assaulted. These findings suggest the need for unique prevention education strategies in rural areas around sexual violence and additional research on gender dynamics in family violence education.

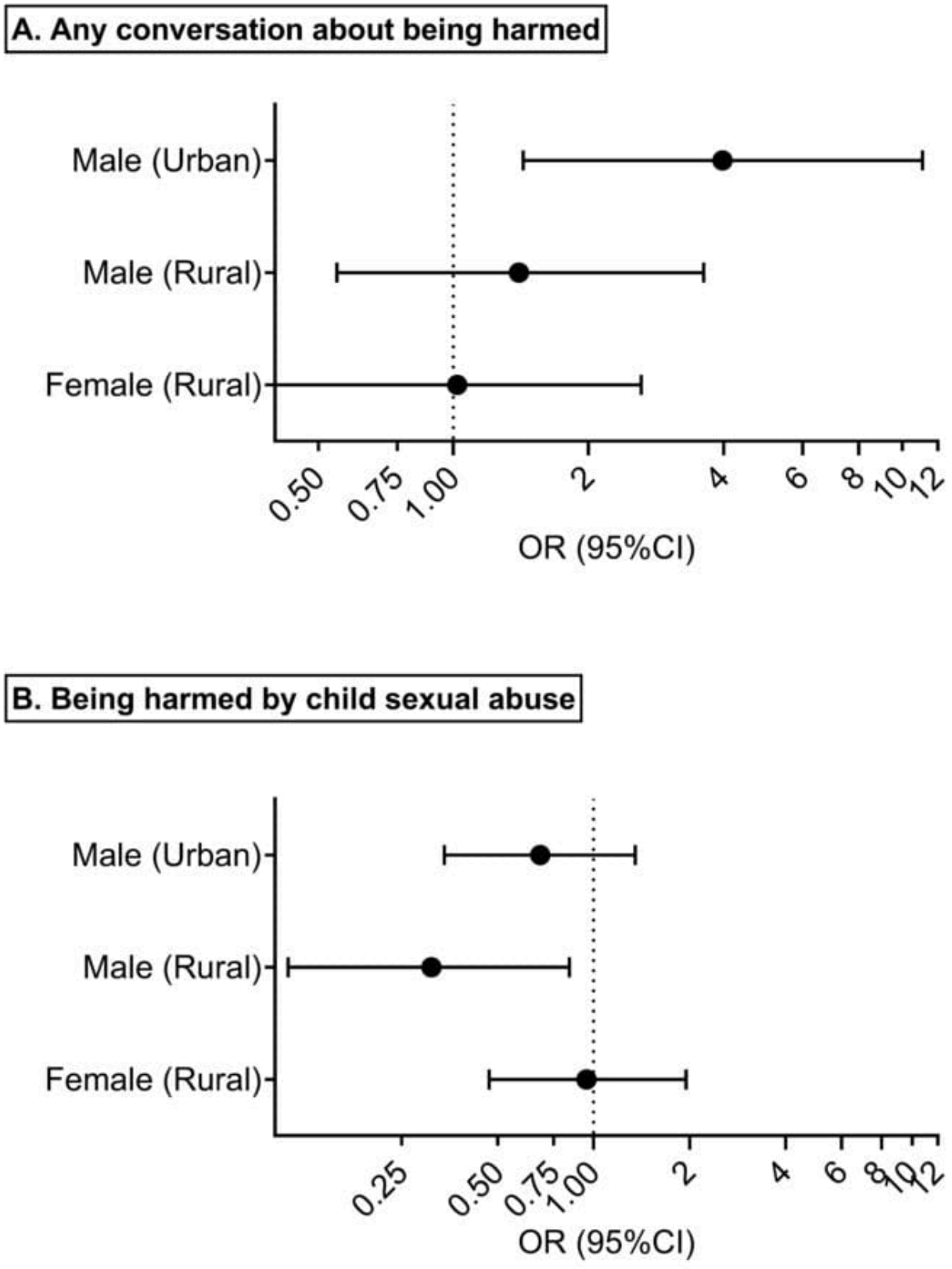


Figure 2. Compared to female urban parents, male parents in urban areas are more likely to talk with their child(ren) about being harmed while male parents in rural areas are less likely to talk with their child(ren) about experiencing childhood sexual abuse.

Mental Health

COVID Mental Health And Soul Study (CMAS Study)- Baseline Data Thomas V. Joshua PhD* Thomas Joshua William V. McCall MD Peter Rosenquist MD Sabina Widner PhD Victoria Burt PhD Debra Williams RN Annette Lynch RN Nori Brown MA

Background: The COVID-19 pandemic exposed significant gaps in public health response to individual/collective health and emotional/social functioning. Disparities in depression screening are evident. African Americans with depression are less likely to seek treatment, become more disabled, and suffer longer illness course. The overall aim of this study is to train Church Health Workers (CHWs) to screen for depression among COVID-19 survivors in a Black church comparing the effectiveness of Screening, Brief Intervention, and Referral to Treatment (SBIRT; Intervention arm) to individuals as Referral As Usual (RAU; Control arm/Usual Care arm) on treatment engagement for depression.

Methods: A 2-arm, single-blind, mixed-methods Randomized Control Trial among COVID-19 survivors within a Black church is currently ongoing. CHWs screened their fellow church members with the Patient Health Questionnaire (PHQ-9) and individuals with depression score ≥ 10 included in the study. Screening of 99 individuals yielded a pool of 8 participants.

Results: 99 subjects were screened and 8 (9.5%) were in moderate and 17 (20.2%) were in mild depression. Descriptive statistics, the mean and standard deviation will be used to describe continuous variables and analyzed at baseline, 3 mos. and 6 mos. after intervention. Simple linear and multiple regression models will be used to estimate the relationship between variables.

Conclusion: We hypothesize that CHWs deployed for church-based depression screening and intervention can help overcome cognitive barriers and increase treatment engagement, defined as attending a depression-related clinical visit for which the subject reports receiving information, referral, counseling, or medication for depression.

Mental Health

Risk and Protective Factors of War-related PTSD in an Israeli Civilian Population in the Aftermath of October 7th Sharon Stein Merkin* Sharon Merkin Liat Orenstein Teresa Seeman Robert Pynoos Alan Steinberg

Background/Objective: Identify risk and protective factors related to post-traumatic stress disorder (PTSD) among civilians during armed conflict.

Methods: Participants (ages ≥18) completed a population-based survey 6 months after the onset of the October 7th war and again 9 months later (n=813). PTSD was based on the PTSD checklist for the Diagnostic and Statistical Manual of Mental Disorders 5th edition (PCL-5, score >31) among those reporting their most bothersome traumatic event (n=435). Sociodemographics, social wellbeing (social support, social integration, resilience) and coping behaviors (sleep, physical activity, weight gain, smoking/alcohol use, volunteering intensity) were based on the baseline survey. Type of exposure to traumatic events included direct (experienced/witnessed), indirect (occurred to family/friend), or secondary (via media or work). Cumulative exposure to trauma included a count of traumatic experiences throughout the follow-up, having a family member in combat and previous trauma.

Results: Overall population prevalence of PTSD was 15.6%, and 29.2% among those reporting a traumatic event. Multivariable models estimated statistically significant risk and protective factors for PTSD after adjusting for all covariates. Risk factors included low income (OR 2.6 95% CI 1.2-5.4), high count of traumatic experiences (OR 3.5 95% CI 1.4-9.1), worse sleep (OR 2.2 95% CI 1.2-4.1) and increased perceived threat (OR 1.3 95% CI 1.1-1.4). Protective factors included resilience (OR 0.8 95% CI 0.6-0.9) and moderate volunteering (OR 0.3 95% CI 0.1-0.8).

Conclusion: These findings indicate that among those who experience traumatic events during wartime, there are several factors that may increase the risk of developing PTSD and other factors that may reduce this risk. Uniquely, this study utilized a civilian population sample during an ongoing war, yielding findings that may inform policy and interventions to prevent and mitigate PTSD during armed conflict.

Mental Health

Cannabis Use Disorder and Postpartum Serious Mental Disorders: Trends and Associations Among Delivering Women in California, 2016-2021 Tosin Oyetunji* LaMecia Ward Sidra J. Goldman-Mellor Tosin Oyetunji

Substance use during pregnancy remains a major public health concern due to its association with fetal and maternal health risks, including mental health problems. Since recreational cannabis was legalized in California in 2016 and use has risen, it is critical to examine how prenatal cannabis use is associated with postpartum women's mental health. Using California statewide linked data on inpatient hospital deliveries and emergency department (ED) visits from January 2016 to December 2021, we examined risk of any ED visit for a serious mental disorder (SMD; psychotic, bipolar, major depressive, anxiety disorders, or suicidal ideation) within 12 months postpartum. Exposure groups were defined as women with cannabis use disorder (CUD), alcohol use disorder (AUD), or neither AUD/CUD, assessed at delivery. Risk ratio (RR) models adjusted for age group, race/ethnicity, insurance type, urbanicity, comorbid psychotic, mood, or anxiety disorder diagnoses at delivery, number of ED visits during pregnancy, and tobacco/nicotine use. Trend analyses showed the prevalence of CUD at delivery increased by 6% per year, and that of AUD increased by 3% per year. Compared with those with no AUD/CUD, individuals with CUD at delivery had 30% higher risk of postpartum SMD (RRadj=1.30; 95% CI:1.21-1.39), while those with AUD had 46% higher risk (RRadj=1.46; 95% CI:1.20-1.77). Findings suggest that prenatal CUD and AUD are independently associated with postpartum serious mental disorder burden, with AUD associated with a slightly higher risk. However, given the substantial rise and increasing prevalence of CUD over time among delivering individuals, CUD may signal a growing mental health threat in this population. These findings highlight the need for intervention and screening strategies for prenatal substance use and mental health.

Mental Health

The Association between 25-Hydroxyvitamin D Levels and Depression 5 years later: A Longitudinal and Mendelian Randomization Analysis of Canadian Longitudinal Study on Aging data Karen Davison* Karen Davison Pulindu Ratnasekera Cherith Somerville Rukshan Mehta Ying Jiang Esme Fuller-Thomson

Depression is a major global health concern. Although vitamin D is involved in central nervous system functioning, its relationship with depression is unclear. Using data from the Canadian Longitudinal Study on Aging, we examined observational and potential causal associations between serum 25-hydroxyvitamin D (25(OH)D) levels (nmol/L) and depression in a prospective cohort of Caucasian adults aged 45–85 who were not taking vitamin D supplements. The variables included: 1) Depression (outcome) measured using the Center for Epidemiologic Studies Short Depression rating scale (score≥10=depression); 2) Transformed 25(OH)D (to remove seasonal effects, 25(OH)D measures were rescaled using a range from 0-lowest to 1-highest level, and the rescaled values were then square-root transformed to satisfy the normality assumptions required for model fitting); and 3) sociodemographic and health-related variables. The causal association between transformed 25(OH)D and depression were investigated using Two Stage Residual Inclusion methodology.

The prevalence of depression at baseline was 13.8% (n = 9,954). At follow-up 1 (approximately four years after baseline) and in Autumn 2020, the proportions of recurrent or incident depression were 12.3% (n = 9,954) and 19.0% (n = 6,608), respectively. Observational association of transformed 25(OH)D were negatively associated with depression at baseline (OR = 0.35, 95% CI: 0.22–0.54), incident depression at follow-up 1 (OR = 0.28, 95% CI: 0.15–0.52), and incident depression in Autumn 2020 (OR = 0.37, 95% CI: 0.19–0.74). In addition, genetically predicted transformed 25(OH)D were negatively associated with baseline depression (OR = 5.9×10^{-6}, 95% CI: 5.9×10^{-10}–1.4×10^{-2}), incident depression at follow-up 1 (OR = 0.26, 95% CI: 0.13–0.51), and incident depression in Autumn 2020 (OR = 0.43, 95% CI: 0.13–1.40). Three genetic variants, rs2012736 (UGT1A), rs4121823 (LIPG), and rs6013897 (CYP24A1; LD2.1/RP2.2) were found to be related to depression via transformed 25(OH)D.

The findings suggest a potentially causal inverse association between transformed 25(OH)D levels and depression. Future studies could help confirm if vitamin D supplementation may help manage depression in those with genetically low levels of 25(OH)D.

LATEBREAKER

Mental Health

Prevalence of prenatal PTSD and co-occurring depressive symptoms among Black women: The role of adverse childhood experiences, sexual harassment and unwanted sexual contact across the lifecourse Sarah C. Haight* Sarah Haight Dawn P. Misra Reema Chande Rosemary Adaji Jaime Slaughter-Acey

OBJECTIVE: Post-traumatic stress disorder (PTSD) during pregnancy may stem from traumatic experiences during childhood or adolescence. In a sample of post-delivery Black women, we investigate the prevalence of prenatal PTSD and co-occurring depressive symptoms and examine associations with adverse childhood experiences (ACEs), sexual harassment, and unwanted sexual contact.

METHODS: Data were from the LIFE-2 cohort of Black women delivering in Detroit (2023-2025). All measures were self-report: PTSD was considered 17 on the 6-item PTSD screener from DSM-5, elevated depressive symptoms were considered 10 on the 10-item Center for Epidemiologic Studies Depression Scale, and elevated ACEs were considered 4 on the ACE-10. Experiences of sexual harassment and unwanted sexual contact was assessed for past year, ever, and age at first occurrence; childhood was defined as <18. Modified Poisson regression produced prevalence ratios (PR) and 95% CIs for prenatal PTSD adjusting for age and education.

RESULTS: Among 519 Black women, 28% experienced prenatal PTSD and 68% of those had co-occurring elevated depressive symptoms. Women with prenatal PTSD were more likely to be younger and unmarried/not living with a partner. In adjusted models, 4 ACEs (PR: 2.7; 95% CI=2.0-3.7), sexual harassment in the past year (PR=1.8, 95% CI=1.2-2.9) and ever (PR=1.7, 95% CI=1.3-2.4), and unwanted sexual contact in the past year (PR=2.8, 95% CI=1.7-4.6), ever (PR=2.3, 95% CI: 1.7-3.1), and during childhood (PR=2.2, 95% CI=1.6-3.0) were all related to an increased likelihood of prenatal PTSD.

CONCLUSION: Among this sample of Black women at delivery hospitalization, 1 in 4 experienced prenatal PTSD and of those, nearly three quarters had co-occurring depressive symptoms. ACEs and experiences of sexual harassment or unwanted sexual contact were significantly related to prenatal PTSD. Findings support the use of trauma-informed care and performing validated PTSD screening in perinatal care settings.


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LATEBREAKER

Mental Health

Extreme heat, mental health conditions, and readmission after heart failure hospitalization among Medicare beneficiaries with type 2 diabetes Christine L Gray* Christine Gray Rebecca Fillipo Sofia Pozsonyiova Lauren E Wilson Elizabeth Rojo Hayden Bosworth Sudha R Raman

Heart failure (HF) mortality among older adults with type 2 diabetes (T2D) in the US is increasing, as are extreme heat events. HF patients are heat sensitive and especially vulnerable in the 30 days after hospitalization. This may be especially true of those with existing mental health conditions. Using Medicare claims data on a cohort of adults with T2D discharged following a heart failure hospitalization between 2015 and 2019, we examined mental health severity, extreme heat event (EHE), and risk of the composite outcome of 30-day re-hospitalization or all-cause mortality. EHE was defined as ≥2 consecutive days with Max Heat Index ≥ county-specific 95th percentile during the warm season (May 1 – September 30). A 1-year lookback ensured capture of an active T2D diagnosis, no prior HF hospitalization, and ability to classify existing mental health status. We focused on the role of mental health, using the presence of ICD-10 diagnosis codes F20-F49 and dispensed medications to define mental health groups (no/low, moderate, and severe). Cox proportional hazard models with time varying EHE exposure adjusted for demographics, climate region, temporal indicators, comorbidities, and county characteristics estimated HRs and 95% CIs. Among 186,201 included individuals, 13,582 were exposed to an EHE over the study period. Compared to those with severe mental health, those with moderate mental health status had reduced risk of the outcome (HR: 0.92; 95%CI: 0.90,0.95) and those with no/low mental health conditions had even more reduced risk (HR: 0.80; 95%CI: 0.78,0.82). We examined modification by mental health severity of the EHE exposure and our outcome, but did not observe statistically significant associations, though data were less powered to detect effects. Mental health status is an important consideration in discharge of T2D patients following heart failure hospitalization. More research on timing of EHEs may elucidate potential heat impacts by mental health status.

Mental Health

Acculturation, Social Support, and Mental Health among Latinos in New York City John Wetmore* John Wetmore Ruth Ottman

Background: Acculturation and social support are central social determinants of mental health among U.S. Latinos, yet their combined effects on depression, anxiety, and stress are not well characterized.

Methods: We analyzed cross-sectional data from 358 Latino residents of northern Manhattan, New York. Acculturation profiles (traditional, bicultural, integrated) were derived using latent class analysis incorporating migration history, language use, and cultural orientation. Social support was measured with the Multidimensional Scale of Perceived Social Support (MSPSS) and dichotomized as high (>5) versus low (≤5). Logistic regression was used to assess associations of acculturation profile with high social support. Depression (PHQ-9), anxiety (GAD-7), and perceived stress (PSS) were modeled using linear regression to estimate marginal means (EMMs). All regression models adjusted for age, gender, education, marital status, and Latino origin subgroup (e.g., Dominican, Mexican).

Results: Prevalence of high social support did not differ among acculturation profiles (all $p \geq 0.32$). Compared with integrated participants, bicultural participants had higher adjusted EMMs for depression (5.4±0.5 vs 3.7±0.6, $p=0.01$) and anxiety (4.6±0.5 vs 3.2±0.6, $p=0.02$). In stratified analyses, acculturation-related differences were most pronounced among participants with low social support, where bicultural participants exhibited markedly higher depression (6.7±0.8 vs 2.8±1.0, $p<0.001$), anxiety (4.8±0.8 vs 2.2±0.9, $p=0.01$), and stress (15.9±1.3 vs 12.7±1.5, $p=0.047$) than integrated participants. Interaction tests supported effect modification by social support for depression.

Conclusions: Acculturation-related differences in depression, anxiety, and stress were evident under conditions of low social support. Social support may buffer acculturation-related mental health risk, underscoring its potential as a modifiable intervention target for reducing mental health disparities among Latinos.

Mental Health

Social Support and Anxiety in Parents of Young Children: A Latent Class Analysis Erin Wissler Gerdes* Erin Wissler Gerdes Nichole Nidey Sarah Nash Jonathan Platt Emily Roberts Andrea Greiner

Introduction: The transition to parenthood is a vulnerable period for both mothers and fathers, yet most parental mental health research focuses on mothers in the immediate postpartum period. Little is known about parental anxiety as children move beyond infancy, despite evidence that support needs remain high. Social support is a key protective factor in mental health, and early interventions may help reduce anxiety and other mental health concerns. This study examines how distinct patterns of interpersonal support relate to anxiety among parents of young children, with the goal of identifying support gaps that may serve as intervention targets.

Methods: Social Support was measured using the Interpersonal Support Evaluation List (ISEL-12) plus one original item, and anxiety was measured using the General Anxiety Disorder Assessment (GAD-7). Among 352 parents with at least one child under the age of five, latent class analysis identified subgroups of social support. Descriptive analyses examined demographic characteristics associated with class membership, and linear regression assessed the relationship between social support and anxiety.

Results: Four distinct classes of social support were identified: 1) High Support, 2) Low Support, 3) Mid-High Support, and 4) Mid-Low Support. Compared to Class 1, parents in Classes 2-4 scored 1.8-4.8 points higher on the GAD-7. Across all classes, the Belonging subscale had the lowest scores, suggesting that feelings of loneliness and reduced social connectedness may be common among parents of young children. Most demographic characteristics were not significantly associated with class membership, although financial insecurity was more likely in Class 2, with members “finding it difficult to get by”.

Conclusion: This study identified four classes of social support and their impact on anxiety severity. Identifying social support gaps offers an opportunity for targeted interventions to reduce anxiety in parents of young children.

Mental Health

Revisiting the Diagnostic Algorithm: Implications for Depression Prevalence Daniel Hagen*
Debbie Huang Daniel Hagen Rasmika Kumar Emily Goldmann

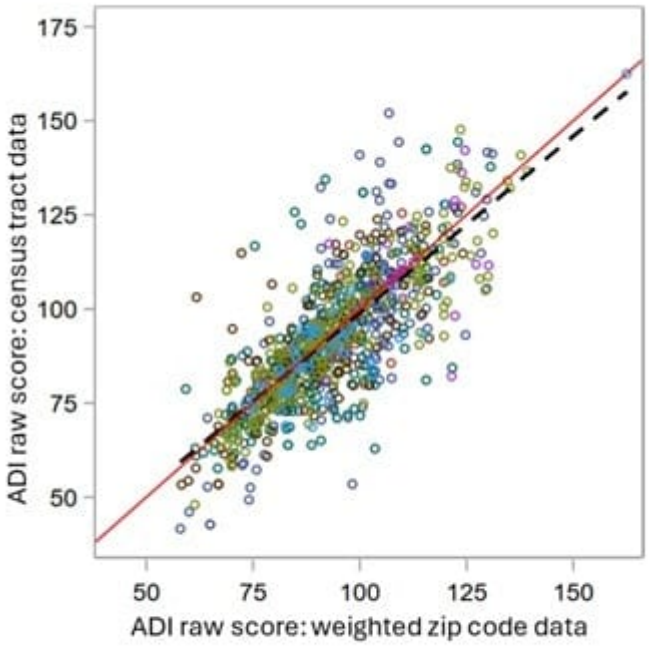
The Patient Health Questionnaire (PHQ)-9 is among the most utilized screeners for major depressive episode (MDE). Despite being devised for screening, many prevalence studies use it, taking a summed score approach (cut-point≥10), which may overestimate prevalence. We employed a data-driven approach to revisit use of the less sensitive but more specific diagnostic algorithm scoring approach – which mirrors Diagnostic and Statistical Manual and Mental Disorders (DSM)-5 criteria for MDE and requires endorsement of at least 5 of 9 PHQ-9 symptoms at least more than half the days in the past 2 weeks, one of which must be depressed mood or anhedonia – in prevalence studies when gold standard diagnostic instruments are not feasible. To first quantify current use of screening instruments in prevalence studies, we conducted a scoping review of studies reporting depression prevalence and indexed in MEDLINE in 2024-25. Second, we analyzed data from the 2021-23 National Health and Nutrition Examination Survey (NHANES) to describe differences in weighted prevalence and sociodemographic, clinical and functioning indicators between adults (18+) who screened positive for depression using both the summed score and diagnostic algorithm approach vs. summed score approach only. Out of 298 studies using screening instruments to measure depression prevalence, 110 (37%) utilized the PHQ-9 with the summed score approach. Using NHANES data, the diagnostic algorithm scoring approach yielded a lower prevalence estimate (5% vs. 12% using summed score). Screening positive with the diagnostic algorithm was highly associated with greater functional impairment and symptom severity, but not with any sociodemographic characteristics. In studies measuring depression prevalence, the diagnostic algorithm may yield more realistic estimates than the summed score approach and identify those with more severe symptoms and greater functional impairment, serving as a better indicator of population need.

Methods/Statistics

Comparing methods for linking neighborhood-level estimates to longitudinal data from the Breast Cancer Surveillance Consortium (BCSC) Erin J Aiello Bowles* Erin Bowles Ladia Albertson-Junkans Gaia Pocobelli Tracy Onega Garth Rauscher Marissa Lawson Al Derus Karla Kerlikowske Anna Tosteson Christoph Lee Brian Sprague Sarah Nyante Janie Lee Rebecca Hubbard Diana L Miglioretti

Methods for obtaining and linking neighborhood-level estimates of social determinants of health (SDOH) often focus on data from one specific timepoint (e.g. one year of the US Decennial Census or American Community Survey), or data from a single level of aggregation (e.g. census tract). We present methods and results from two area-based methods used to obtain SDOH among people receiving multiple breast imaging exams over time in the Breast Cancer Surveillance Consortium (BCSC). We linked >3.6M exams performed at 135 breast imaging facilities between 2005-2023 on women ages 18+ years from eight regional registries in California, Illinois, New Hampshire, North Carolina, Vermont, and Washington state. Regional BCSC registries geocoded addresses from self-report and administrative data at each exam using ArcGIS. For one method, registries linked geocodes to US census tracts over time (e.g. exams from 2010-2019 used 2010 census tracts) and then linked census tracts to publicly available SDOH indices (e.g. Area Deprivation Index [ADI]) by exam year. The second method linked zip codes to SDOH indices to reduce missingness (~40%) due to addresses that could not be geocoded and PO boxes. Zip-code-level indices were weighted by census tract using US Department of Housing and Urban Development residential ratios that describe the portion of each census tract within a zip code. We compared ADI raw scores from census tract and weighted zip code data to understand concordance between the two methods. Scatter plots of a random sample showed good agreement between the two methods with some variation by registry (see figure). Analyses using area-level data should consider trade-offs between missingness and data variability when linking to different neighborhood-level estimates and SDOH indices.

Scatter plot comparing two methods for generating ADI

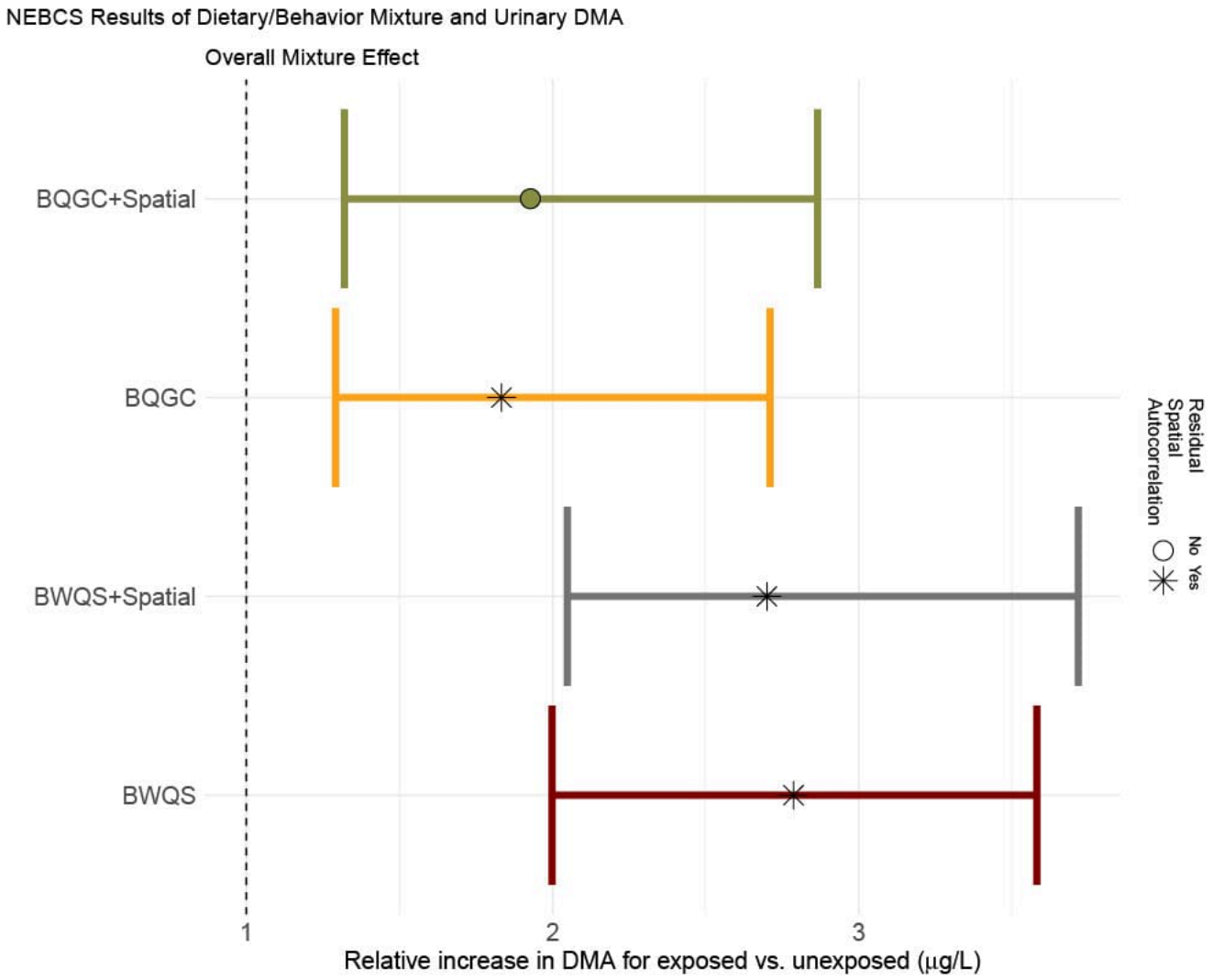


Key: different color circles = registries
Dashed black line = regression line fit to data
Solid red line = perfect agreement

Methods/Statistics

Analysis of Complex Mixtures Using Flexible Bayesian Quantile-Based G-Computation Maria Kamenetsky* Maria Kamenetsky Sung Duk Kim Stella Koutros Margaret R. Karagas Alison Johnson Dalsu Baris Debra T. Silverman Alexander P. Keil

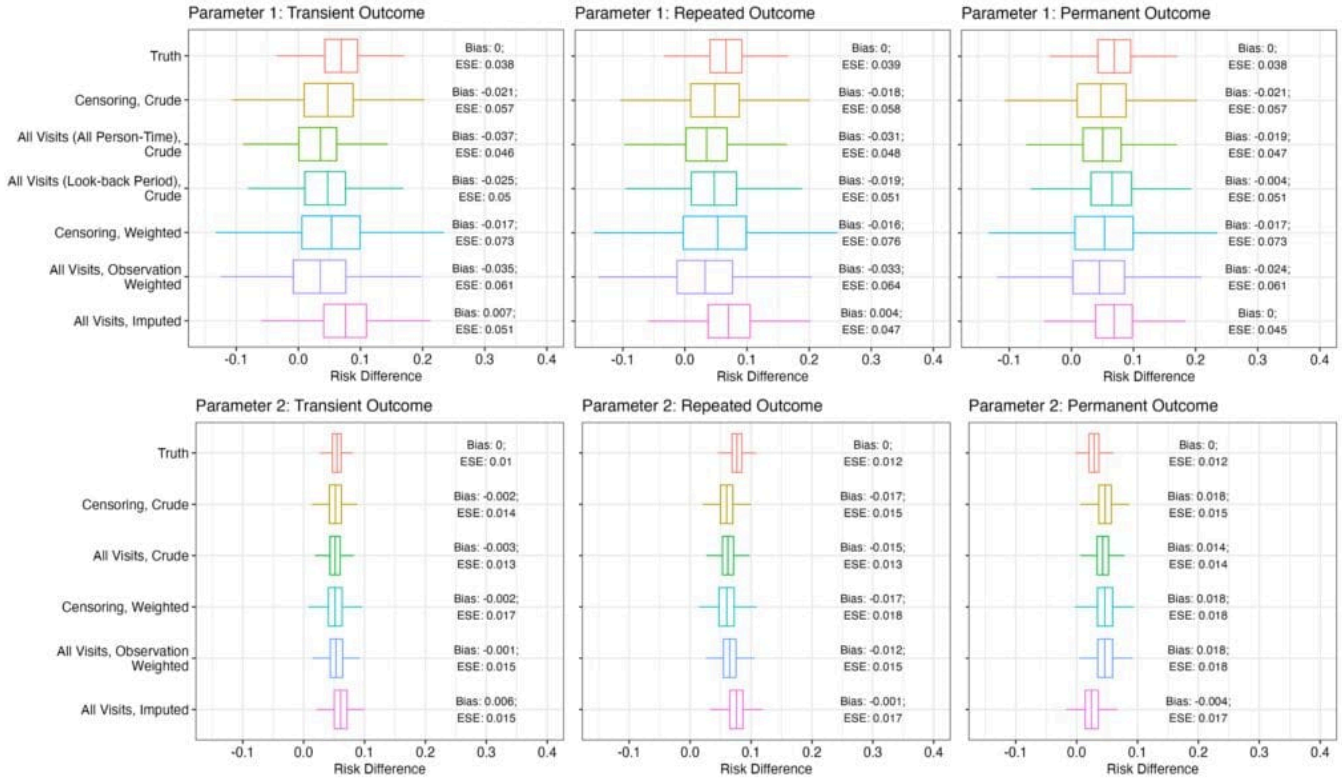
Methods for environmental mixtures (“mixtures analyses”) consider the overall effect of multiple concurrent exposures instead of solely one exposure at a time. Mixtures analyses are particularly important for environmental exposures as overall effects can differ from effects of any single exposure alone. Data on these exposures are often collected in small sample sizes and exhibit complex dependence structures, such as spatial or temporal correlation and hierarchical exposure groupings. However, commonly-used mixtures methods that target a single overall effect are limited in their ability to formally model these features, potentially results in biased inference and poor prediction. To address this limitation, we develop a novel flexible Bayesian quantile-based g-computation (BQGC) approach to mixtures. This Bayesian framework allows for the integration of more data complexities and common characteristics of environmental mixtures. We demonstrate our approach using dietary data from the New England Bladder Cancer Study (NEBCS), a large population-based case-control study. Exposure to arsenic, a known carcinogen, is primarily through contaminated drinking water and diet. Arsenic is metabolized into dimethylarsinic acid (DMA), monomethylarsonic acid (MMA), and inorganic arsenic (iAs), with DMA comprising the largest proportion in human urine. We explore the association between a mixture of dietary exposures and urinary DMA in the region among control participants (N=1,109). Using BQGC with integrated spatial dependence (BQGC+Spatial), those exposed to the dietary mixture had urinary DMA values that were 93% higher than compared to those never exposed (95% credible interval: 32%, 187%), with no evidence of residual spatial autocorrelation. Our innovations improve the accuracy of statistical evidence of the mixture’s effect on disease risk and expand the flexibility of mixtures analysis in public health.


NEBCS Results of Dietary/Behavior Mixture and Urinary DMA
Overall Mixture Effect
BQGC+Spatial
BQGC
BWQS+Spatial
BWQS
1
2
3
Relative increase in DMA for exposed vs. unexposed (μg/L)
Residual Spatial Autocorrelation
No
Yes

Methods/Statistics

Mind the Gap: addressing missing person time when estimating time-fixed effects in longitudinal data Jacqueline Rudolph* Jacqueline Rudolph Rachael Ross Lauren Zalla Bryan Lau Catherine Lesko

Longitudinal data often include gaps in observation when outcomes (and other variables) are unmeasured, due to missed study visits or drop out. Previously we examined how to handle data gaps when estimating outcome incidence; here, we extend that work to examine the estimation of time-fixed effects in longitudinal data. We generated 1000 simulation iterations of 1000 individuals followed across t=5 study visits; individuals were allowed to miss visits or drop out of the study. We generated 3 outcome types: transient, repeated, and permanent. In each simulation, we had two target parameters: (1) average causal risk difference (RD) at t=5 by baseline exposure ($E[Y(5)x(0)=1,\bar{m}(5)=0]$-$E[Y(5)x(0)=0,\bar{m}(5)=0]$) and (2) time-specific average causal RD by concurrent exposure ($E[Y(t)x(t)=1,\bar{m}(t)=0]$-$E[Y(t)x(t)=0,\bar{m}(t)=0]$), where Y(t) denotes outcome, X(t) denotes exposure, and M(t) denotes missingness at t. Here, we present results under a data generating mechanism where missingness was informative (affected by a baseline outcome predictor and exposure). We estimated parameter 1 by taking the contrast in the complement of the Kaplan-Meier survival estimators by baseline exposure; we estimated parameter 2 using linear binomial models with generalized estimating equations (exchangeable correlation), obtaining the information-weighted average of the time-specific estimates. We estimated bias and empirical standard errors for crude (e.g., censor at missed visit, include all observed visits) and adjusted (e.g., censor with censoring weights, multiple imputation) approaches to account for missed visits. Results are summarized in the Figure. For parameter 1, most crude and adjusted approaches underestimated RD; multiple imputation was least biased. For parameter 2, bias was minimal regardless of approach with a transient outcome; otherwise, multiple imputation had the lowest bias. In future work, we will examine additional data generating mechanisms, including those with time-varying confounders.


Parameter 1: Transient Outcome
Parameter 1: Repeated Outcome
Parameter 1: Permanent Outcome
Truth
Censoring, Crude
All Visits (All Person-Time), Crude
All Visits (Look-back Period), Crude
Censoring, Weighted
All Visits, Observation Weighted
All Visits, Imputed
Bias: 0; ESE: 0.038
Bias: -0.021; ESE: 0.057
Bias: -0.037; ESE: 0.046
Bias: -0.025; ESE: 0.05
Bias: -0.017; ESE: 0.073
Bias: -0.035; ESE: 0.061
Bias: 0.007; ESE: 0.051
Bias: 0; ESE: 0.039
Bias: -0.018; ESE: 0.058
Bias: -0.031; ESE: 0.048
Bias: -0.019; ESE: 0.051
Bias: -0.016; ESE: 0.076
Bias: -0.033; ESE: 0.064
Bias: 0.004; ESE: 0.047
Bias: 0; ESE: 0.038
Bias: -0.021; ESE: 0.057
Bias: -0.019; ESE: 0.047
Bias: -0.004; ESE: 0.051
Bias: -0.017; ESE: 0.073
Bias: -0.024; ESE: 0.061
Bias: 0; ESE: 0.045
-0.1 0.0 0.1 0.2 0.3 0.4
Risk Difference
Parameter 2: Transient Outcome
Parameter 2: Repeated Outcome
Parameter 2: Permanent Outcome
Truth
Censoring, Crude
All Visits, Crude
Censoring, Weighted
All Visits, Observation Weighted
All Visits, Imputed
Bias: 0; ESE: 0.01
Bias: -0.002; ESE: 0.014
Bias: -0.003; ESE: 0.013
Bias: -0.002; ESE: 0.017
Bias: -0.001; ESE: 0.015
Bias: 0.006; ESE: 0.015
Bias: 0; ESE: 0.012
Bias: -0.017; ESE: 0.015
Bias: -0.015; ESE: 0.013
Bias: -0.017; ESE: 0.018
Bias: -0.012; ESE: 0.015
Bias: -0.001; ESE: 0.017
Bias: 0; ESE: 0.012
Bias: 0.018; ESE: 0.015
Bias: 0.014; ESE: 0.014
Bias: 0.018; ESE: 0.018
Bias: 0.018; ESE: 0.018
Bias: -0.004; ESE: 0.017
-0.1 0.0 0.1 0.2 0.3 0.4
Risk Difference

Methods/Statistics

Bias analysis adjustment for time-to-event outcomes Richard MacLehose* Richard MacLehose Pam Lutsey Katherine Giorgio Sanaz Sedaghat

Introduction

Misclassification is a threat to the validity of epidemiologic studies. Bayesian, frequentist, and probabilistic bias analysis (PBA) methods have been developed to adjust for misclassification, but little methodological development has focused on outcome misclassification in a time-to-event setting. We present methods to adjust for outcome misclassification in discrete-time follow-up analyses using both Bayesian and PBA approaches. We evaluate these approaches in simulations and apply them in a longitudinal cohort study of risk factors for time to dementia onset.

Methods

We assume that the true outcome status is unobserved at each discrete time point and once it occurs, it never resolves (an absorbing state). Outcome risk varies over time intervals and is a function of observed risk factors. The true disease state is latent and the observed outcome is misclassified. The influence of sensitivity and specificity is specified through prior distributions. We fit an absorbing-state hidden Markov model using Bayesian methods and approximated via a PBA algorithm. The methods are compared in a simulation study and illustrated in a longitudinal cohort study of dementia risk, following participants from adulthood into late life.

Results

Simulations showed both methods remove nearly all bias due to misclassification when the bias parameters were correctly specified (bias <0.01 and greater than 99% coverage). The Bayesian approach required more technical expertise and took 5 times the computational time. When these methods were applied to an existing cohort study, risk of dementia increased relative to methods that did not adjust for misclassification. Interval estimates were wider for the bias-adjusted risks because they incorporated uncertainty in the bias parameters.

Discussion

We presented two novel methods to adjust for outcome misclassification in time-to-event studies. Both methods had little bias and good coverage, with PBA maintaining an advantage in speed.

LATEBREAKER

Methods/Statistics

Illusions of Equity: When Real-World Data Sources Blur the True Benefits of Structural Interventions Jerzy Eisenberg-Guyot* Jose Plascencia Jimenez Jerzy Eisenberg-Guyot Sarah Conderino

Background

Real-world data (RWD) is increasingly used to identify targets for reducing racial disparities, but data-retrieval processes (e.g., measurement, selection, restriction) can distort prevalence and absolute risk differences, quantities that determine how much disparity an intervention can remove. We asked if RWD distorts the observed reduction in the Black–White gap in uncontrolled diabetes when evaluating a hypothetical intervention to eliminate insurance gaps.

Methods

Using published nationally representative prevalence estimates for race, insurance coverage, and uncontrolled diabetes (HbA1c >9%) as our benchmark, we calibrated a source population propagating parameter uncertainty via probabilistic simulation. Our causal estimand was the proportion of disparity eliminated (PDE): the percentage reduction in the Black–White absolute risk difference under a hypothetical intervention do(E=0). We simulated three RWD data-source mechanisms: (1) EHR data, (2) hospital-cohort, and (3) claims data restriction, representing differential outcome misclassification, selection, and collider stratification bias. We calculated source-driven instability as the probability of observing a minimal or reversed effect (PDE <5% or PDE <0) conditional on a true baseline PDE ≥20%.

Results

In the benchmark, eliminating the coverage gap reduced the racial disparity by a median of 18% (IQR 3%–39%). Simulated EHR misclassification attenuated the benefit to 4% (−5% to 18%), with a 19% probability of inverting the direction of effect. Hospital selection reversed the effect to −5% (−23% to 17%), with a 45% instability rate. Insured restriction eliminated the signal (0%, −1% to 2%), with a 80% reversal rate.

Conclusions

RWD can decrease or reverse the observable effects of structural interventions on disparity reduction. Health equity research using RWD should report absolute disparity estimands (e.g., PDE) and conduct quantitative bias analyses to account for data-source bias mechanisms.

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Methods/Statistics

Considerations for synthetic control generation in difference-in-differences via Gaussian process: A use-case Hayden Smith* Hayden Smith

Background: Emergency Department (ED) patients that left without being seen (LWBS) present a clinical challenge. Evaluation of interventions to reduce LWBS rates requires methods to account for temporal trends. Conventional difference-in-differences (DID) approaches may be biased when pre-intervention trends are not parallel. Objective: To present an example of using a Gaussian process-based synthetic control DID (GPSDID) model and describe limitations.

Methods: A GPSDID framework was used to examine LWBS rates after the implementation of an ED staffing change. One-year of data was collected before and after the change from three EDs (i.e., study center and two control centers) in the same Midwestern health system. The GP was trained on pre-intervention data to capture nonlinear temporal trends and to generate a synthetic post-period counterfactual. Differences between the post-intervention LWBS rates and synthetic control were used to compute the average treatment effect on treated (ATT), with 95% credible intervals (Crl) derived from GP posteriors.

Results: There were 88,000 ED encounters across the reviewed centers. The GP-based synthetic control had nominal coverage of the pre-intervention observations (Figure). Post-intervention data failed to reveal an effect relative to synthetic control with ATT being 1.97% (95% CrI: -1.89%, 2.05%). Modeling considerations included the smoothness of trends, interpretability of latent functions, sparse controls, covariate adjustment, complexities for covariance in uncertainty measures, and extrapolation concerns – these topics will be expanded upon at the conference.

Conclusions: GPSDID provides a flexible and interpretable framework for assessing interventions by capturing nonlinear trends and providing uncertainty quantification via Bayesian posteriors. The approach may enable robust causal inference in complex settings and can be possibly applied to outcomes with dynamic trends. Of note, GP may not be without limitations.

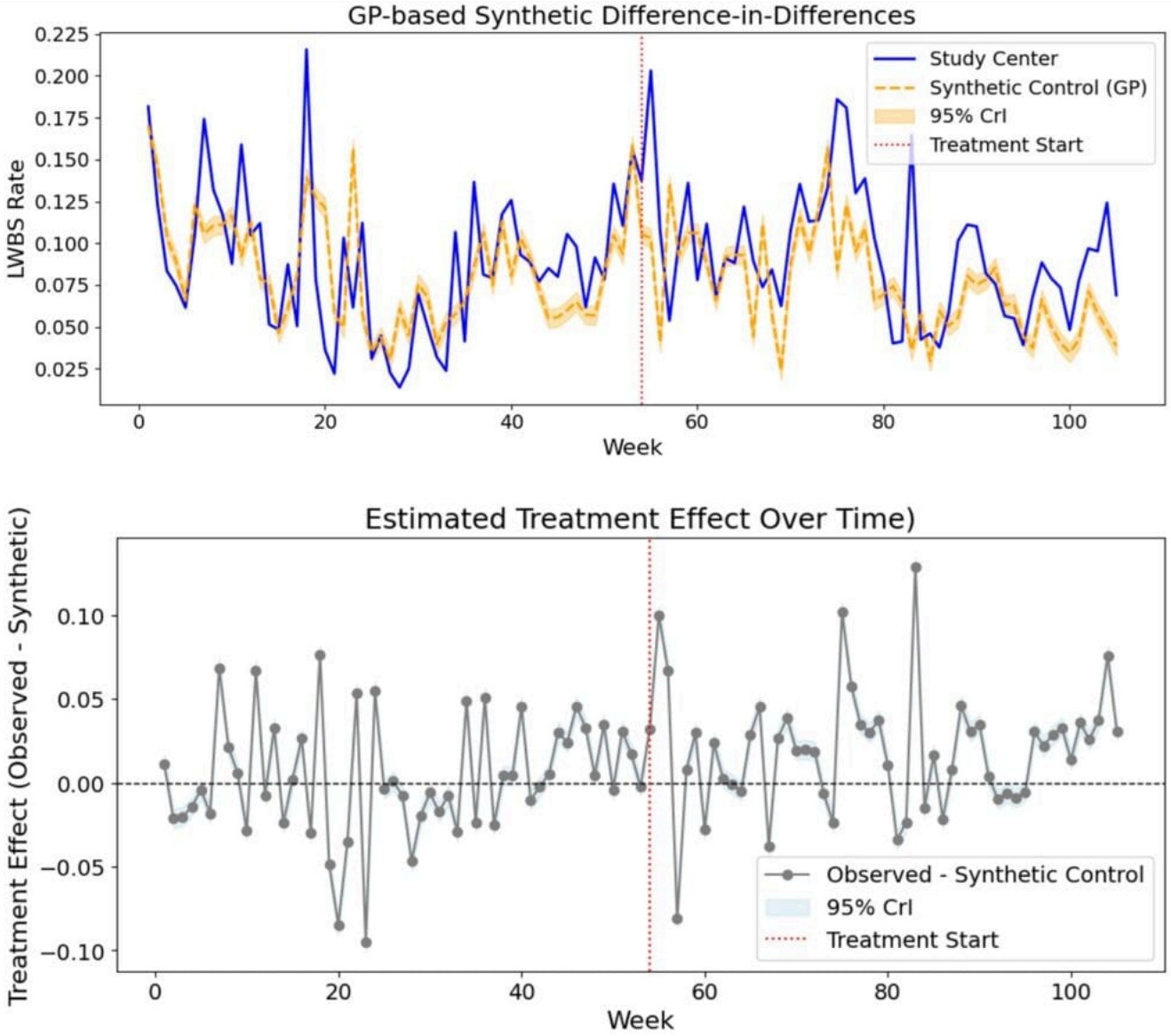


Figure. Top pane: plotted left without being seen rates for study center receiving a staffing intervention versus synthetic control group values calculated using Gaussian process (GP). Bottom pane: Differences in LWBS rates between study center and synthetic control.

Methods/Statistics

A Unified Multi-State Approach for Investigating the Dynamics of Chronic and Infectious Diseases Ming Ding* Ming Ding

Infectious diseases and chronic diseases are two major fields in epidemiology that have traditionally been studied separately because of their distinct etiologies and modeling methods. Infectious disease data are typically collected as aggregated data and are modeled using compartmental models, with the most commonly susceptible (S), infectious (I), and recovered (R) (SIR) model. While for chronic disease, data are usually collected as individual-level data and are analyzed using multi-state survival models. Previous studies have pointed out the link between compartmental models and survival analysis by reconstructing the aggregated infection disease data into individual-level data. However, these studies have largely focused on the two-state transition from S to I state, and few studies have simultaneously modeled the three-state process, S, I, and R. In this abstract, we propose to use a discrete-time multi-state framework to model the three-state transition of infectious disease. We first introduce and compare modeling approaches for infectious disease and chronic disease dynamics, then show the link between compartment models and multi-state models, and finally present how infectious disease parameters can be estimated using multi-state models under the two scenarios: 1) all S, I, and R states are observed, and 2) only the I state is observed, with the R state treated as latent. In the application, we applied the multi-state approach to describe the dynamics of influenza using the data in a British boarding school in 1978. The estimated recovery rate was 0.42 and the corresponding contact rate was 0.91 (95% CI:0.84, 0.98). The basic reproductive number was 2.17 (95% CI: 2.00, 2.33), and declined to approximately 1 by day 6, and continued to decrease thereafter, indicating that the turning point reached at around day 6. Overall, we propose a unified multi-state approach for modeling infectious and chronic disease progression, which may provide key evidence to inform timely and effective infectious disease prevention.

Table 1. A comparison of infectious disease and chronic disease progression.

	Infectious Disease	Chronic Disease
Disease etiology	Caused by transmissible pathogens	Caused by risk factors that vary across individuals
Disease duration	Typically short	Long-term; may take decades
Data collected	Aggregated population-level data	Individual-level longitudinal data
Models	Compartment models $\frac{dS(t)}{dt} = -\beta S(t)I(t)$ $\frac{dI(t)}{dt} = \beta S(t)I(t) - \gamma I(t)$ $\frac{dR(t)}{dt} = \gamma I(t)$	Multi-state models $\frac{dS_0(t)}{dt} = -\lambda_{01}(t)S_0(t)$ $\frac{dS_1(t)}{dt} = \lambda_{01}(t)S_0(t) - \lambda_{12}(t)S_1(t)$ $\frac{dS_2(t)}{dt} = \lambda_{12}(t)S_1(t)$
Model characteristics	• Disease dynamics are characterized by the contact rate (β) and the recovery rate (r). • β and r are largely determined by pathogen, with minimal individual-level difference. • The S→I transition rate depends on the proportion of infected individuals, $I(t)$. • The S→I transition rate is time-varying, while the I→R transition rate is constant.	• Disease dynamics are characterized by transition rates between states. • Transition rates are largely determined by individual-level risk factors. • Transition rates are independent of the proportion of participants in each state. • Transition rates can be time-varying.
Estimated parameters	Population-level parameters: • Contact rate (β) • Recovery rate (r) • Basic reproductive number (R_0)	Population-level parameters: • Coefficients of risk factors with transition rates Individual-level parameters: • Transition rates • Survival probabilities

Methods/Statistics

Beyond per-capita rates: Urban scaling of female firearm homicides in the United States
Roni Barak Ventura* Roni Barak Ventura Maurizio Porfiri

Epidemiologic rates are typically standardized by population size, however, growing evidence suggests that rural and urban systems differ in more fundamental ways that are not fully captured by per-capita measures. Urban Scaling Theory models cities as complex systems analogous

to biological organisms, whose behaviors are better described by scaling laws such as Kleiber's Law and Ideal Gas Law. Empirical studies show that urban infrastructure (e.g., roads, cables, and built area) scales sublinearly with population size, whereas socioeconomic phenomena (e.g., GDP, patents, and social interactions) scale superlinearly. By explicitly accounting for population-dependent nonlinearities, urban scaling enables more equitable comparisons across spatial units of different sizes.

Urban scaling provides an appropriate framework for modeling epidemiologic variables such as event incidence, risk factors, and the distribution of resources to mitigate them across the urab-rural continuum. We demonstrate the utility of this approach by examining the distribution of female firearm homicides across U.S. cities. We analyzed data from 917 U.S. cities for three periods: pre-pandemic (2018–2019), during the pandemic (2020–2021), and post-pandemic (2022–2023). For each period, we fit a power-law model relating homicide counts to city population size and recorded the corresponding scaling exponent β. Female firearm homicides exhibited strictly sublinear scaling across all periods, indicating a disproportionate burden in less populous, more rural areas. However, the scaling exponent increased significantly during the pandemic ($\beta = 0.711 \in [0.668, 0.754]$ in 2018-2019 and $\beta = 0.804 \in [0.761, 0.846]$ in 2020-2021) and following the pandemic ($\beta = 0.903 \in [0.872, 0.933]$ in 2022-2023). This finding suggests a growing incidence of these homicides in more densely populated cities. These results align with reports of increased domestic violence and femicide during and following the COVID-19 pandemic.

LATEBREAKER

Methods/Statistics

Maternal Mortality and Racial Disparities Health Indicators in Historical US Data: Does Nonstationarity matter? Anthony Kondracki* Anthony Kondracki Manouchehr

Background: Maternal mortality and racial disparities, key health indicators and quantitative metrics of high-priority issues in the US, have been drawing sustained attention from current academic research, public health service agencies, and policymakers. Most time series models assume data stationarity for valid estimates and future predictions. Limited attention has been paid to examine data properties before selecting models, and how research findings may affect the policymaking process. Our objective was to conduct a time series analysis for these health indicators to verify data properties, which is crucial for conducting analyses, valid inferences, and forecasting.
Methods: We performed a retrospective time series analysis of aggregate population-level data (1960-2016) from the US National Center for Health Statistics. Time plots were generated to analyze data points reported consistently every two years to identify broad behaviors and trends. The Augmented Dickey-Fuller (ADF) test, differencing, and transformation techniques were applied to verify data properties and to achieve stationarity.
Results: The analysis of data points revealed instability in patterns and drifting trends characteristic of a nonstationary process, which was confirmed by the ADF test. Data were transformed to achieve stationarity. Stationarized data are analyzed using standard statistical models for valid estimates and for predicting future values. Maternal mortality rates rise contingent on permanent effects of specific events or shocks which accumulate and integrate into future values, rather than dissipating over time.
Conclusions: Maternal health research should explicitly address and test time series data to verify data properties to avoid errors in estimates, invalid inferences, and misguiding strategic policy decisions.

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Neurology

Tinnitus Burden among Young to Middle-Aged Adults in the United States: the National Longitudinal Study of Adolescent to Adult Health (Add Health) Chuan-Ming Li* Chuan-Ming Li Howard J. Hoffman Christi L. Themann Bryan K. Ward Gregory A. Flamme

Objective: To estimate tinnitus incidence, prevalence, and risk factors among adults aged 24–51 years.

Methods: The National Longitudinal Study of Adolescent to Adult Health (Add Health) is a nationally representative cohort of students recruited in grades 7–12 during 1994–1995. Participants in Wave 4 (2008; ages 24–32; n=15,701), Wave 5 (2016–2018; ages 33–43; n=12,300), and Wave 6 (2022–2025; ages 39–51; n=11,979) were asked whether they experienced bothersome tinnitus lasting ≥5 minutes in the past 12 months. Multivariable logistic regression was used to estimate ORs and 95% confidence intervals (CI) while simultaneously adjusting for potential risk factors.

Results: Overall, 22.0% of participants reported tinnitus at least once across the three waves. Among 8,846 participants completing all three waves, tinnitus prevalence increased from 6.3% in Wave 4 (6.7% males; 5.8% females) to 10.7% in Wave 5 (12.7% males; 9.2% females) and 15.4% in Wave 6 (17.4% males; 13.4% females). Tinnitus prevalence in Wave 5 increased from 27.3% to 64.4% for individuals in Wave 4 who reported their onset of tinnitus from <3 months to ≥15 years. Tinnitus prevalence in Wave 5 also increased from 28.7% to 73.8% as the frequency of occurrence in Wave 4 increased from “less than once a month” to “almost always”. In Wave 5, significant risk factors included male sex (OR=1.9; CI: 1.5, 2.7), head trauma (OR=1.5; CI: 1.2, 1.9), headaches (OR=1.8; CI: 1.5, 2.2), anxiety (OR=1.3; CI: 1.0, 1.6), balance/dizziness problems (OR=2.7; CI: 2.2, 3.3), and report of moderate or worse hearing trouble (OR=16.2; CI: 10.9, 24.1). In Wave 6, tinnitus prevalence increased from 47.1% to 85.7% as tinnitus severity in Wave 5 increased from “no problem” to “a very big problem”.

Conclusions: Tinnitus is common in young adults and increases steadily with age. The Add Health longitudinal study provides insight into how risk factors contribute to the increasing prevalence of tinnitus with age.

Neurology

Associations between a summary Measure of Social Determinants of Health/Health Equity and Subjective Cognitive Decline Status among Mississippi Adults Vincent.L.Mendy* Vincent L. Mendy Princess C. Sule Anika Tasrin Monika Tawandra Rowell-Cunsolo

Background

Subjective cognitive decline (SCD) is associated with mild cognitive impairment, Alzheimer disease and all-cause dementia. The prevalence of Alzheimer's disease and related dementias among Mississippi Medicare beneficiaries aged 65 years or older is 12.9%, which exceeds the national average. Mississippi adults experiencing multiple social determinants of health/health equity risk factors may have increased odds of SCD compared to those experiencing no social determinants of health/health equity risk factors. We examined the association between a summary measure of SDOH/HE and SCD among Mississippi adults.

Methods

Using the SDOH and Health Equity (SDOH/HE) Module data from 2395 respondents who self-identified as non-Hispanic Blacks or Whites and 45 years or older in the 2023 Mississippi Behavioral Risk Factor Surveillance System survey, we conducted multivariable logistic regression models to examine the association between a SDOH/HE summary measure and SCD.

Results

Mississippi adults 45 years or older experiencing SCD is 19.3%. Mississippians 45 years or older experiencing 1 (adjusted odds ratio [AOR], 3.63), 2 (AOR, 6.29), 3 (AOR, 7.07) and 4 or more (AOR, 16.35) of SDOH/HE risk factors had higher odds of SCD compared to those experiencing no SDOH/HE risk factors respectively.

Conclusions

Mississippi adults with multiple SDOH/HE risk factors had significantly higher odds of SCD than those with no SDOH/HE risk factors. These findings highlight the importance of addressing multiple SDOH/HE factors of cognitive decline outcomes and the need for targeted interventions among Mississippi adults experiencing multiple SDOH/HE risk factors.

Neurology

Associations of Interleukin-6 and Interleukin-18 with Incident Epilepsy in Older Adults: Results from the Atherosclerosis Risk in Communities (ARIC) Study Derartu Ahmed* Derartu Ahmed Russell T. Shinohara Adam Naj Ramon Diaz-Arrastia James J. Gugger Rebecca F. Gottesman Emily L. Johnson Christie M. Ballantyne Andrea L. C. Schneider

Background:

The highest burden of epilepsy occurs among older adults (aged 65+ years) and, notably, a significant proportion of these late-onset epilepsy diagnoses lack an identifiable cause. Recent research suggests a potential link between inflammation and epilepsy. Therefore, we investigated associations of two pro-inflammatory cytokines, interleukin-6 (IL-6) and IL-18, with incident epilepsy.

Methods:

Using data from the Atherosclerosis Risk in Communities (ARIC) Study, we conducted a prospective cohort analysis with follow-up extending from 2011-2013 through 12/31/2022. IL-6 and IL-18 were measured from plasma collected in 2011-2013 using high-sensitivity enzyme-linked immunosorbent assays (categorized into quartiles). Incident epilepsy was defined using International Classification of Diseases, Ninth and Tenth Revision (ICD-9/10) codes. Cause-specific Cox proportional-hazards regression models were used to separately model associations of IL-6 and IL-18 with incident epilepsy with covariate adjustment for age, sex, race/center, education, smoking, alcohol consumption, hypertension, diabetes, cognitive status, stroke, and APOE 4 genotype. Missing covariate data were imputed via multiple imputation using chained equations.

Results:

We included 5,552 participants (mean age 75 years, 56% female, and 21% Black race) with IL-6 and IL-18 data without prevalent epilepsy in the analytic population. Participants were followed for a median of 12 years, over which 4% developed incident epilepsy and 37% died. In adjusted models, IL-6 was not statistically significantly associated with incident epilepsy. In contrast, the upper three higher quartiles of IL-18 were associated with similar increased risk of incident epilepsy (Q2: HR=1.98, 95%CI=1.27-3.07, Q3: HR=2.23, 95%CI=1.45-3.45, and Q4: HR=1.61, 95%CI=1.01-2.55) compared to the lowest quartile (Q1) (Figure).

Conclusions:

Among older adults, higher IL-18, but not IL-6, was associated with risk of incident epilepsy.

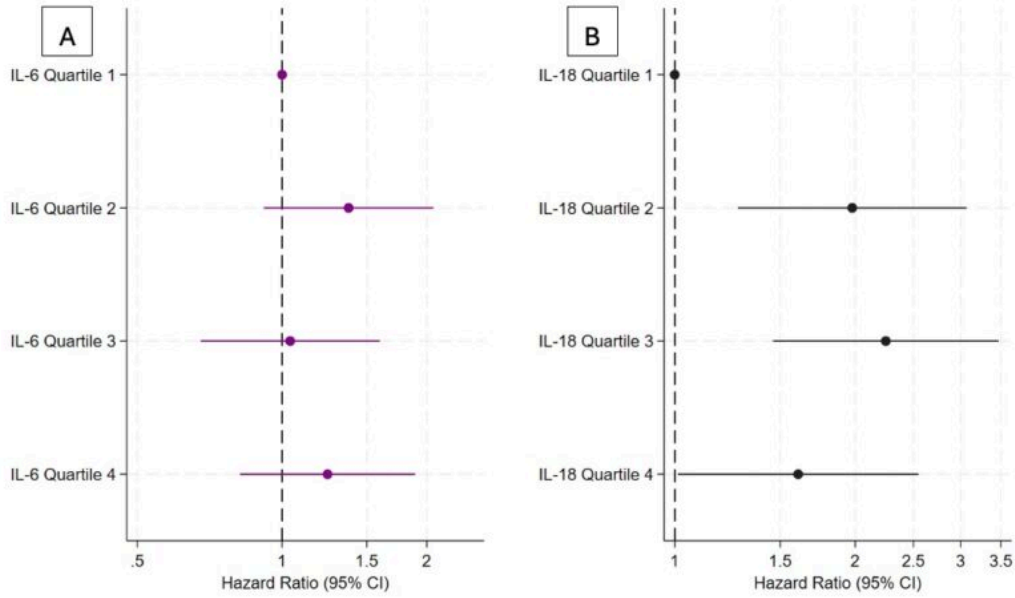
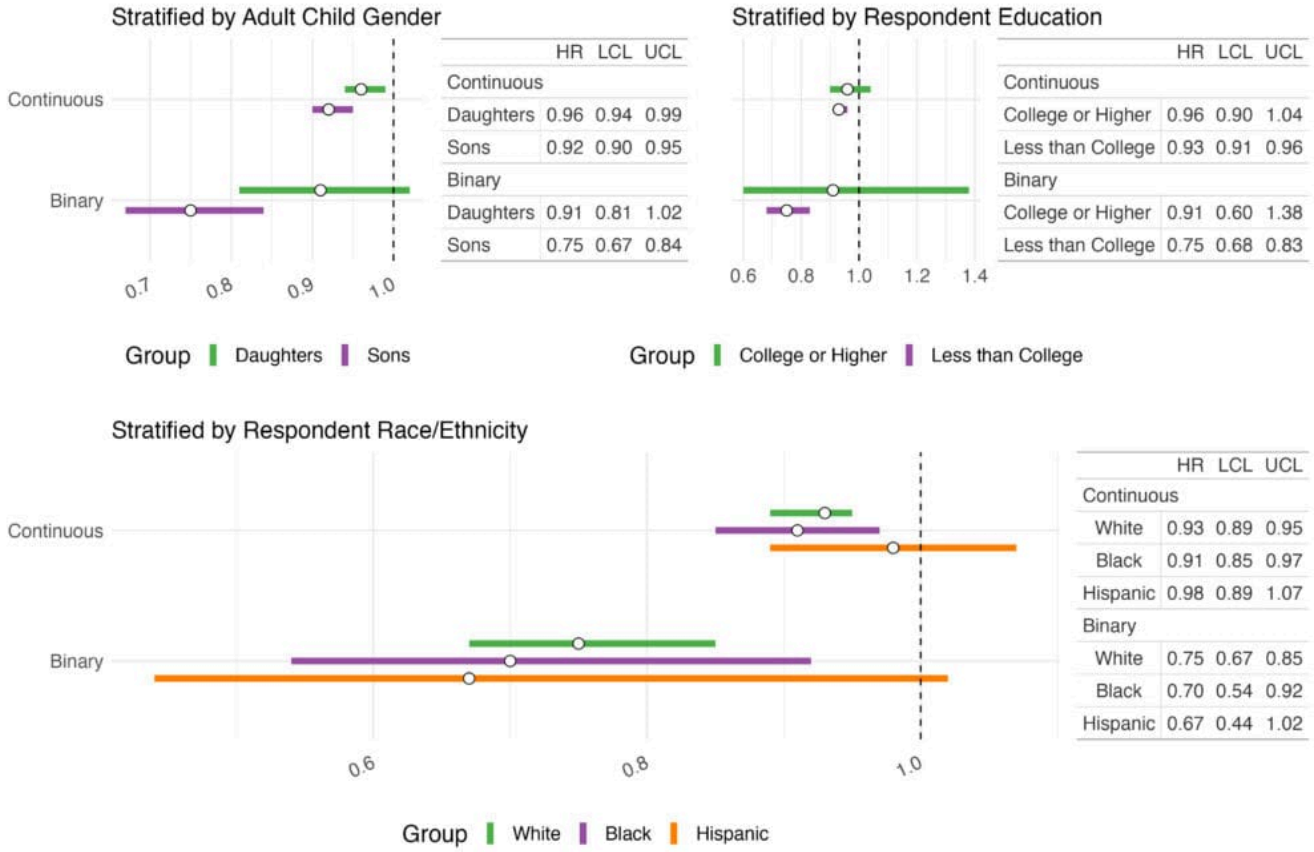


Figure. Hazard ratios and 95% confidence intervals for the associations of interleukin-6 (Panel A) and interleukin-18 (Panel B) with incident epilepsy. Cause-specific Cox proportional hazards regression models were adjusted for age, sex, race/center, education, smoking, alcohol consumption, hypertension, diabetes, cognitive status, stroke, and APOE $\varepsilon 4$ genotype.

Neurology

Is the Educational Attainment of Adult Children Associated With Their Parents' Risk of Incident Stroke? Michelle Caunca* Michelle Caunca Karla R. Flores Romero Ruben Vargas Sirena Gutierrez Jennifer Weuve M. Maria Glymour Jacqueline Torres

Adult children's education is associated with several measures of better health among their parents. This association is hypothesized to operate via mechanisms such as financial support, navigating health systems, and modeling healthy behaviors. Evidence on the association of adult children's education and parental stroke is limited, despite the public health importance of stroke. We followed 13,788 stroke-free HRS respondents from baseline (1994) through 2018 until incident stroke, mortality, study drop-out, or last observed visit (106,346 respondent-waves). Adult children's educational attainment was estimated by the mean years of education across a respondent's children aged ³25 years at baseline, modeled continuously and dichotomously (³13 years vs. <13 years). Stroke status was determined via self-report of physician diagnosis. We fit discrete time hazards models adjusted for the respondent's baseline age, gender, race/ethnicity, education, childhood health and financial status, childhood rural residence, and parental and spousal education. The analytic sample had a mean age of 64 years (SD=8) and consisted of 60% women and 12% Black, 7% Hispanic, and 78% non-Hispanic white participants. Each 1-year increment in adult child educational attainment corresponded to an 8% lower stroke risk (OR [95% CI]: 0.92 [0.90, 0.95]). Participants whose children were at least college-educated had 27% lower stroke risk than did those whose children did not have a college education (OR [95% CI]: 0.73 [0.66, 0.81]). The association was larger with respect to sons' educational attainment (vs. daughters'), among respondents with less than a college education, and among those identifying as either non-Hispanic White or Black (Figure). Overall, this evidence suggests that greater educational attainment among older adults' children is protective against incident stroke for their parents. This research should be replicated in a setting with adjudicated stroke cases.



	HR	LCL	UCL
Continuous			
Daughters	0.96	0.94	0.99
Sons	0.92	0.90	0.95
Binary			
Daughters	0.91	0.81	1.02
Sons	0.75	0.67	0.84

	HR	LCL	UCL
Continuous			
College or Higher	0.96	0.90	1.04
Less than College	0.93	0.91	0.96
Binary			
College or Higher	0.91	0.60	1.38
Less than College	0.75	0.68	0.83

	HR	LCL	UCL
Continuous			
White	0.93	0.89	0.95
Black	0.91	0.85	0.97
Hispanic	0.98	0.89	1.07
Binary			
White	0.75	0.67	0.85
Black	0.70	0.54	0.92
Hispanic	0.67	0.44	1.02

Nutrition/Obesity

Consumption of antioxidant-rich foods attenuates respiratory and cardiovascular health effects in a population highly exposed to air pollution Adeladza Kofi Amegah* Adeladza Kofi Amegah Kelvin Yeboah Evans Quarshie Patricia Amonoo Divine Benjamin Saverio Stranges Ngianga-Bakwin Kandala Patrick Attey-Yeboah

Background: Diet and nutrition have shown promise in attenuating air pollution health effects. However, to date, no study has been conducted in an occupationally exposed population who experience high levels of very complex air pollution mixtures on a daily basis.

Objectives: We therefore evaluated the effectiveness of regular consumption of antioxidant-rich foods in attenuating respiratory and cardiovascular health effects among street vendors in Accra, Ghana.

Methods: We used a quasi-experimental design of 12-month duration, assigning 307 street vendors to either an intervention group (n = 155) to receive weekly supply of antioxidant-rich foods or control group (n = 152) who maintained their usual dietary pattern.

Results: Participants regularly consuming antioxidant-rich foods were assigned to the intervention group with those consuming less of these foods assigned to the control group. The primary outcomes were self-reported respiratory and cardiovascular symptoms, and impaired lung function. The intervention participants were found to have reduced odds of cough (AOR=0.45; 95% CI: 0.33, 0.63), difficulty breathing (AOR=0.40; 95% CI: 0.25, 0.65), irregular heartbeat (AOR=0.08; 95% CI: 0.05, 0.13), and hospital visits (AOR=0.34; 95% CI: 0.16, 0.72) compared to the control participants. Surprisingly, we observed a decline in lung function among the intervention participants compared to the control participants.

Conclusions: We found regular consumption of antioxidant-rich foods to attenuate adverse air pollution health effects among this vulnerable population. Risk communication among this group and other outdoor workers should emphasize this nutrition intervention.

Nutrition/Obesity

Ultra-processed foods, dietary inflammation, and diet quality in relation to mortality risk in U.S. adults Penias Tembo* Penias Tembo James R. Hebert Xuehong Zhang Longgang Zhao

Background: Prior studies have examined ultra-processed foods (UPF), dietary inflammatory potential, and diet quality separately, limiting inference on their independent and joint associations with mortality. We aimed to evaluate the independent and joint associations of UPF, inflammatory diet, and diet quality with mortality risk among U.S. adults.

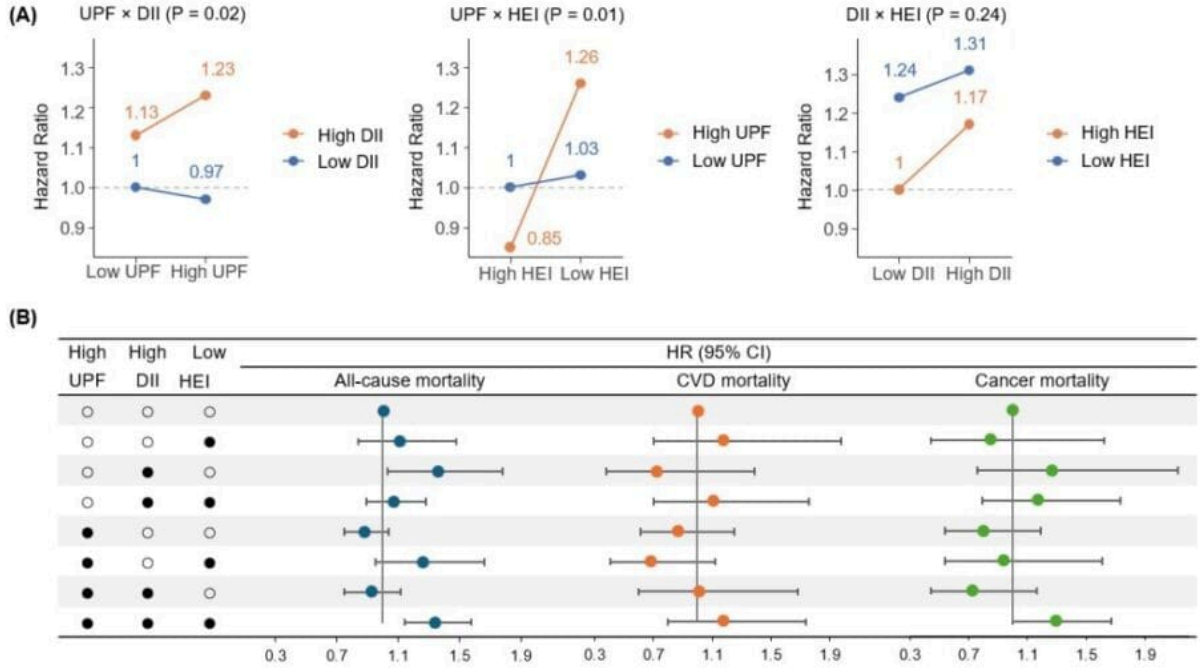
Methods: This longitudinal study analyzed data from the National Health and Nutrition Examination Survey (NHANES) cycles from 2005–2018, including a representative sample of 25,506 U.S. adults. Exposures of interest were UPF intake and Dietary Inflammatory Index (DII) and Healthy Eating Index (HEI) scores. The primary outcome was mortality. Hazard ratios (HRs) and 95% confidence intervals (CIs) were estimated by survey-weighted Cox proportional hazards regression models.

Results With a median 7.6 years of follow-up, we documented 2577 deaths. Higher UPF and DII scores were associated with increased all-cause mortality (HR Quintile 5 vs. 1 [95% CI]: UPF, 1.30 [1.07–1.59]; DII, 1.55 [1.28–1.88]), and HEI was inversely related to mortality (0.75 [0.62–0.91]). When modelled jointly, DII (1.48 [1.20–1.82]) and HEI (0.79 [0.65–0.97]) remained independently associated with mortality, whereas UPF was attenuated (1.15 [0.93–1.41]). Significant interactions were observed between UPF and both DII (P = 0.02) and HEI (P = 0.01); higher mortality risk was evident only among individuals with high DII or low HEI. Joint analyses showed the highest risk among participants with high UPF, high DII, and low HEI (1.34 [1.14–1.58]). Among UPF subcategories, beverages (HR Tertile 3 vs. 1 [95% CI]: 1.16 [1.01–1.34]) and ready-to-eat/heat meals (1.14 [1.00–1.31]) were positively associated with mortality, whereas sauces/cheese spreads showed an inverse association (0.81 [0.70–0.94]).

Conclusions UPF intake was associated with higher mortality risk, particularly among individuals with poor diet quality or high dietary inflammation.

Figure. Effect Modification and Joint Associations of Ultra-Processed Food Intake, Dietary Inflammatory Index, and Healthy Eating Index with Mortality

(A) Associations between ultra-processed food (UPF) intake, DII and HEI. Interaction terms were tested using multiplicative models. (B) Joint associations of UPF intake and diet quality/inflammatory potential with all-cause and cause-specific mortality. Participants were categorized into joint exposure groups based on dichotomized levels of UPF and DII or HEI (median as cutoff values), with the low-UPF, high-HEI, and low-DII group as the reference. Hazard ratios (HRs) and 95% confidence intervals (CIs) were adjusted for age, sex, race/ethnicity, education, income, physical activity, BMI, waist circumference, smoking, alcohol, total energy intake, and major comorbidities.



Nutrition/Obesity

Sugar-Sweetened Beverage Intake and Uric Acid in Adolescents: Longitudinal Pathways Through Adiposity and Blood Pressure Pei-Wen Wu* Pei-Wen Wu Yu-Ting Chin Sharon Tsai Wei-Ting Lin Chien-Hung Lee

Background: Uric acid (UA) dysregulation in adolescence is increasingly recognized as an early marker of cardiometabolic risk. Sugar-sweetened beverage (SSB) intake, a major source of dietary fructose, may elevate UA directly through hepatic metabolism and indirectly via effects on adiposity and blood pressure (BP). Because BMI and BP vary over time and reflect both stable between-individual differences and within-individual change, this study examined longitudinal associations between SSB intake and UA, with BMI and BP as potential mediators. **Methods**: A six-wave cohort of 909 adolescents (aged 12–13 years) in southern Taiwan was followed at 6-month intervals from 2015 to 2018. Between- and within-individual temporal dynamics of BMI and BP were analyzed using random-intercept (RI) cross-lagged panel models. Direct and indirect pathways from baseline SSB intake to follow-up UA through time-varying BMI and BP were estimated within a structural equation modeling framework, adjusting for covariates. **Results**: At the between-person level, BMI and BP were temporally stable. Within individuals, higher-than-usual BMI predicted higher subsequent systolic BP (adjusted $s\beta = 0.06–0.08$, $p < 0.05$), and autoregressive paths for BMI and systolic BP were significant. Adolescents consuming ≥500 mL/day SSB had higher UA at wave 1, which was associated with higher RI-BMI, and RI-BMI in turn predicted higher UA at wave 6 (adjusted $s\beta = 0.11$, 0.56, and 0.19; all $p < 0.05$). Mediation analysis showed that the pathways ≥500 mL/day canned SSB → wave 1 UA → wave 6 UA and ≥500 mL/day canned SSB → wave 1 UA → RI-BMI → wave 6 UA accounted for 78.8% and 16.7% of the total mediation effect, respectively. **Conclusion**: Excessive SSB intake in adolescence predicts elevated UA over time, primarily through direct metabolic pathways and secondarily through stable adiposity, underscoring early metabolic consequences of SSB consumption.

LATEBREAKER

Nutrition/Obesity

Periconceptional dietary diversity and metabolic syndrome risk at 3 years postpartum

Qianhui Jin* Qianhui Jin Sara Parisi Lisa Bodnar Ashley Naimi

Objective: We evaluated the association between periconceptional dietary diversity, reflected by evenness in energy distribution across foods, and metabolic syndrome risk at 3 years postpartum and whether this association differs by diet quality.

Methods: We analyzed data from 4025 participants in Nulliparous Pregnancy Outcomes Study: monitoring mothers-to-be Heart Health Study. Periconceptional dietary intake was assessed using a food frequency questionnaire. Dietary diversity was operationalized as energy distribution evenness across foods using Pielou's Index. Multivariable logistic regression was used to estimate the association between energy evenness and incident metabolic syndrome (defined using AHA/NHLBI criteria), adjusting for total energy intake and maternal characteristics. We stratified analyses using Healthy Eating Index-2020 scores representing lower (HEI <60) and higher (HEI ≥60) diet quality.

Results: Periconceptional energy evenness differed by diet quality. Among those with lower-quality diets, participants with energy intake more evenly distributed across foods had a lower percent energy from sugar-sweetened beverages (e.g., regular soda: 2.1% vs. 7%) and a higher percent energy from many refined grains and fat sources (e.g., bagel: 2.3% vs. 1.6%; butter: 1.5% vs.1%) compared to those with energy concentrated in fewer foods. Percent energy differences were minimal in higher-quality diets. Postpartum metabolic syndrome occurred in 14% of participants (n=602). Among those with lower-quality diets, the adjusted risk of metabolic syndrome was stable until approximately the median of energy evenness and then increased steadily. No association was observed among those with higher-quality diets.

Conclusions: Among individuals with suboptimal periconceptional diets, high energy evenness may indicate dispersion of energy intake across many nutrient-poor, energy-dense foods, potentially increasing postpartum metabolic syndrome risk.

Occupational

Validating a Task-Based Asbestos Job Exposure Matrix for Screening Pulmonary Disease in Trade Workers: A Calibrated Approach for Surveillance and Prevention Sundus Siddique* Sundus Siddique Anne Golden Grace N. Sembajwe Melissa C. Friesen Alexis Descatha Jerome Lavoue Jacqueline Moline

Background: Cumulative asbestos exposure causes respiratory impairment and malignancies, highlighting the need for industry specific job-exposure matrices (JEMs) for surveillance and risk assessment.
Methods: We constructed a task-based JEM for 492 unionized workers using Northwell Occupational Lung Registry data. Three indices (linear & two nonlinear frequency weightings) integrated 29 tasks, exposure frequency, duration, and employment era. Cronbach's α, principal component analysis and kappa were used to examine reliability, dimensions and agreement. Associations with fibrosis, pleural plaques and impaired pulmonary function were estimated via logistic regression. We examined discrimination (AUC), sensitivity, specificity, and calibration; analyses adjusted for trade, stratified by smoking.
Results: Median age was 61 years; ~60% had smoked. Rates of FEV1 < 80%, FVC < 70%, fibrosis, and pleural plaques were 22%, 7%, 15%, and 17%. JEM indices were reliable (Cronbach's $\alpha > 0.87$), unidimesional and high in agreement (kappa ≥ 0.7). High scores were associated with radiological and functional impairment ($p < 0.01$); the highest JEM quartile accounted for most adverse outcomes. Associations between JEM scores and radiological outcomes were significant after adjusting for trade and stratifying by smoking. Discrimination for fibrosis was moderate (AUC 0.68-0.70); calibration was excellent ((Brier 0.119-0.124), nonsignificant Hosmer-Lemeshow test, decile calibration plots showed agreement between observed and predicted outcomes). Using optimized cut-points, 35% of workers were classified as high-risk (sensitivity 63-67%, specificity 68-69%). Risk assignment was concordant across JEM types.
Conclusions: We validated that our task-based asbestos JEM was associated with adverse pulmonary outcomes and was a reliable and accurately calibrated tool. Both linear and nonlinear task scoring provided consistent risk classification, supporting the use of this approach in surveillance.

Occupational

Occupational exposure and risk of bladder cancer: findings from the Agricultural Health Study Shuai Xie* Shuai Xie Shuai Xie Melissa Friesen Debra Silverman Sarina Murray Christine Parks Dale Sandler Laura Beane Freeman Stella Koutros

Background: Occupational exposures are a leading cause of bladder cancer, with numerous agents (e.g., engine exhausts, solvents, and metal-working fluids) suspected as carcinogens. Farmers are frequently exposed to some of these agents during farm tasks (e.g., repairing engines, painting, and welding metal).

Methods: We evaluated the association between farming tasks and bladder cancer risk in the Agricultural Health Study, a large prospective cohort study which includes farmers in Iowa and North Carolina. Farmers (n=22,234) reported the frequency of farm tasks at enrollment (1993–1997). We used Cox proportional hazards models with age as the time scale to estimate HR and 95% CI for a 28-year follow-up period (1993-2021), adjusting for cigarettes smoking, sex, race, body mass index, and pipe smoking.

Results: Overall, 312 farmers were diagnosed with bladder cancer and provided information about farm tasks. Driving diesel tractors (90%), driving gasoline tractors (68%), and driving trucks (67%) were the most frequently reported farming tasks. The frequency of grinding metal was strongly correlated with welding (r=0.66) and moderately correlated with engine repair (r=0.43). We observed elevated risk with weekly/daily grinding metal (HR=1.26, 95% CI: 0.92-1.71), monthly welding (HR=1.31, 95% CI: 1.01-1.73), and monthly engine repair (HR=1.42, 95% CI: 1.08-1.86). Additionally, the frequency of painting was moderately correlated with solvent use (r=0.42). Monthly solvent use was associated with a higher risk of bladder cancer (HR=1.59, 95% CI: 1.08-2.36).

Conclusions: Farming tasks are important sources of exposure to potential bladder carcinogens among farmers. Increased risks observed from welding, engine repair, and solvents add to emerging literature supporting a link between these occupational exposures and bladder cancer etiology. As some farmers are also employed off the farm, additional exploration of these exposures in occupations off-farm are warranted.

Occupational

Mediating role of biological aging in the relationship between long working hours, poor sleep quality, and mortality in the U.S. working population Xiang Li* Xiang Li Liwei Chen Jian Li Onyebuchi Arah Xuyuehe Ren

Long working hours (LWH) and poor sleep quality (PSQ) are each associated with increased mortality risk, yet their joint effects remain understudied. Biological age, a composite biomarker-based measure of biological aging, has been increasingly evaluated in chronic disease research, but its role as a potential pathway linking work- and sleep-related exposures to mortality among workers has rarely been examined. We analyzed a nationally representative sample of 13,491 employed adults (aged 18-85 years) from the U.S. National Health and Nutrition Examination Survey (NHANES 2005–2014), with mortality follow-up through 2019 via linkage to the National Death Index. LWH was defined as working ≥55 hours per week, and PSQ as having one or more adverse sleep characteristics (diagnosed sleep disorder, self-reported trouble sleeping, or sleep duration <7 or >9 hours). Biological age was estimated using the PhenoAge algorithm based on 11 clinical biomarkers. Causal mediation analysis using G-Computation was applied to estimate the total effect (TE) of joint exposure to LWH and PSQ on all-cause mortality, as well as the total indirect effect (TIE) mediated through biological age; effects were reported as marginal RRs with 95% CIs. Models adjusted for age, sex, race and ethnicity, income, education, marital status, and baseline cardiometabolic conditions (diabetes, hypertension, or cardiovascular disease). During a mean follow-up of 9.85 years, 344 deaths were observed. Compared with workers with neither LWH nor PSQ, those exposed to LWH and PSQ had higher all-cause mortality (TE RR = 1.47, 95% CI: 1.42-1.53). The indirect pathway through biological aging was small in magnitude (TIE RR = 1.03, 95% CI: 0.99-1.07), accounting for approximately 13% of the total effect. These findings suggest that co-occurring long working hours and poor sleep quality are associated with elevated mortality risk among U.S. workers, with biological aging contributing slightly to this association.

LATEBREAKER

Occupational

Recent changes at the Centers for Disease Control and Prevention and their impacts on workforce mental health Candice Johnson* Candice Johnson Xuantao Li Laurel Harduar Morano Danielle R. Gartner A. Emiko Blalock Kipling M. Bohnert

Background: In late January 2025, the leadership of the newly-elected federal government instituted policies and initiatives that resulted in one-third of employees at the Centers for Disease Control and Prevention (CDC) being terminated, retiring, or resigning. CDC cycled through permanent and acting leaders and long-standing scientific and agency operations underwent disruptive changes. We characterized the mental health of CDC workers, who have experienced rapid and continuous changes to their work environment since then.

Methods: In late February 2026, we distributed an anonymous survey to current and former CDC workers through formal and informal professional networks. We asked about self-reported mental health, anxiety, and depression. Study recruitment is ongoing; we present preliminary descriptive results from participants enrolled to date.

Results: We included 446 participants in our preliminary analysis, of whom 70% were still working at CDC and 30% were terminated or left CDC after January 20, 2025. Over half (54%) described their current mental health as fair or poor. Among the 54% of participants who had ever been diagnosed with anxiety, 99% said that changes at CDC made their anxiety worse; 72% either started medications or increased their medication dosage in response. Among the 41% who had ever been diagnosed with depression, 97% said these changes made their depression worse; 65% started medication or increased their dosage. Overall, 38% of participants knew of a CDC worker who attempted to harm themselves or thought about harming themselves due to the changes at CDC.

Conclusions: Our preliminary results indicate that the changes at CDC have negatively affected the mental health of CDC workers. Although those who responded to our survey may be more likely to have been affected than non-responders, these high levels of worsening mental health indicate the potential need for a more stable work environment to improve workforce mental health.

Occupational

Military occupation and sleep trends over time: longitudinal results from the Annual Periodic Health Assessment of active duty US Navy and Marine Corps personnel, 2017-2021 James K. Romine* James Romine Amber L. Dougherty Andrew J. MacGregor

Introduction: US military personnel are less likely than civilians to obtain the recommended 7-9 hours of sleep per night, increasing risk of impaired performance and safety issues. There is little understanding of occupation-specific sleep trajectories. Estimates of expected changes in sleep quality have yet to be quantified.

Materials and Methods: The Periodic Health Assessment (PHA) was used to examine the relationship of military occupation with trends of sufficient sleep among active duty US Navy and Marine Corps personnel from 2017 to 2021. Sufficient sleep was defined as ≥7 hours “on most days” during the previous 2 weeks (self-reported). Occupational titles were derived from Defense Manpower Data Center codes. Population-averaged generalized estimating equations were used to estimate the prevalence of sufficient sleep at baseline and the percent change over time, accounting for repeated measures. Covariates were age, sex, and number of deployments.

Results: The total sample (n=496,079) was 59% Navy and 41% Marine Corps. Across 48 Navy occupations, the baseline prevalence of sufficient sleep ranged from 21.4% to 52.0%. The Navy’s average prevalence of sufficient sleep decreased by 2.9 -%/yr (95% CI, 2.6-3.2 -%/yr). Law Enforcement (21.4%), Food Service Personnel (21.7%), and Material Receipt, Storage and Issue (22.7%) showed the lowest baseline sleep prevalence. The fastest decreases were observed among Aircraft Launch Equipment (21.19 -%/yr); Metalworking (17.70 -%/yr); Religious, Morale and Welfare (8.69 -%/yr); and Food Service (8.32 -%/yr). Across 55 Marine Corps occupations, the baseline prevalence ranged from 22.7% to 49.2%. Average prevalence decreased by 4.1 -%/yr (95% CI, 3.5-4.6 -%/yr). Cyberspace Maintenance (22.7%), Administration (23.0%), and Food Service (23.5%) showed the lowest baseline sleep prevalence. The fastest decreases were observed among Other Mechanical and Electrical Equipment (15.7 -%/yr), Metalworking (12.7 -%/yr), Motor Transport (11.1 -%/yr), and Unmanned Vehicle System (UVS) Operation (10.7 -%/yr).

Conclusion: This study demonstrates a method to identify at-risk occupations that could be targeted for interventions to prevent sleep deterioration over time. Future studies are needed to understand how occupations contribute to sleep quality over time.

LATEBREAKER

Perinatal & Pediatric

Reduction in time-to-initiation of weight-loss medication after initiating antipsychotic between 2020 and 2024: Management of antipsychotic-induced weight gain in youth

Kareshma Mohanty* Kareshma Mohanty Susan dosReis

Background: While second-generation antipsychotics (SGAs) effectively treat symptoms of hallucinations and mania with fewer neurologic side effects, 80% of youth experience ≥10% weight gain within six months of initiating an SGA. Clinicians acknowledge the critical need to manage this rapid weight gain, yet the uptake of adjunctive weight-loss medication (WTRx) is low, and there is limited evidence on when to initiate this preventive therapy in youth. Our preliminary findings showed an increase in WTRx uptake over time. In this study, we examined changes in time-to-initiation of WTRx from 2020 to 2024.

Methods: We conducted a new-user, retrospective cohort study using IQVIA PharMetrics® Plus Closed Health Plan claims data. Youth aged 5-21 years newly initiating an SGA (index date) from January 01, 2020, through June 30, 2024, with ≥6 months of continuous health insurance, and no SGA or WTRx use in the 6-month baseline period, were included. Beneficiaries were followed from the index date through December 31, 2024, to identify the first WTRx. Jonckheere-Terpstra test assessed trends in time-to-initiation. Multivariable generalized linear models assessed change in time-to-WTRx-initiation, adjusted for baseline covariates and stratified by sex.

Results: We included 954 (out of 26,936) youth who initiated WTRx; the majority were female (64.6%), older than 15 years (61.3%), on aripiprazole (48.9%), and prescribed metformin (86.6%). Only 4.9% co-initiated a WTRx. Median time to WTRx initiation decreased significantly from 2020 to 2024 (Fig. 1; p-trend<0.001). The time-to-WTRx-initiation ratio for each additional year, from 2020 to 2024, was 0.70 (95% CI: 0.63-0.77), with no significant difference by sex.

Conclusion: We observed a 30% reduction in the time-to-WTRx-initiation over the years. Studies in adults have shown that co-initiation, rather than initiation after SGA-induced weight gain, is more effective; thus, reducing the time to initiation is imperative in youth.

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Perinatal & Pediatric

Exploring Effects of PM2.5 and Neighborhood Stress on Inflammation in Pregnancy Teresa Janevic* Teresa M. Janevic Sarah Nowlin Demina Williams Rushna Tubassum Anna Rommel Alison Lee Teresa Janevic

Exposure to ambient fine particulate matter (PM2.5) during the first and second trimesters of pregnancy may increase inflammation in the third trimester measured through inflammatory indicator, HS-CRP. The relationship may be modified by stress due to neighborhood-based structural racism. We analyzed data from a New York City pregnancy cohort of individuals recruited between 2020-2022 who had an assayed sample of HS-CRP within the third trimester of pregnancy (> 196 days gestation), excluding samples taken a week within delivery and twin births. These analyses include 747 women with geocoded address data during pregnancy. We used the XIS-PM model of daily estimates of PM2.5 which we averaged by trimester. We used the Structural Racism Effect Index (SREI) to characterize neighborhood stress. To preserve temporality, we modeled first and second trimester-averages PM2.5 to estimate associations with percentage changes in third trimester log-transformed HS-CRP using linear regression. We included Race-ethnicity, Medicaid (yes/no), maternal age at enrollment, and gestational age at sample as covariates. We assessed effect modification by dividing SREI into quartiles where the fourth quartile represented the highest level of neighborhood stress. We excluded race-ethnicity from the interaction model with SREI. We found an association between first trimester PM2.5 and HS-CRP(adjusted percent change=4.67%, 95% CI=0.57%,8.88% per 1-unit increase in ug/m3).No association was observed between second trimester PM2.5 and HS-CRP(adjusted percent change=0.40%, 95% CI= -3.54%,4.34%). While no interaction was present, we observed a trend for second trimester PM2.5 in the fourth quartile supporting our hypothesis in highest SREI neighborhoods(adjusted percent change=7.6%, 95% CI= -0.06%,15.82%).This suggests that PM2.5 exposure in early gestation may be associated with higher inflammation in the third trimester and that women in highest-stress neighborhoods may be more susceptible.

Perinatal & Pediatric

The Role of Gravity and Informative Censoring in Explaining the Association Between Pregnancy Loss and Subsequent Hypertension Sabrina Chiodo* Sabrina Chiodo Kristian B. Filion Sonia M. Grandi

Background: Pregnancy loss is linked to hypertension risk, but prior studies have not accounted for the potential influence of reproductive history or informative censoring. We examined how accounting for gravidity and informative censoring impacts the association between pregnancy loss and the five-year incident hypertension risk.

Methods: This population-based retrospective cohort study used administrative health data from British Columbia, Canada (1994–2016). Participants were nulliparous women (15–49 years) with a recorded pregnancy and no prior hypertension. Pregnancy loss (miscarriage/stillbirth) was identified via ICD codes. We used inverse probability of treatment and censoring weights to account for confounding and informative censoring. Time to incident hypertension was estimated using Weibull accelerated failure time models under three analytic strategies: (1) gravidity excluded from weighting/outcome models; (2) gravidity in the treatment weighting model only; and (3) gravidity in both the weighting and outcome models.

Results: Among 309,608 pregnancies (27,044 losses), losses were linked to older age, higher BMI, and higher gravidity. Without accounting for gravidity, pregnancy loss was associated with a 15% shorter time to hypertension (Time Ratio [TR] 0.85, 95% CI 0.80, 0.90). When gravidity was included in the treatment weighting model only, pregnancy loss remained associated with earlier hypertension onset (TR 0.91, 95% CI 0.86, 0.97), though this association was attenuated after additionally accounting for informative censoring (TR 0.96, 95% CI 0.90, 1.03). When gravidity was included in both the weighting and outcome models, pregnancy loss was no longer associated with hypertension (TR 0.95, 95% CI 0.90, 1.02).

Conclusion: The observed association between pregnancy loss and earlier hypertension may largely be driven by reproductive history and informative censoring. Future studies must explicitly account for these factors to avoid biased inference.

Perinatal & Pediatric

Pattern of maternal chronic conditions among stillbirth pregnancies Anne Marie Darling*
Anne Marie Darling Steven Kerr Martha Werler Julie Peteresen Sarah Fisher Meredith Howley Wendy Nembhard Mahsa Yazdy Eirini Nestoridi

Background: Several maternal chronic conditions have been linked to stillbirth, but most research has examined them individually. Patterns of co-occurrence may reflect distinct etiologic pathways, yet they remain poorly characterized. Identifying chronic condition clusters may help guide future etiologic research on stillbirth and clinical care.

Objective: To estimate the prevalence of maternal chronic conditions among women with pregnancies ending in stillbirth enrolled in the Birth Defects Study to Evaluate Pregnancy exposureS (BD-STEPS), and to identify distinct chronic condition profiles.

Methods: We estimated the prevalence of 23 chronic conditions, as well as the occurrence of multiple chronic conditions (≥2 conditions) and complex multimorbidity (≥3 conditions across ≥3 body systems), among 366 BD-STEPS participants whose pregnancies ended in a stillbirth and were unaffected by birth defects. We used latent class analysis (LCA) to identify chronic condition profiles among those reporting ≥2 conditions. We selected the final model based on statistical fit criteria and clinical interpretability.

Results: A majority of women (58.2%, 95% CI 53.1-63.2) reported multiple chronic conditions. Nearly one third (31.1%, 95% CI 26.4, 35.9) met the criteria for complex multimorbidity. Among those reporting ≥2 conditions (n=213), LCA identified two distinct classes of chronic conditions based on modal posterior assignment. The larger class (69%) was characterized by a moderate burden of cardiometabolic conditions and a lower burden of mental health conditions while the smaller class (31%) was characterized by a high burden of mental health conditions and a relatively lower burden of cardiometabolic conditions.

Conclusion: Maternal chronic conditions appear to commonly co-occur among women with pregnancies ending in stillbirth. LCA identified subgroups reflecting differing frequencies of cardiometabolic and mental health conditions. Future research could help determine whether these chronic condition phenotypes are associated with stillbirth risk.

Perinatal & Pediatric

A prospective preconception cohort study of the association between miscarriage history and fecundability in Kenyan women trying to conceive Hanna Shephard* Hanna Shephard Erica Lokken Walter Jaoko John Kinuthia Kishor Mandaliya R. Scott McClelland

Background: Emerging evidence suggests that a prior miscarriage might impair subsequent fecundability, defined as the per-menstrual cycle probability of conception. However, existing studies are from high-income settings, leaving a gap in the evidence from low- and middle-income countries. The Microbiota and Pre-term Birth (MPTB) Study is a prospective, preconception cohort of HIV-negative Kenyan women trying to conceive.

Objective: To test the hypothesis that miscarriage history is associated with reduced fecundability among women in the MPTB Study.

Methods: At enrollment, participants reported outcomes of prior pregnancies (miscarriage, termination, ectopic pregnancy, stillbirth, or live birth). Participants were followed prospectively for up to six months. At monthly visits, participants reported the date of their last menstrual period and underwent pregnancy testing to ascertain incident pregnancies. The exposure was self-reported miscarriage history prior to enrollment, defined as spontaneous abortion at <20 weeks' gestation. We fit discrete-time proportional probability models to estimate fecundability ratios (FRs) and 95% confidence intervals (CI) comparing women with a history of one or more miscarriages to women with no history of miscarriage.

Results: Among 423 gravid participants, 22.5% had a history of one or more miscarriages. In unadjusted analyses, miscarriage history was associated with slightly reduced fecundability (FR 0.88, 95% CI: 0.66—1.17), although confidence intervals were wide. After adjustment for age at enrollment. study site, education, body mass index, regularity of menses, vaginal washing and condomless sex behavior, and sexually transmitted infections, the association was further attenuated (FR 0.93, 95% CI: 0.69—1.25) and confidence intervals remained wide.

Conclusions: Among MPTB study participants, miscarriage history may be associated with slightly associated lower fecundability, but estimates were imprecise and confidence intervals encompassed the null.

LATEBREAKER

Perinatal & Pediatric

Community Influenza Activity During Pregnancy and Cerebral Palsy in Offspring Cole King*
Cole King Haoran Zeyan

Background:

Cerebral palsy (CP) is the most common childhood movement disorder, and its incidence varies seasonally. Influenza, a common seasonally varying pathogen, has been associated with poor birth and neurodevelopmental outcomes. However, no studies have examined whether community influenza activity is associated with CP risk.

Methods:

A cohort of 4.47 million live births in California from 2007-2015 was linked to CP diagnostic records through 2021 from a statewide diagnostic system, yielding 4,679 cases. Weekly influenza-like illness (ILI) surveillance data were obtained from the California Department of Public Health and averaged for each pregnancy and trimester to estimate community influenza circulation. Logistic regression was used to estimate the odds ratio (OR) and 95% confidence intervals (CI) for CP diagnosis based on community influenza activity, adjusted for maternal, neighborhood, and environmental factors. Temporal negative controls were used to evaluate uncontrolled confounding bias, and causal mediation analyses were conducted to identify potential causal pathways for the associations found.

Results:

Increased influenza activity during the first trimester was associated with CP diagnosis (OR 1.07 [95% CI 1.02-1.13]), especially for years dominated by the H1N1 viral subtype (OR = 1.18 [95% CI 1.11-1.26]). This relationship was robust to temporal negative controls that assessed community influenza activity before and after pregnancy. Mediating effects were noted for preterm birth and very preterm birth (mediated percentages 9.6% and 17.92%, respectively) but not for preeclampsia (mediated percentage <1%).

Conclusions:

Maternal exposure to increased community influenza during the first trimester of pregnancy is associated with increased CP risk, especially in years dominated by descendants of the 2009 novel H1N1 virus. Given continued emergence of novel respiratory pathogens, the potential implications of these findings merit further investigation.

LATEBREAKER

Perinatal & Pediatric

Development of an Intervention to Reduce Risk for PTSD Following Birth Trauma Katherine Bowers* Katherine Bowers Robert T. Ammerman Alonzo Folger

Background: Posttraumatic stress disorder following traumatic birth (PTSD-BT) is an underrecognized perinatal mental health outcome disproportionately affecting medically and socially high-risk populations. In our home visiting birth cohort, 22.6% screened positive for clinically significant PTSD symptoms at 1 month postpartum, increasing to 33% among those with labor complications (used as a proxy for birth trauma). These results highlight the need for early identification and scalable community-embedded support.
Methods: We are conducting a mixed-methods study to characterize the epidemiology of PTSD-BT and inform the development of a trauma-informed intervention within a home visiting program. Quantitatively, we are enrolling a prospective pilot birth cohort (target n=50) using validated birth trauma and PTSD measures to estimate prevalence and examine associations with risk/protective factors. Qualitatively, we conducted four design studios with parents, home visitors, clinicians, and other stakeholders to co-develop ideas about participant eligibility, engagement approaches, and potential intervention models.
Results: Preliminary quantitative data (20 prenatal visits; 5 postpartum follow-ups) demonstrate the feasibility and acceptability of structured birth trauma screening (preliminary associations will be presented). Across design studios, participants emphasized autonomy, cultural competence, non-stigmatizing communication, and normalization of postpartum trauma. Priority components include advocacy coaching, birth process education, and social support mobilization, delivered with flexible or risk-tiered formats.
Conclusion: PTSD-BT is prevalent and insufficiently addressed in high-risk postpartum populations. Integrating trauma-informed screening and support into home visiting is a feasible, acceptable, and population-relevant strategy. Ongoing data collection will refine intervention components and strengthen evidence for scalable implementation.

Perinatal & Pediatric

Pre-pregnancy calcium supplementation on the risk of gestational hypertension and proteinuria: A per-protocol analysis of a randomized trial Chase D. Latour* Chase Latour Kyle R. Busse Gabriela Cormick Stefanie N. Hinkle José Belizán Enrique F. Schisterman Sunni L. Mumford Ellen C. Caniglia

Introduction: Adhering to pre- and early-pregnancy low-dose calcium supplementation may reduce the risk of preeclampsia. However, its effect on preeclampsia physiology—specifically, gestational hypertension and proteinuria—is unclear.

Methods: We analyzed data from a double-blind, placebo-controlled trial of daily, low-dose (500mg) calcium supplementation from pre-conception through 20 weeks' gestation among women with prior preeclampsia in Zimbabwe, South Africa, and Argentina (2011-16). Persons who had chronic hypertension with proteinuria at screening were excluded. Gestational hypertension and proteinuria were assessed during study visits at 20 and 32 weeks' and from medical records based on blood pressures (systolic ≥140 or diastolic ≥90 mmHg) and urine protein (≥2 on urine dipstick or elevated urinary protein laboratory values). Participants were adherent if they took their assigned tablets at least 5 days/week, on average, as determined by counts taken every 12 weeks. We used parametric g-computation to estimate per-protocol RRs for gestational hypertension and proteinuria. We addressed missing values via multiple imputation (m=10) and estimated CIs via bootstrap (n=500).

Results: Among 1,355 participants (678 calcium, 677 placebo), 60% adhered to their assigned treatment. Adhering to pre- and early-pregnancy low-dose calcium supplementation versus placebo had minimal to no effect on the risk of gestational hypertension (33.6% versus 35.2%, RR=0.95 [95% CI: 0.90, 1.05]) or gestational proteinuria (20.7% versus 21.6%, RR=0.95 [95% CI: 0.87, 1.04]).

Conclusions: Adhering to pre- and early-pregnancy low-dose calcium supplementation did not decrease the risk of gestational hypertension or proteinuria. These results seem to conflict with a previous analysis, finding adherence associated with a decreased risk of preeclampsia. However, discrepancies may reflect bias towards the null due to non-differential outcome misclassification in secondary trial outcomes.

Perinatal & Pediatric

Continuation of ACE inhibitor dispensing into the first trimester and risk of non-live birth and major congenital malformations: a target trial emulation using US claims data Jeremy Brown* Jeremy Brown Elizabeth Diemer Krista Huybrechts Brian Bateman Sonia Hernández-Díaz

Background

ACE inhibitor exposure in the second and third trimester of pregnancy is considered a cause of fetopathy, but it is unclear whether first trimester exposure increases the risk of malformations. We emulated a target trial using US MarketScan commercial insurance claims data to estimate the effect of continuation of ACE inhibitor dispensing into the first trimester on the risk of non-live birth and major congenital malformations (MCM).

Methods

Eligible individuals were pregnant women aged 16-55 years with an ACE inhibitor dispensation in the 90 days prior to conception. Treatment strategies were discontinuation defined by no further dispensations vs. at least one further dispensation within a grace period from conception to end of remaining drug supply + 4 weeks. Pregnancies were cloned and then censored when non-compliant with the assigned strategy. Censoring weights were estimated by pooled logistic regression adjusted for potential confounders.

Results

There were 6,070 eligible pregnancies with an ACE inhibitor dispensation in the 90 days prior to conception. Among 4,315 live births, 1,679 (38.9%) received an ACE inhibitor dispensation within the grace period. Compared to discontinuers the relative risk was 1.12 (95% CI 1.03-1.22) for spontaneous abortions, 1.81 (1.48-2.28) for elective terminations, 1.19 (1.11-1.28) for any non-live birth, and 1.08 (0.74-1.54) for MCM prevalence. No specific pattern of MCM was identified. The proportion of terminations accompanied by a fetal anomaly claim was not higher in continuers vs. discontinuers (2.4%, 6/255 vs. 5.7%, 9/158).

Discussion

Findings provide some reassurance regarding risk of MCM with unintentional exposure to ACE inhibitors in the first trimester. Potential explanations for an increase in elective terminations include more unplanned pregnancies among continuers, termination due to concerns around ACE inhibitor fetotoxicity, and ACE inhibitor continuation among women planning to terminate.

Outcome	No. events	Risk continuer - % (95% CI)	Risk discontinuer - % (95% CI)	Risk difference - % (95% CI)	Risk ratio (95% CI)
Non-live birth	1979	35.0 (33.3, 37.0)	29.4 (27.8, 31.0)	5.6 (3.2, 8.0)	1.19 (1.11, 1.28)
Spontaneous abortion	1571	26.8 (25.1, 28.5)	23.9 (22.3, 25.2)	2.9 (0.8, 5.1)	1.12 (1.03, 1.22)
Elective termination	339	7.6 (6.4, 8.6)	4.2 (3.5, 4.9)	3.4 (2.2, 4.7)	1.81 (1.48, 2.28)
MCM among live births	147	6.5 (4.7, 8.4)	6.0 (4.8, 7.2)	0.5 (-1.7, 2.7)	1.08 (0.74, 1.51)
Live birth with MCM	147	4.3 (3.1, 5.4)	4.3 (3.4, 5.1)	0.0 (-1.4, 1.5)	1.00 (0.69, 1.37)

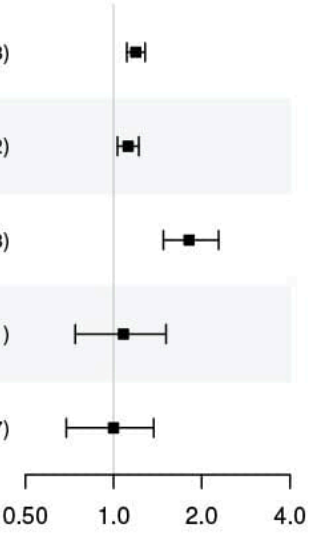


Figure 1: Risk of non-live birth outcomes and MCM among ACE inhibitor continuers and discontinuers

Perinatal & Pediatric

Maternal early pregnancy blood heavy metal(loid)s and low fish consumption in relation to child Dyslipidemia at the age of 7 years Fengxiu Ouyang* Fengxiu Ouyang Yanlin Li Yichun Xuan Ting Zhang Junxia Liu Jian Xu Chong-Huai Yan Jun Zhang

Objective: Dyslipidemia can lead to complex cardiometabolic diseases, and prenatal exposure to selected heavy metal(loid)s may increase risk of dyslipidemia in children. We sought to investigate the association between maternal heavy metal(loid)s exposure, fish consumption and children's serum lipids at the age of 7 years.

Material and Methods: In 1393 mothers and their children from the Shanghai Birth Cohort, we measured maternal whole blood concentrations of 13 metal(loid)s including mercury (Hg), arsenic, cadmium, lead, magnesium, calcium, manganese, iron, copper, zinc, selenium, rubidium, and strontium in mothers at early pregnancy. The intake frequency of sea-fish and river-fish in the past three months (<1 time, 1-3 times, and >3 times per week) was asked using food frequency questionnaire at early pregnancy. Children's fasting serum total cholesterol (TC), triglyceride (TG), low-density lipoprotein (LDL), high-density lipoprotein (HDL) cholesterols, lipoprotein (a) [Lp (a)], apolipoprotein E (Apo E), apolipoprotein A (Apo A), and apolipoprotein B (Apo B) were measured. Blood heavy metal(loid)s was examined both as continuous variables by natural logarithm transformation values and in tertiles (low, medium and high).

Results: The detection rate of maternal blood concentrations of these metals and metalloids ranged 98.3-100%. Early pregnancy blood Hg concentrations Log Hg (mg/L) were associated with higher risk of child fasting serum TC≥5.17 mmol/L, TG≥1.12 mmol/L, LDL≥3.36 mmol/L at the age of 7 years. Among mothers with sea-fish intake frequency 3 time/week (interaction test p=0.003). Similar results were observed in river-fish intake frequency (interaction test p=0.049 for the >3 time/week consumption group). Consistently, positive association of maternal Log Hg (mg/L) with child serum LDL, non-HDL, and Apo B were observed in sea-fish or river-fish intake frequency 3 time/week.

Conclusions: In this prospective birth cohort, despite relatively low maternal Hg exposure, maternal Hg during early pregnancy was positively associated with higher child fasting serum lipids at the age of 7 years, while higher sea-fish or river-fish consumption showed counteracting effect.

Perinatal & Pediatric

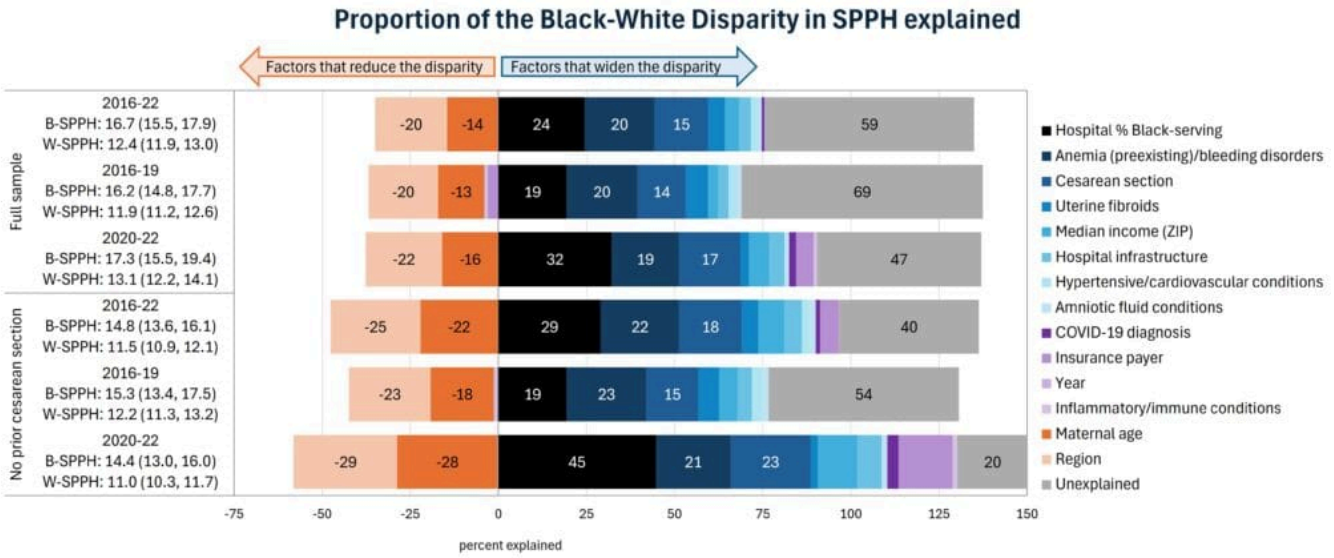
The Contribution of Cesarean Birth to Black-White Disparities in Severe Postpartum Hemorrhage Lindsay Mallick* Lindsay Mallick Eugene Declercq Michel Boudreaux Ron Iverson Sandra Quinn Marie Thoma

Disparities in US maternal morbidity are well established and seen in a heightened risk for Black women for both cesarean section (CS) and its potential complications, like postpartum hemorrhage (PPH). It remains unclear whether disparities in PPH are driven primarily by higher CS prevalence or higher risk of PPH following CS.

We used 2016–2022 National Inpatient Sample data to examine the contributions of CS to the Black–White disparity in severe PPH (SPPH: PPH with shock, hysterectomy, or disseminated intravascular coagulopathy). The sample comprised 2,672,991 singleton, term, cephalic deliveries to non-Hispanic Black and White women without indications for CS for hemorrhage risk. Race-stratified adjusted linear probability models estimated risk differences in SPPH across maternal and hospital characteristics. Oaxaca-Blinder decomposition analyses quantified the proportion of the Black–White disparity in SPPH accounted for by measured factors. Analyses were further stratified by year (2016-19 and 2020-22) and repeated among a subgroup of 2,212,257 deliveries with no prior CS.

SPPH befell 16.6 (95% CI: 15.5-17.8) and 12.4 (95% CI: 11.8-13.0) per 10,000 deliveries to Black and White women, respectively. CS was associated with higher risk of SPPH for both races. Overall, CS, pre-existing anemia, and higher hospital percent Black-serving patients were the largest contributors to the Black–White SPPH disparity (15%, 20%, and 24%, respectively). Age and regional distribution attenuated the disparity; 59% was unexplained by measured factors (Figure). In 2020-22, COVID diagnoses contributed little (2%), but the contribution of greater Black-serving hospitals grew to 32%, leaving less unexplained. Subgroup analyses (no prior CS) found similar patterns but a smaller Black-White disparity in SPPH (14.8 vs. 11.5 per 10,000).

With stark racial disparities in severe maternal morbidity, interventions to improve access to high-quality, equitable maternity care are urgently needed.



Note: SPPH: Severe postpartum hemorrhage (a postpartum hemorrhage diagnosis accompanied by shock, hysterectomy, or disseminated intravascular coagulopathy); B-SPPH: Black SPPH per 10,000 deliveries; W-SPPH: White SPPH per 10,000 deliveries. Pre-existing anemia (e.g., iron or nutrition-related anemia, aplastic, and hereditary anemias, except in crisis and also encompasses bleeding disorders like hemophilic or hemorrhagic disorders; hypertensive or cardiovascular disorders include pregestational or gestational hypertension, mild or moderate pre-eclampsia eclampsia prior to birth, preexisting cardiac disease, and pulmonary hypertension; amniotic conditions include polyhydramnios and chorioamnionitis; inflammatory and autoimmune conditions include pregestational diabetes, gestational diabetes, body mass index (BMI) of 40+, autoimmune conditions, and renal disease. Survey weights were applied to produce nationally representative estimates and account for complex sample design.

Perinatal & Pediatric

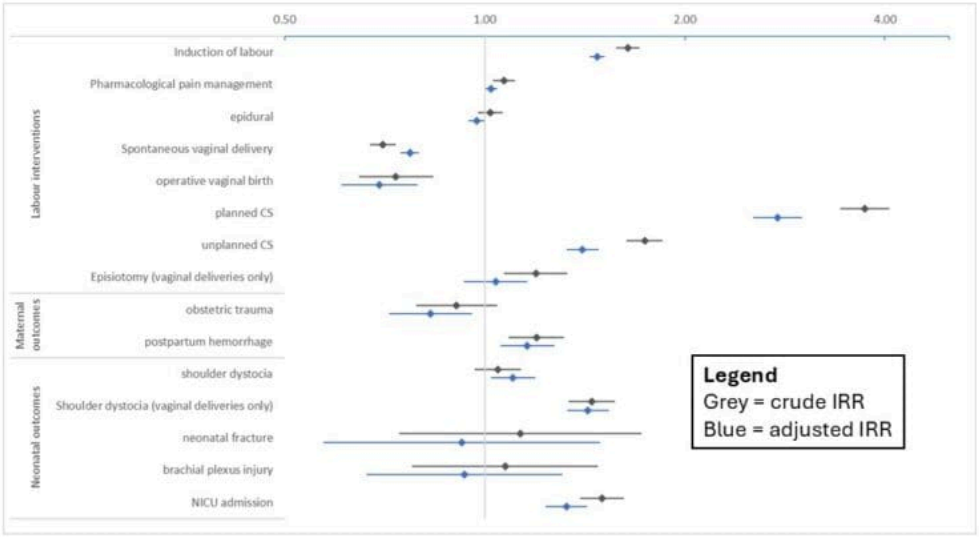
Ultrasound suspicion of fetal large for gestational age and maternal and neonatal outcomes Samantha Krueger* Samantha Krueger Giulia Muraca

Objective: To compare maternal and neonatal outcomes among large-for-gestational-age (LGA) neonates with and without prenatal ultrasound suspicion of LGA.

Study Design: We conducted a population-based cohort study of term LGA births in Ontario, Canada (2012–2021) using linked health administrative data. LGA births with documented prenatal ultrasound suspicion of LGA were treated as exposed and compared with LGA births without such documentation. Outcomes included labor interventions, maternal complications, and neonatal outcomes. Propensity scores with overlap weights were applied in modified Poisson regression models. To explore potential mediating factors and misclassification bias, sensitivity analyses included 1) removing gestational hypertension variables from the propensity score and 2) including those without a documented complication of suspected LGA but a late third trimester ultrasound to the exposed group.

Results: Among 82,385 LGA births, 3,969 (4.8%) had prenatal ultrasound suspicion of LGA. After adjustment, suspected LGA had higher rates of labour induction (39.0% vs 64.0%; aIRR [adjusted incidence rate ratio] 1.48, 95% CI 1.44–1.52), planned cesarean delivery (4.3% vs 16.0%; 2.76, 2.54–3.00), unplanned cesarean delivery (15.9% vs 27.6%; 1.40, 1.33–1.48), postpartum hemorrhage (9.5% vs 11.4%; 1.16, 1.06–1.27), shoulder dystocia (15.4% vs 16.1%; 1.10, 1.02–1.19), and neonatal intensive care unit admission (12.1% vs 18.1%; 1.33, 1.23–1.43; Figure 1). Operative vaginal delivery and obstetric trauma rates were lower among deliveries with suspected LGA (8.2% vs 6.1%; 0.69, 0.61-0.79 and 5.7% vs 5.2%; 0.83, 0.72-0.96 respectively). Results from the two sensitivity analyses were similar to the main analysis.

Conclusion: Prenatal ultrasound suspicion of LGA is associated with increased interventions without improved maternal or neonatal outcomes other than a decrease in operative vaginal delivery and obstetric trauma.


0.50
1.00
2.00
4.00
Induction of labour
Pharmacological pain management
epidural
Spontaneous vaginal delivery
operative vaginal birth
planned CS
unplanned CS
Episiotomy (vaginal deliveries only)
obstetric trauma
postpartum hemorrhage
shoulder dystocia
Shoulder dystocia (vaginal deliveries only)
neonatal fracture
brachial plexus injury
NICU admission
Labour interventions
Maternal outcomes
Neonatal outcomes
Legend
Grey = crude IRR
Blue = adjusted IRR

Perinatal & Pediatric

Diet quality components and arterial stiffness in children: evidence from a birth cohort

Xuanxuan Zhu* Xuanxuan Zhu Diane L. Putnick Priscilla K. Clayton Tzu-Chun Lin Edwina Yeung

Background. Arterial stiffness is a risk factor for hypertension and eventually increases the risk of cardiovascular and cerebrovascular diseases. Arterial stiffening is a gradual process that begins early in life and progresses over time. Experts recommend that risk factors be addressed as early as childhood to slow its progression. Yet, its association with diet quality remains understudied in children. This study aimed to examine the association of diet quality components (food groups and eating behaviors) with arterial stiffness in middle childhood.
Methods. On 7- and 9-year questionnaires, mothers reported their children's daily intake of various foods (e.g., whole wheat bread, vegetables, snacks) and weekly intake of fast food, breakfast, and multivitamins. Accordingly, the Youth Healthy Eating Index (YHEI) was calculated (0-90), with higher scores indicating better diet quality. Pulse wave velocity (PWV), a measure of arterial stiffness, was taken in duplicate using the SphygmoCor XCEL device at clinic visits at 9-10 years. Generalized linear models estimated associations, adjusting for sociodemographics, pre-pregnancy body mass index, breastfeeding duration, etc.
Results. Among 324 children with measures (mean age 9.46±0.58 years), the mean PWV was 4.39±0.86 m/s. YHEI total and component scores were not associated with PWV (Table 1). Only a crude association of a higher YHEI score in the fast-food category (reflecting lower intake) with lower PWV was observed and it attenuated after adjusting for covariates (-0.05 m/s per unit fast-food YHEI; 95% confidence interval: -0.10, 0.01). Associations were similar after additionally adjusting for obesity status at the time of dietary report (i.e., at 7-9 years, 14.23% were reported as obese).
Conclusion. Diet quality was not associated with arterial stiffness in children. Future studies are needed to explore the association in longer follow-up or in adolescence.

Table 1. Diet quality and Pulse Wave Velocity (PWV), Upstate KIDS Study (N = 324).

	Estimate, 95% CI	
YHEI	Model 1	Model 2
Whole grains	-0.02 (-0.05, 0.01)	-0.02 (-0.05, 0.01)
Vegetables	-0.01 (-0.04, 0.02)	-0.01 (-0.05, 0.03)
Fruits	-0.02 (-0.05, 0.02)	-0.003 (-0.05, 0.04)
Dairy	0.02 (-0.01, 0.05)	0.01 (-0.03, 0.05)
Meat ratio	0.002 (-0.02, 0.03)	-0.0006 (-0.03, 0.03)
Snack foods	0.02 (-0.02, 0.05)	0.02 (-0.01, 0.06)
Sweetened beverages	-0.04 (-0.10, 0.02)	-0.03 (-0.10, 0.04)
Multivitamin use	-0.02 (-0.07, 0.02)	-0.03 (-0.08, 0.02)
Fast foods	**-0.06 (-0.11, -0.02)**	-0.05 (-0.10, 0.01)
Eat breakfast	-0.05 (-0.22, 0.12)	-0.11 (-0.31, 0.08)
Dinner with family	-0.01 (-0.18, 0.16)	0.01 (-0.17, 0.20)
Total	-0.01 (-0.01, 0.004)	-0.004 (-0.01, 0.01)

Estimates present unstandardized betas for continuous PWV (m/s).
YHEI is the Youth Healthy Eating Index.
Model 1 is the unadjusted model.
Model 2 is adjusted for maternal age at delivery (years), race/ethnicity (non-Hispanic White vs. not), marital status (y/n), maternal education (less than college vs. college vs. advanced degree), private insurance (y/n), fertility treatment (No treatment vs. OI/IUI vs. ART), WIC (y/n), maternal smoking (never/ever smoked), pre-pregnancy BMI, nulliparous (y/n), child age at outcome, child sex, plurality (singleton/twin), breastfeeding duration (months), child moderate-to-vigorous physical activity at outcome (Q1 vs. Q2 vs. Q3 vs. Q4), and time to introduce fruits and vegetables (< 5, 5-8, 9-12 months).
Bolding indicates statistically significant results (p <.05).

LATEBREAKER

Pharmacoepidemiology

Impact of Phenobarbital-Based Regimens on Clinical Outcomes in Critically Ill Patients with Alcohol Withdrawal Syndrome: A Propensity Score-Matched Cohort Study Zeeshan Rizwan* Zeeshan Rizwan

Objectives: Alcohol withdrawal syndrome (AWS) in the intensive care unit (ICU) often requires escalating sedative therapy and is associated with respiratory complications and prolonged length of stay (LOS). Phenobarbital (PHB) is increasingly used for benzodiazepine (BZD)-refractory AWS, yet comparative effectiveness data in critically ill patients remain limited. We evaluated whether PHB-based regimens were associated with differences in LOS and early safety outcomes compared with non-PHB strategies.

Design: Multicenter retrospective cohort study using multiple imputation and propensity score matching to estimate the average treatment effect in the control (ATC).

Setting: ICUs at four Mayo Clinic sites from June 30, 2017 to July 1, 2024.

Patients: Adults (≥18 years) admitted with AWS (CIWA-Ar ≥10) who received either a PHB-based or non-PHB pharmacologic strategy. Patients admitted after surgical intervention were excluded. The matched cohort included 1,216 patients (PHB n=345; non-PHB n=871).

Measurements and Main Results: Primary outcomes were ICU and hospital LOS. Safety outcomes included hypotension and respiratory compromise (new intubation or aspiration) within 48 hours of treatment initiation. In adjusted ATC analyses, PHB was not associated with significant differences in ICU LOS (+1.18 days; 95% CI −0.08 to 2.44; p=0.067) or hospital LOS (+1.39 days; 95% CI −0.87 to 3.65; p=0.228). Adjusted odds of hypotension and intubation were similar between groups. Aspiration within 48 hours occurred less frequently with PHB (7.8% vs 12.6%; p=0.017). CIWA-Ar reductions at 24 and 48 hours were comparable.

Conclusions: In this multicenter ICU cohort, PHB-based regimens were safe and effective for AWS management but were not associated with improved LOS in an all-comers population. Pragmatic randomized trials are needed to define effectiveness, cost-effectiveness, and identify subgroups most likely to benefit.

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Pharmacoepidemiology

Comparative effectiveness of oral antihypertensives initiation during pregnancy in a California Medicaid population, 2016-2020. Catherine Psaras* Catherine Psaras Rebecca Baer Clare Cutri-French Gretchen Bandoli

To extend findings from the Chronic Hypertension and Pregnancy (CHAP) trial, we compared initiation of labetalol, nifedipine, and methyldopa by 23 weeks' gestation among pregnant patients with chronic hypertension, focusing on effectiveness and safety. We used California Medicaid claims linked to the California Study of Mothers and Infants for deliveries from 2016-2020. Exposure was defined as at least one paid fill for labetalol, extended-release nifedipine, or methyldopa by 23 weeks' gestation among patients with no oral antihypertensive use from 90 days before last menstrual period (LMP) through LMP. As in CHAP, the composite effectiveness outcome included preeclampsia with severe features, preterm birth <35 weeks, placental abruption, and fetal or neonatal death. Small for gestational age birth (SGA) was evaluated as a safety outcome. The cohort included 2,282 singleton births (1,496 labetalol, 653 methyldopa, 133 nifedipine). Composite outcome incidence differed modestly by medication (labetalol 23%, methyldopa 19%, nifedipine 25%). Compared with labetalol, methyldopa was associated with lower risk (adjusted risk ratio [aRR] 0.82; 95% CI 0.68-1.00), while nifedipine showed no difference (aRR 1.03; 95% CI 0.74-1.43). Nifedipine versus methyldopa yielded an aRR of 1.25 (95% CI 0.80-1.70). For SGA, results were similar (aRR (95% CI): methyldopa vs. labetalol: 0.81 (0.62, 1.05); nifedipine vs. labetalol: 1.06 (0.65, 1.74); nifedipine vs. methyldopa: 1.32 (0.62, 2.01)). Labetalol and nifedipine showed comparable effectiveness and safety, while methyldopa was associated with lower risks of adverse outcomes. Limited overlap between treatment groups and potential residual confounding warrant cautious interpretation. Further research is needed to determine whether the apparent advantage of methyldopa reflects a true therapeutic benefit or underlying bias.

Pharmacoepidemiology

Postpartum COVID-19 vaccination and risk of lactational mastitis Yihe G Daida* Yihe Daida Jingran Cao Kimberly K Vesco Gabriela Vazquez-Benitez Malini B DeSilva Elisabeth M Seburg Kirsten Ehresmann Elyse O Kharbanda Abbey Sidebottom Heather S Lipkind Kristin Palmsten

Purpose: Mastitis could occur as a vaccination-related adverse effect, if vaccination were associated with reduced breastfeeding frequency, leading to subsequent inflammation. We aimed to assess the association between maternal postpartum COVID-19 vaccination and risk of lactational mastitis.

Method: We conducted a retrospective study using electronic health record (EHR) data from four integrated health systems. Eligible patients had a live birth between December 2020–September 2022, were linked to an infant with ≥1 well visit before 60 days of life and had documentation of ever breastfeeding in the EHR. State immunization information system supplemented EHR data on COVID-19 vaccination. The primary outcome was an International Classification of Diseases, Tenth Revision (ICD-10) Clinical Modification mastitis diagnosis (N61.0 or O91.2x) in the 180 days postpartum; the secondary outcome was mastitis plus antibiotic dispensing within 3 days. Cox proportional hazards models with time-dependent exposure estimated adjusted hazards ratios (aHR) and 95% CI, accounting for site, maternal age, insurance, race and ethnicity, infant gestational age at birth, smoking status, neighborhood-level socioeconomic characteristics (education, poverty level, medium household income) and year and month of delivery with stabilized inverse probability of treatment weights. Person-time was classified as unexposed until vaccination and as exposed thereafter. Patients were censored at first mastitis diagnosis or 180 days postpartum, whichever occurred first.

Results: Among 18,446 individuals; 36.2% were vaccinated in the 180 days postpartum. Overall, 5.5% were diagnosed with mastitis. There was no significant association between vaccination and lactational mastitis (aHR 1.10, 95% CI: 0.83-1.46) or mastitis diagnosis plus antibiotic dispensing (aHR 1.17, 95% CI: 0.87-1.59).

Conclusion: COVID-19 vaccination was not associated with a higher lactational mastitis risk in the 6 months after delivery.

Pharmacoepidemiology

Dispensations of prescription pain medications and opioids during the first year postpartum among TRICARE beneficiaries, 2013-2022 Celeste Romano* Celeste Romano Jackielyn Lanning Clinton Hall Ava Marie S. Conlin Marissa Seamans

Objective: To describe person-time with any prescription pain medication and prescription opioids during the first year postpartum.

Methods: Birth and Infant Health Research program data were used to identify patients with a live birth while enrolled in TRICARE, the health insurance program for US military families, 2013–2022. Live births were identified using diagnostic and procedure codes in administrative medical records and confirmed via linkage to enrollment data. Patients were followed until 1-year postpartum, with loss to care and return to care accounted for in estimation of person-time. Dispensed pain medications, excluding those for opioid use disorder treatment, were identified in outpatient pharmacy records. The mean number of days on 1) any pain medication and 2) opioid medications were calculated overall and by military status. Mean differences comparing military vs non-military patients were estimated and bootstrap resampling was used to obtain estimates of precision.

Results: Overall, 1,037,793 live deliveries were identified, with 59% of postpartum patients filling a pain medication prescription and 41% filling an opioid prescription. Across 10.4 million person-months, 3% of person-time was spent on any prescription pain medication (mean ± SD: 10.3 ± 29.0 days) and 1% was spent on an opioid medication (mean ± SD: 3.7 ± 15.5 days). Approximately one-third of time spent on pain medications occurred within the first 2 weeks postpartum (34%). Compared to non-military patients, postpartum military service members, who comprised 17% of the sample, spent an additional 3.7 days, on average, on any pain medication (95% CI: 3.6-3.9), although time on opioid medications was comparable (mean difference: 0.4 days; 95% CI: 0.3-0.4).

Conclusions: Pain medications were frequently dispensed during the first year postpartum, particularly among military service members. Although opioid dispensations were also common, time on opioids was low, indicating good stewardship.

LATEBREAKER

Policing/Incarceration

Association Between Residential Proximity to Carceral Facilities and Asthma ED Visits in California Beier Li* Beier Li Yiran Liu

Background: The United States operates roughly 6,300 correctional facilities, clustered around environmental hazards, with new facility construction ongoing. While research has shown the health harms associated with high incarceration rates, less is known about the health of communities living near prisons and jails.

Methods: We conducted a cross-sectional ecological analysis at the census tract level to examine the association between residential proximity to jails or prisons and asthma emergency department (ED) visit rates in California. We generated buffers of varying distance thresholds around facilities (0.25, 0.5, and 1 mile for jails; 1, 2, and 5 miles for prisons) and classified tracts overlapping a buffer as proximate. Multivariable linear models assessed the tract-level association between jail or prison proximity and asthma ED visits, adjusting for urbanicity, percent Black, unemployment rate, median household income, percent uninsured, primary care provider shortage, ozone concentration, and particulate matter (PM)2.5.

Findings: At the 1-mile threshold, 655 census tracts (8.2%) with over 3 million residents were classified as proximate to a jail, while 543 tracts (6.8%) were proximate to a prison. Jail proximity was significantly positively associated with asthma ED visit rates after controlling for covariates across all distance thresholds tested. Effects did not monotonically decrease with increasing distance (0.25-mile: β=3.6; 0.5-mile: β=5.6; 1-mile: β=4.5). Prison proximity was not significantly associated with asthma ED visit rates at any distance threshold.

Conclusions: California census tracts proximate to jails experience a greater burden of asthma ED visits than explained by measured socioeconomic and environmental covariates. While causality remains unclear, the findings suggest potential health risks associated with jail proximity, with implications for the health of incarcerated individuals, staff, and surrounding communities.

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Policing/Incarceration

The effect of prison visitation on post-incarceration risk of reincarceration and mortality, Rhode Island, 2009-2019 Molly Remch* Molly Remch Daniel Westreich Sara N Levintow Brian W Pence Paul N Zivich Tonya Van Deinse Lauren Brinkley-Rubinstein

Receiving visitors is an opportunity for incarcerated people to maintain connection to their social networks. We estimate the causal effect of receiving visitors on post-release mortality and, separately, on reincarceration using a cohort of 12,588 people released from the Rhode Island Department of Corrections between 2009 and 2019. We used g-computation with accelerated failure time models and a generalized gamma distribution to estimate the effect of potential interventions in which the mean monthly visits, median monthly visits, number of visits in the last month of incarceration, and percent of months with visits were each increased. We estimated survival curves and risk differences between one- and five-years post-release. During five years post-release, 418 (3.3%) people died and 8,153 (64.8%) people were reincarcerated. Although we did not observe an effect on mortality, the interventions had a protective effect on risk of reincarceration. The five-year risk difference for reincarceration under an intervention that increased everyone’s mean monthly visits by two was -0.04 (95% CI: -0.04, -0.03). These results speak to the importance of social networks in preventing reincarceration. Implementation and evaluation of policies that increase the accessibility of visitation are needed.

Reproductive

Weight stigma during pregnancy: The association between prepregnancy body mass index category, gestational weight gain, and adequate prenatal care communication Lisa Miller* Lisa Miller Sarah Haight Habibah A. Ijaiya Dawn P. Misra Jaime Slaughter-Acey

Background
Women with obesity frequently cite physicians as a source of weight bias, potentially limiting adequate prenatal care (PNC). We examined the association between prepregnancy body mass index (pBMI) and PNC provider communication and whether gestational weight gained (GWG) modifies this relationship.

Methods
Data were from the 2009 – 2011 Life-course Influences of Fetal Environments study, restricted to respondents with ≥ 1 PNC visit (N=1090). GWG was categorized per CDC guidelines as “less than recommended”, “recommended”, or “more than recommended”, and pBMI was classified as “overweight” (25-29.9 kg/m2), “obese” (≥30kg/m2), or “healthy weight” (18-24.9 kg/m2), with “healthy weight” as the reference. PNC communication covered 8 topics (e.g. early labor pains and alcohol use) and was operationalized as adequate (discussed/given guidance) or inadequate (not discussed). Logistic regression was used to estimate odds ratios (OR) and 95% CI for pBMI with PNC communication. Effect modification of pBMI across GWG levels was assessed. Models were adjusted for health behaviors (e.g. smoking), PNC adequacy, and sociodemographics.

Results
Among those who gained more weight than recommended, overweight participants were less likely to receive communication about early labor pains (OR: 0.41; 95% CI: 0.22-0.78) and obese participants were less likely to receive guidance on sleep (OR: 0.59; 95% CI: 0.37-0.95). Among those who gained less than weight recommended, overweight participants were less likely to receive guidance on sleep (OR: 0.32; 95% CI: 0.11-0.96) and obese participants were less likely to receive guidance about chronic health (OR: 0.40; 95% CI: 0.19-0.86) and alcohol use (OR: 0.37; 95% CI: 0.16-0.87).

Conclusion
Participants with an overweight or obese pBMI who deviate from GWG recommendations are less likely to receive adequate PNC communication. Findings indicate PNC providers may differentially prioritize communication depending on body size and GWG.

Reproductive

Opioid Use on Pregnancy Outcomes and Congenital Anomalies Xiaoyi Shan* Xiaoyi Shan

The increased opioid use has been a public health concern for the past two decades. The misuse and abuse of the prescription opioid among women, especially during pregnancy also has been rising significantly. The consequences of the opioid use disorder (OUD) on reproductive health have been reported. The review aims to provide a most up-to-date summary focusing on the pregnancy outcomes and congenital abnormalities. Pubmed search was used for published research on human subject in English between 2005-2025. The keywords combined ‘opioid use disorder’, ‘pregnancy outcome’ ‘spontaneous abortion’, ‘stillbirth’, ‘congenital anomalies’ and ‘birth defect’. Most relevant studies with full text available and were included. Most studies reported chronic opioid use increased the risk of adverse pregnancy outcomes including spontaneous abortion, preterm birth, intrauterine growth restriction, as well as small for gestation age infants. Majority studies reported elevated risk of overall birth defects. The highest risk reported was over two folds, though some studies didn’t find a statistically significant association between OUD and birth defects. Congenital heart defects showed a strong association with opioid exposure during pregnancy, and was the most frequently reported group of anomalies. Other reported congenital anomalies including neural tube defects, gastroschisis, clefts, and limb deficiencies. Due to the complexity of prescription drug abuse such as social stigma, there is lack of data and in-depth analysis on the subject. Some studies had very small sample sizes, and many faced potential methodological challenges. There is a critical need for research to better understand the adverse effects of opioid use on pregnancy outcomes and identify risk factors as well as effective intervention strategies and evidence based recommendations for safe prescription use.

LATEBREAKER

Reproductive

Stillbirth and risk of Alzheimer's disease and other related dementias: Findings from the Utah Population Database (1977–2024) Karen Schliep* Karen Schliep Brian Avery Emily Guinto Christine Cliatt Brown Ken Smith Jennifer Majersik Norman Foster Jean Wactawski-Wende Truls Ostbye JoAnn Tschanz James Padbury Julio Facelli Michael Varner

Introduction:
Prior studies suggest stillbirth increases dementia risk in women, but findings are inconsistent and largely based on non-U.S. cohorts with self-reported reproductive histories and limited assessment of dementia subtypes. Stillbirth is linked to maternal vascular and stress-related conditions characterized by inflammation and thrombosis, biological pathways that also contribute to neurodegeneration We examined associations of stillbirth with dementia overall and dementia subtypes in a large U.S. population.

Methods:
We conducted a retrospective cohort study using the Utah Population Database. Assigned females at birth aged 15–55 with ≥1 pregnancy (1978–2023) were followed for dementia and death through 2024. Stillbirth was identified from fetal death records and dementia from electronic medical records and death certificates. Cox models estimated hazard ratios (HR) for all-cause dementia and dementia subtypes with 95% confidence intervals (CI). Models used age as the analysis time scale, censoring on out-migration, death, or end of follow-up. Early (<65) vs late-onset (≥65) dementia were prespecified to reflect clinically and etiologically distinct onset periods. Models adjusted for birth year, baseline parity, and age at index pregnancy.

Results:
The cohort included 910,322 women and 4,916 dementia cases (Table 1). Overall, 11,795 women experienced ≥1 stillbirth (73 dementia cases). Stillbirth history was associated with increased risk of any dementia (HR = 1.32, 95% CI 1.05–1.66), driven by early-onset dementia (HR = 1.50, 95% CI 1.07–2.11), particularly non-Alzheimer's (namely vascular dementia), early-onset subtype (HR = 1.54, 95% CI 1.05–2.26). No associations were observed for late-onset dementia or Alzheimer's disease.

Conclusion:
Stillbirth was linked to elevated dementia risk, particularly early-onset and non-Alzheimer's subtypes. This pattern suggests that reproductive vascular insults may increase neurodegenerative vulnerability.


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Respiratory

Real-world effectiveness of infant RSV preventative interventions: a target trial emulation study using a novel analytic approach Sara S Kim* Sara Kim Emily Wu Connor Van Meter Ashley Tippett Marina Bruck David Benkeser Elizabeth Rogawski McQuade

Respiratory syncytial virus (RSV) is the leading cause of infant hospitalization in the United States. In 2023, long-acting monoclonal antibodies (mAbs) and maternal bivalent prefusion F vaccination (RSVpreF) were approved to protect infants. To estimate real-world effectiveness of each intervention, we applied a novel target trial emulation (TTE) method that targets a similar estimand to matching-based studies designed to emulate phase 3 randomized controlled trials (RCTs) while leveraging data from all observed individuals without requiring matching to identify a randomization time.

Using claims data, we identified 165,516 infants eligible to receive mAbs or maternal RSVpreF and followed them from birth until an RSV-related event, insurance lapse, or study end. We estimated effectiveness of mAbs and RSVpreF against RSV hospitalization and medically attended illness (MAI) using a g-computation-based estimator. For each intervention, we estimated cumulative incidence with ($\psi 1$) and without ($\psi 0$) the intervention by fitting separate Cox proportional hazards models among infants who received the intervention and among those who had not yet received it and marginalizing over covariates and time of receipt. We defined effectiveness as ($1- \psi 1/\psi 0$). For RSVpreF, we assumed protection from birth and began follow-up at birth for all infants.

At 150 days post-intervention, mAbs reduced the risk of RSV hospitalization by 82% (95% CI: 74-88%) and RSV MAI by 75% (95% CI: 70-78%). RSVpreF reduced risk of RSV hospitalization by 96% (95% CI: 91-99%), but protection against RSV MAI was lower (48% (95% CI: 16-67%)).

Both interventions performed similarly as in their respective phase 3 RCTs, indicating sustained effectiveness in real-world settings and illustrating the utility of the target trial emulation approach.

Science Communication & Media

Sociodemographic Factors Associated with Withdrawal from a National Brain Health Cohort Azmat Sidhu* Azmat Sidhu Zelin Wang Zhao Chen

Background:

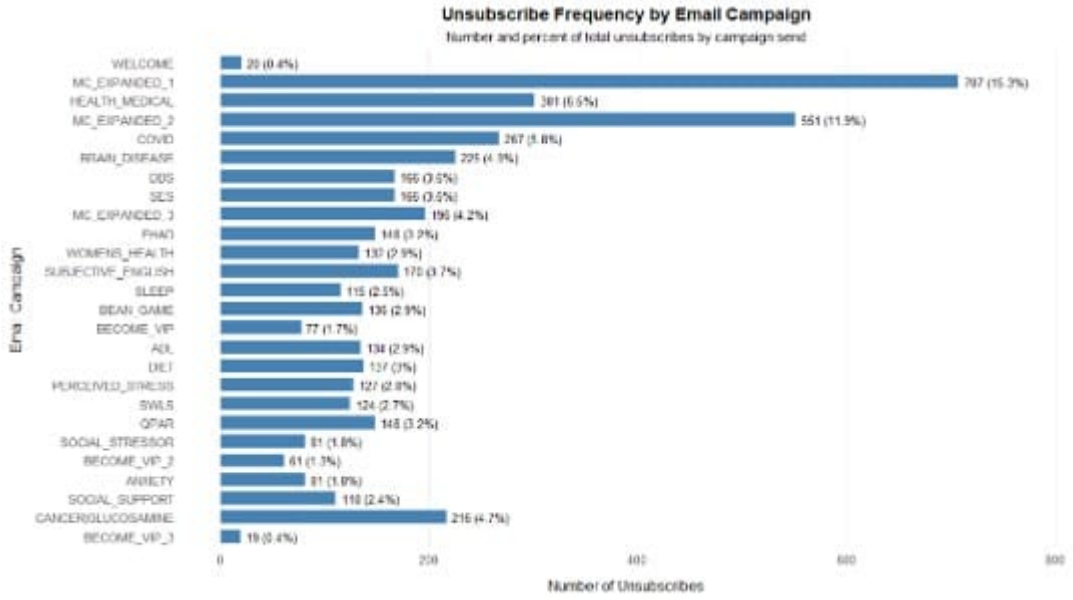
Internet-based cohorts are critical for brain health research, but participant withdrawal threatens representativeness and longitudinal follow-up. In digital studies, email unsubscription provides a measurable indicator of disengagement. We examined sociodemographic factors associated with withdrawal from MindCrowd, a national online brain health cohort.

Methods:

We conducted a retrospective cohort study of U.S. MindCrowd participants engaged in automated email communications between June 2022 and August 2025. Adults (≥18 years) with valid email addresses were included. The outcome was confirmed email unsubscription. Predictors included age, sex, race, Hispanic/Latino ethnicity, education, number of chronic conditions, and neighborhood socioeconomic vulnerability (CDC Social Vulnerability Index). Logistic regression models estimated unadjusted and adjusted odds of unsubscription.

Results:
Among 80,930 participants, 4,615 (5.7%) unsubscribed. Mean time to unsubscription was 71.6 days. Older age was strongly associated with withdrawal; participants aged 70–79 (aOR=1.94, 95% CI: 1.64–2.29) and ≥80 (aOR=2.24, 95% CI: 1.80–2.80) had higher odds compared with ages 18–29. Black participants (aOR=0.59, 95% CI: 0.50–0.69) and Hispanic/Latino participants (aOR=0.77, 95% CI: 0.69–0.87) were less likely to unsubscribe than White and non-Hispanic participants. Higher education was associated with greater withdrawal, while residence in highly socioeconomically vulnerable areas was associated with lower odds of unsubscription (aOR=0.83, 95% CI: 0.74–0.92). Sex and chronic conditions burden were not independently associated.

Discussion:
Withdrawal from a national online brain health cohort is socially patterned. Targeted, age- and education-sensitive engagement strategies may reduce attrition and improve representativeness in large-scale digital brain health research.


Unsubscribe Frequency by Email Campaign
Number and percent of total unsubscribes by campaign send
Email Campaign
WELCOME
MC_EXPANDED_1
HEALTH_MEDICAL
MC_EXPANDED_2
COVID
BRAIN_DISEASE
DDS
SES
MC_EXPANDED_3
PHAD
WOMENS_HEALTH
SUBJECTIVE_ENGLISH
SLEEP
BRAIN_GAME
BECOME_VIP
ADL
DIET
PERCEIVED_STRESS
SWLS
QPAR
SOCIAL_STRESSOR
BECOME_VIP_2
ANXIETY
SOCIAL_SUPPORT
CANCERGLUCOSAMINE
BECOME_VIP_3
20 (0.4%)
707 (15.3%)
301 (6.5%)
551 (11.9%)
267 (5.8%)
195 (4.2%)
148 (3.2%)
133 (2.9%)
170 (3.7%)
115 (2.5%)
136 (2.9%)
77 (1.7%)
134 (2.9%)
137 (3%)
127 (2.8%)
124 (2.7%)
148 (3.2%)
81 (1.8%)
61 (1.3%)
81 (1.8%)
110 (2.4%)
216 (4.7%)
19 (0.4%)
0
200
400
600
800
Number of Unsubscribes

Screening

Using facility zip code level mammography utilization to overcome biases that plague survey data on screening utilization Garth Rauscher* Garth Rauscher Sarah Lomahan Teresita Macarol Anne Marie Murphy

Introduction: National and local survey data on mammography screening suffer from self-report inaccuracies (mostly in the form of over-reporting) and low survey participation, where participants are more likely than the general population to have been previously screened. As a result, survey data overestimate screening and may mask disparities in screening. We obtained population-level prevalence estimates of screening mammography in Chicago, while avoiding the low response rates and over-reporting issues that plague survey data. Methods: For calendar year 2019, we requested zip code-level counts of screening mammograms for sites within and around the city of Chicago. Counts were aggregated to the zip code and divided by the number of women aged 40-79 to obtain approximate utilization rates. Next, we linked zip code compositional characteristics (e.g., segregation, disadvantage) and estimated prevalence differences (PD) associations between zip code characteristics and screening utilization. We also compared estimates to those from the BRFSS and HCS. Results: Utilization estimates were lower than those obtained from survey data. Mean zip code utilization rate was 29% when assigning all screening mammograms to women aged 40-79, versus 48.5% in the past 12 months using BRFSS data. Higher utilization was associated with greater zip code-level income, education, and private health insurance. Predominantly minority zip codes had utilization rates that were approximately 10 percentage points lower than those of non-minority zip codes (95% CI: -0.18, -0.02); this disparity was statistically eliminated when zip code socioeconomic status was added to the models (PD=-0.01, 95% CI: -0.16, 0.15). Updated results will be presented. Conclusion: Self-reported data on mammography utilization provides an overly optimistic picture of screening utilization and masks existing disparities in utilization.

Screening

Comparative Performance of Metabolic Risk Indices for Predicting MASLD in Adolescents: Evidence from the Ewha Birth and Growth Study Hyeseung Jang* Hyeseung Jang Seunghee Jun Hyelim Lee Hye Ah Lee Hyesook Park

Background

With the increasing prevalence of obesity, insulin resistance, and dyslipidemia among adolescents, metabolic dysfunction–associated steatotic liver disease (MASLD) has emerged as an important public health concern. Because pediatric MASLD is often asymptomatic and imaging-based diagnosis is limited in large-scale settings, noninvasive metabolic indices are widely used. Although most indices were developed in adults, recent studies highlight the need for pediatric-specific criteria, including cutoff values based on the fatty liver index (FLI) and hepatic steatosis index (HSI).

Methods

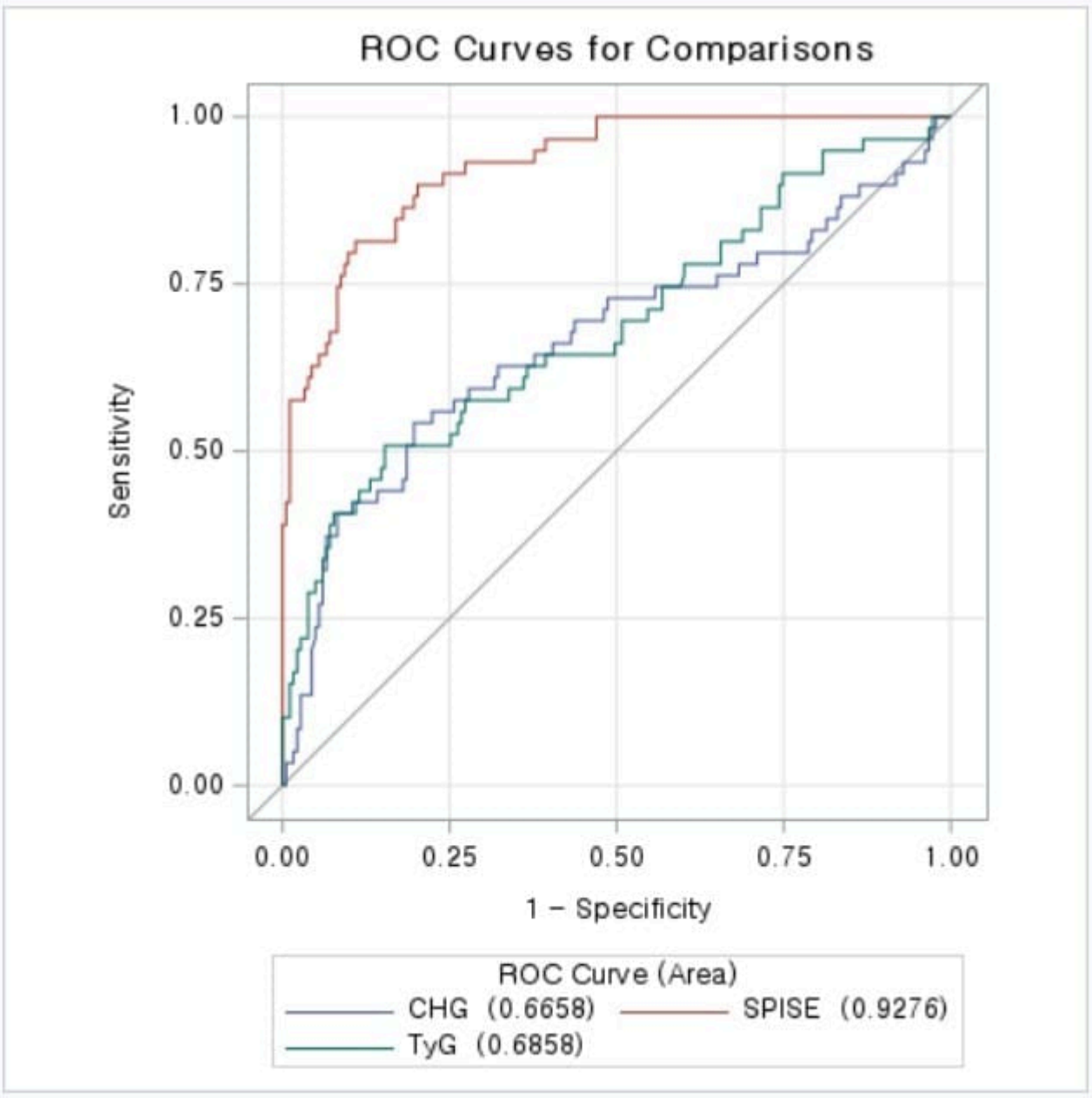
This study included 242 adolescents aged 13–15 years from the Ewha Birth and Growth Cohort and compared the predictive performance of the cholesterol–glucose index (CHG), triglyceride–glucose index (TyG), and single-point insulin sensitivity estimator (SPISE) for MASLD. MASLD was defined using pediatric-specific cutoff values (FLI ≥20 or HSI ≥30). Associations were evaluated using logistic regression. Predictive performance was assessed using receiver operating characteristic (ROC) curves and area under the curve (AUC), with between-index differences tested using ROC contrast tests. Optimal cutoffs for the metabolic indices were determined by maximizing the Youden index.

Results

The prevalence of MASLD defined by pediatric criteria was 24.4%. All three indices were significantly associated with MASLD. In adjusted analyses, CHG and TyG showed positive associations with MASLD risk, whereas SPISE showed an inverse association. In ROC analysis, SPISE demonstrated the highest predictive performance (AUC = 0.928, 95% CI 0.893–0.962), significantly outperforming TyG (AUC = 0.686) and CHG (AUC = 0.666). At the optimal cutoff, SPISE achieved high sensitivity (82.8%) and specificity (88.9%). CHG and TyG showed lower sensitivities (55.2% and 51.7%) and specificities (80.7% and 84.2%), respectively.

Conclusion

Using pediatric MASLD criteria proposed in prior studies, this study compared the predictive performance of CHG, TyG, and SPISE in adolescents. Among the candidate indices, SPISE showed superior predictive accuracy, supporting its utility as a simple tool for identifying MASLD risk in adolescents when imaging-based diagnosis is not feasible.


ROC Curves for Comparisons
Sensitivity
1.00
0.75
0.50
0.25
0.00
0.00
0.25
0.50
0.75
1.00
1 − Specificity
ROC Curve (Area)
CHG (0.6658)
SPISE (0.9276)
TyG (0.6858)

Social

Leveraging Epidemiologic Mixture Methods to Understand Early Child Development Through a Socio-Ecological Lens Amanda Dorsey* Amanda Dorsey Shakira F Suglia Anke Hüls

Background: Exposures at the individual, interpersonal, and neighborhood levels have been individually shown to affect child development. We examined which levels of modifiable exposures are most impactful for three-year old child development, using two types of mixture models.

Methods: We used Future of Families and Child Wellbeing Study data, a longitudinal birth cohort from 18 large U.S. cities. Two mixture models, self-organizing maps (SOM) and quantile g-computation, included individual resource (income, material hardship, educational toys), interpersonal (aggravation in parenting, mother-child activities), and neighborhood (collective efficacy) exposure scales. Development outcomes at age 3 were measured with the Adaptive Social Behavior Inventory, Child Behavior Checklist, and Peabody Picture Vocabulary Test. Covariates included maternal race and ethnicity and child sex.

Results: Among 1,552 families, three SOM clusters were identified. Cluster 1 was most privileged across all exposures; cluster 2 had the lowest interpersonal exposure scores but moderate privilege regarding neighborhood collective efficacy and educational toys; cluster 3 had the lowest neighborhood exposure scores but moderate privilege regarding material hardship and aggravation in parenting. Compared to cluster 1, mean developmental scores in clusters 2 and 3 were 0.22-0.63 standard deviations lower across developmental domains. Clusters 2 and 3 experienced marginally smaller differences in social and behavioral scores, respectively. Adjusted quantile g-computation further showed that improving all exposures by one quantile was associated with 0.21 (95% CI: 0.09, 0.33; social domain) to 0.59 (95% CI: 0.47, 0.71; behavioral domain) SD higher child development scores.

Conclusion: Greater privilege across these exposures was collectively associated with improved child development, particularly behavioral. These results support multi-level interventions for well-rounded child development.

Social

Stratification and accumulation? Explaining changing mortality inequities between business owners and non-owners in the US (1984-2022) Jerzy Eisenberg-Guyot* Jerzy Eisenberg-Guyot Seth J. Prins Anita Minh Anjum Hajat Audrey Renson

Background: Consolidating power among business owners, reflected in plunging labor-union density and growing precarious employment, may be fueling mortality inequities across social classes. However, the issue remains understudied. Thus, we quantified and explained temporal changes in mortality inequities between business owners ("owners") and non-owners in the US.

Methods: Our sample included respondents ages 18-66 in the 1984, 1989, 1994, and 1999-2013 Panel Study of Income Dynamics waves with mortality follow-up through 2022. Owners were those who themselves or whose family units owned a business or had a financial interest in a business in the prior year. Using parametric g-computation, we estimated how inequities between owners and non-owners in 10-year age-adjusted mortality risks changed from 1984-2013. Next, we analyzed whether any changes in the inequities across years could be attributed to shifting gendered, racialized, and socioeconomic stratification. Finally, we analyzed whether growing income and wealth disparities between owners and non-owners exacerbated inequities across years.

Results: Our sample included 23,859 respondents and 115,161 observations. In 1984, non-owners had 1.34-times (95% CI: 1.07, 1.70) greater 10-year age-adjusted mortality risks than owners; the 2013 figure was 2.20 (95% CI: 1.72, 2.96) (Figure 1), for a ratio of risk ratios (RRR) across years of 1.64 (95% CI: 1.13, 2.38). After social-stratification-adjustment, within-year inequities lessened; however, increases across years attenuated only somewhat (RRR for 2013 vs 1984: 1.46 [95% CI: 1.01, 2.04]). Finally, we estimated increases in the inequities across years would not have meaningfully lessened if income and wealth distributions had remained at 1984 levels.

Conclusions: We estimated growing mortality inequities between owners and non-owners in the US, which cannot be fully explained by shifting social stratification and individual-level income and wealth distributions.

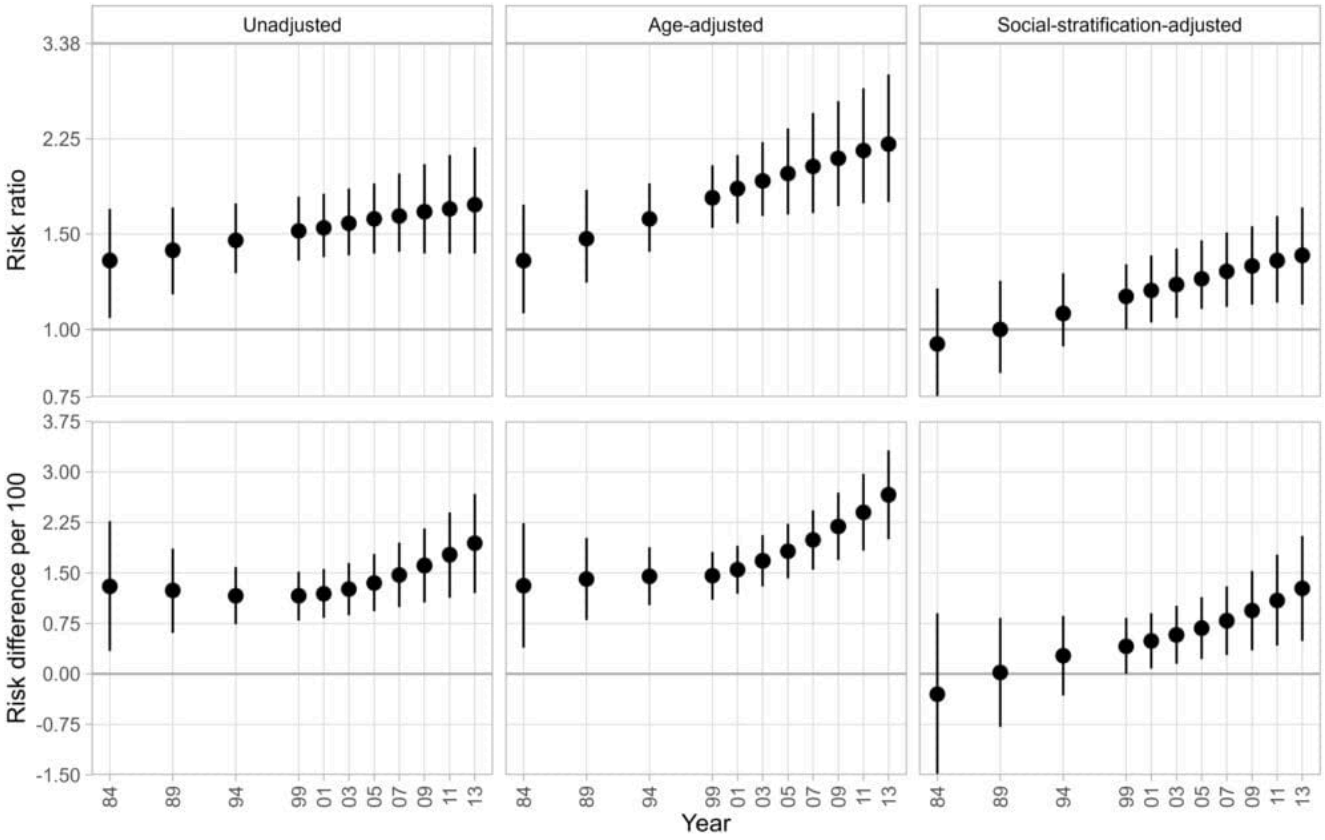


Figure 1. 10-year risk of mortality among non-owners vs owners in each survey year, adjusted for given covariate set.

Social

Association of Neighborhood Social Environment and Psychological Wellbeing in the Health and Retirement Study: Moderation by Personality Traits Sana A. Khan* Sana Khan Breanna Rogers Kosuke Tamura

Purpose: Despite perceived neighborhood social environments associated with older adults' well-being, the extent to which personality traits may moderate these associations remain understudied. Thus, we examined the associations of perceived neighborhood social cohesion and physical disorder with psychological well-being (PWB), and whether these associations are moderated by personality traits.

Methods: Cross-sectional data came from the 2022 Health and Retirement Study (n=2,984; mean age=70.4). PWB was measured using a self-report scale. Perceived neighborhood social cohesion (trusting neighbors) and physical disorder (trash/litter) were assessed using self-report scales. Weighted regression models were used to examine associations of neighborhood social cohesion and physical disorder with PWB, stratified by personality traits (openness, conscientiousness, extraversion, agreeableness, neuroticism) and adjusted for covariates.

Results: Overall, higher social cohesion and physical disorder were associated with higher and lower PWB, respectively (β=0.09, 95% CI [0.06, 0.13]; β=-0.06, 95% CI [-0.09, -0.03]) (Table 1). In stratified analyses, higher social cohesion was associated with higher PWB among participants with both high and low openness. Similar associations were observed across strata for the other traits (all $p<.05$). Higher physical disorder was associated with lower PWB in participants with low levels of each trait when analyzed separately, except neuroticism, for which associations were observed at both high and low levels (all $p<.05$).

Conclusion: Neighborhood social cohesion was related to well-being across personality strata, while physical disorder was linked to well-being generally in low-trait groups. Future research should continue to explore how individual-level personality traits may differentially moderate the relationship between perceived neighborhood contexts and well-being in later life.

Table 1. Associations of neighborhood social cohesion (X)[a] and physical disorder (X)[a] with psychological well-being (Y)[b] in overall and stratified by personality traits

	Social Cohesion	**Physical Disorder**
	β (95% CI)	**β (95% CI)**
Overall, n = 2,984	0.09 (0.06, 0.13)***	-0.06 (-0.09, -0.03)***
Openness		
High, n = 1,596	0.07 (0.03, 0.11)**	-0.04 (-0.08, 0.00)
Low, n = 1,388	0.10 (0.06, 0.15)***	-0.07 (-0.11, -0.03)**
Conscientiousness		
High, n = 2,004	0.07 (0.03, 0.11)***	-0.03 (-0.06, 0.01)
Low, n = 980	0.11 (0.56, 0.16)***	-0.09 (-0.14, -0.03)**
Extraversion		
High, n = 1,686	0.07 (0.03, 0.12)**	-0.04 (-0.08, 0.00)
Low, n = 1,298	0.08 (0.04, 0.13)***	-0.07 (-0.11, -0.03)***
Agreeableness		
High, n = 1,723	0.08 (0.04, 0.12)***	-0.03 (-0.07, 0.01)
Low, n = 1,261	0.07 (0.02, 0.11)**	-0.08 (-0.12, -0.03)***
Neuroticism		
High, n = 1,509	0.10 (0.06, 0.14)***	-0.06 (-0.10, -0.02)**
Low, n = 1,475	0.09 (0.04, 0.13)***	-0.06 (-0.11, -0.01)*

Note. *p<.05; **p<.01; ***p<.001; [a]X = Exposure Variable; [b]Y = Outcome Variable; 95% CI = 95% Confidence Interval; Continuous personality trait scores were dichotomized using a median split; Models adjusted for age, sex (male/ female), race (White/ Non-White), education (less than high school/ high school and above), marital status (married/ not married), physical activity (weighted composite sum score of mild, moderate, and vigorous activity), current smoker (Yes/ No), Ever drink alcohol (Yes/ No), and perceived stress.

Social

Locus of Control and Subsequent Physical and Mental Health: An Outcome-Wide Longitudinal Approach Siqi Wu* Siqi Wu Richard Silverwood George Ploubidis

Existing research has shown that locus of control is a key psychological construct influencing both physical and mental health. Individuals with a more internal locus of control tend to exhibit or experience more positive health behaviors and outcomes, better well-being and greater resilience, while a more external locus of control is often linked to worse health outcomes and higher psychological distress. These associations span across diverse cultural and demographic contexts and have been observed in areas such as chronic disease management, healthcare use, and lifestyle choices. Building on this theory, our study examines the impact of locus of control in early adulthood using data from Next Steps, a cohort of approximately 16,000 people in England born in 1989-90. We examine associations between locus of control at age 15 and 18 outcomes at age 32 spanning three domains: health behaviors (9), physical health outcomes (4), and mental health and well-being (5), adjusting for 11 demographic, familial, and baseline health covariates measured at age 14. We apply an outcome-wide longitudinal approach that enables the systematic examination of a single exposure across multiple outcomes using consistent confounding control, reducing selective reporting, and providing a more comprehensive assessment of the diverse effects of locus of control on health and well-being. Preliminary results indicate that a more internal locus of control is associated with lower disability, better self-rated health, lower smoking prevalence, more frequent fruit and vegetable intakes, higher life satisfaction, lower risk of depressive disorder, and lower loneliness. By applying this novel outcome-wide approach and accounting for a rich set of covariates, the study both extends existing evidence on locus of control and offers insights into how supporting adolescents' locus of control may contribute to healthier trajectories into adulthood.

Social

Historicizing instrumental variables: Insights from an IV for racial segregation Mark Hernandez* Mark Hernandez Gabriel L. Schwartz

Background: Instrumental variables are increasingly sought-after for use in studies of social exposures and health, given how difficult (and unethical) social exposures are to randomize. Epidemiologists are thus looking to economics studies to find potential IVs. However, many IVs' impacts on social exposures may be historically contingent and change across time and space. Here, we examine an instrumental variable for residential segregation used in health research as a case study of the importance of historicizing health econometrics.

Methods: We examine an instrumental variable developed by Ananat, who showed that the quasi-random degree to which cities built their railroad networks in a grid in the late 1800s/early 1900s served as an instrument for how racially segregated those cities became during the Great Migration. We focus on the first stage of IV analyses using this instrument, regressing metro area anti-Black segregation on Ananat's railroad index. We specifically examine whether different cities' segregation trajectories vary over time and space in response to the IV.

Results: We find that railroad configuration-induced changes in segregation are historically contingent. The IV not only caused affected cities to become more segregated initially, it also slowed the degree to which segregation declined even many decades later, well after railroads were dismantled. As such, the strength of the IV grows as time passes, requiring careful first-stage modeling.

Conclusion: Instrumental variables for social exposures in one time or place cannot be assumed to operate similarly in others, even when an IV performs well on average across study sites and years. First stage models ignoring this heterogeneity will produce less precise estimates that could have been strengthened, particularly, with better mapping between (A) detailed historical grounding and sociologic theory and (B) how first stage models are operationalized.

LATEBREAKER

Social

Transient and sustained effects of family income change on adolescent health and academic achievement Ekaterina Sadikova* Ekaterina Sadikova Henning Tiemeier Margot Rémeau Divyangana Rakesh

Background

Effects of transient and sustained transitions into and out of poverty on adolescent outcomes are not well studied and would be helpful to guide policy decisions.

Methods

Using g-computation, we calculated the effects of transitions into and out of poverty for those living above and below 200% of the national poverty line, respectively, on adolescent BMI, broad psychopathology and academic achievement in the Adolescent Brain Cognitive Development study. For those starting in poverty (N=3,959), we assessed effects of sustained (5 years) and transient (1-4 years) transitions out of poverty. For transient transitions, direct and total effects were calculated, with the latter capturing mediation by naturally fluctuating family income after a hypothetical intervention to alleviate poverty. Analogous analyses were conducted to assess transitions into poverty for those starting above 200% of the poverty line (N=7,909). Mean differences (MDs) and bootstrapped confidence intervals were reported.

Results

Transitioning into poverty for as little as 1 year significantly harmed academic achievement (e.g. the direct effect MD=-0.5(-0.8,-0.2) for the first year only), while a minimum of 2 years in poverty were needed to increase BMI (e.g. the direct effect MD=1.2(0.4,1.9) for years 1 and 2). Transitions out of poverty needed to be sustained longer to have an impact. Two or more consecutive years out of poverty was sufficient to improve academic achievement, while 4 to 5 years out of poverty were needed to lower BMI. Total effects generally exceeded direct effects, indicating lingering impacts of income transitions. We found no significant effects of income transitions on parent-reported broad psychopathology.

Conclusions

Transitioning into poverty – even transiently – had stronger effects on BMI and academic achievement than transitioning out of poverty. Policies should aim to transition youth out of poverty for sustained periods of time to affect health and academic outcomes.

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Structural

GPS-Derived Mobility Profiles and Neighborhood Context Among Transwomen of Color in New York City: The TURNNT Cohort Study Giselle A. Barreto* Giselle Barreto Dustin T. Duncan Tan Li Mary Jo Trepka Seann D. Regan Adam Whalen Diana M. Sheehan

Transwomen of color (TWOC) face barriers in healthcare engagement due to neighborhood structural conditions. Traditional residential measures overlook broader environments experienced daily. Global Positioning System (GPS)-derived activity spaces provide a more practical picture of neighborhood exposure, but the impact of structural disadvantage, safety, and service access on mobility, especially for TWOC, remains less understood. We examined how weighted census tract characteristics (assessed with GPS activity spaces) shape mobility profiles among TWOC in New York City. We identified latent mobility profiles using one week of GPS data collected at baseline (2020–2023) from 130 TWOC aged 18–55. Adjusted odds ratios and 95% confidence intervals were estimated using logistic regression (SAS 9.4), considering factors such as socioeconomic disadvantage, socio-structural vulnerability, crime, and availability of healthcare providers collected from public census and municipality data. Two profiles emerged: short-range movers with localized activity spaces and long-range movers who traveled across more census tracts and greater distances. After adjusting for demographic characteristics, participants who spent more time in census tracts with greater socioeconomic disadvantage and socio-structural vulnerability had significantly higher odds of short-range mobility (aOR = 2.98, 95% CI: 2.56–3.46 and aOR = 1.57, 95% CI: 1.38–1.80 respectively). However, a lower odds of short-range mobility was associated with greater time spent in areas with higher levels of crime, including violent crime (aOR = 0.36, 95% CI: 0.30–0.43) and nonviolent crime (aOR = 0.29, 95% CI: 0.24–0.35). Similarly, those who spent more time in areas with below-median availability of trans-competent healthcare services (aOR = 0.27, 95% CI: 0.23–0.30) and primary care providers (aOR = 0.85, 95% CI: 0.74–0.98) also had lower odds of short-range mobility. Short-range mobility appears rooted in areas marked by socioeconomic disadvantage, while long-range mobility reflects movement through higher-crime and lower healthcare service neighborhoods. These patterns reveal how mobility reflects neighborhood opportunity structures and shapes differential exposure to structural barriers that may impede healthcare engagement.

Study Design

Validation of self-reported hypertension, blood pressure, and anthropometry variables in the Nurses' Health Study 3 Hikaru Morooka* Hikaru Morooka Jamie E. Hart Francine Laden Kathryn M. Rexrode Jorge E. Chavarro Janet Rich-Edwards

Self-report measures are simple, cost-effective methods for data collection. We aimed to validate self-reported blood pressure (BP) and anthropometric measures against clinical measures using data from the Chronic Disease Biospecimen Collection (CDBC), a sub-study of the Nurses' Health Study 3 (NHS3).

From 2022 to 2025, a total of 1,215 CDBC participants visited Quest Laboratories to collect anthropometry data (height, weight, and waist circumference) and BP measurements. Mean age of CDBC participants was 47.6±7.4 years at CDBC visit. Main study questionnaires assessed BP and anthropometric measures (up to 4 years) and height and hypertension (up to 15 years) prior to the CDBC visit. BPs were self-reported in categories of 5 mmHg; hypertension and use of antihypertensive medications were combined to represent 'ever' self-report of hypertension. Hypertension at CDBC was defined as BP ≥140/90 mmHg and/or use of anti-hypertensive medications. We calculated correlations, agreement, sensitivity, and specificity of the self-reported variables with the CDBC measured variables. We used paired t-tests to assess differences between measured and self-reported height, weight and waist circumference.

Sensitivity and specificity of self-reported 'ever' hypertension were 76.0% and 93.7%. Correlation coefficients of ±5 mmHg adjacent categories for self-reported and measured systolic and diastolic BP were 0.44 and 0.42, while agreement was 53%, and 65%. Correlation coefficients for height, weight, and waist circumference were 0.95, 0.97, and 0.85, respectively. Absolute differences between measured and self-reported height, weight and waist circumference were 0.22 cm, 0.46 kg, and -2.30 cm, respectively.

Self-reported categorical BPs were modestly correlated with clinical measures up to 4 years later. While the sensitivity of hypertension up to 15 years later was modest, specificity remained high. The validity of self-reported height, weight and waist circumference was high.

Study Design

Guiding Principles for Returning Results to Participants in the Connect for Cancer Prevention Study Marie-Josephe Horner* Marie-Josephe Horner Megan Frone Nicolas Wentzensen Andrea Burnett-Hartman Paul Han Jackelyn Payne Nyahne Bergeron Carmit McMullen Christine Neslund-Dudas Raheem Young Christopher Rayburn Aileen Cunnane Camella Rising Deanna DePietro Mia Gaudet

Today’s study participants may ask or expect to receive timely research results, which embodies a shift from passive study involvement toward active engagement and partnership in the research process. However, implementing return of results in modern, general population cohorts is not straightforward. The what, when, and how of returning different types of results require careful consideration of ethical principles, and potential benefits and harms to participants and the study. On the one hand, return of a particular result can build trust and partnership with participants, enhance the participant experience, and improve retention and engagement. But it can also cause unforeseen negative impacts on the study and potential harms to participants, such as false positive results that lead to unnecessary clinical follow-up. Furthermore, analytic and clinical uncertainties surrounding a given result must be clearly conveyed to a lay audience, which can be challenging. During cohort study design, researchers need to find a balance between potential benefits, harms, and practical feasibility. Here, we will discuss our Guiding Principles for Returning Results in a new cohort, the Connect for Cancer Prevention Study (Connect). Early feedback in Connect shows that some participants desire full and timely access to results, captured by the sentiment, “we want it all, we want it now”, while others are less interested in receiving results, and cite altruism—rather than the desire for research results—as their primary motivation for participating in the study. In the context of these varied expectations, we outline six Guiding Principles: transparency of the research process, respect for participant autonomy, participant ownership of donated data, education, and privacy and confidentiality. We also share our framework to support thoughtful decision-making about how to return different types of results and explore trade-offs in modern cohort study design.

LATEBREAKER

Study Design

Achieving recruitment and retention successes in a community-engaged randomized clinical trial: lessons from The Misoprostol-Only Regimen Evidence (MORE) Study pilot

Katherine Key* Katherine Key Ruvani Jayaweera Sydney Reese Desiree Williams Awa Youm Sarah Baum Lori Gawron Heidi Moseson

Low uptake and high attrition threaten the validity of randomized controlled trial (RCT) clinical research across contexts. These challenges are further exacerbated when healthcare is politicized, as in the case of abortion. In this session, we will present a case study of an RCT designed to evaluate a single drug medication abortion (MA) regimen in the United States and discuss how community engaged methods and high-touch, intentional follow-up protocols enabled rapid recruitment and nearly 100% retention in the 6-week pilot.

From October 2025 to March 2026, we piloted study materials, instruments, and systems for The Misoprostol Only Regimen Evidence (MORE) Study at one clinical site in Utah. Enrolled participants were randomized 1:1 to receive either the standard combined regimen or an endorsed misoprostol only regimen. Abortion completion, physical experiences, care-seeking, and satisfaction were assessed with daily surveys in the first 3 days, and subsequent weekly surveys at 7, 14, 21, 28, and 35 days. We also conducted cognitive interviews and convened clinical, advocate, and community advisory boards to inform the conduct and design of the study. Further, to improve respondent experience, response rates, and data quality, we utilized strategies including phone, email and text message survey distribution, automated incentive distribution, password-protection features, and a combination of automated and manual reminders. We also utilized piped survey text across time points to reduce respondent fatigue.

In the pilot phase, we observed recruitment and retention successes that we attribute to the high degree of community input into the study design, as well as the survey structure and follow-up procedures. We enrolled ~6 patients per week, exceeding our expectation of ~4 patients per week. Retention was also high, with 93% completing the final survey, above the 85% we anticipated. Additionally, in the final survey, respondents reported positive experiences participating in the study.

Results from this pilot phase indicate that person-centered, community-engaged strategies in RCT design and implementation can contribute to recruitment and retention success, as well as positive respondent experiences. The specific strategies adopted could translate well to other clinical epidemiology studies.

Substance Use

Educational Attainment and Prenatal Substance Use Cessation: A National Analysis of PRAMS Data, 2016-2021 Rylie Fode* Andrew Williams Rylie Fode Taylor Lange Jaksen Perrin

Background: In the United States, 6.5% of pregnancies are exposed to cigarettes, 3.8% to e-cigarettes, and 5.4% to cannabis. Women with low education are more likely to use substances prenatally. This study aimed to examine the association between educational attainment and perinatal substance use, and whether healthcare provider conversations about nicotine and cannabis use moderate these associations.

Methods: National 2016-2021 PRAMS participants (weighted n=110,568) self-reported cigarette smoking, e-cigarette use, and marijuana use for the 3-months preconception and during pregnancy. Substance use change categories were derived from preconception to pregnancy: (never used, no change, increased use, decreased use, quit using). Education was derived from birth certificates linked to PRAMS. Participants reported whether healthcare providers discussed nicotine or cannabis use during pregnancy. Logistic regression estimated odds ratios and 95% confidence intervals for the association between education and substance use. Healthcare provider discussions were included to estimate effect modification in the association between educational attainment and substance use. Regression models were adjusted for maternal factors and weighted to account for survey design.

Results: Participants with >high school education were 2.5 times more likely to quit using marijuana (OR:2.51; CI:1.32,4.76), 1.6 times to quit smoking tobacco (OR:1.56; CI:1.34,1.85), and 1.4 times to quit smoking e-cigarettes (OR:1.37; CI:1.04,1.81) than those with ≤high school education. Healthcare provider discussions did not significantly moderate any outcomes.

Conclusion: Low educational attainment is a strong predictor of prenatal substance use, and healthcare provider discussions did not modify substance use. Prenatal substance use discussions require improvement to benefit this high-risk group.

Substance Use

Intersectional patterns in cigar use with cigarettes and e-cigarettes by race and ethnicity, education, and sex: Insights from 10-Years of PATH data James Buszkiewicz* James Buszkiewicz Maria Robayo Luz Sánchez-Romero Luis Zavala-Arciniega Yoonseo Mok Jihyoun Jeon Ritesh Mistry Jamie Tam David Levy Rafael Meza

Background: Few studies have examined US cigar use disparities at the intersection of race and ethnicity, education, and sex, and none have documented intersectional trends—work critical to designing tailored tobacco control strategies.

Methods: Using nationally representative Population Assessment of Tobacco and Health data, Waves 1 (2013–2014) to 7 (2022–2023), we examined current cigar use prevalence trends at the intersection of race and ethnicity (Hispanic, non-Hispanic Black, non-Hispanic White, non-Hispanic other), education (high school degree, General Educational Development (GED), or less; some college; or college degree or more), and sex among US adults aged 25 or older. We also examined current dual and polytobacco use with cigarettes and e-cigarettes. For all trends, we estimated average annual percentage changes (AAPC) using segmented log-linear regression.

Results: Among non-Hispanic White adults, cigar use declined among females (AAPC = -7.0%; 95% CI = -13.3%, -0.2%) and males (AAPC = -1.2%; 95% CI, -1.5% to -0.9%) with some college education, and among females with a college degree or more (AAPC = -11.8%, 95% CI = -20.9%, -1.6%), but increased among males with a college degree or more (AAPC = 4.1%; 95% CI, 2.3%, 5.9%). Among non-Hispanic White adults with a college degree or more, exclusive cigar use (AAPC = 4.0% 95% CI = 2.0%, 6.1%) and dual e-cigarette use (AAPC = 10.6%, 95% CI = 4.7, 17.0%) increased. Current dual cigarette use decreased or remained stable for all subgroups. Polytobacco use increased among non-Hispanic Black adults with a high school degree, GED, or less (AAPC = 16.8%, 95% CI = 3.5%, 31.8%) and a college degree or more (AAPC = 24.5%, 95% CI = 1.8%, 52.8%).

Conclusion: We documented persistent intersectional cigar use disparities and new emerging trends in dual and polytobacco use with cigarettes and e-cigarettes, highlighting the need for equity-focused interventions addressing intersectional determinants of US adult cigar use.

Substance Use

Effect of State-Wide Alcohol Ban in Bihar, India on Suicides: A Synthetic Difference-in-Difference Analysis Siddhesh Zadey* Siddhesh Zadey Dana E. Goin Charles C. Branas Christopher N. Morrison

Statement of Purpose: Suicides have a large mortality burden in low- and middle-income countries. Chronic and acute alcohol use can increase the suicide risk through complementary pathways, by driving more frequent suicidal ideation and attempts. Whether a population-level reduction in alcohol consumption reduces suicide incidence in this context remains an open question. In 2016, the northern Indian state of Bihar enforced a statewide alcohol ban. The aim of this study was to assess the effect of this ban on the overall suicide death rates and the proportions of deaths involving alcohol.

Methods: The Indian National Crime Records Bureau provided annual, uninterrupted state-level counts of overall suicide deaths and those involving alcohol/drug use from 2012 to 2022. We used 2012-2015 as the pre-intervention period and 2017-2022 as the post-intervention period, with Bihar as the intervention state and 28 other states and union territories as control states. Given the limited pre-intervention period and the potential bias in effect estimates arising from choosing control states, we estimated the average treatment effect on the treated using synthetic difference-in-differences (synthdid package in R 4.4.3).

Results: The alcohol ban was not associated with a significant reduction in overall suicide rate (ATT [95% CI]: -0.23 [-8.94, 8.49]) or proportion of suicide deaths involving alcohol injuries (-0.21 [-8.48, 8.06]).

Conclusion: We found that the Bihar alcohol ban did not significantly reduce the proportion of alcohol-involving suicides or the overall rate of suicide deaths. While the ban has been known to have affirmative impacts on other health outcomes, we did not observe effects related to suicide prevention.

Significance: This is the first study investigating the impact of Bihar’s alcohol ban on suicides.

Substance Use

Association between social determinants of health and substance use disorder among reproductive-aged women Ishu Karki* Ishu Karki George Pro

Background: Substance use disorder (SUD) is a significant public health concern in the U.S. Prior research has documented associations between social determinants of health (SDOH) and SUD. Although recent evidence indicates an increase in SUD among women, studies examining the relationship between SDOH and SUD among reproductive-aged and pregnant women remain limited.

Objective: To examine the association between SDOH and past-year SUD among women and assess whether pregnancy status moderates these associations.

Methods: We conducted a secondary analysis of the 2024 National Survey on Drug Use and Health, restricting the sample to females aged 12-49 years (N = 24,714). The primary outcome was past-year SUD. SDOH proxy measures included poverty, employment, high school graduation, enrollment in higher education, health insurance, English speaking, and lifetime arrest history. Multiple logistic regression models examined the main effects of SDOH on SUD and tested interactions with pregnancy status.

Results: Overall, 16.9% of women had past-year SUD. In the main effects model, lifetime arrest history was the strongest SDOH associated with SUD (AOR = 3.007, 95% CI = 2.53-3.56). In the interaction model, pregnancy status significantly moderated the relationship between arrest history and SUD (B = -0.95, p = 0.02), such that arrest history was not as strong of a predictor of SUD among pregnant women.

Conclusion: Criminal justice involvement was associated with increased SUD risk among women. The weaker association observed among pregnant women may reflect greater engagement with healthcare services, increased motivation to reduce substance use due to health concerns, or the influence of policies related to substance use during pregnancy. The findings suggest that pregnancy may represent a critical window for intervention, during which enhanced access to healthcare and social support could help mitigate the elevated risk of SUD associated with arrest history among women.

Substance Use

Integrating Telehealth into Syringe Service Programs to Improve HIV Prevention Among People Who Use Drugs Jessica Beetch* Jessica Beetch M. Kumi Smith Kadel Adelsheim

Background: People who use drugs (PWUD) experience disproportionate HIV risk yet face persistent structural barriers to prevention and care, including stigma, limited access to specialty providers, and challenges navigating health systems. Syringe service programs (SSPs) are trusted community-based harm reduction settings that provide sterile injection supplies and other preventive services and may facilitate alternative care delivery models.

Methods: We launched a National Institutes of Health–funded pilot study evaluating a telehealth intervention integrated within four SSPs in Minnesota, USA. The intervention aims to improve access to HIV prevention and related services by (1) connecting PWUD to clinicians trained in infectious disease and addiction medicine, (2) providing case management support for healthcare navigation and insurance enrollment, and (3) implementing trauma-informed care training and structural protocol changes to reduce stigma. During Phase 1, we conducted formative qualitative research to inform intervention design. Two trained interviewers conducted semi-structured interviews with 30 racially and geographically diverse PWUD recruited from the four participating SSPs. Interviews lasted approximately 60 minutes and participants received cash compensation for their time and expertise. Audio-recorded interviews were transcribed verbatim and coded in Dedoose using a dual-coder approach to identify recurring themes.

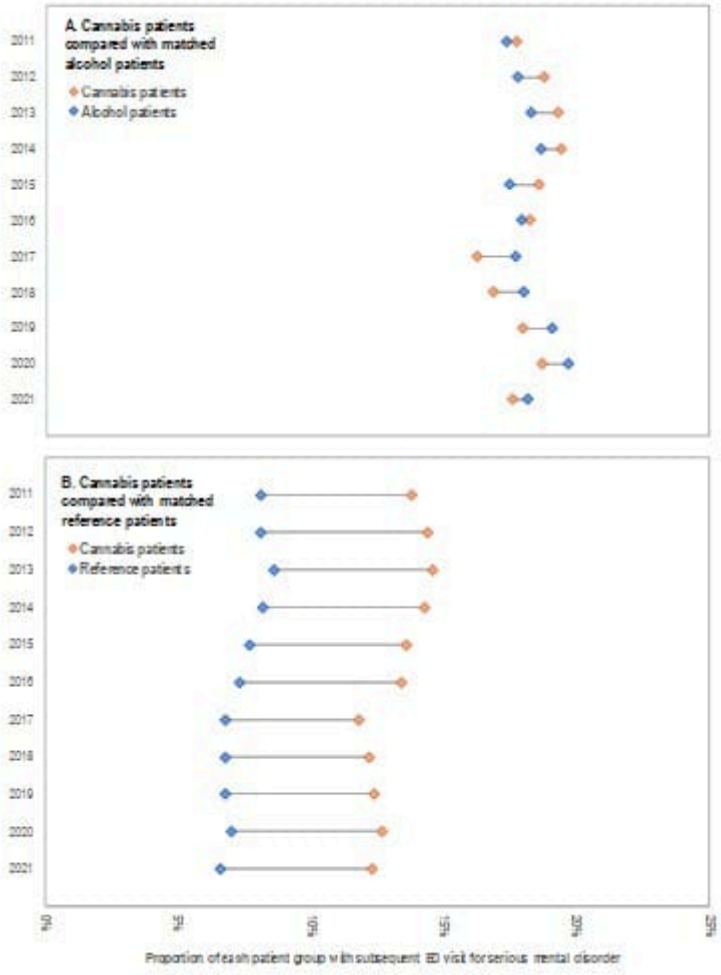
Outcomes: Key themes included lack of provider understanding of substance use, experiences of judgment and stigma in healthcare settings, and reports of being denied pain management or adequate care due to their drug use history. Participants also identified multiple barriers to healthcare access including transportation challenges, unstable housing, long wait times, limited access to working phones, and lack of health insurance coverage. Notably, awareness of pre-exposure prophylaxis (PrEP) differed by geographic location. While 59% of participants in urban settings reported having heard of PrEP, only 15% of participants in rural settings reported PrEP awareness.

Conclusions: Findings from this formative phase highlight the importance of community-informed intervention design and emphasize the need for services that meet PWUD where they are both physically and emotionally within trusted harm reduction settings. By embedding telehealth services within SSPs, this study evaluates a health system–level approach to improving HIV prevention and care access for PWUD. Findings will inform scalable strategies to reduce HIV-related disparities in populations disproportionately affected by structural barriers and healthcare stigma.

Substance Use

Recreational cannabis legalization and serious mental disorder among cannabis patients in California: A statewide longitudinal study Sidra Goldman-Mellor* Sidra Goldman-Mellor Madeline Meier Magdalena Cerda

More than 50% of U.S. residents live in states with legalized recreational use of cannabis. Cannabis use is associated with adverse mental health outcomes, and research suggests that recreational cannabis legalization (RCL) has led to population-level increases in incidence of serious mental disorder. No studies, however, have examined whether RCL is associated with changes in such risk among individuals with problematic cannabis use (the most vulnerable group). Using statewide linked emergency department (ED) data from California, we examined 12-month risk of serious mental disorder ED visits among >500,000 cannabis ED patients presenting before vs. after RCL in CA (2011-2016 vs. 2017-2021), comparing such risk to that of (a) alcohol ED patients and (b) a random sample of other ED patients. Patients were matched on sociodemographic characteristics and comorbid mental health and substance use. Using risk ratio models with interaction terms, we found that risk of mental disorder ED visits was equivalent among cannabis and alcohol patients prior to RCL, but that cannabis patients' risk significantly decreased after RCL while alcohol patients' risk remained stable (interaction term RR=0.91, $p<0.001$). Compared to the ED random-sample patients, cannabis patients had elevated mental disorder risk prior to RCL; both patient groups' risk declined after RCL, but the decrease was greater among the random-sample patients (interaction term RR=1.03, $p<0.001$). These overall patterns were largely due to shifts in incidence of ED visits specifically for major depression, anxiety, and suicidal behavior. In summary, cannabis ED patients exhibited a decrease in mental disorder risk after RCL, but our findings may reflect population-wide shifts in mental disorder vulnerability rather than a distinct effect of RCL. More research is needed to understand longer-term patterns and potential subgroup-specific effects in the association between RCL and mental disorder among cannabis patients.


A. Cannabis patients compared with matched alcohol patients
Cannabis patients
Alcohol patients
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2021
B. Cannabis patients compared with matched reference patients
Cannabis patients
Reference patients
2011
2012
2013
2014
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2021
Proportion of each patient group with subsequent ED visit for serious mental disorder

LATEBREAKER

Substance Use

Access, continuity, and comprehensiveness of primary care and their impact on the successful induction of opioid agonist treatment among patients with opioid use disorder.

Imen Farhat* Imen Farhat Dimitra Panagiotoglou

Background: Opioid use disorder (OUD) is a major public health challenge. While effective treatment with opioid agonist therapy (OAT) exists, initiating and successfully completing induction remains difficult. Primary care is an ideal setting for OAT delivery, providing both an entry point into care and ongoing coordination with other services. The specific ways in which access, continuity of care, and comprehensiveness of primary care affect OAT induction success are not well understood.

Objective: To assess the causal association between primary care dimensions and first successful OAT induction among people diagnosed with OUD.

Methods: We conducted a population-based cohort study of patients first diagnosed with OUD in British Columbia, Canada (2014–2018). We used Fine and Gray's proportional subdistribution hazards models to account for deaths. Inverse probability of treatment weighting was used to control for confounding. Analyses were also stratified by rurality.

Results: Among 17,184 patients, 34% achieved their first successful OAT induction, and 6% died during follow-up. Greater access to primary care was associated with a 24% increased likelihood of successful OAT induction (HR=1.24, 95% CI: 1.17-1.31). Continuity of care showed a weaker association (HR=0.96, 95% CI: 0.90-1.02). Comprehensiveness of primary care physicians was associated with a lower likelihood of successful OAT induction (HR=0.73, 95% CI: 0.67-0.81). Stratified analysis by setting showed that access to care is more crucial in rural areas (HR=1.47, 95% CI: 1.23-1.77) than in urban areas (HR = 1.25, 95% CI: 1.18-1.33).

Conclusions: Primary care dimensions influence successful OAT induction differently. Greater access facilitates successful induction, but higher comprehensiveness of care, which reflects the diversity of primary care physicians' practice, may be associated with lower successful induction rates. More research is needed to understand how primary care impacts OUD patient outcomes.

LATEBREAKER

Substance Use

Estimating the effect of initiating medication for opioid use disorder (OUD; MOUD) on overdose risk among people with HIV and OUD in Baltimore, Maryland, 2019-2025: a target trial emulation Michael H. Chiu* Michael Chiu Anthony T. Fojo Oluwaseun O. Falade-Nwulia LaQuita N. Snow Jeanne C. Keruly Lauren C. Zalla Y. Joseph Hwang Lorraine T. Dean Nicholas P. Schweizer Richard D. Moore Jarratt D. Pytell Catherine R. Lesko

In people with opioid use disorder (OUD), medications for OUD (MOUD) prevent overdoses, but their effects are not well-studied in people with HIV (PWH) and OUD. PWH have unique access to and patterns of care engagement. We estimated the effect of initiating MOUD on overdose risk in a clinical cohort of PWH engaged in HIV continuity care in Baltimore, Maryland. MOUD was defined as self-reported methadone use or prescribed or dispensed buprenorphine. Overdose (due to any drug) was defined as any of: overdose as coded on the death certificate, an inpatient or outpatient overdose diagnosis, or self-report of ≥1 overdose in the prior 6 months on a patient-reported outcome survey asked regularly at clinic visits. Following index OUD diagnoses from 1 January 2019 to 31 March 2025, we cloned observations and assigned each to one of two treatment strategies: 1) initiate MOUD within a month or 2) do not initiate MOUD over 5 years of follow-up. We censored clones when participants stopped following the assigned treatment strategy. We adjusted for selection bias due to protocol violations using stabilized inverse probability of censoring weights estimated conditional on a comprehensive set of demographic, clinical, and social covariates. We fit weighted survival curves and calculated the risk difference. 95% confidence intervals (CI) were based on percentiles of the distribution of 500 estimates from bootstrap resamples. We included 1,280 incident OUD diagnoses from 365 PWH (57% Male, 83% Black, median age 57 years). The overall incidence rate was 7.7 overdoses per 100 person-years (95% CI: 6.8, 8.9). In the weighted analysis, initiating MOUD within a month of OUD diagnosis was associated with an 8.4% (95% CI: -1.7, 17.7) lower 5-year risk of overdose. Timely initiation of MOUD among PWH and OUD reduces the risk of overdose. More research is needed to improve MOUD uptake and persistence in this patient population to address the public health burden of the opioid epidemic.

Translational & Implementation Science

Causal Decision Modules in the EHR: Bedside Care in Acute Decompensated Heart Failure
Ishan Suthar* Ishan Suthar Dr. Anwar T. Merchant

Epidemiological analyses of large volumes of electronic health records (EHRs) have largely focused on retrospective estimation and prediction. Most EHR based Clinical Decision Support (CDS) still remain predictive rather than causal and rarely inform interventional knowledge at the moment of care, limiting their utility. To answer a clinician's question, "what's next?", we propose a deployable, EHR-native causal inference framework that generates interpretable, action-oriented recommendations for inpatient acute decompensated heart failure (ADHF) decisions.

We propound a theory-driven causal inference framework that embeds target trial emulation directly within ADHF inpatient workflows to align causal estimation with real clinical decision points. ADHF care is framed as a sequence of target trials at key decisions (initial decongestion, escalation, therapy, discharge readiness), each with prespecified eligibility, treatment options, and decision-aligned estimands. Eligibility is reassessed at each decision point, enabling rolling enrollment and avoiding artificial baselines. Intervention strategies reflect bedside actions: IV loop diuretic intensity/continuation vs temporary holding of guideline-directed therapy, addressing treatment–confounder feedback.

Clinical notes are leveraged to measure time-varying severity as confounders while accounting for documentation bias and measurement error. Causal effects are identified using doubly robust g-methods with flexible nuisance models using ML, under assumptions of consistency, sequential exchangeability, and positivity. To emulate real-world timing, we use cloning–censoring–weighting to address immortal time and selection biases.

Each target trial is packaged as a reusable EHR-based causal decision module and evaluated prospectively in silent mode before clinician-facing release to assess safety, equity, and decision concordance. This provides a feasible path to transparent, causal-based bedside decision support for ADHF.

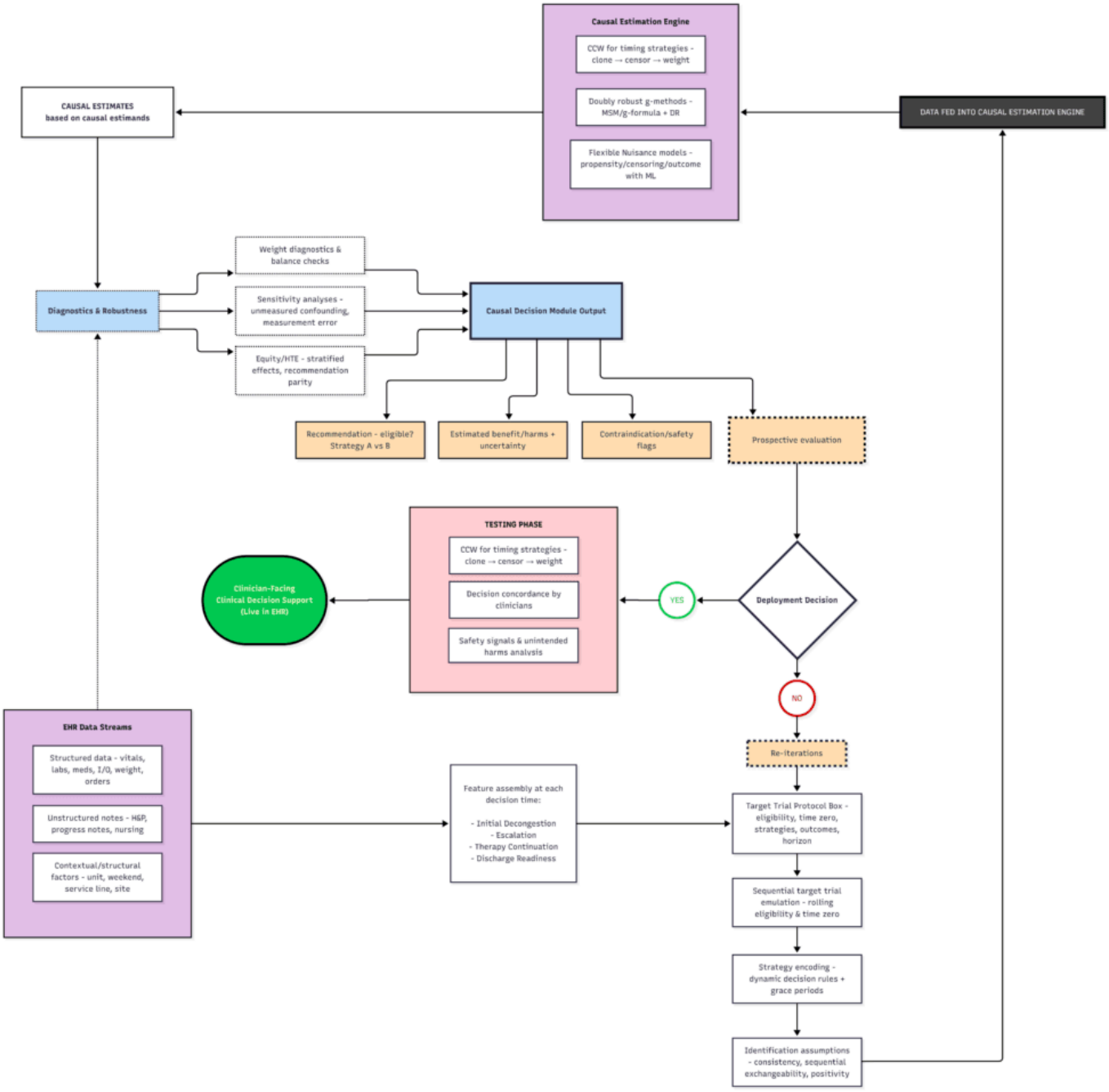


Figure: Framework for translating EHR-based causal inference into bedside decision support in ADHF. Sequential target trials are defined at recurrent clinical decision points, estimated with CCW and doubly robust g-methods, stress-tested via diagnostics/sensitivity/equity checks, and packaged into reusable decision modules. Outputs are prospectively evaluated in silent mode to support a staged transition to clinician-facing CDS.

LATEBREAKER

Translational & Implementation Science

Implementation of the Community Health Worker Medi-Cal benefit across California: Barriers and facilitators of early adoption Yessica Martinez Mulet* Yessica Martinez Mulet Joann Lee Joe Lee Patricia Rodriguez Espinosa

Community health workers (CHWs) have well-documented effectiveness in health promotion and patient navigation. Medicaid policy allow billing for CHW services – adopted by 29 states to-date; yet implementation challenges exist. Using a mixed-methods community-based participatory research design, we examined implementation barriers and facilitators of the Medicaid CHW Benefit across California.

Key-informant interviews (N=39) and surveys (N=38) were conducted with community-based organizations, health plans, and health jurisdictions. Surveys included: Organizational Readiness for Change Assessment, Program Sustainability Assessment Tool, and Organizational Readiness for Implementation Assessment. Quantitative data was analyzed using descriptive statistics. Qualitative data was analyzed using a hybrid inductive-deductive coding approach, informed by the Consolidated Framework for Implementation Research.

Findings revealed significant implementation barriers including financial sustainability concerns, low reimbursement rates, and administrative burden. All stakeholders, particularly community-based organizations, endorsed not having the necessary financial resources for implementation (2.9 on 1-5 scale). Interviews revealed ramp-up costs (including billing IT systems) as an implementation barrier, particularly for small organizations. High enthusiasm and leadership support were reported (5.9 on 1-7 scale); yet stakeholders emphasized staffing limitations. Conversely, facilitators included external funding sources, technical assistance support, and high commitment to implement the benefit (4.5 on 1-5 scale).

Infrastructure changes are necessary to further support program implementation. Additional avenues for financial sustainability and strategies to reduce administrative burden are recommended as priorities. Study findings provide actionable insights for timely solutions that better support the social services landscape through further integration of the CHW workforce.

Women’s Health

The Association between Maternal Nativity and Treatment Engagement Kendria Kelly-Taylor* Kendria Kelly-Taylor Sara Aghaee Joshua Nugent Nina Oberman Ai Kubo Charles Quesenberry Kathryn Ridout Mibhali Bhalala Lyndsay Avalos

Racial/ethnic disparities in prenatal depression diagnosis and treatment engagement are well-documented; less is known how maternal nativity (US-born vs. non-US-born) is associated with treatment initiation and type. This study examines differences in treatment initiation and type by maternal nativity among a cohort of pregnant individuals universally screened for depression. We conducted a retrospective cross-sectional analysis (2013-2019) of Kaiser Permanente Northern California members newly diagnosed with depression between the first day of LMP to the day before a live birth (n=27,044). Nativity, determined from birth records, and treatment initiation (any vs. none), type (antidepressant medication vs. psychotherapy), and covariates (e.g., maternal age, Medicaid, anxiety, parity, substance use, depression severity via Patient Health Questionarrie-9) ascertained from electronic health records. Logistic regression models estimated the adjusted odds ratio (aOR) and 95% CIs. In models excluding depression severity, non-US-born individuals had 22% higher odds of initiating treatment compared with US-born (aOR:1.22;95%CI:1.12-1.34), yet the associated attenuated after adjusting for severity. Of those who initiated treatment, non-US-born individuals had greater odds of engaging in psychotherapy (vs. medication), persisting after adjustment for depression severity (aOR:1.29;95%CI:1.05-1.58). Findings suggest differences in treatment engagement by maternal nativity may hinge on the severity of depression symptoms, which could mediate the pathway between nativity and treatment initiation. Prior research among KPNC pregnant individuals showed non-US -born individuals presented equivalent or higher depression severity than US-born counterparts. Nativity differences vanish after adjusting for severity, underscoring severity’s possible mediating effect. Further, findings offer clinical insight for tailoring depression treatment options during pregnancy based on nativity.

Women’s Health

Respectful Maternity Care and Postpartum Emotional Distress: The Mediating Role of Baby-Friendly Hospital Initiative Practices and Moderation by Support Chidinma Oli* Chidinma Oli MaryBeth Rhomberg Cynthia Garvan Deepthi S. Varma Victoria Evans Shanting Chen Adetola Louis-Jacques

Introduction: Respectful maternity care (RMC) is a critical component of high-quality maternal care, yet its relationship with postpartum emotional distress remains underexplored. This study examined whether Baby-Friendly Hospital Initiative (BFHI) practices mediate the association between respectful maternity care and postpartum emotional distress, and whether emotional and practical support modify this relationship.

Methods: We analyzed cross-sectional postpartum survey data from 207 women receiving care at a U.S.-based academic medical center. Respectful maternity care was measured using the Mothers on Respect Index (MORi), and postpartum emotional distress was modeled as a latent construct comprising nervousness, sadness, anhedonia, and worry. We used Structural Equation Modeling with bootstrapped confidence intervals (n=5,000) to test for mediation and simple slope analysis to explore moderation by support.

Results: The median (SD) MORi score was 77.0 (12.0). RMC was associated with lower postpartum emotional distress [β = -.224; 95% CI [-.390, -.059]]. The indirect effect of RMC on postpartum emotional distress through BFHI practices was significant [β = -.044; 95% CI [-.102, -.003]]. Emotional support moderated the association between Respectful Maternity Care and postpartum emotional distress (β = 0.15, p = .014). Specifically, higher RMC was associated with lower distress among women with low emotional support (p < .001), but not among those with high emotional support (p = .884). Practical support showed no moderating effect.

Conclusions: RMC may reduce postpartum emotional distress in part, through the implementation of BFHI practices. The protective effect of Respectful Maternity Care is strongest for women with lower emotional support, highlighting the importance of institutional and social support for all women, especially those with low emotional support.

Women’s Health

Hospital costs of severe maternal morbidity across race/ethnicity and insurance status: a national serial cross-sectional study Amelia Srajer* Amelia Srajer Amity Paul Erin Amy

Objective: Medicaid covers over 40% of United States births and disproportionately serves racial minority groups who already face elevated obstetrical risks. Coverage gaps relative to private insurance may further exacerbate these adverse outcomes and their associated healthcare costs. We assessed the odds and hospital costs of severe maternal morbidity (SMM) at the intersection of race/ethnicity and insurance status.

Methods: We analyzed 23.5 million weighted obstetric deliveries from 2015-2022 using the National Inpatient Sample. Ten interaction terms were created to compare Medicaid versus private insurance across White, Black, Hispanic, Asian, and Native American groups. The 21 SMM complications were defined per CDC criteria using International Classification of Disease codes. Multivariable logistic regression and generalized linear models assessed SMM odds and associated hospital costs respectively, adjusting for a validated obstetric comorbidity score, discharge year/quarter, mode of delivery, and hospital region.

Results: Medicaid insured 43.8% of deliveries, with higher coverage among Native American (67.6%), Black (66.7%), and Hispanic (66.6%) patients compared to White (32.3%) and Asian (27.9%) patients. Adjusted odds of composite SMM were higher among all intersectional groups compared to privately insured White patients ($p<0.001$). Within each racial category, Medicaid was associated with higher odds of SMM. SMM-related costs were generally higher among Black, Hispanic, and Asian patients across insurance types whereas Native American Medicaid patients demonstrated significantly lower costs (Fig 1).

Conclusion: Racial disparities in SMM risk are significantly amplified for those with Medicaid, yet race appears to be the primary driver of the disproportionate financial burden. Addressing these inequities requires policy reform that targets both insurance coverage and the structural biases inherent to clinical care and resource allocation.

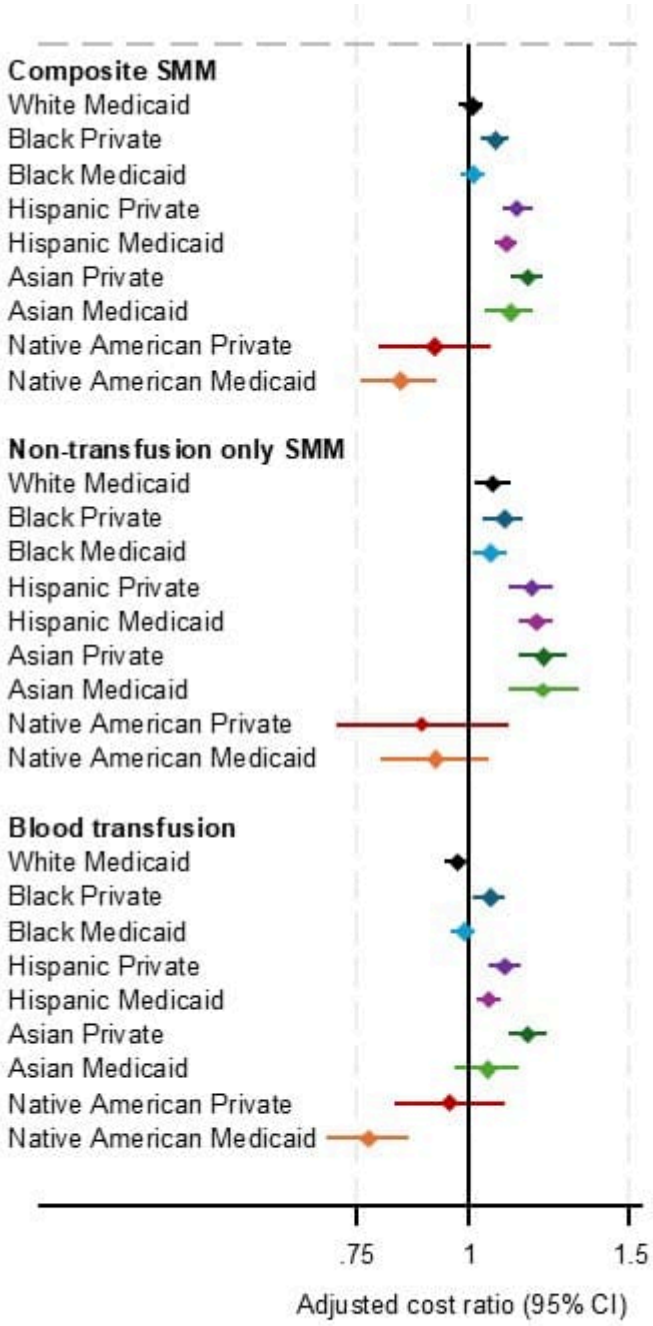


Figure 1. Adjusted cost ratios for severe maternal morbidity (SMM) complications by race and insurance type, in comparison to White Private insurance patients.

Women’s Health

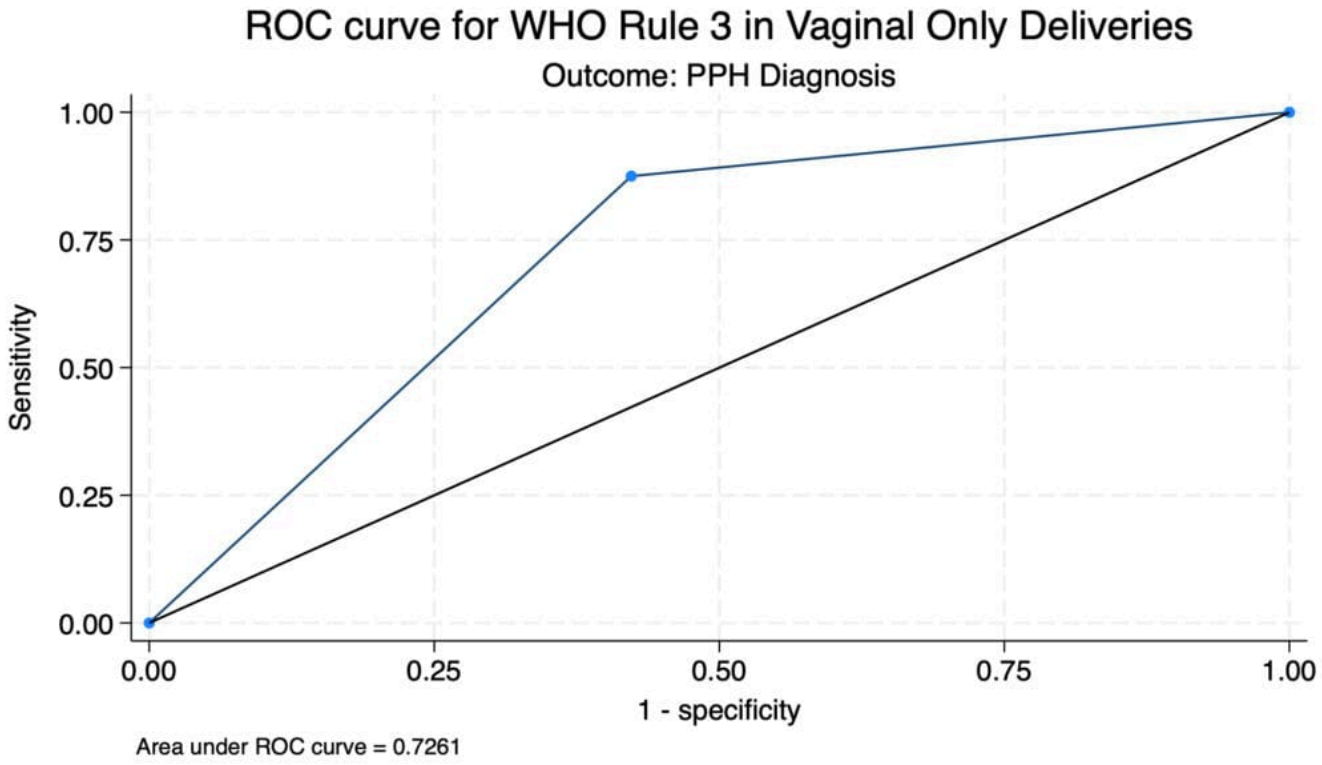
Applying WHO Prognostic Blood Loss Clinic Markers in a US-based Pregnancy Cohort
Nelson Barba* Nelson Barba Elise Erickson

Background: Postpartum Hemorrhage (PPH) is the number one cause of mortality in childbirth globally and contributes significantly to pregnancy-related morbidity. In 2025, the WHO published new prognostic markers using vital sign data for predicting severe morbidity due to blood loss in pregnancy. WHO guidelines did not use data from US-based participants, and studies were primarily vaginal deliveries.

Methods: Using a cohort of 669 deliveries with data abstracted from medical records, we applied WHO guidelines regarding abnormal levels of blood loss, systolic & diastolic blood pressure, shock index, and heart rate. Diagnostic outcomes were pulled from abstracted data. Sensitivity (sens) and specificity (spec) were calculated for this cohort using the three diagnostic rules from WHO. Data was analyzed for the whole cohort and then by delivery type.

Results: In our study population (median age: 29 years (IQR: 25-33), 53.6% Hispanic, 74.3% vaginal delivery), the WHO rule 3 — 300 mL of blood loss with 1 abnormal clinical marker or a blood loss of 500 mL— showed a 91.4% (sens) & 43.3% (spec) for a diagnosis with PPH and it showed a 85.7% (sens) and 44.7% (spec) for symptoms of hypovolemia which were slightly short of the WHO goal of 80/50 for sens/spec. In vaginal deliveries, rule 3 achieved 87.5% 9 (sens) and 57.7% (spec), and for c-sections, it was 100% (sens) and 1.2% (spec). When the blood loss guideline levels were raised in the c-sections by 500 mL to 800/1000 mL, the specificity increased to 34.7%

Conclusion: This research suggests that the guidelines from the WHO may be practical to populations within the United States for vaginal births but not for c-sections. For c-section deliveries, 97.8% reached the higher blood loss threshold (500 mL), which adversely impacted the specificity. Data suggests that deliveries via c-section will require higher blood loss cutoffs, and additionally, they may require adjusted cutoffs for abnormal vital sign data.


ROC curve for WHO Rule 3 in Vaginal Only Deliveries
Outcome: PPH Diagnosis
Sensitivity
1.00
0.75
0.50
0.25
0.00
0.00
0.25
0.50
0.75
1.00
1 - specificity
Area under ROC curve = 0.7261

LATEBREAKER

Women’s Health

Sociodemographic risk factors for endometriosis diagnostic delay: Findings from the ARCHES retrospective cohort Karen Schliep* Karen Schliep Saskia Spiess Benjamin Brown Nancy West Tiffany Ho Leslie Farland Emily Wickens Emmaline Haderlie

Introduction: Endometriosis diagnostic delay can exacerbate pain and infertility, contribute to mental-health burdens, and increase economic strain. Women in underrepresented, underserved, and under-reported (U3) groups may face even greater barriers, contributing to disparities that remain poorly understood. Our objectives were to characterize the distribution of endometriosis diagnostic delay within a large population-based cohort and quantify sociodemographic disparities.

Methods: We used the Utah Population Database to build a cohort of women with pelvic pain and assess burden of endometriosis diagnostic delay. U3 status was characterized by race/ethnicity, education, and residence. Diagnostic delay was calculated as the time between first pelvic pain and endometriosis diagnosis, with a six-month washout period. Associations between U3 characteristics and continuous diagnostic delay were analyzed using generalized linear models (gamma distribution) to produce adjusted geometric mean ratios (GMRs) with 95% CIs.

Results: Among our cohort of 29,154 women, diagnostic delay averaged 7.4 years (median 5.67; range 0.50–29.02 years). 28.9% had one U3 characteristic and 7.5% had two or more (Figure 1). After adjusting for age at baseline and other U3 characteristics, women who identified as Hispanic or non-white had a 6% higher aGMR delay compared with those who identified as non-Hispanic and white (95% CI 3%, 9%). Women with some high school or less had a 7% higher aGMR delay than those with higher education (95% CI 4%, 10%). Living in rural or frontier areas, compared to urban, showed no difference in diagnostic delay (aGMR -3%, 95% CI -6, 0% and aGMR 2%, 95% CI -3%, 8%).

Conclusion: Among this population-based Utah cohort, average endometriosis diagnostic delay exceeded seven years and was longer for women who identified as Hispanic or non-white, and those with lower-education. Further exploration of geographic residence in relation to diagnostic delay is warranted.

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Women’s Health

Understanding the dynamic relationship between LDL-C and statin therapy through the menopause transition: A time-varying Bayesian analysis of the Study of Women’s Health Across the Nation James Matuk* James Matuk Elizabeth A Jackson Maria Brooks Carol A. Derby Rebecca C. Thurston Daniel H. Solomon Samar R. El Khoudary

Background: Low-density lipoprotein cholesterol (LDL-C) increases rapidly during the menopause transition (MT), which is linked to higher cardiovascular disease (CVD) risk. This makes the MT a critical prevention window for initiating lipid-lowering medications such as statins. We investigated the dynamic relationship between timing of statin initiation relative to the final menstrual period (FMP) and longitudinally measured LDL-C, hypothesizing that earlier initiation reduces the MT related increase in LDL-C compared to later initiation.

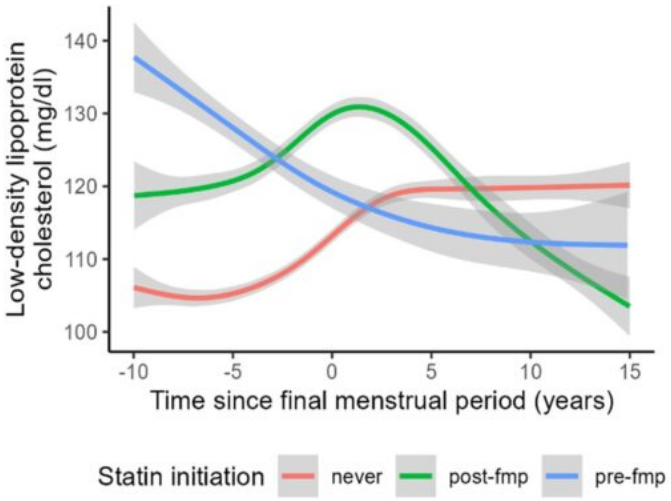
Methods: We used data from the Study of Women’s Health Across the Nation, a multi-site, multi-racial/ethnic cohort that follows women through the MT to document its health sequelae. We included participants with at least three LDL-C measurements over 18 years, on average, centered on the FMP. We employed a longitudinal Bayesian time-varying coefficient mixed model to flexibly capture MT associated changes in LDL-C and the dynamic effect of statin use.

Results: The 2676 participants’ average age was 46.5 years (2.7 SD) at baseline, 52.4 years (2.8 SD) at the FMP, where 45.9% had an imputed FMP age and 36.8% eventually initiated statins. Our model inferred that later statin initiation resulted in a faster rate of decline in LDL-C levels. However, women initiating statins before the FMP reached lower LDL-C levels earlier compared to women initiating later in life. Eventually, the LDL-C levels of women starting statins prior to the FMP were comparable to those initiating after the FMP (Figure panel A). This model also enabled prediction of how statin initiation prior to FMP could dramatically alter one’s LDL-C trajectory (Figure panel B).

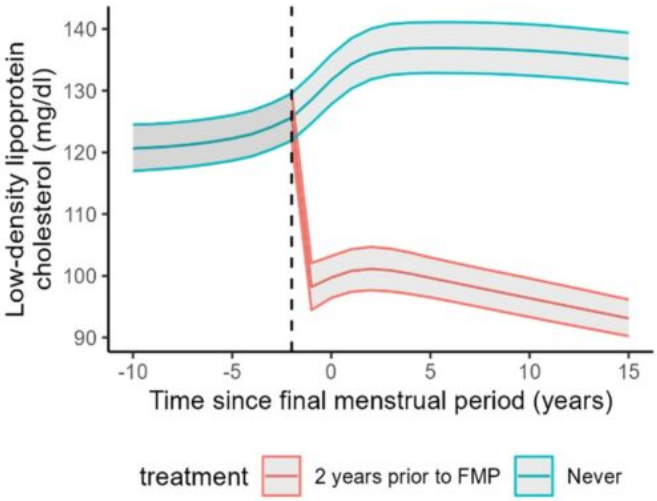
Conclusion: Our findings suggest that perimenopause is a crucial, women-specific period in lipid screening and clinical decision-making, and could extend current guidelines. Future research should determine if early MT initiation of lipid-lowering medication reduces the risk of future CVD events.

Funding Acknowledgment: The Study of Women’s Health Across the Nation (SWAN) has grant support from the National Institutes of Health (NIH), DHHS, through the National Institute on Aging (NIA), the National Institute of Nursing Research (NINR) and the NIH Office of Research on Women’s Health (ORWH) (Grants U01NR004061; U01AG012505, U01AG012535, U01AG012531, U01AG012539, U01AG012546, U01AG012553, U01AG012554, U01AG012495, and U19AG063720). The content of this article abstract is solely the responsibility of the authors and does not necessarily represent the official views of the NIA, NINR, ORWH or the NIH

A: Inferred trajectories of LDL-C across the MT for statin initiation subgroups



B: Predicted trajectories for a hypothetical participant based on never initiating statins compared to initiating prior to the FMP



Models adjust for race/ethnicity, study site, education, financial hardship, body mass index, systolic blood pressure, physical activity, comorbidities, hormone use, non-statin lipid-lowering medication use, and insurance status.

Women’s Health

Interconceptional Exposure to Common Plasticizers and Fetal Growth Kim Cajachagua-Torres* Kim Nail Cajachagua Torres Linda G. Kahn Teresa Herrera Hediyeh Baghsheikhi Shilpi Mehta-Lee Yuyan Wang Wenging Yang Kurunthachalam Kannan Mengling Liu Leonardo Trasande

Maternal exposure to common plasticizers prior to conception may impact fetal growth, but evidence remains limited. Participants were women enrolled with two successive pregnancies in a NYC birth cohort (2016-2021, interpregnancy interval median=2.5 years, 90% range=0.99-4.9). Exposure data from the first pregnancy (up to three measurements) were used as the interconceptional exposure for the second pregnancy, for which fetal growth and birth outcome data were available in 139 and 173 dyads, respectively. We averaged concentrations of urinary phthalate metabolites and bisphenols across timepoints, adjusted for urinary dilution, and natural log-transformed them. Repeated fetal biometry measures from clinical ultrasounds were used to predict growth parameters at 20, 30, and 36 weeks using linear mixed-effects models assuming nonlinear effects of gestational age. Information on birth outcomes was obtained from electronic health records. We used mixed models to test associations with fetal growth across gestation and linear regression for birth outcomes. Interactions with fetal sex was significant, so we conducted sex-stratified models. In male fetuses, higher maternal interconceptional levels of mono-ethyl phthalate were positively associated with estimated fetal weight, biparietal diameter, and head circumference. We also found positive associations of mono(2-ethylhexyl) phthalate with abdominal circumference and femur length. In contrast, higher mono-(2-carboxyheptyl) phthalate was associated with shorter femur length. In female fetuses, higher mono(2-carboxymetylhexyl) phthalate was associated with smaller abdominal circumference. Interconceptional levels of phthalate metabolites were positively associated with gestational length but negatively associated with birth length z-scores. There were no associations with bisphenols. Interconceptional exposure to phthalates may influence fetal growth, with males and females affected differently.

Women’s Health

Correlates of iron deficiency in non-pregnant women of reproductive age 15-49 years, NHANES 2021-2023 Mollie Killion* Mollie Killion Maria Elena D. Jefferds Laura Hendrickson Yaw Addo

Background: Iron deficiency (ID) is prevalent but frequently undiagnosed in women of reproductive age (WRA), leading to morbidity despite availability of effective treatment. Using a physiologically-based (PB) approach, the threshold to identify early iron-deficient erythropoiesis is higher than the current CDC 1998 threshold, which is based on limited data and expert opinion.

Objectives: We estimated ID prevalence among non-pregnant WRA using inflammation-adjusted serum ferritin (SF). We compared the CDC guideline (CDC-ID) and PB SF (PB-ID) thresholds. We also identified correlates associated with PB-ID.

Methods: Using NHANES 2021–2023, we estimated ID prevalence classified as CDC-ID (SF<15 µg/L) and PB-ID (SF<25 µg/L). We used quasibinomial log-link models to estimate adjusted prevalence ratios (aPR, 95%CI), identifying underlying, immediate, and biological correlates associated with PB-ID, with alpha of $p<0.05$. Analyses used R survey package and phlebotomy weights.

Results: CDC-ID prevalence was 23.1% and PB-ID was 40.0%. Age 15–19 was associated with increased PB-ID prevalence compared to age 31–40 (aPR 1.4; 95%CI: 1.0, 1.9). Compared to non-Hispanic White, Mexican American and Other Hispanic race/ethnicity were associated with higher PB-ID prevalence (1.4; 1.0, 2.0 & 1.5; 1.1, 1.9, respectively). Having regular menstruation and BMI > 30 kg/m2 were also positively associated with PB-ID (2.5; 1.6, 4.0 & 1.3; 1.0, 1.6) compared to no regular menstruation and normal BMI. Alcohol use, iron intake, food security status, poverty level, health insurance status, and education were not associated with PB-ID.

Conclusion: ID prevalence among WRA in the U.S. is high, with meaningful differences (17 percentage points) between prevalence based on CDC versus PB thresholds. Predominantly biological correlates were associated with PB-ID. Understanding factors associated with ID can help identify WRA at risk of ID-related adverse outcomes and inform updated screening guidance.

Aging

Cadmium Exposure and Incidence of All-Cause Dementia and Alzheimer's Disease in US Adults Erika Walker* Erika Walker Yanelli Rodriguez-Carmona Xin Wang Bhramar Mukherjee Laura Arboleda-Merino Wei Hao Hiroko Dodge Roger L. Albin Henry L. Paulson Sung Kyun Park Kelly M. Bakulski

Introduction: Longitudinal population studies aid in understanding risk factors for long-latency disorders like Alzheimer's disease (AD) and all-cause dementia. Environmental exposures with neurotoxic effects, such as non-essential metals, may be modifiable risk factors for these conditions. We evaluated the association between cadmium exposure and AD/all-cause dementia incidence in US adults.

Methods: National Health and Nutrition Examination Survey (NHANES) III (1988-1994) and continuous NHANES (1999-2016) data were linked with Medicare claims to identify incident AD and dementia cases through 2018. Urinary and/or blood cadmium were measured during NHANES. We used covariate-adjusted, survey-weighted Cox proportional hazard models to evaluate the associations between cadmium exposure biomarkers and AD/dementia over follow-up.

Results: In NHANES III (N=6,122), baseline age was 53.9±0.5 years and urinary cadmium was 0.8±0.02 ug/L. Over a follow-up of 20.4±0.3 years, 743 AD and 1,508 all-cause dementia cases occurred. Urinary cadmium was not associated with AD (HR: 1.01, 95% CI: 0.9-1.0) nor all-cause dementia incidence (HR: 1.02, 95% CI: 0.96-1.08). In continuous NHANES (urinary cadmium N=2,833; blood cadmium N=8,038), baseline age was 64.1±0.2 years, urinary cadmium was 0.5±0.03 ug/L, and blood cadmium was 0.6±0.01 ug/L. Over 9.5±0.1 years, 587 AD and 1,260 all-cause dementia cases occurred. Urinary and blood cadmium showed no associations with AD (HR [95% CI]: 1.09 [0.9, 1.4]; 1.06 [0.9, 1.2]) nor all-cause dementia (HR [95% CI]: 1.07 [0.9, 1.3]; 1.06 [0.95, 1.2]).

Conclusion: No associations between cadmium exposure and AD/dementia incidence were observed. Our null findings should be interpreted while considering potential methodological issues and verified by subsequent studies.

Aging

Iodine Status and Bone Fracture Prevalence among Adults in the United States Alexander Hill* Alexander R Hill Durdana Najli Ashley J

Background: Excess or insufficient iodine intake can affect thyroid function and abnormal thyroid function can impact bone health and increase fracture risk. However, there are few studies on iodine status and bone health outcomes in older adults. To our knowledge, this study is the first to examine whether deficient or excess iodine status is associated with increased fracture prevalence among adults in the United States.

Methods: The study included 1,202 adults aged 50 years and over from the National Health and Nutrition Examination Survey (NHANES 2017 – 2020). We determined iodine status via urinary iodine concentrations adjusted for creatinine (UICadj). We defined iodine status as iodine-deficient (UICadj < 100 µg/L), excess (UICadj ≥ 300 µg/L), or normal (UICadj = 100-299 µg/L). We conducted survey-weighted, covariate-adjusted logistic regression models to examine associations between iodine status and prevalence of hip, spine, or wrist fracture for all participants and stratified by sex.

Results: Participants were 64 years old on average. Approximately, 28% of participants were iodine deficient, while 23% had excess UICadj levels. Approximately 19% of participants reported having had a bone fracture, with 13%, 5% and 3% reporting prior wrist, spine or hip fracture, respectively. Men with excess UICadj had higher odds of having had a hip fracture (OR: 3.70; 95%CI: 1.33 – 10.33; p = 0.01) compared to those with normal UICadj. There were also trends of associations of excess UICadj with higher odds of hip fracture in the overall sample of men and women (OR: 2.33; 95%CI: 0.92 – 5.93; p = 0.11), and spine fracture in men (OR: 3.41; 95%CI: 0.72 – 16.16; p = 0.13) compared to those with normal UICadj.

Conclusions: Excess iodine intake may be an underrecognized risk factor for bone fracture among men. Longitudinal studies are needed to examine associations between iodine status and bone health, as well as mediation by thyroid function, and sex-specific effects.

Aging

Purpose in Life vs. Satisfaction with Life: Which is more essential for longevity with preserved physical and cognitive function? Nicole S. Pippard, MPH* Nicole Pippard Andrea Z. LaCroix, PhD Aladdin H. Shadyab, PhD Humberto Parada Jr., PhD Linda C. Gallo, PhD Caroline Nievergelt, PhD

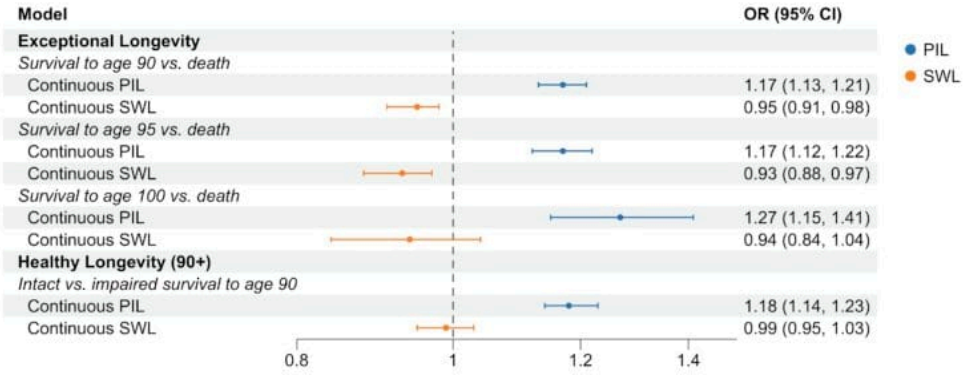
As populations age, understanding determinants of healthy aging is increasingly important. Epidemiologic research predominantly focuses on risk factors for morbidity and mortality, with limited attention to psychosocial health assets that may promote longevity and preserve cognitive and physical functioning. This study aimed to examine associations of purpose in life (PIL) and satisfaction with life (SWL) with exceptional and healthy longevity.

We studied 25,050 postmenopausal women in the Women's Health Initiative who completed a psychosocial questionnaire in 2012 (baseline) and had potential to survive to age 90 or older. PIL and SWL were assessed using validated self-report measures. Exceptional longevity was defined as survival to ages 90, 95, or 100 vs. death prior to these ages. Healthy longevity was defined as survival to age 90 with intact mobility and cognitive function vs. impaired survival. Logistic regression models estimated ORs and 95% CIs, with sequential adjustment for sociodemographic, health, and psychosocial factors. Mediation analyses explored underlying psychological and behavioral pathways for significant associations.

A total of 18,406 women survived to age 90 or older. After adjustment, a 1-SD increase in PIL was associated with greater odds of survival to age 90 (OR 1.2; 95% CI 1.1-1.2; $P < 0.001$), age 95 (OR 1.2; 95% CI 1.1-1.2; $P < 0.001$), and age 100 (OR 1.3; 95% CI 1.2-1.4; $P < 0.001$). Women with higher PIL had greater odds of intact survival to age 90 (OR 1.2; 95% CI 1.1-1.2; $P < 0.001$). SWL and longevity associations were attenuated after adjustment for health and psychosocial factors. Resilience and physical activity partially mediated these associations.

PIL was independently associated with exceptional longevity and intact survival in later life, while SWL was not consistently associated with these outcomes after adjustment. Findings highlight meaningful differences in how dimensions of psychological well-being may shape healthy aging.

Associations of Purpose in Life (PIL) and Satisfaction With Life (SWL) with Longevity Outcomes



OR = odds ratio; CI = confidence interval; All estimates represent a 1-standard-deviation increase in PIL or SWL; Reference line at OR = 1

LATEBREAKER

Aging

The older adult with HIV population in North America: a meta-analysis of repeated cross-sectional data Derek Manis* Derek Manis Joseph Daniels Mike Todd Heather Ross Jennifer Watt Colleen Webber Chantal Backman Wenshan Li Paul Katz Angel Algarin Allie Peckham Claire Kendall David Coon

HIV infection catalyzes aging, leaving older adults with HIV (OAWH) to manage multiple chronic and intersecting health conditions that likely increase their need for home and community-based services and unpaid caregiving. There is a substantial knowledge gap to understand the impact of aging with HIV at a continent-level to adapt systems and services for this population. HIV prevalence and incidence trends were examined among older adults (i.e., ≥ 50 years of age) and younger individuals (i.e., < 50 years of age). Repeated cross-sectional data of annual prevalences and incidences of HIV in California and Ontario were analyzed from 2010 to 2023; California and Ontario are the most populous jurisdictions in the U.S. and Canada, respectively, which makes them ideal for deriving continent-level estimates. Age-stratified prevalence and incidence case numerators in each year and jurisdiction were meta-analyzed with a random effects model and expressed per 100,000 individuals using jurisdiction-level denominators. The pooled prevalence among OAWH ranged from 68 to 143 per 100,000 individuals over the study period. There were 75 (95% CI [45, 108]) more OAWH per 100,000 individuals in 2023 relative to 2010, which represented a 2.09 (95% CI [1.60, 2.73]) times relative increase in the prevalence of HIV among older adults. Compared to those under 50 years of age in 2023, there were 28 (95% CI [12, 62]) more OAWH per 100,000 individuals, and this represented a 1.24 (95% CI [1.20, 1.28]) times relative increase in prevalence of HIV among older adults. Trends in the incidence of HIV among older adults and younger individuals were mostly consistent over the study period. These continent-level estimates affirm that the burden of HIV is now disproportionately borne by older adults. There is a clear need to adapt home and long-term care services and treatment strategies (i.e., long-acting antiretroviral injectables that reduce pill burden) to meet the needs of this population.

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Aging

Changes in financial well-being and epigenetic age acceleration in middle-aged and older US adults Sarah E. Weber* Sarah Weber Jeanine I. Nasser Allison E. Aiello Adina Zeki Al Hazzouri Katrina L. Kezios

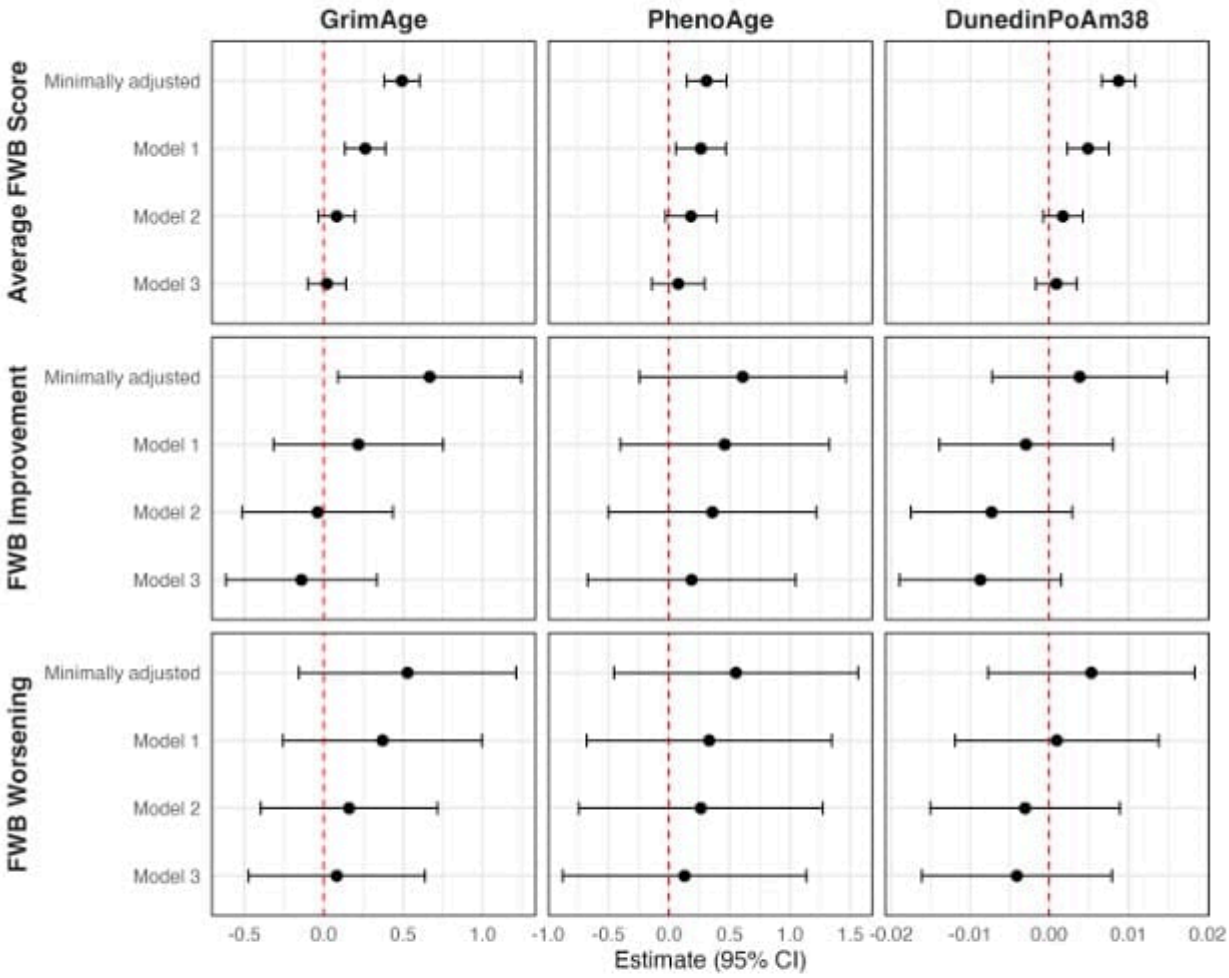
Financial insecurity is a common stressor among older adults that may accelerate epigenetic aging, which is the accumulation of DNA-methylation changes that reflect biological aging and predict health outcomes. Research on financial well-being (FWB) and epigenetic aging is limited. Using data from 2,539 adults >50 years in the Health and Retirement Study, we investigated how FWB impacts epigenetic age acceleration.

We measured FWB in 2010 and 2014 or 2012 and 2016 using a validated index (range: 0-8; higher scores=worse FWB). FWB was defined as average score and worsening (increase in 2+ points) or improvement (decrease in 2+ points) over the 4-year period. We assessed epigenetic aging in 2016 with 3 clocks: GrimAge, PhenoAge, and DunedinPoAm38. GrimAge and PhenoAge were calculated as residuals of epigenetic age regressed on chronological age, and DunedinPoAm38 reflects epigenetic years gained per 1 chronological year. We used linear regression to estimate effects of each FWB exposure on each clock, with sequential adjustment for confounders (see Figure 1 footnote).

The mean average FWB score was 1.4; 8% had worsening and 12% improving FWB. Across all clocks, higher average FWB score was associated with faster epigenetic age acceleration in models adjusted for sociodemographics, but results attenuated after adjusting for baseline health behaviors and conditions (e.g., GrimAge model 1: b=0.261 years of greater epigenetic aging per 1-unit increase in average FWB score, 95% CI 0.133-0.389 vs. model 3: b=0.019, 95% CI -0.101-0.139). Estimates for FWB improvement and worsening were imprecise and inconsistently patterned, suggesting no associations with epigenetic aging.

The association between poor FWB and epigenetic aging was largely attenuated after adjusting for baseline health factors. Future work disentangling life course roles of socioeconomic status and health is critical for determining whether improving financial security can meaningfully slow biological aging.

Figure 1. Linear regression results with sequential adjustment[1] for associations between average FWB score, FWB improvement, and FWB worsening and epigenetic age acceleration from three clocks, GrimAGE,[2] PhenoAge,[3] and DunedinPoAm38.[4]



Abbreviations: FWB = financial well-being.

[1]Minimally adjusted model adjusted for age and cell type proportions. Model 1 additionally adjusted for race, ethnicity, sex, birthplace, years of education, parental years of education, marital status, labor force status, health insurance type, occupational skill level, wealth, and income. Model 2 additionally adjusted for smoking, alcohol use, and body mass index. Model 3 additionally adjusted for number of health conditions, and depressive symptoms.

[2]GrimAge clock trained on surrogate DNA methylation biomarkers of physiological risk and stress factors with plasma proteins and smoking pack years.

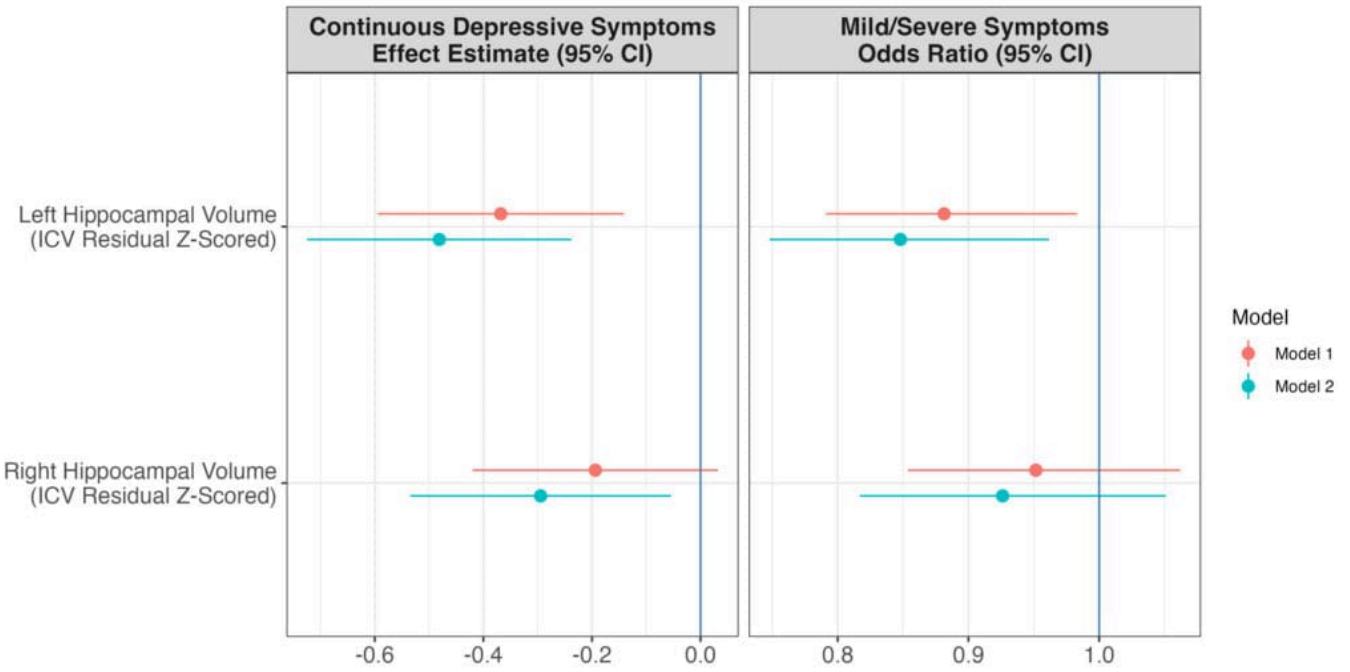
[3]PhenoAge trained on age and markers of tissue and immune function: albumin, creatinine, serum glucose, CRP, lymphocyte percent, mean (red) cell volume, red cell distribution width, alkaline phosphatase, white blood cell count.

[4]DunedinPoAm38 clock trained on 18 biomarkers that measure rate of aging in cardiovascular, metabolic, renal, hepatic, pulmonary, periodontal, and immune systems.

Aging

Lateral differences in the relationship between hippocampal volume and depressive symptoms in a cohort of ethnically diverse older adults Suhani Amin* Suhani Amin Evan Fletcher Eleanor Hayes-Larson

Reduced hippocampal volume is associated with depression diagnosis and symptoms in older adults. However, findings on hemispheric differences remain mixed and evidence is limited in ethnically diverse samples. Using the Health and Aging Brain Study (HABS-HD) cohort (n = 2280), we examined the effects of left and right hippocampal volumes on depressive symptoms measured by the 30-item Geriatric Depression Scale (GDS). Outcomes were analyzed both continuously and dichotomously as mild-to-severe (GDS score >= 10) vs. little-to-no symptoms. Model 1 was unadjusted, and Model 2 adjusted for age at imaging, gender, ethnicity (White, Hispanic, Black), education, income, and scanning protocol. Hippocampal volumes were residualized for intracranial volume and z-scored. The sample had a mean age of 69.1 (SD = 6.4), 59.6% female, a racial/ethnic distribution of 42.9% White, 32.8% Hispanic, and 24.3% Black participants, and 17.2% of the sample met criteria for mild-to-severe symptoms. Larger left and right hippocampal volumes were associated with lower GDS scores after adjustment, with a stronger effect for the left hippocampus (β = -0.481 z-score units, 95% CI [-0.725, -0.238], p < 0.001). When modeled dichotomously, only the left hippocampus volume was associated with meaningful reduction in odds of mild-to-severe depressive symptoms (OR = 0.848, 95% CI [0.748, 0.962] p = 0.01). Our analyses find an association between hippocampal volumes and late-life depressive symptoms in an ethnically diverse cohort and identify lateralized effects. Taken together, these findings suggest a notable role of the left hippocampus, which is known to be involved in episodic, contextual, and self-relevant memories, in late-life depressive symptoms.



Aging

Trajectories of depressive symptoms among older adults by spousal dementia status: a sequence analysis approach Michelle Flesaker* Michelle Flesaker Lucia Pacca Anusha M. Vable Marcia Pescador Jimenez

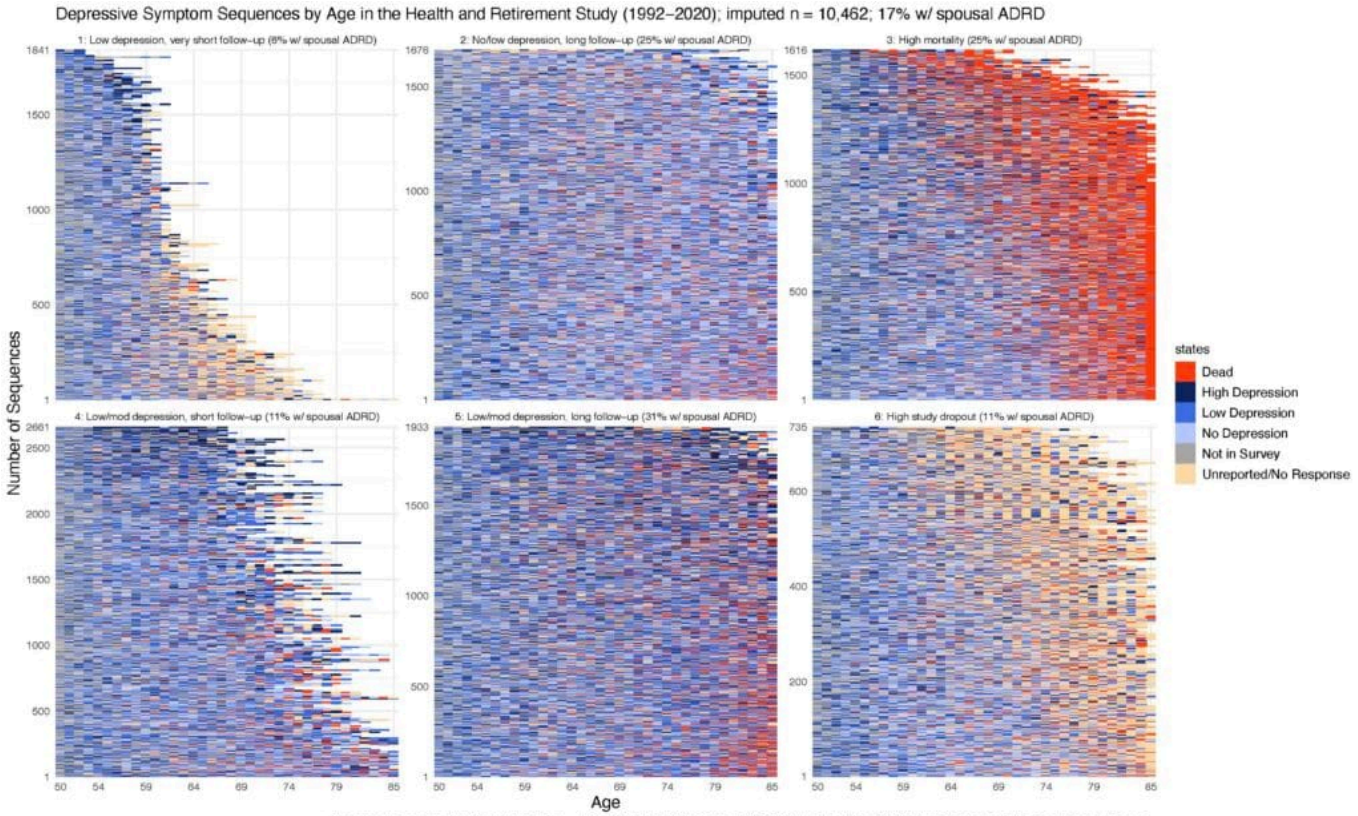
Introduction: One in 10 US older adults have Alzheimer's Disease and Alzheimer's Disease Related Dementias (ADRD). Spouses of people with ADRD have higher depression incidence than those without.1 Studies on depressive symptoms by spousal ADRD status have not examined complex trajectories of symptoms over time. We characterize trajectories of depressive symptoms from age 50-85 in older adults and variations by spousal ADRD status through novel applications of sequence and cluster analyses.

Method: We used data from the Health and Retirement Study (HRS), a longitudinal study of older adults in the US. We included 5,231 married people, 890 (17%) of whom had spousal ADRD. We classified each year of participants' lives from ages 50-85 into one of the following mutually exclusive categories using the modified Center for Epidemiologic Studies-Depression Scale (0-8): no depression (0), low (1-3), high (>4), unreported, dead. We used multiple imputation to complete initial and intermediate missing data. We calculated dissimilarity between individual trajectories of depressive symptoms using sequence analysis and grouped similar sequences using cluster analysis. We quantified relationships between spousal ADRD status and resultant clusters.

Results: We identified 6 clusters of depressive symptom trajectories. Clusters varied by symptom severity, follow-up time, and survival. Spousal ADRD status was differentially distributed among clusters: more participants with spousal ADRD were in the low/moderate depression, long follow-up (Cluster 5; 31% with spousal ADRD, 69% without), high mortality (Cluster 3; 25% with spousal ADRD), and no/low depression, long follow-up clusters (Cluster 2; 25% with spousal ADRD).

Discussion: We found a different distribution of spousal ADRD by unique clusters of depressive symptoms over time in a large national sample of older adults. Future research should consider the impact of complex longitudinal depressive symptom patterns.

1. Joling KJ, van Hout HP, Schellevis FG, et al. Incidence of depression and anxiety in the spouses of patients with dementia: a naturalistic cohort study of recorded morbidity with a 6-year follow-up. Am J Geriatr Psychiatry. 2010;18(2):146-153

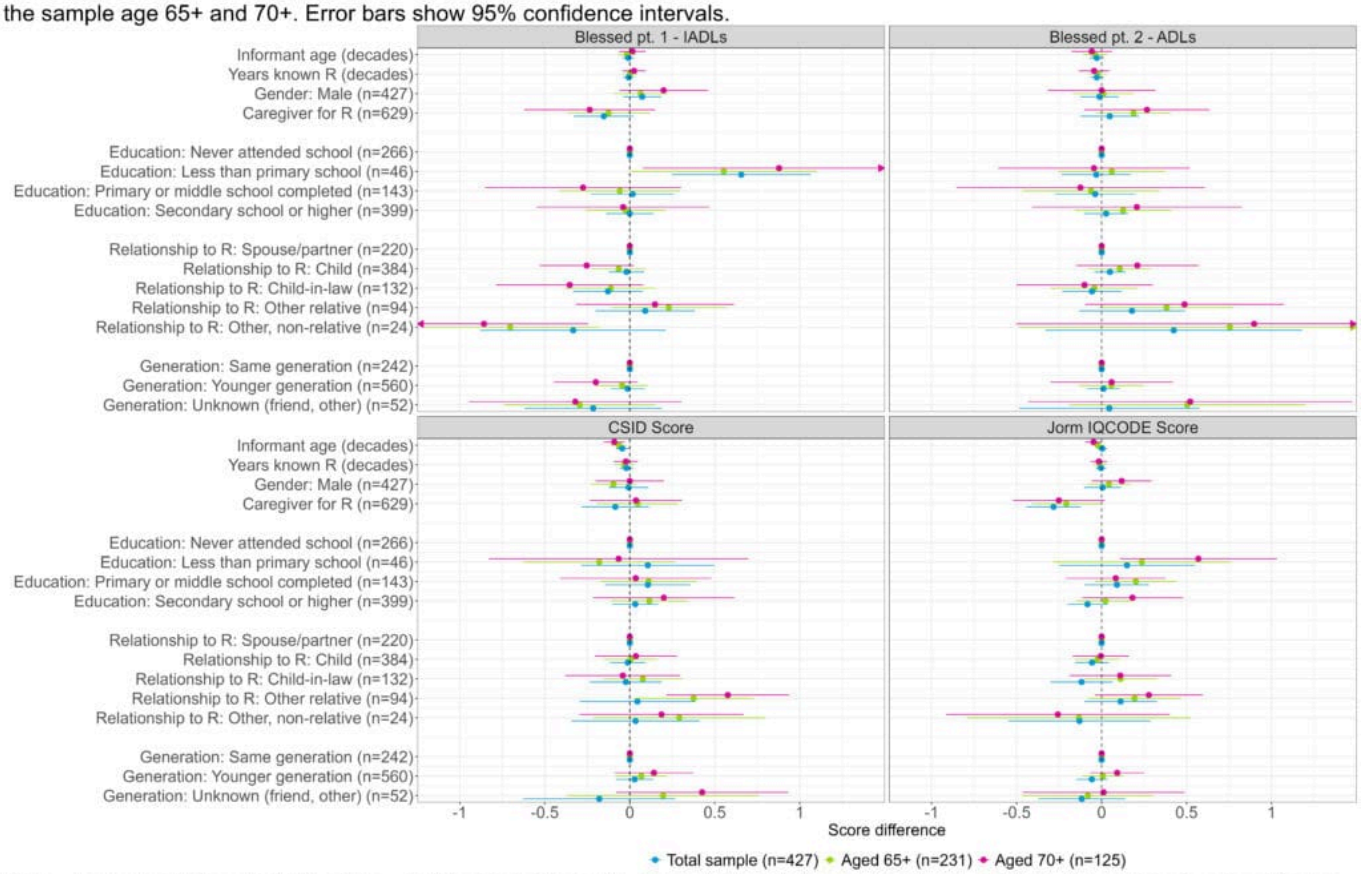

Depressive Symptom Sequences by Age in the Health and Retirement Study (1992–2020); imputed n = 10,462; 17% w/ spousal ADRD
1: Low depression, very short follow−up (8% w/ spousal ADRD)
2: No/low depression, long follow−up (25% w/ spousal ADRD)
3: High mortality (25% w/ spousal ADRD)
4: Low/mod depression, short follow−up (11% w/ spousal ADRD)
5: Low/mod depression, long follow−up (31% w/ spousal ADRD)
6: High study dropout (11% w/ spousal ADRD)
Number of Sequences
Age
states
Dead
High Depression
Low Depression
No Depression
Not in Survey
Unreported/No Response
Among our sample (n after imputation = 10,462; 17% with spousal ADRD), we identified 6 distinct clusters of depressive symptoms.
Those with spousal ADRD were overrepresented in the no/low depression, long follow−up, (2), high mortality (3), and low/moderate depression, long follow−up (5) clusters.

Aging

The effect of informant characteristics on reports of impairment in cognition and daily functioning in India: Findings from a multiple informant, within-person design Emma Nichols* Emma Nichols Sarah Gao Pranali Khobragade Alden L Gross Lindsay C Kobayashi Kenneth M Langa Erik Meijer Jinkook Lee

Informant reports of respondents' cognitive and everyday functioning are commonly used in studies of older adults to inform dementia diagnoses. However, characteristics of the informant may influence reporting, leading to bias. While existing literature suggests this source of bias may be important, evidence comes from between-person comparisons adjusting for respondent characteristics, and residual confounding due to links between informant and respondent characteristics is a concern. We used multiple informant data from four informant scales in the Longitudinal Aging Study in India – Diagnostic Assessment of Dementia (LASI-DAD) innovation sample (2024-2025; N=858) to estimate the within-person effect of informant characteristics using linear regression models with fixed effects for each respondent. Respondents were on average 66.7 years old (inter-quartile range = 62-70); 56.7% of the sample were women. Included informants were most commonly spouses or partners (25.8%), children (44.9%), or children-in-law (15.5%), who lived with the respondent (88.0%), and provided care to the respondent (73.3%). A large proportion of respondents (10.8%-21.5% across scales) had at least a 1 standard deviation difference in scale scores between informants. However, findings on the effects of informant characteristics were less consistent, with some evidence of differences by caregiving status, relationship with the informant, and frequency of contact. Effects were larger among older adults and were different across informant scales (Figure 1). Findings highlight the variability in scores across informants, but evidence on systematic differences by informant characteristics was inconsistent across scales and weaker compared to prior evidence from between-persons designs. Bias may be a concern predominantly for older respondents with less knowledgeable informants, such as distant relatives, non-relatives, or those who see respondents infrequently.

Figure 1. Within-person differences in four informant scales by characteristics of the informant in the Longitudinal Aging Study in India Diagnostic Assessment of Dementia (LASI-DAD) innovation sample (N=858). Results are shown for the total sample (60+) as well as the sample age 65+ and 70+. Error bars show 95% confidence intervals.



*IADLs = Instrumental Activities of Daily Living; ADLs = Activities of Daily Living; CSID = Community Screening Instrument for Dementia; IQCODE = Informant Questionnaire on Cognitive Decline in the Elderly.

Aging

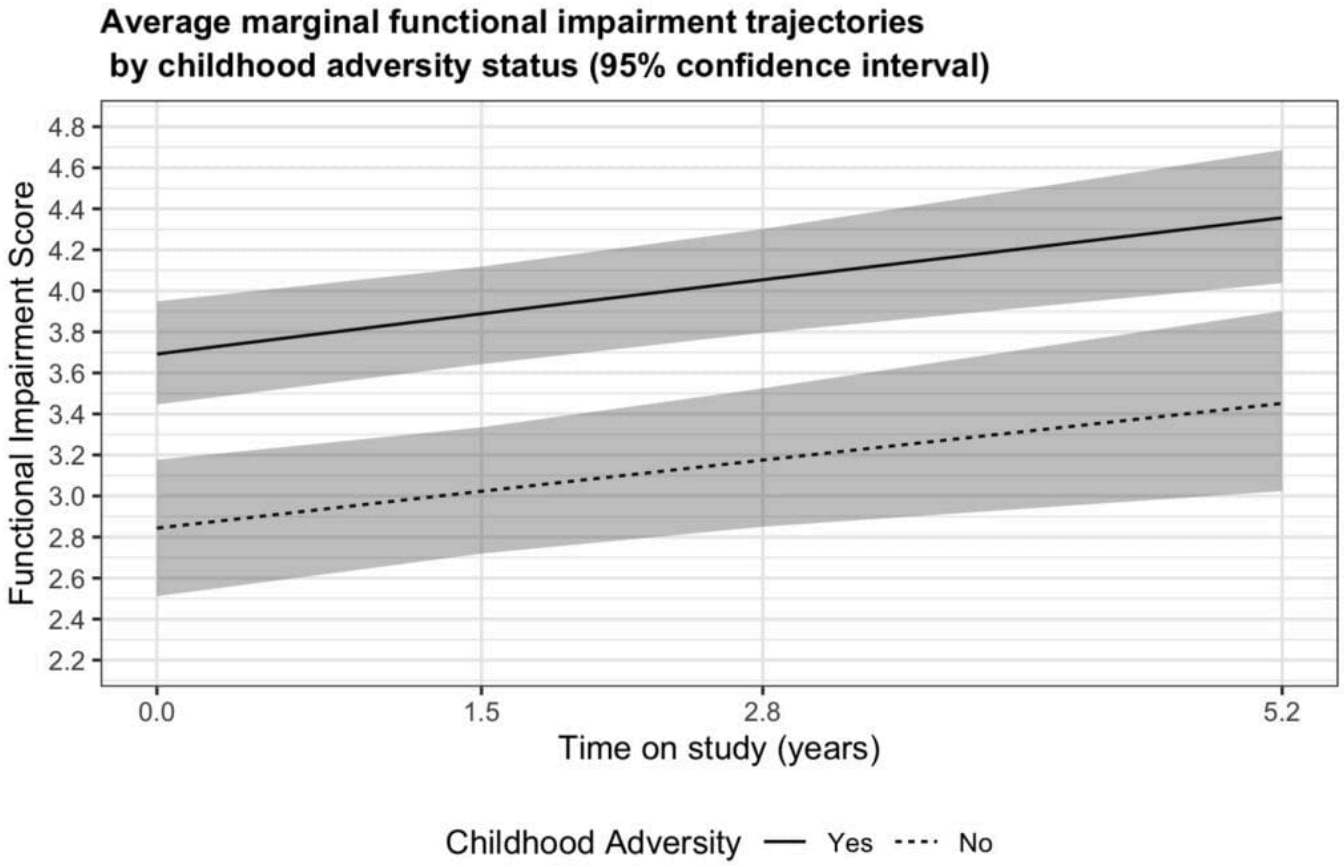
The impact of adverse childhood experiences on functional impairment in a diverse cohort of older adults Gina E. Nam* Gina Nam Paloma Rojas-Saunero M. Maria Glymour Rachel Whitmer Elizabeth Rose Mayeda Paola Gilsanz Eleanor Hayes-Larson

Background: The possible impact of childhood adversity on functional impairment in late life is unknown.

Methods: We included community-dwelling adults aged 65+ from the Kaiser Healthy Aging and Different Life Experiences Study. Childhood adversity was defined as reporting at least one adverse experience (parental separation, parental remarriage, witnessed domestic violence, family substance abuse, parental job loss, parental incarceration, and serious illness of a family member) versus none. Functional impairment was a composite score summing 12 Likert (0-4) items of activities of daily living (ADL), instrumental ADL, and mobility domains (range: 0-36), measured over up to 4 waves (2017-2025). We fit generalized estimating equations for functional impairment scores by childhood adversity, adjusting for follow-up time, early-life demographic, and socioeconomic variables. We estimated marginal mean functional impairment scores by childhood adversity status at each study wave, accounting for attrition (dropout/death), and calculated mean differences.

Results: Among 1,709 participants (mean [SD] baseline age, 76.0 [6.8] years; 60% female), 67% reported experiencing at least one type of childhood adversity. Mean baseline functional impairment score was 3.2 (SD = 4.3). Those with a history of childhood adversity had higher baseline levels of functional impairment than those without adversity (mean difference = 0.85; 95% CI, 0.44-1.26). Average functional impairment scores increased over time for both groups, and differences in change between exposure groups were small (Figure). By wave 4 (5.2 years), mean difference in functional impairment between those with and without childhood adversity was 0.90 (95% CI, 0.36-1.45).

Conclusion: Childhood adversity was associated with higher levels of functional impairment, with differences persisting over follow-up. More research is needed to understand the impact of childhood adversity on functional impairment over the lifecourse.


Average marginal functional impairment trajectories
by childhood adversity status (95% confidence interval)
Functional Impairment Score
4.8
4.6
4.4
4.2
4.0
3.8
3.6
3.4
3.2
3.0
2.8
2.6
2.4
2.2
0.0
1.5
2.8
5.2
Time on study (years)
Childhood Adversity
Yes
No

Aging

Epigenetic aging mediates the association between oral health and mortality in the United States Hyeji Seo* Hyeji Seo Yoosoo Chang Seungho Ryu Kyeezu Kim

Periodontitis and tooth loss are linked to mortality, but the role of epigenetic aging in this relationship remains unclear. This study investigated the associations of oral health with DNA methylation-based epigenetic age acceleration (EAA) and evaluated whether EAA mediates the link between oral health and mortality.

We analyzed data from 1,764 participants from the National Health and Nutrition Examination Survey (1999-2002) and linked mortality data from the National Death Index up to December 2019 (median follow-up: 17.4 years; IQR: 10.4, 18.8). Periodontitis severity was classified as mild, moderate or severe based on CDC/AAP definitions. Number of teeth was categorized into four groups: ≥ 20, 10–19, 1–9 and 0 (edentulous). Seven EAA measures were examined: IEAA, EEAA, PhenoAA, SBAA, GrimAA, Grim2AA and DunedinPoAm. We evaluated the associations using multivariable linear and Cox proportional hazards models, and assessed the mediating role of EAA adjusting for demographic characteristics, lifestyle behaviors, and anthropometric parameters.

Participants with periodontitis exhibited higher EAA across all measures except IEAA compared to those without periodontitis (b range: 0.897–1.902, all $p < 0.05$). Similarly, compared to those with ≥ 20 teeth, individuals with < 20 teeth showed higher EAA (b: 1.164 [95% CI: 0.29, 2.038] for Grim2AA; b: 1.051 [0.206, 1.896] for GrimAA). Mediation analyses revealed that Grim2AA partially mediated the association between tooth loss and mortality, accounting for 29.0% of all-cause mortality (95% CI: 13.0, 68.9), 19.8% of CVD mortality (2.0, 97.5), and 23.1% of lower respiratory disease mortality (8.6, 51.0). However, no mediation was observed for periodontitis.

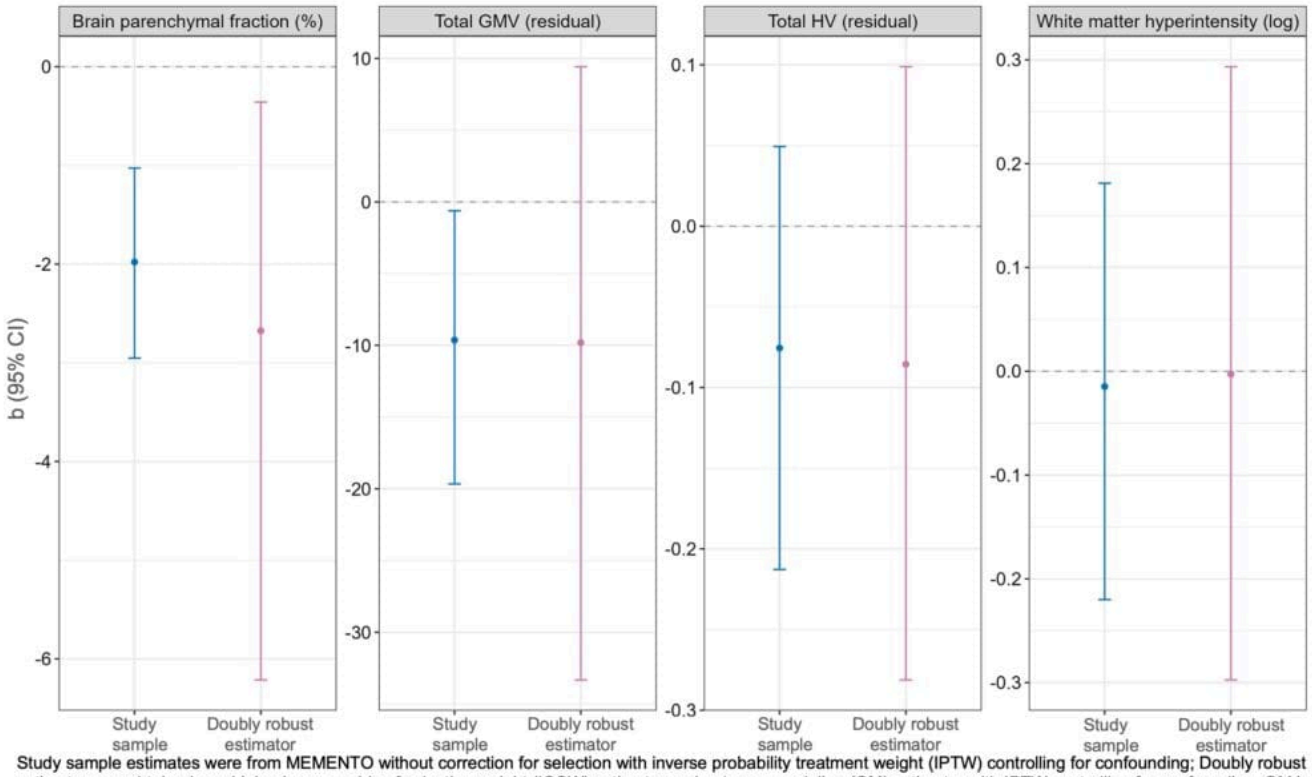
Epigenetic age acceleration, particularly Grim2AA, serves as a key biological mechanism linking tooth loss to increased mortality risk. Our findings suggest that maintaining optimal oral health may be crucial for slowing biological aging and promoting longevity.

Aging

Estimated effects of diabetes on neuroimaging biomarkers: Extending estimates from the MEMENTO cohort to the French population of older adults Yingyan Wu* Yingyan Wu Eleanor Hayes-Larson Carole Dufouil Laura E. Gibbons Rachel Whitmer Daniel Westreich Marissa J. Seamans M. Maria Glymour Elizabeth Rose Mayeda

Neuroimaging studies show that people with type 2 diabetes have worse neuroimaging biomarkers of Alzheimer's disease and related dementias. However, neuroimaging samples are often highly selected, raising concerns about generalizability to broader populations. We aimed to extend estimated effects of type 2 diabetes on neuroimaging biomarkers from a clinic-based French neuroimaging sample to the French population of older adults. We used data from the French MEMENTO neuroimaging cohort (n=2,057), which recruited participants aged 60-90 years from memory clinics who had subjective cognitive complaints or mild cognitive impairment, and the survey-weighted French component of the Survey of Health, Ageing, and Retirement in Europe (SHARE-France; n=3,459) to represent 13.8 million French adults aged 60-90 years. After harmonizing and pooling datasets, we compared characteristics between MEMENTO and survey-weighted SHARE-France. We used a doubly robust transportability estimator to extend estimates from MEMENTO to the target population. We estimated inverse odds of selection weights and inverse probability of treatment weights using age, sex, education, self-rated health, and hypertension. We fit outcome models in the MEMENTO sample and combined with weighting to obtain transported doubly robust estimates. Compared with the French population represented by SHARE-France, MEMENTO participants were healthier and more highly educated. Despite these differences, associations between type 2 diabetes and neuroimaging biomarkers were qualitatively similar in the original MEMENTO sample and the transported estimates (e.g., mean difference in brain parenchymal fraction by diabetes status: MEMENTO b=−1.98% [95% CI −2.95%, −1.03%] vs. transported b=−2.68% [−6.21%, −0.36%]) (**Figure 1**). Despite substantial selection into the neuroimaging cohort, associations between type 2 diabetes and neurodegeneration were robust when extended from a clinic-based sample to the French population.

Figure 1. Estimated mean differences in neuroimaging biomarkers by type 2 diabetes status. Negative effect estimates of brain parenchymal fraction, total gray matter volume (GMV), total hippocampal volume (HV) and positive values of white matter hyperintensity volume represent worse brain health for people with type 2 diabetes.



Study sample estimates were from MEMENTO without correction for selection with inverse probability treatment weight (IPTW) controlling for confounding; Doubly robust estimator was obtained combining inverse odds of selection weight (IOSW) estimator and outcome modeling (OM) estimator with IPTW controlling for confounding. OM is the outcome model to predict outcome in the targeted population represented by survey-weighted SHARE-France sample. Grey dotted lines denote null value.
GMV: grey matter volume; HV: hippocampal volume.

Aging

Associations of shift work with longitudinal cognitive decline among a diverse cohort of older adults: The KHANDLE study Hilary L. Colbeth* Hilary Colbeth Alexander Ivan B. Posis Ellen A. Eisen Charles DeCarli Paola Gilsanz Rachel A. Whitmer

Background: Studies on the impacts of work patterns on cognitive decline are scarce due to challenges collecting exposure and repeated late-life cognitive data over decades; few investigated shift work with cognitive change.

Methods: We included 1,643 Kaiser Health Aging and Different Life Experiences (KHANDLE) study participants. Using the American Time Use Survey, we determined if participant's self-reported main lifetime occupation was characterized by night shifts (23:00–6:00), long hours (≥8hr days), or included weekends. Executive function (EF) and verbal episodic memory (VM) were measured using the Spanish and English Neuropsychological Scales across up to 4 interview waves and z-scored to baseline. To test associations of long hours, nights, or weekend work, respectively, and cognitive change, we fit joint models that use linear mixed effects and Cox proportional hazards sub-models to account for the competing risk of death. Time to all-cause mortality was calculated from baseline to death.

Results: Participants (mean age=75 years SD:6.71[range:65-90]; 59% female; 51% ≤some college) were 25% Asian, 26% Black, 20% Latinx, and 29% White; 43% worked long hours, 42% night shifts, and 20% weekends. During a mean follow-up of 3.98 years (SD:1.82[0-7.65]), 14% died. In joint models, shift work (nights and weekends, respectively) and long hours were associated with lower EF and VM scores at baseline compared to standard schedules (Figure 1). Night work and long hours were not associated with rates of decline for EF and VM. However, weekend work was associated with faster decline in EF and VM (both β:-0.02, 95% CI:-0.04,-0.00).

Conclusions: Within an ethnoracially diverse cohort, shift work and long hours were associated with lower baseline cognition and weekend work was associated with slightly faster decline than weekday shifts only. Further research will examine industry-specific impacts of work patterns on cognitive function.

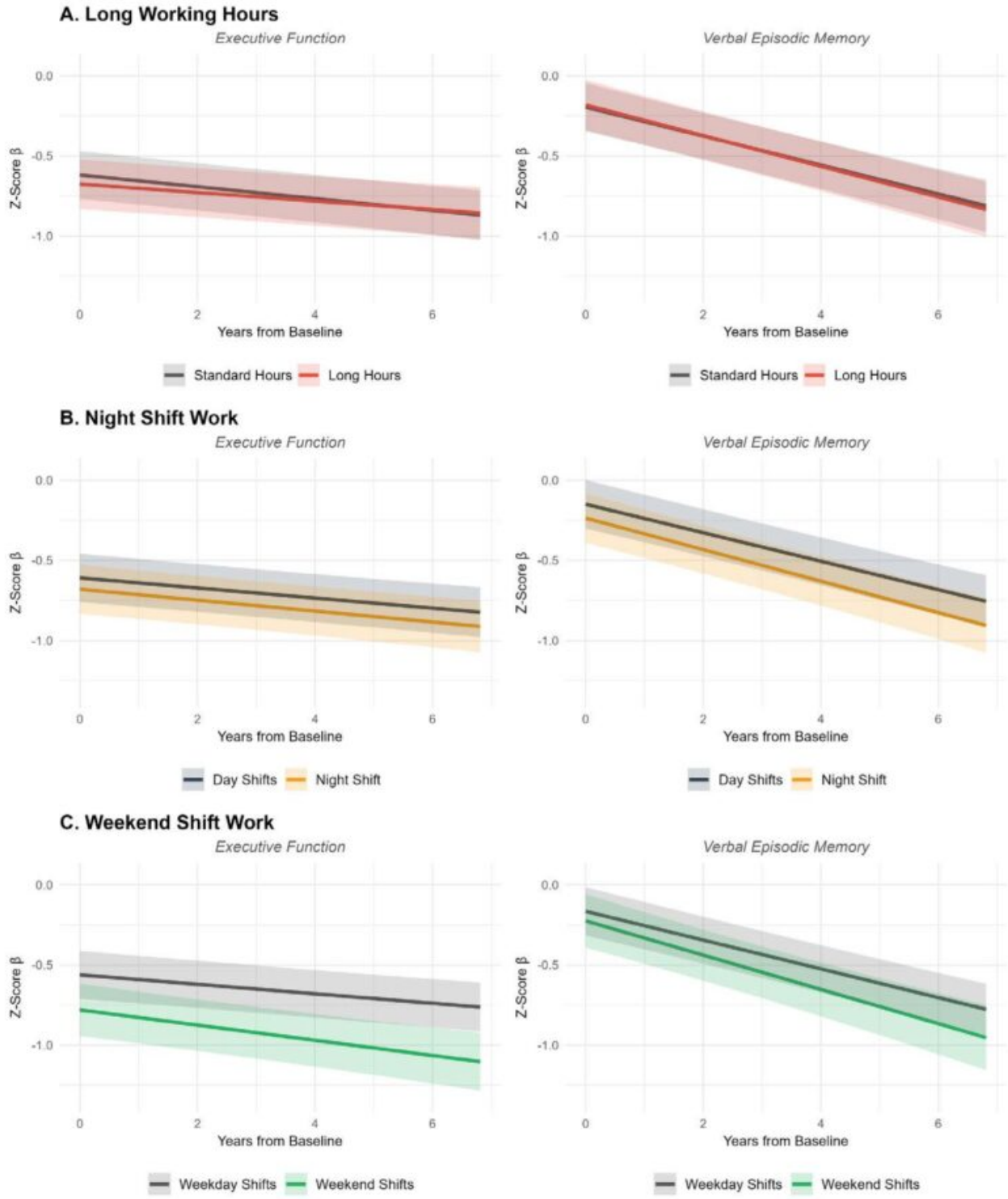


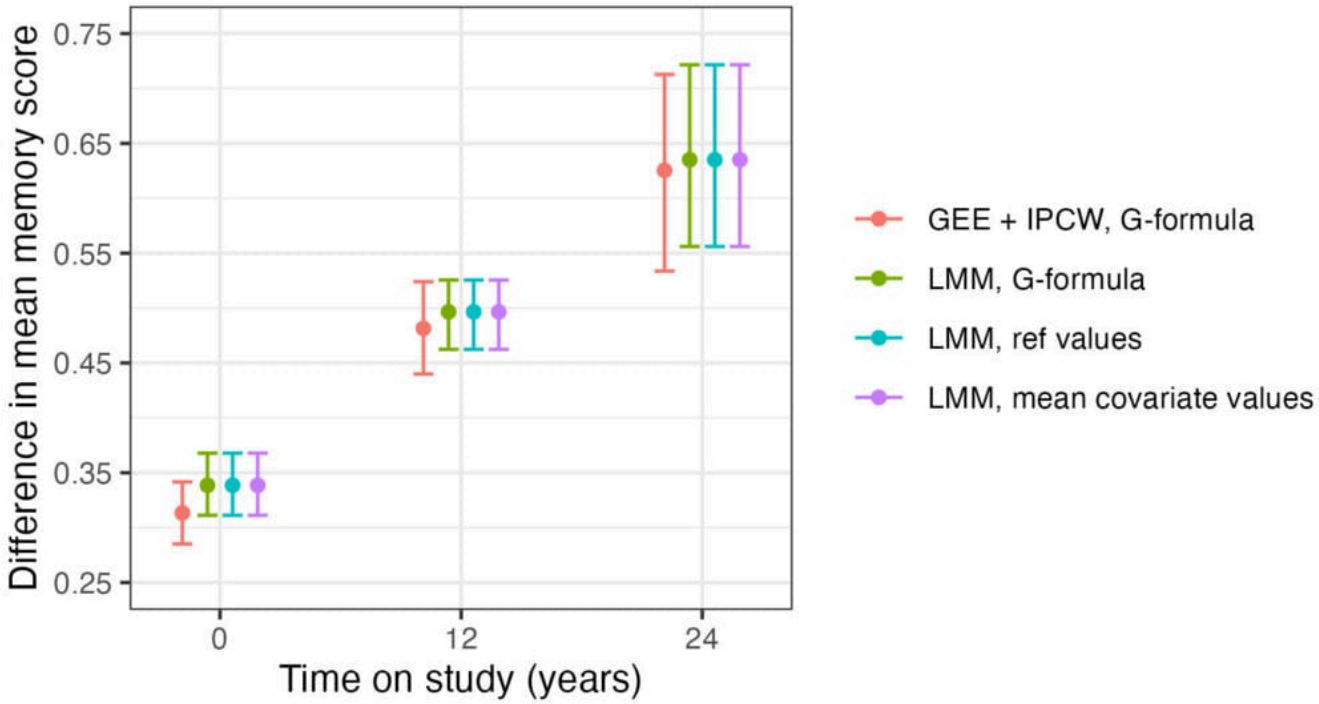
Figure 1. Cognitive function decline as measured by executive function and verbal episodic memory in association with long hours, night shifts, and weekend shifts.

Aging

Estimating Effects of Exposures on Memory Trajectories With Death and Dropout: Comparing Modeling Frameworks and Prediction Strategies L. Paloma Rojas-Saunero* L. Paloma Rojas-Saunero Yixuan Zhou Taylor M. Mobley Elizabeth Rose Mayeda

Observational studies on the effect of time-fixed exposures on memory decline in older adults commonly use linear mixed-effects models (LMMs) and summarize results by evaluating predicted memory trajectories at reference or mean covariate values, which differ from marginal estimates obtained from generalized estimating equations (GEE). We used data from the Health and Retirement Study to estimate the effect of completing high school versus not on memory decline over 24 years of follow-up. We included participants with a memory score assessment in 1998 (n=19208, mean baseline age=66.3 years) and constructed a binary indicator for high school educational attainment (yes/no). We estimated mean differences in memory function over time using a g-formula approach based on GEE with inverse probability censoring weights (IPCW) for attrition due to death and dropout. We also estimated mean differences in memory function over time from a single LMM with random intercepts, estimated using three prediction strategies: the g-formula, prediction at reference covariate values, and prediction at mean covariate values. For both GEE and LMM, we included exposure, practice effects, time with natural splines, interaction between time and exposure, baseline age, sex/gender, southern birth, parental educational attainment, and interaction between covariates and time. For the IPCW, we additionally included race/ethnicity and time-varying health-related variables. We calculated 95% confidence intervals with 500 bootstraps. High school attainment was associated with higher memory scores, with mean differences increasing over time. Mean differences estimated using GEE were slightly smaller than those based on LMM, and all three LMM-prediction approaches yielded identical estimates (Figure). Overall, mean differences over time varied across modeling approaches, not across prediction strategies; GEE with IPCW is a more explicit strategy for accounting for potentially informative attrition.

Figure. Estimated mean differences in memory function at baseline comparing high school attainment vs. not, at baseline, 12, and 24 years of follow-up, comparing modeling frameworks and prediction strategies

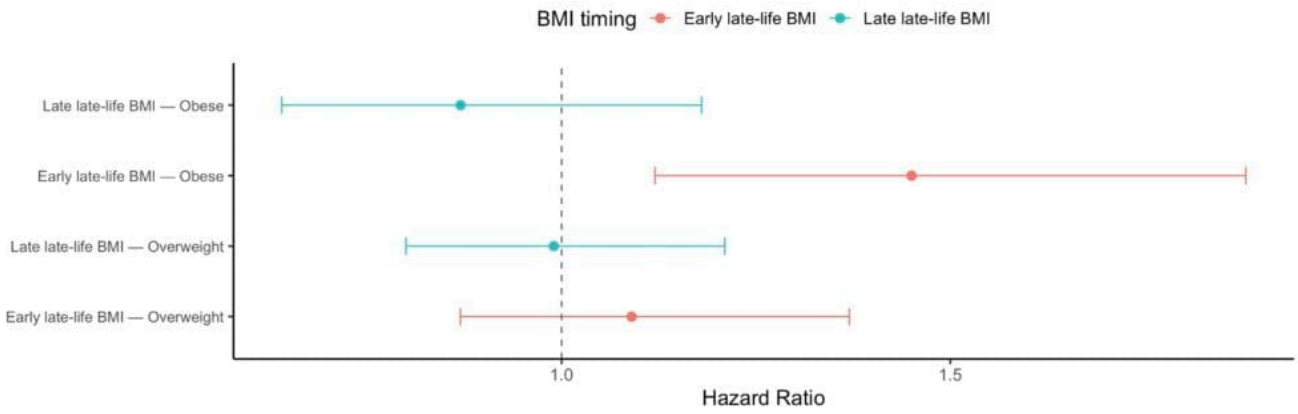


Aging

Body mass index at different late-life stages and risk of all-cause mortality in a diverse population with exceptional longevity: LifeAfter90 Study Claire Meunier* Claire Meunier Paola Gilsanz Maria Corrada Kristen M. George Michelle C. Odden Rifat Alam Rachel A. Whitmer

The association between late-life obesity and all-cause mortality varies across older age. Among the younger-old populations, obesity is associated with a higher mortality risk. However, studies among oldest-old have reported null or protective effects, with little known about diverse populations. We examined the association of BMI measured at different stages of late-life and all-cause mortality in 849 participants who lived until 90 years in the LifeAfter90 study. Early late-life BMI (mean age 79.9; range 73.8-95.1) was defined as the first clinically measured BMI obtained at age 65 from electronic health records beginning in 2005. Late late-life BMI (mean age 91.7; range 89.2-104.6) was defined as the BMI measure closest to study baseline. Time to mortality, which was ascertained from the EHR, was calculated as years since baseline. Cox proportional hazards models estimated the association between BMI and mortality adjusting for demographic variables. BMI distributions differed by timing, early late-life: 30% normal, 46% overweight, 25% obese; late late-life: 48% normal, 39% overweight, 13% obese. During six years of follow-up, 53% of participants died. In models accounting for demographics, age at BMI, and baseline age, obesity in early late-life was associated with a higher hazard of mortality after age 90 compared with normal BMI (HR(95% CI):1.45(1.12,1.88)). Obesity measured in late late-life was not associated with mortality, though point estimates suggest a lower risk of mortality (HR:0.87(0.64,1.18)). For both late-life time points, overweight BMI was not associated with mortality (Figure 1). In this diverse cohort of the oldest-old, obesity in early late-life was associated with increased mortality risk, whereas obesity in late late-life was not. The reversal of point estimates later in late life may reflect age specific effects of obesity, selective survival, or reverse causality due to illness-related weight loss prior to death.

Figure 1: The hazard ratio of early late-life and late late-life BMI with all-cause mortality



Estimates adjusted for age at BMI, age at baseline, education, race, and sex from Cox proportional hazards models. Hazard ratios; normal BMI is the reference.

Aging

Sex-specific associations between thyroid hormones and biological aging Rebecca Stutz*
Rebecca Stutz Zhongzheng Niu Marina Oktapodas Feiler

Background: Thyroid hormones are master regulators of the metabolic function, which is a core component of biological aging. DNA methylation-based epigenetic clocks, particularly DunedinPoAm, are promising biomarkers of the rate of biological aging, i.e., how fast one ages biologically. However, the thyroid hormonal regulation of the rate of biological aging in adults remains largely unexplored.

Objective: To investigate the association of thyroid hormones with DunedinPoAm using the representative sample from the National Health and Nutrition Examination Survey (NHANES).

Methods: NHANES, a cross-sectional survey of the U.S. non-institutionalized population, assesses lifestyle, nutrition, and health status. From 1999 to 2002, thyroid hormones, including thyroxine (T4) and thyroid-stimulating hormone (TSH) were measured by immunoassay. Among these participants, 831 also had DunedinPoAm estimates from DNAm. We used linear regression models to examine the independent and interactive associations of T4 and TSH with DunedinPoAm, adjusting for demographics, lifestyle factors, and comorbidity. The analysis was stratified by sex to evaluate sex-specific effects.

Results: In males, T4 appeared to accelerate the rate of aging, with a 1-unit increase in T4 associated with a 0.80% (95% CI: 0.28, 1.33) higher DunedinPoAm age acceleration after adjusting for confounders. There is a small, but significant interaction between T4 and TSH where the beta for the interaction term was 0.04% (95% CI: -0.03, 0.11). In females, T4 and TSH both appeared to decelerate aging (T4: β = -0.8%, 95% CI: -1.4, -0.2, TSH: β = -1.7%, 95% CI: -3.5, 0) in the fully adjusted model. T4 and TSH also showed positive and significant interaction (β = 0.3%, 95% CI: 0.07, 0.5).

Conclusion: Among people older than 50 years, thyroid hormones had sex-specific associations with the rate of biological aging, where T4 can accelerate DunedinPoAm in males, but T4 and TSH can decelerate DunedinPoAm in females.

Aging

Quantifying bias from reverse causation in observational studies of dementia risk factors: A simulation study informed by reverse Mendelian Randomization Jingxuan Wang* Jingxuan Wang Minhyuk Choi Sarah F. Ackley Ruijia Chen Willa D. Brenowitz Thomas J. Hoffmann Scott C. Zimmerman Katrina L. Kezios Adina Zeki Al Hazzouri Elizabeth Rose Mayeda Rebecca E. Graff Jacqueline M. Torres M. Maria Glymour

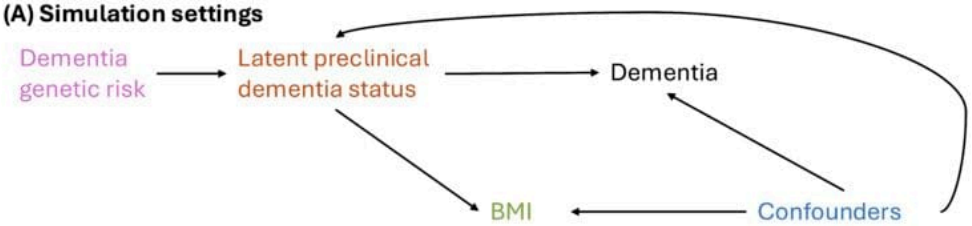
Background: Observational studies are central to identifying modifiable determinants of dementia, yet its long preclinical phase can induce reverse causation, biasing associations even in longitudinal analyses. Using simulations informed by prior reverse Mendelian randomization (MR) findings, we quantified the magnitude of reverse causation bias in observational analyses of the effects of body mass index (BMI) on dementia.

Methods: For a hypothetical cohort study (n=20,000), we simulated longitudinal trajectories of BMI and dementia risk from ages 45 to 90 years (Figure: causal directed acyclic graph). Data generating rules were calibrated to align with previously published evidence on age-specific dementia incidence, BMI trajectories across age, and age-specific associations of dementia genetic risk with BMI from reverse MR studies. We generated the data such that BMI had no effect on dementia incidence and that any observed association would reflect bias due to reverse causation. For each simulation, we selected a baseline age for study entry (45 to 80), and simulated a study where BMI was measured at baseline, and participants were followed until age 90. We estimated the association between z-standardized BMI at study entry and dementia incidence using Cox models and quantified bias as the deviation of the estimated HR from the null. Each simulation was repeated 300 times.

Results: The magnitude of reverse causation bias increased with older baseline age (HR decreased). For example, when follow-up began at age 65, the estimated HR for BMI and dementia was 0.82 (95% CI: 0.71-0.96). When follow-up began at age 80, the HR decreased to 0.61 (95% CI: 0.53-0.71).

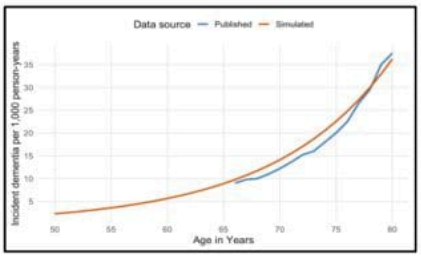
Conclusion: Our flexible, simulation-based tool can help quantify reverse causation bias in dementia research. Our findings, consistent with prior hypotheses, indicate reverse causation bias for dementia risk factors can be large and lead to qualitatively incorrect conclusions.

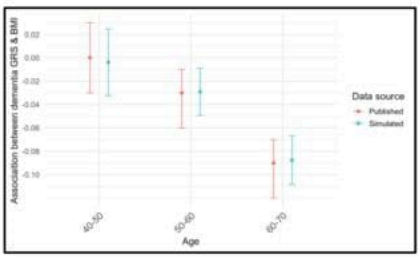
(A) Simulation settings

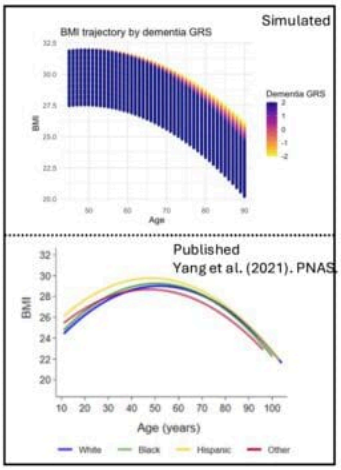


- Cohort sample size N = 20,000
- Dementia genetic risk score (GRS) ~ N(0,1)
- Female ~ Bernoulli(0.5)
- High school ~ Bernoulli(0.4)
- Measured C ~ N(0,3)
- Unmeasured U ~ N(0,1)

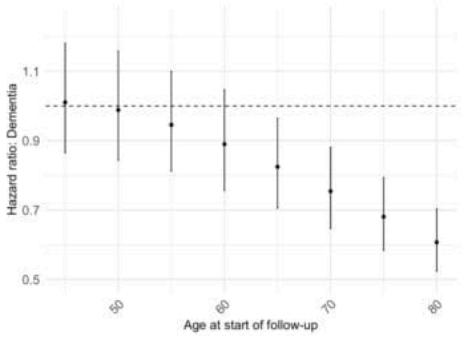
- Latent preclinical dementia status = -10.2 + 0.09 × age + [0.003 ×(age-45) + 0.0003 (age- 45)^2] × GRS - 0.5 × female - 0.5 × high school + 0.05 × U - 0.05 × C
- BMI = 27 - 0.5× Latent preclinical dementia status -0.004 × (age - 55)^2 + 1.5 × female + 1.2 × high school + 0.1 × U + 1.0 × C + ε , ε ~ N(0,1)
- logit(P(dementia=1)) = Latent preclinical dementia status







(B) Simulation results



Aging

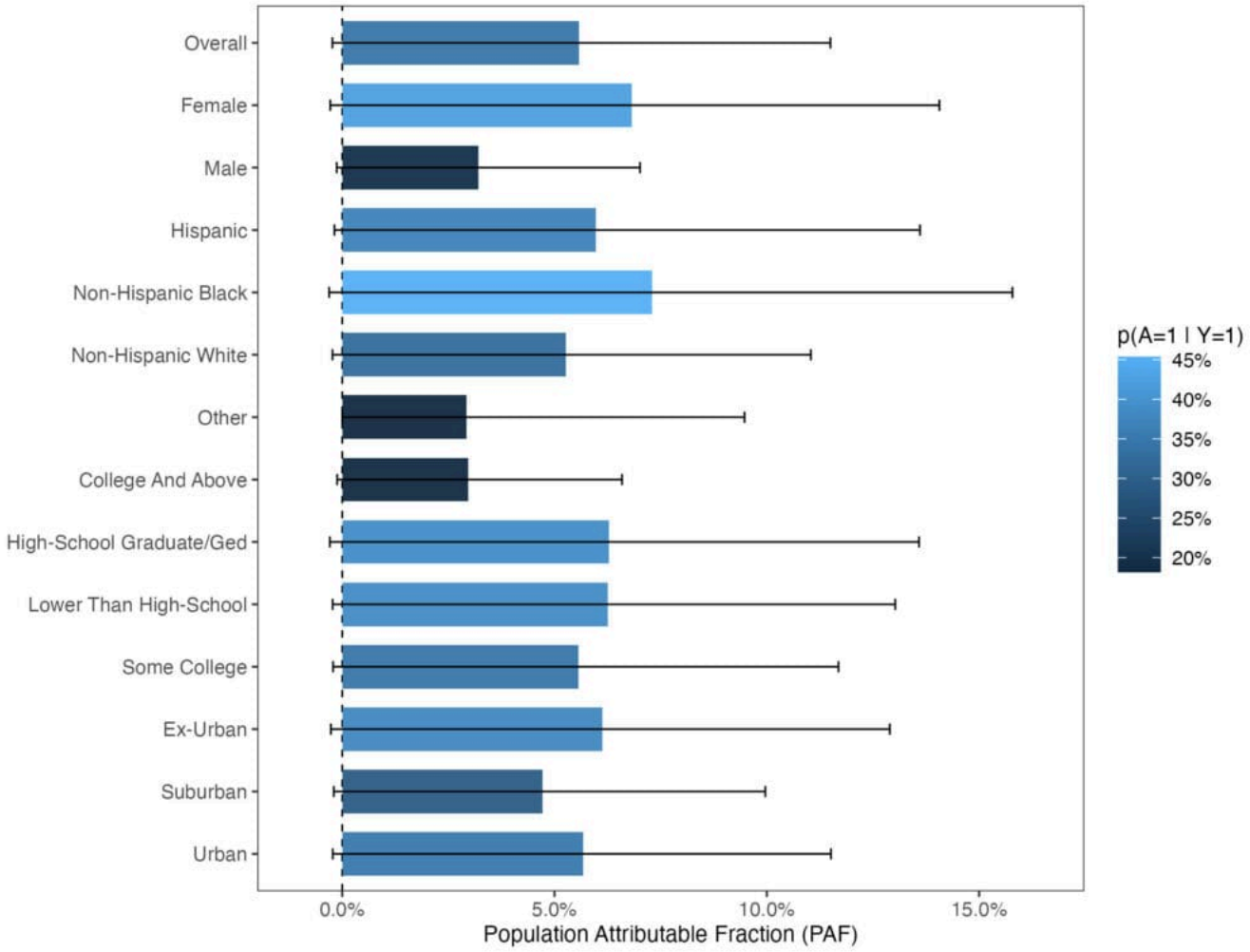
Heterogeneity in the Population Attributable Fraction of Social Isolation for Incident Dementia Dylan Tran* Dylan Tran Andrew Philips Afzalbek Fayzullaev Koichiro Shiba Audrey R. Murchland Kendra D. Sims Yulin Yang Jacqueline M. Torres Maria M. Glymour Roch Nianogo Ruijia Chen

Social isolation is a potentially modifiable risk factor for dementia, but its population impact may vary across sociodemographic subgroups. We examine heterogeneity in the estimated population attributable fraction (PAF) of incident dementia attributable to social isolation.

Data were from the 2008–2020 Health and Retirement Study. Social isolation was measured at baseline using a six-item composite variable capturing marital status, living alone, monthly contact with children/family/friends, and participation in social activities with participants in the top quintile classified as isolated. Baseline exposure was defined as the first available assessment from 2008 or 2010. Incident dementia was defined using the Langa–Weir cognitive classification. We fit discrete-time pooled logistic models adjusting for age, sex, race and ethnicity, education, and urbanicity. Heterogeneity in RR was assessed using interaction terms and likelihood ratio tests. We computed Miettinen PAFs using the baseline prevalence of isolation among incident cases within subgroups and the overall RR when there was no evidence of interaction.

Among 11,402 participants followed for up to 12 years (mean age [SD] = 64.8 [11.7]), 58% women, 21.4% were classified as socially isolated at baseline (ranging from ~18% to ~45% across subgroups), and 598 (5.2%) developed incident dementia. Social isolation was associated with higher dementia risk (RR=1.19, 95% CI:0.99 to 1.45). Tests for interaction provided no evidence of effect heterogeneity, supporting the use of a common RR. The estimated PAF was 5.6% (95% CI: −0.23% to 11.5%). Although a common RR was used, subgroup-specific PAF point estimates varied (e.g. 6.8% for women, 3.2% for men), reflecting differences in the subgroup prevalence of social isolation.

These findings suggest that while RRs were similar across sociodemographic groups, population-level impact as measured by the PAF differed due to variation in the prevalence of social isolation.


Overall
Female
Male
Hispanic
Non-Hispanic Black
Non-Hispanic White
Other
College And Above
High-School Graduate/Ged
Lower Than High-School
Some College
Ex-Urban
Suburban
Urban
0.0%
5.0%
10.0%
15.0%
Population Attributable Fraction (PAF)
p(A=1 | Y=1)
45%
40%
35%
30%
25%
20%

Aging

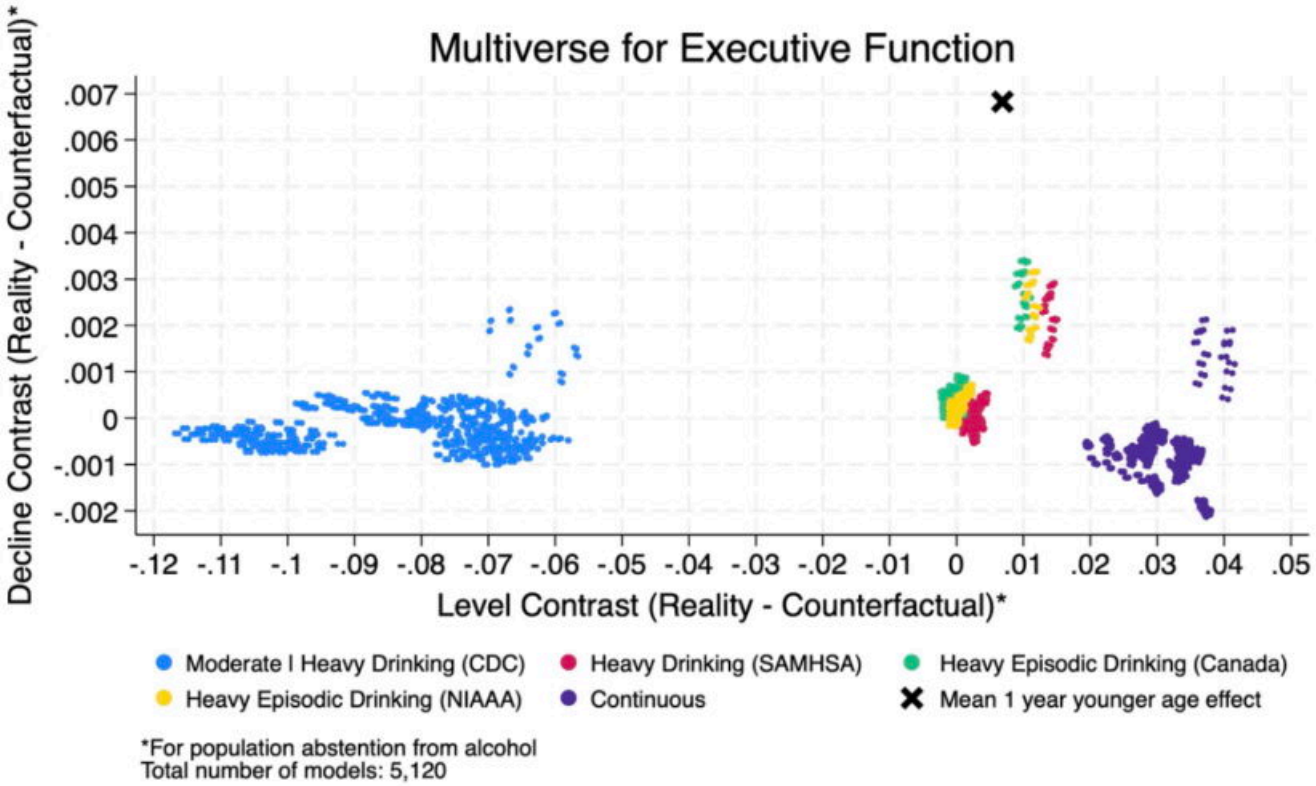
Assessing the Impact of Differential Alcohol Consumption Operationalization and Covariate Adjustment on Cognitive Outcomes in KHANDLE: A Multiverse Analysis David Kapaon* David Kapaon Shelli Vodovozov Anna M. Pederson Scott C. Zimmerman Ruijia Chen Paola Gilsanz Elizabeth Rose Mayeda Rachel Whitmer Laura A. Schmidt Suzanna M. Martinez Yvette C. Cozier Rebecca E. Graff Cynthia I. Campbell Stacy A. Sterling M. Maria Glymour

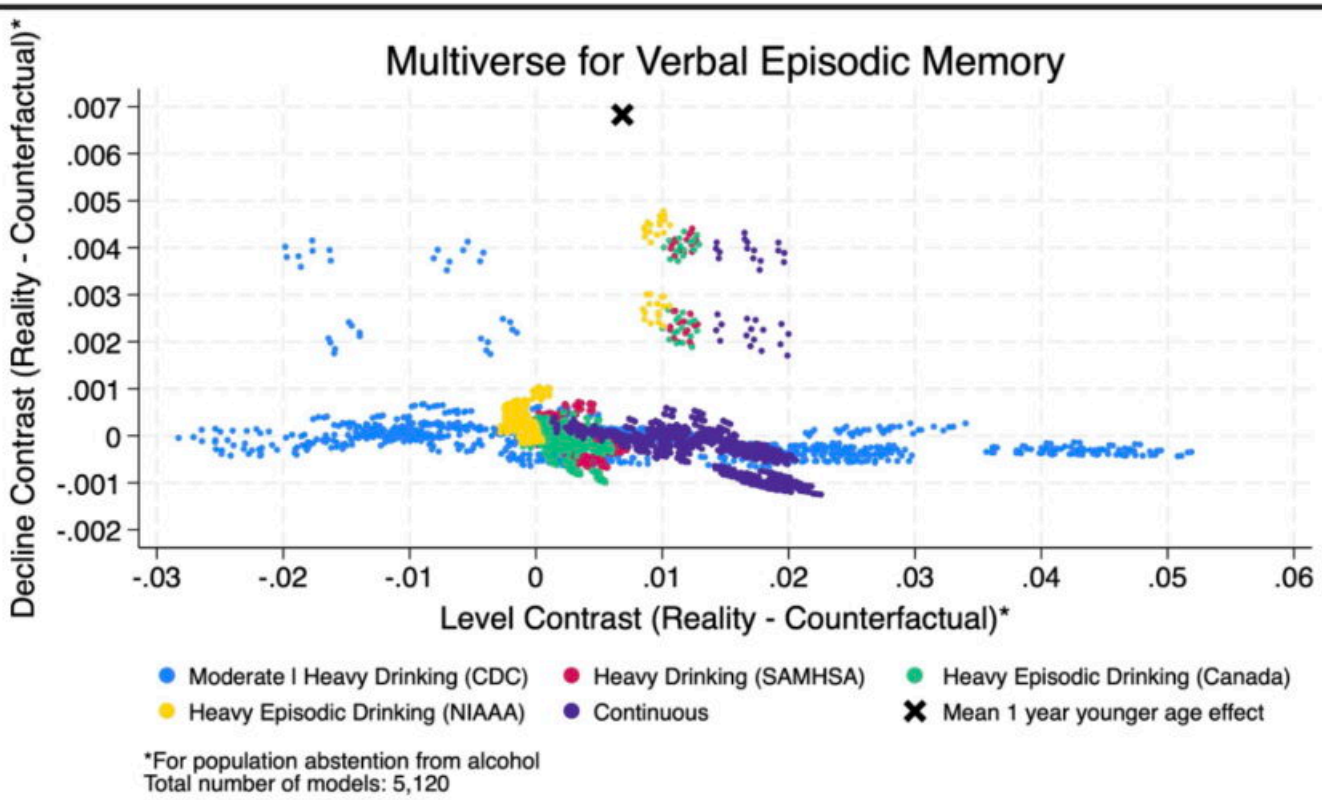
Research indicates heavy drinking harms older adults' cognition. However, evidence on low-to-moderate drinking is mixed, in part due to variability in operationalizing alcohol consumption. We used multiverse analysis to assess alternative measures of alcohol consumption and differential covariate adjustment on cognition.

In the Kaiser Healthy Aging and Different Life Experiences Study, executive function (EF) and verbal episodic memory (VM) scores were z-standardized to wave 1. Each wave, participants reported the number of days/week drinking in the past 3 months (frequency: 0; 1-6; 7) and drinks/day when drinking (volume: 0; 1; 2; 3; 4+). We derived a continuous measure of alcohol consumption (drinks/week) and four sex-specific measures using definitions from US/Canadian federal agencies. Using parametric g-computation, we looped through all exposure-covariate combinations and ran linear mixed models with random intercepts (10,240 models). All models adjusted for sex, race/ethnicity, and age (linear; linear & quadratic). Covariates in the multiverse included sociodemographic, anthropometric, psychosocial and behavioral factors, interview mode, and enrollment cohort. For each model, we estimated contrasts in cognitive levels and declines between the observed world and a counterfactual world where all respondents abstained from drinking.

75% of the sample reported no alcohol consumption. Models with the CDC's drinking definitions showed the greatest heterogeneity in estimated effects, ranging from moderately worse outcomes (EF level = -0.12 SD; 95% CI: [-0.21, -0.02]) to small improvements (VM level = 0.05 SD; [-0.05, 0.15]) for abstention across models. No models showed substantial differences in average rates of EF or VM decline.

Abstention achieved small population impacts on cognition, likely due to high proportions of non-drinkers. Multiverse analysis revealed effects differed in sign depending on alcohol consumption operationalization and covariate adjustment.


Multiverse for Executive Function
Decline Contrast (Reality - Counterfactual)*
.007
.006
.005
.004
.003
.002
.001
0
-.001
-.002
-.12 -.11 -.1 -.09 -.08 -.07 -.06 -.05 -.04 -.03 -.02 -.01 0 .01 .02 .03 .04 .05
Level Contrast (Reality - Counterfactual)*
Moderate I Heavy Drinking (CDC)
Heavy Drinking (SAMHSA)
Heavy Episodic Drinking (Canada)
Heavy Episodic Drinking (NIAAA)
Continuous
Mean 1 year younger age effect
*For population abstention from alcohol
Total number of models: 5,120


Multiverse for Verbal Episodic Memory
Decline Contrast (Reality - Counterfactual)*
.007
.006
.005
.004
.003
.002
.001
0
-.001
-.002
-.03 -.02 -.01 0 .01 .02 .03 .04 .05 .06
Level Contrast (Reality - Counterfactual)*
Moderate I Heavy Drinking (CDC)
Heavy Drinking (SAMHSA)
Heavy Episodic Drinking (Canada)
Heavy Episodic Drinking (NIAAA)
Continuous
Mean 1 year younger age effect
*For population abstention from alcohol
Total number of models: 5,120

Aging

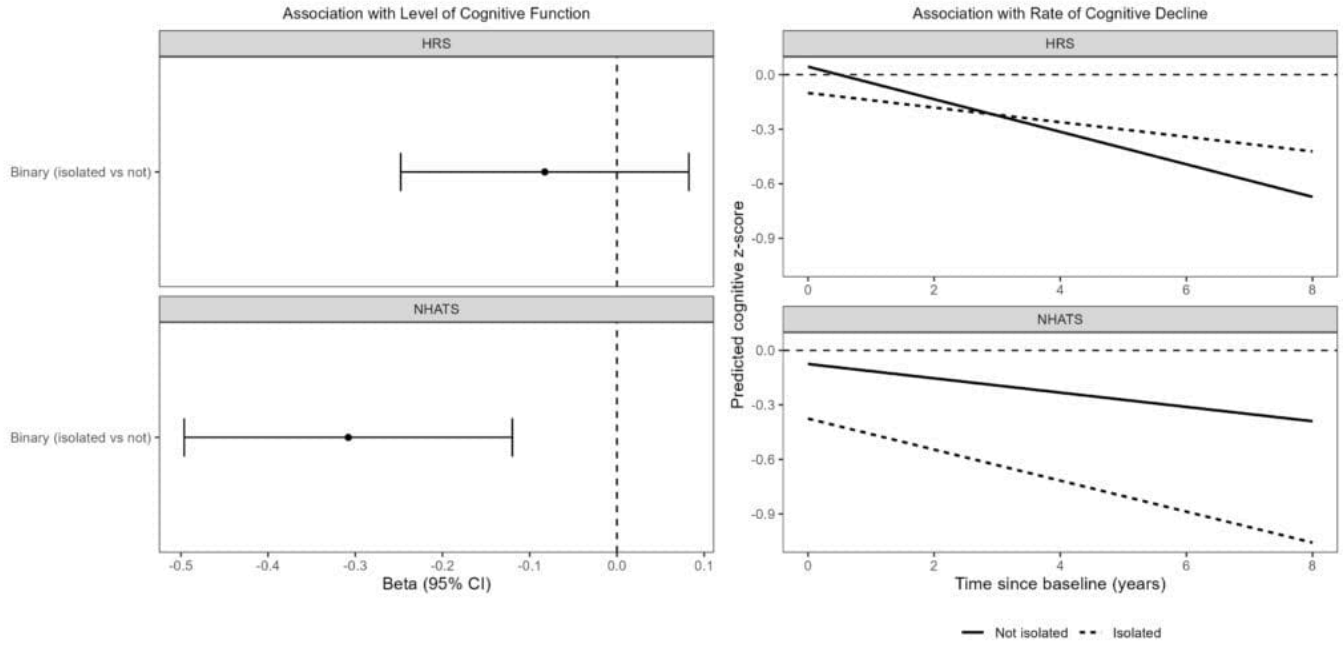
Triangulating Evidence on Social Isolation, Cognitive Function, and Dementia Risk Among Adults Aged 90 Years and Older Andrew Philips* Andrew Philips Dylan Tran Eleanor Hayes Larson Afzalbek Fayzullaev M. Maria Glymour Maria Corrada Elizabeth Rose Mayeda Ruijia Chen

Social relationships change with age, and the impact of social isolation may differ in those aged ≥90 years. However, evidence on associations of social isolation with cognitive aging in this age group is limited.

We used the 2012-2020 Health and Retirement Study (HRS) and the National Health and Aging Trends Study (NHATS), restricted to participants ≥90 years (HRS n=416, NHATS n=396). In both cohorts, social isolation was operationalized using items conveying marital status, living arrangement, frequency of contact with network members, and social participation (HRS: 0-5, NHATS: 0-4). Social isolation was modeled both as a continuous and binary measure (top quintile in HRS, ≥2 in NHATS). Cognitive function in HRS (range 0–27) and NHATS (range 0–33) was assessed using measures capturing memory and orientation, with scores standardized to baseline mean and SD. Dementia was defined using the Langa-Weir algorithm for HRS and AD-8 for NHATS. We fit linear mixed-effects models for cognitive level and decline, and Cox proportional hazards models for dementia risk for those without prevalent dementia at baseline, adjusting for baseline age, sex, race, education, and depression. Inverse probability weights accounted for attrition due to death and loss to follow-up.

In NHATS, greater social isolation was associated with lower cognitive levels (-0.21, 95% CI: -0.3, -0.12) and faster annual rate of decline (-0.03, 95% CI: -0.05, -0.01), with similar findings for the binary measure. However, no such associations were observed in HRS. 33% of HRS participants and 53% of NHATS participants developed dementia during follow-up, but social isolation was not associated with dementia risk in either cohort.

Social isolation may be associated with lower cognitive function and faster cognitive decline among those aged ≥90 years, although findings were inconsistent across cohorts. More data and a harmonized measurement approach is needed to strengthen evidence in this population.


Association with Level of Cognitive Function
HRS
Binary (isolated vs not)
NHATS
Binary (isolated vs not)
-0.5
-0.4
-0.3
-0.2
-0.1
0.0
0.1
Beta (95% CI)
Association with Rate of Cognitive Decline
HRS
NHATS
Predicted cognitive z-score
0.0
-0.3
-0.6
-0.9
0
2
4
6
8
Time since baseline (years)
Not isolated
Isolated

Autoimmune Disease

Hospitalization Trends and Projections of Autoimmune Diseases in the United States: A Nationwide Analysis, 2000-2030 Minkyo Song* Minkyo Song Choa Yun Ana F. Best

Autoimmune diseases impose a growing healthcare burden, yet population-level evidence remains limited. We examined hospitalization trends of 28 autoimmune diseases in the U.S. using a nationally representative database, and projected rates over the next decade.

We analyzed the Nationwide Inpatient Sample, restricting analyses to autoimmune conditions with annual rates >10 per 100,000 hospitalizations. Age- and sex-standardized rates were analyzed using joinpoint regression and summarized as annual and average annual percentage changes (APC, AAPC). Hospitalization rates were projected through 2030 using ARIMA and AAPC.

We analyzed >66 million autoimmune disease-related hospitalizations. In 2022, rates ranged from 21 to 2,368 per 100,000 hospitalizations, highest for type I diabetes mellitus, inflammatory bowel disease, and rheumatic fever/rheumatic heart disease. Joinpoint analysis showed consistently increasing APC trends for 15 of 28 diseases, declining trends for one, and mixed or multi-phase patterns for the remainder. From 2000 to 2022, 25 diseases increased significantly, with the largest AAPCs observed for celiac disease (AAPC=11.1%, 95% CI: 10.6% – 12.0%), autoimmune hepatitis (10.9%, 7.5% – 14.5%), and autoimmune thyroiditis (9.1%, 8.7%-9.6%), while type 1 diabetes mellitus (−1.0%, −1.3% – −0.5%) and pernicious anemia (−3.2%, −3.5% – −2.8%) declined. Projections indicated increases for most diseases through 2030 with type 1 diabetes, inflammatory bowel disease, and rheumatoid arthritis remaining most prevalent. Trends were consistent across forecasting methods and in analyses excluding the pandemic period.

Hospitalizations for most autoimmune diseases increased over the past two decades in the U.S., reflecting a growing healthcare burden. These trends likely reflect changes in disease burden, diagnosis, and healthcare utilization. Further research is warranted to identify underlying drivers and inform prevention and health system planning.

LATEBREAKER

Behavior

Impact of neighborhood characteristics on leisure-time physical activity among school employees working on the Texas-Mexico border Zuber D. Mulla* Zuber Mulla Jennifer J. Salinas

Aim: Reporting both relative and absolute measures of association allows for a comprehensive assessment of the public health impact of exposures. Our aim was to quantify the association between selected neighborhood characteristics (and demographics) and the outcome of leisure-time physical activity among school employees working on the Texas-Mexico border.

Methods: Subjects were school employees working in El Paso County who participated in a pilot study of a walking challenge intervention trial. Cross-sectional analyses were performed in which the binary outcome was the frequency of leisure-time physical activity during the majority of the past year: Subjects who spent most of their leisure time without engaging in much physical activity (the sedentary group) were compared to those who were more active. Predictors included neighborhood environment variables. Adjusted prevalence ratios (PR), adjusted prevalence differences (PD) and 95% confidence limits (CL) were calculated.

Results: Mean age of the 80 employees was 44.4 y. Of the 80, 35% were classified as sedentary. No associations on the relative scale between the following neighborhood environment factors and the outcome of being sedentary were found: Crime rate; high traffic; and presence of sidewalks. Subjects >=50 y of age were 92% more likely than those <50 to be sedentary (Adjusted PR=1.92, 95% CL: 1.11, 3.31, p=0.02). The age-adjusted PD for subjects who somewhat agreed or strongly agreed that the crime rate in their neighborhood makes it unsafe to go on walks at night was -22.6% (95% CL: -42.3%, -2.9%, p=0.02).

Discussion: We found a positive correlation between age and sedentary behavior during leisure time on the relative scale and an inverse association between neighborhood crime and sedentary behavior on the absolute scale. It is possible that individuals who live in neighborhoods that are not conducive to walking outdoors may be engaging in physical activity at home, work, and/or in fitness centers.

Behavior

Associations of Weight Teasing and Related Distress with Orthorexic Eating among College Students Cynthia Yoon* Cynthia Yoon Craig

Background: Orthorexic eating (OE) refers to preoccupation with foods perceived as healthy accompanied by rigid dietary rules. OE is prevalent among college students and associated with adverse health outcomes, highlighting the need to identify modifiable and preventable risk factors.

Objective: To examine the associations of weight teasing and weight teasing related distress with OE among college students.

Methods: Data were drawn from 1,647 college students in 2022-2023 (Mage=20.5±3.3 years; 58.7% female). Independent variables included self-reported weight teasing by friends or family members and related distress. Dependent variable, OE, was assessed using the ORTO-15 (<35 points). Covariates included age, sex, ethnicity/race, parental educational attainment, and BMI. Modified Poisson regression examined associations of weight teasing and related distress with OE.

Results: Students who experienced weight teasing from friends or family each had 1.24 (95% CI=1.04-1.48) and 1.22 times (95% CI=1.03-1.44) the prevalence of OE, respectively, compared to those not teased, after adjustments. Among students teased by friends, those reporting distress ‘a little ’ or ‘a lot’ had 1.25 (95% CI=0.74-2.11) and 1.90 (95% CI=1.13-3.20) times the prevalence of OE, respectively, compared to those not distressed. Among those teased by family members, students reporting distress ‘a lot’ had 1.32 (95% CI=0.86-2.04) times the prevalence of OE compared to those not distressed.

Conclusion: Weight teasing and related distress were associated with greater OE prevalence among students, with stronger associations observed for teasing by friends and higher levels of perceived distress. OE prevention efforts may benefit from incorporating strategies that reduce weight-based teasing and stigma within peer and campus environments.

LATEBREAKER

Big Data/Machine Learning/AI

Depression Risk and Potential Benefit from Social Participation among Japanese Older Adults: A Machine Learning Based Approach Yuta Takemura* Yuta Takemura Kosuke Inoue Naoki Kondo

Depression is a major global public health challenge, and social participation (SP) is a key preventive factor. A previous study found that the association between SP and reduced depression risk is particularly pronounced among older adults with low socioeconomic status (SES), suggesting its potential to reduce mental health disparities. However, the extent to which baseline risk is correlated with the magnitude of benefit derived from SP remains unclear. Using data from Japan Gerontological Evaluation Study data for adults aged ≥65, we aimed to (i) develop a prediction model for depression, (ii) identify key predictors, and (iii) evaluate the correlation between predicted risk and preventive benefit to identify populations at high risk and high benefit. Using baseline covariates in 2016 as predictors and depressive symptoms (GDS≥5) in 2022 as the outcome, we compared logistic regression, lasso regression, random forest, XGBoost, and SuperLearner models. For the model with the highest AUC and lowest Brier score, we assessed variable importance. We then examined the correlation between predicted depression risk and individual-level benefit of SP from causal forest model using Spearman's rank correlation. Among all models, lasso regression outperformed others (AUC=0.741 [95% CI: 0.724-0.759]; Brier score of 0.12). The most influential predictors in the model were 10 baseline GDS items. Predicted depression risk was positivity correlated with the predicted benefit of SP (ρ=0.40). Individuals in the high-risk and high-benefit group were more likely to be older and have lower SES, characterized by unemployment, unmarried or living alone, and lower educational attainment and household income. These findings indicate that individuals at higher risk of depression are also those who derive greater preventive benefit from SP. Promoting SP may therefore be an effective strategy to both prevent depression and reduce socioeconomic disparities in mental health.

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LATEBREAKER

Big Data/Machine Learning/AI

MOMENTS: a linked maternal–infant database for rural, social-context epidemiology in South Dakota Christine Hockett* Christine Hockett Traci A Bekelman Semhar Michael Lacey A McCormack Fredrick Berendse Tianna Beare Madison Palecek Katelyn Strasser Heather Petermann Amy Elliott Kimberlee McKay

Machine-learning (ML) prediction models are increasingly used in epidemiology to identify high-risk patients from electronic health records (EHRs), but equity and interpretability improve when clinical data are paired with social context and service-use information. Maternity Outcomes, Metrics and Evidence for periNaTal Services (MOMENTS) is a board-governed South Dakota (SD) maternal–infant database that integrates individual-level EHR data with individual- and community-level social determinants of health (SDoH) and public/health-service utilization data. MOMENTS includes pregnant people receiving perinatal care at Avera Health-an integrated rural system spanning 72,000 sq. miles-and their infants (>26,000 dyads; >70% rural) from one year pre-pregnancy through one year postpartum. The database includes demographic, clinical, health services use, and social variables at the individual, household and community levels (e.g. Area Deprivation Index, SNAP/WIC participation). Key strengths include linkage of health-system records with state administrative data, longitudinal time-varying measures, referral services received, high data quality, and governed access under a formal policy structure. An example use case is a project recently funded by NIH focused on developing a trimester-specific ‘whole-person’ obstetric risk scores to reduce maternal morbidity. Outcomes include clinical and social sub-scores and an ensemble “whole-person” score using explainable statistical and machine learning models (e.g. XGBoost with SHAP-based variable ranking), internal training/validation, and performance metrics. Two stages of qualitative interviews will be conducted to help understand strategies to support the reach, effectiveness, adoption, implementation, and maintenance of the risk score. MOMENTS provides an opportunity to accelerate equitable use of ML research, while acknowledging its limitations of generalizability, data missingness, and misclassification related to EHR data, and small-area re-identification risk related to the inclusion of rural/frontier areas. This presentation will 1) describe MOMENTS development and governance, 2) highlight a use case, and 3) share lessons learned for other states or single-payer systems.

Big Data/Machine Learning/AI

Improving Detection of Adolescent Prescription Opioid Misuse Using Machine Learning with Synthetic Oversampling Asef Raiyan* Asef Raiyan Hoque Dang Huu Thien Nguyen

Background: Prescription opioid misuse among adolescents is a major public health concern. Population-based surveillance systems provide valuable data for developing predictive models to support early identification of youth at risk of opioid misuse. However, supervised machine learning models applied to these datasets often face severe class imbalance, resulting in misleadingly high accuracy and area under the receiver-operating characteristic curve (AUC), driven primarily by correct classification of non-misuse cases. Consequently, model sensitivity is often low, limiting the ability to identify adolescents at risk.
Methods: This study utilized the CDC's nationally representative Youth Risk Behavior Surveillance System (YRBSS) data from 2017-2021. We evaluated performance of eight supervised machine learning models. To address pronounced outcome imbalance, the Synthetic Minority Over-sampling Technique (SMOTE) was applied to the training data to assess whether correcting class imbalance improves minority-class detection without substantially compromising overall performance. Model performance was evaluated using accuracy, sensitivity, specificity, ROC AUC, precision, and F1-score.
Results: Across all models, application of SMOTE improvement sensitivity and F1-score, indicating improved detection of adolescents at risk of prescription opioid misuse. Random Forest and Extreme Gradient Boosting demonstrated the most favorable performance metrics, with the largest gains in sensitivity 18.37% to 84.33% and 21.10% to 87.39%, respectively. These improvements indicate a marked reduction in false negative classification. While accuracy declined for some models, ROC AUC and F1-score improved consistently, and specificity remained high.
Conclusion: Application of SMOTE resulted in substantial improvements in sensitivity and F1-score across models, enabling more accurate identification of adolescents at risk of prescription opioid misuse. These gains were achieved with minimal loss in specificity, preserving strong classification of non-misuse cases. Our findings suggest that resampling approaches such as SMOTE can be a practical and effective tool for improving case detection when applying machine learning to imbalanced public health data.

Cancer

Life’s Essential 8 and Cancer Risk: A Multistate Causal Mediation Analysis of Incident Cardiovascular Disease Minji Jung* Minji Jung Zhengyi Deng Marvin Langston Benjamin I. Chung

Background: Life’s Essential 8 (LE8) is a comprehensive measure of cardiovascular health (CVH), with higher scores indicating better CVH. Higher LE8 has been linked to lower cancer risk, but the extent to which incident cardiovascular disease (CVD) mediates this association is unclear.

Methods: In UK Biobank (2006–2010 enrollment; follow-up to May 2022), we analyzed 172,053 adults free of cancer and CVD at baseline with complete LE8 and covariates. LE8 (0–100) was categorized as High (80–100), Middle (50–79), and Low (0–49). Incident cancers were ascertained via cancer registries, and incident CVD was identified from hospital records. HRs were estimated using multivariable Cox models. Mediation by CVD was assessed using multistate causal mediation methods for time-to-event data and summarized as the proportion eliminated (PE) at 5, 10, and 15 years.

Results: Mean (SD) age at baseline was 55.2 (8.1) years; 49.0% were male; 95.7% were White. Participants were 19.4% High, 73.6% Middle, and 7.1% Low LE8. Lower LE8 was associated with higher overall cancer risk (Middle vs High: HR=1.15, 95% CI: 1.10–1.20; Low vs High: HR=1.41, 95% CI: 1.32–1.50). Low vs High LE8 was associated with higher risk of breast (HR [95% CI]=1.24 [1.06–1.46]), colorectal (1.57 [1.29–1.90]), pancreatic (2.03 [1.36–3.04]), kidney (2.09 [1.45–3.03]), uterine (2.54 [1.77–3.66]), and lung cancer (6.43 [4.90–8.44]). Incident CVD mediated up to 10.61% (95% CI: 0.23–21.08) of the LE8–overall cancer association (maximum PE across 5, 10, and 15 years), and up to 8.39% (lung), 12.56% (uterine), 20.42% (colorectal), 30.52% (pancreatic), and 63.58% (kidney).

Conclusions: Better CVH, assessed by LE8, was associated with lower risk of overall and several site-specific cancers. Incident CVD partially mediated these associations, modestly for overall cancer but substantially for certain sites, suggesting both CVD-mediated and CVD-independent pathways.

Cancer

Physical Activity and Breast Cancer Outcomes in the Kaiser Pathways Cohort Study of Breast Cancer Survivors Tanvi Srivastava* Tanvi Srivastava Lia L D'Addario Erin L Van Blarigan Janise M Roh Lawrence H Kushi

Physical activity (PA) improves survival and quality of life in breast cancer (BCa) survivors. Yet, limited research to date has been conducted in racially and ethnically diverse cohorts. We examined post-diagnosis PA in relation to cancer outcomes among women with BCa in the Pathways Study at Kaiser Permanente Northern California.

The cohort of 4,504 recently diagnosed BCa patients enrolled between Jan 2006 and May 2013 provided data through surveys and medical records. The cohort was followed for recurrence and mortality outcomes, with follow-up through Dec 31, 2022 for our study. We classified PA at enrollment based on meeting the World Health Organization (WHO) guideline of at least 7.5 MET-hours/week (yes/no). We first explored racial/ethnic variation in participant PA levels using $\chi 2$ tests and multinomial logistic regression. We used Cox Proportional Hazards models to examine associations of PA with BCa recurrence, BCa progression (recurrence or mortality), and all-cause mortality. We applied Multiple Imputation using Chained Equations to address missing data.

Among 4,386 BCa survivors with baseline PA data, 79% of non-Hispanic White (NHW), 73% Asian American (AA), 73% Hispanic, and 70% non-Hispanic Black (NHB) patients met the WHO PA guideline. The median PA level was 23 MET-hrs/wk among NHW, 18 MET-hrs/wk among AA, 17 MET-hrs/wk among Hispanic, and 14 MET-hrs/wk among NHB patients. Across race/ethnicity, meeting the WHO guideline was associated with a 22% lower rate [Adj. HR= 0.78 (0.68, 0.90)] of all-cause mortality and a 15% lower rate of BCa progression [Adj. HR= 0.85 (0.75, 0.96)] compared to not meeting the guideline. We found no statistically significant associations between PA and BCa recurrence.

These findings support promotion of guideline-level PA among breast cancer survivors and highlight the need to address barriers to physical activity among racially and ethnically minoritized groups of breast cancer survivors.

Cancer

Beyond Body Surface Area: Microsimulation of Muscle-informed Chemotherapy Dosing to Improve Treatment Completion for Colon Cancer Anlan Cao* Anlan Cao Alexandra Binder Kathryn H. Schmitz Jeffrey A. Meyerhardt Bette Caan Elizabeth Cespedes Feliciano

Chemotherapy is primarily dosed by body surface area (BSA) despite wide variability in drug distribution and clearance, contributing to frequent toxicities that lead to dose reductions/delays and compromise efficacy. Since low muscle mass is a predictor of toxicities, muscle-informed dosing may improve tolerability. We used microsimulation to evaluate whether muscle-informed dosing improves treatment completion.

We analyzed 94 patients with stage II-III colon cancer treated with FOLFOX at Kaiser Permanente. Body composition was quantified from CT scans. Chemotherapy delivery was obtained from the electronic health record (EHR), and toxicities were collected each cycle. We developed a cycle-by-cycle microsimulation to model: (1) delivered doses of 5-FU and oxaliplatin, (2) dose modifications, delays, and discontinuation, and (3) toxicities. Delivered doses influenced toxicities, and toxicities affected the subsequent dose changes. Predictors were selected using cross-validated grouped LASSO; discrimination and calibration were evaluated with cross-validation and recalibrated out-of-sample if needed. We simulated BSA- and muscle-informed dosing, respectively. The primary outcome was relative dose intensity (RDI; 0-100%, higher=better completion).

Sub-models showed moderate-to-good performance (AUC 0.68-0.92 with acceptable calibration). Under BSA-dosing, the mean RDI was 77.0% (IQR: 72.7-82.0), similar to observed RDI (78.7%, IQR: 72.0-92.0, P=0.34), indicating acceptable simulation performance. Under muscle-informed dosing (38.5 mg/cm2 for 5-FU and 1.2 mg/cm2 for oxaliplatin), projected RDI was 82.0% (IQR: 68.2-94.8), representing a 5% increase compared to the BSA-dosing (95% CI: 2.1-7.8, P<0.001).

Muscle-informed dosing may improve chemotherapy completion. Next, we will perform a target trial emulation in an EHR cohort (N~2,000) to estimate survival benefits. Our findings could transform personalized cancer treatment by informing future trials and dosing guidelines.

Cancer

Sources of financial support accessed by AYA cancer survivors using fertility cryopreservation strategies Taylor Ellington* Taylor Ellington Jama Brookes Ariana Khan Austin R. Waters Anne C. Kirchhoff Salene M.W. Jones Renata Abrahão Mallory Casperson Chun R. Chao Marlaine Figueroa Gray Kathryn J. Ruddy Candice A.M. Sauder Karen J. Wernli Jessica Chubak Erin E. Hahn Theresa H.M. Keegan Lawrence H. Kushi Hazel B. Nichols

Clinical guidelines recommend fertility counseling for adolescent and young adults (AYAs) undergoing gonadotoxic cancer treatments. Fertility preservation strategies such as sperm, oocyte, or embryo cryopreservation are expensive and often not covered by insurance, potentially leading to financial hardship. We assessed the relation between use of cryopreservation strategies at cancer diagnosis and accessing external financial support among 3,410 survey respondents in the VOICE Study. Participants were diagnosed with 10 common AYA cancers at ages 15-39 years in California and North Carolina during 2013-2022 and surveyed in 2023-24. External financial support was measured with 9 items including savings, family, community, government, employer, student loans, crowdfunding or donations, hospitals, and other sources. Multivariable Poisson regression was used to calculate prevalence ratios (PR) and 95% confidence intervals (CIs) for accessing any external financial support according to use of cryopreservation and adjusted for the following characteristics at cancer diagnosis: age, sex assigned at birth, diagnosis year, income, employment, children, partner status, and cancer stage. Overall, 13% (N=458) of survivors used cryopreservation; 65% reported accessing ≥1 source of external financial support, with 44% accessing ≥2 sources. In multivariable models, survivors who used cryopreservation at diagnosis had a 20% higher prevalence of accessing external financial support (PR 1.2; 95% CI 1.1, 1.4) compared to those who did not. The association between cryopreservation and external financial support was similar by sex (males: PR 1.2; 95% CI 1.0, 1.4; females: PR 1.3; 95% CI 1.1, 1.5). Our analyses highlight the high proportion of AYA cancer survivors who access external sources of financial support to meet their cancer-related costs. Ongoing efforts focused on financial navigation may help facilitate fertility preservation for AYAs with cancer.

Cancer

Understanding Colorectal Cancer Etiology: The Paradigm III Conceptual Model Tanvi Srivastava* Tanvi Srivastava David H Rehkopf Melissa L Bondy Erin L Van Blarigan Salma Shariff-Marco John S Witte Michael B Potter Alan Venook Robert A Hiatt

Colorectal cancer (CRC) is the second leading cause of cancer-related death in the US. By 2030, ~25% of CRC cases are projected to occur in individuals under age 50. To better understand the multifactorial etiology of CRC and early-onset CRC (EO-CRC), we developed a dynamic conceptual model to guide research efforts and improve risk communication to the public.

Building on the Paradigm II breast cancer etiology model, we conducted a literature review to identify risk factors for CRC and EO-CRC. Each factor was assessed for data quality, strength of evidence, and potential interactions, and classified within four domains: biologic, behavioral, social, and environmental. We graded the strength of association as strong (RR > 2.0), modest (RR = 1.5–2.0), or weak (RR < 1.5), and rated overall evidence quality as high, medium, or low according to US Preventive Services Task Force criteria, considering study design, internal validity, consistency, precision, directness and applicability to the target population.

We identified 31 factors of potential etiologic importance across the four domains associated with CRC and EO-CRC. High-quality evidence shows higher EO-CRC incidence in Hispanic populations. Alcohol intake and obesity modestly raise overall CRC risk. Enterotoxigenic Bacteroides fragilis and inflammatory bowel disease (IBD) strongly increase overall CRC incidence. IBD also modestly raises EO-CRC risk. Medium-quality evidence shows that higher vegetable consumption modestly reduces CRC incidence. Low-quality evidence suggests that lower area-level income may weakly increase CRC risk. The Paradigm III framework will be publicly available as an interactive, evidence-based online tool.

This conceptual model provides a novel framework for examining multiple etiologic factors that affect CRC risk and supports ongoing mathematical modeling of long-term benefits of interventions targeting modifiable biologic, behavioral, social, and environmental factors.

Cancer

Sources of dietary sugar and site-specific cancer risk in the NIH-AARP Diet and Health Study Lynn Ferro* Lynn Ferro David Wahl Linda Liao Paul Albert Rashmi Sinha Erikka Loftfield Emily Vogtmann

Background: In the US, the average daily intake of added sugar, of which 24% is comprised of sugar sweetened beverages (SSBs), is higher than the recommend amount of <10% of daily calories. Added sugar intake is associated with obesity, diabetes, and cardiovascular disease, but inconsistent evidence exists for cancer risk. We investigated the association of added sugar and SSB intake with site-specific cancer risk in the NIH-AARP Diet and Health Study.

Methods: Sex-specific quintiles of added sugar and quartiles for consumers of SSBs (grams/1000kcal/day) were calculated from food frequency questionnaires. SSBs included caffeinated and decaffeinated soda, sweet tea, and fruit flavored drinks (<100% fruit juice). Site-specific cancer incidence was identified by cancer registry linkage through 2018. HRs and 95% CIs were estimated and adjusted for demographic and lifestyle characteristics. Additional models evaluated further adjustment for diabetes and body mass index (BMI), given their potential to be mediators.

Results: At baseline, participants had a mean age of 62 years and 59% were male. After a median follow-up of 19.6 years, 114,149 cancer cases were identified. Added sugar and SSB intake were not associated with most cancers, however they were associated with an increased risk of prostate cancer (added sugar HRQ5vs.Q1:1.22 [1.18-1.27], SSBs HRQ4vs.non-consumers:1.31 [1.27-1.36]) (**Figure 1**). Added sugar and SSB intake were inversely associated with pancreatic cancer, added sugar was inversely associated with rectal cancer, and SSBs were inversely associated with lung adenocarcinoma, however these associations were null after adjustment for diabetes and BMI.

Conclusion: Few associations were observed for added sugar and SSB intake with site-specific cancer risk. While positive associations have been observed for added sugar and SSBs with colorectal and breast cancer risk in some studies, there was no convincing evidence for these associations in the NIH-AARP study.

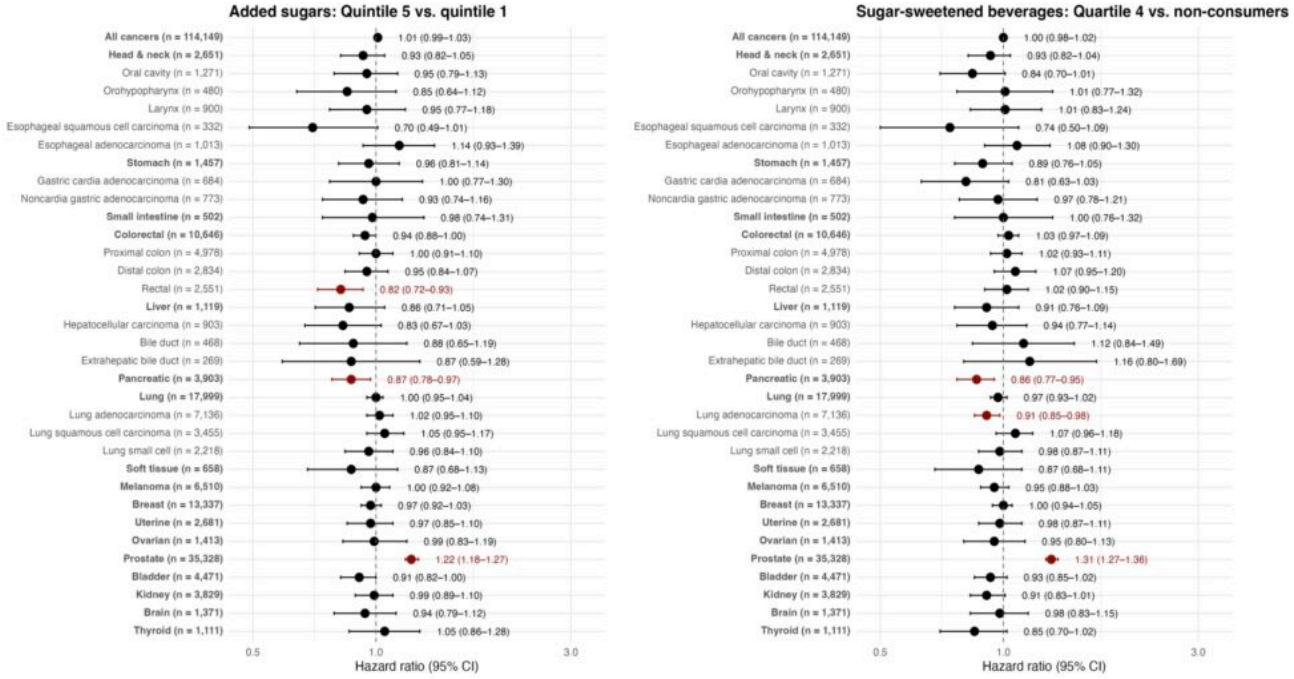


Figure 1. Added sugars and sugar sweetened beverages with site-specific cancer risk in the NIH-AARP Diet and Health Study. Hazard ratios and 95% confidence intervals (CI) for site-specific cancer risk by energy-adjusted grams of added sugar consumption comparing the highest (Q5) to lowest (Q1) quintiles[1] and sugar sweetened beverage consumption comparing the highest quartile (Q4) to non-consumers[2]. Cox proportional hazards regression models adjusted for sex, race/ethnicity, education, marital status, caloric intake, alcohol use, coffee consumption, physical activity, smoking status, and overall health status. Female-specific cancers were also adjusted for years of oral contraceptive use and number of live births. Overall cancer includes those listed and other, rarer cancers that were not analyzed individually.

[1]Median (range) for Q1 and Q5 of added sugars (grams/1000kcal/day):
Males – Q1: 9.85 (0.38-12.61), Q5: 45.27 (34.72-231.56)
Females – Q1: 10.81 (0.42-13.69), Q5: 45.51 (34.71-230.26)
[2]Median (range) for non-consumers and Q4 of SSBs (grams/1000kcal/day):
Males – Non-consumers: 0, Q4: 316.83 (189.90-2266.63)
Females – Non-consumers: 0, Q4: 326.0 (187.35-2260.78)

Cancer

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

Introduction

The Connect for Cancer Prevention Study is a prospective cohort focusing on cancer etiology, risk prediction, and early detection, with a goal to recruit 200,000 participants from 10 U.S. integrated healthcare systems. Baseline activities include online surveys and biospecimen collections, and new biospecimen activities are planned.

Methods

The current baseline protocol collects urine, mouthwash, and blood (serum, EDTA plasma, Streck Nucleic Acid tubes). Biospecimens are shipped in temperature-controlled coolers to a central NCI lab for processing and long-term storage. Mouthwash is also collected at home via mailed kits. Follow-up collections approximately every three years after study entry will mirror the baseline protocol, with modifications possible in the future. A cancer early-detection subcohort will include blood tubes optimized for liquid biopsy assays, collected annually in between follow-up collections. Fecal collections will be research-specific collections using mailed kits validated for human microbiome analyses. Participants will complete surveys of pre-analytical factors relevant to each collection.

Results

As of January 2026, 61,941 of 88,363 Connect participants (70%, 46%-81% across sites) donated baseline biospecimens, with collections still ongoing. Participation in biospecimen donations was similar by sex and race but increased with age. Over 46% of mouthwash samples were collected via home kits (return rate of 75%) which were received a median of 9 days from shipment (IQR 6-20 days). Over 90% of participants who donated biospecimens completed the biospecimen survey. The majority of participants donated specimens within one month of consent.

Conclusion

After successful implementation of baseline biospecimen collections at multiple healthcare sites, plans are in process to collect follow-up biospecimens and other new collections. Data and biospecimens from the Connect Study will be available to the research community in the future.

Cancer

Risks of subsequent primary cancers among the World Trade Center rescue and recovery workers diagnosed with cancer Charles B. Hall* Charles Hall Baozhen Qiao Tabassum Insaf Rachel Zeig-Owens Jiehui Li Andrew Todd James Cone Mark Farfel Moshe Shapiro Nikolina Icitovic Christopher Dasaro Paolo Boffetta

Purpose: We assessed the incidence of subsequent primary cancers (SPCs) among the World Trade Centers (WTC) exposed rescue and recovery workers diagnosed with cancer.

Materials and Method: The incidences of SPCs among WTC-exposed cancer patients with the first primary cancer diagnosed during 2002-2022 in New York state were evaluated using standardized incidence ratios (SIRs), with cancer patients without WTC exposure as the reference population. We calculated SIRs for specific combinations of first and subsequent cancers, also by date of first arrival at WTC site and status of participation in WTC Health Program (WTCHP). Additionally, we conducted multivariate sub-distribution hazard regression analyses to evaluate the association between WTC exposure and SPCs.

Results: 827 (12.8%) SPCs were identified among 6,474 WTC cancer patients. Compared to non-WTC cancer patients, WTC cancer patients showed an increased risk of subsequent cancers for all cancers combined (SIR:1.08; 95% CI: 1.01-1.16), prostate (SIR:1.52; 95% CI: 1.30-1.77), and thyroid (SIR:1.54; 95% CI: 1.08-2.14) cancers. Elevated SIRs were also observed for specific combinations of first and subsequent cancers. Earlier arrival at the WTC site and participation in WTCHP were associated with an elevated risk of subsequent cancers. Multivariate modeling showed similar findings.

Conclusions: Our study found elevated overall SPCs risk among WTC cancer survivors, most prominently for subsequent prostate and thyroid cancers. Even though heightened medical surveillance likely played a major role for these increases, WTC exposure could also be a plausible contributor. Further research is warranted to continuously monitor the impact of WTC exposure on risk of SPCs.

Cancer

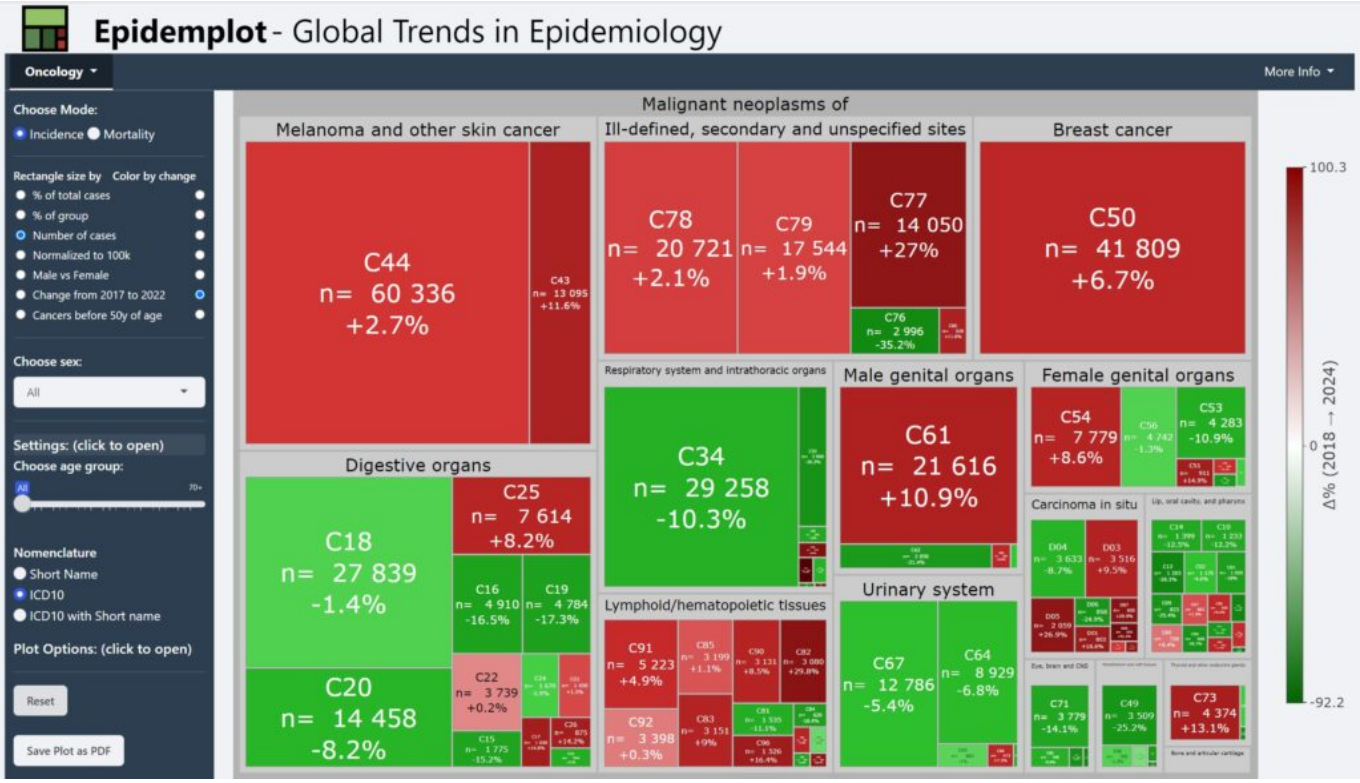
Temporal patterns of cancer incidence and mortality in Hungary: Evidence from nationwide population data Janos Tibor Fekete* Janos Tibor Fekete Zsolt Nagy Balazs Gyorffy

Background: Hungary has a sustained high cancer burden, however, population-based analyses of long-term trends in incidence, mortality, and prevalence across major tumor types remain scarce. Characterizing these temporal patterns is essential for informing cancer surveillance, screening strategies, and healthcare planning.

Methods: ICD10 classification was used to identify cancer diagnoses from the nationwide administrative records of the Hungarian National Health Insurance Fund. Data was analyzed for five major tumor types: breast (C50), colorectal (C18), lung (C34), prostate (C61), and stomach cancer (C16). Annual incidence, mortality, and prevalence were derived for each cancer type over a five-year period (2018 -2024). All metrics were accumulated across both sexes and all age groups.

Results: Temporal trends varied in the five tumor types, but represented consistent nationwide shifts. Breast cancer showed a 6.7% increase in incidence, and a 56.2% surge in mortality, while prevalence increased from 37,887 to 41,809. Lung cancer showed a 10.3% decrease in incidence and a 3.02% reduction in mortality, while prevalence decreased from 31,829 to 29,258. Incidence of colorectal cancer changed minimally (–1.4%), but mortality increased by 25.4%, and prevalence decreased from 28,589 to 27,839. Prostate cancer demonstrated a 10.9% rise in incidence and substantial 40.4% upsurge in mortality, with prevalence rising from 19,046 to 21,616. Stomach cancer exhibited a 16.5% reduction in incidence and a 4.5% lessening in mortality, while prevalence declined from 5,770 to 4,910. A web-based real-time analytical platform was developed to facilitate analysis of further tumor types (www.epidemplot.com).

Conclusion: Nationwide data from Hungary reveal measurable heterogeneous temporal trends of cancer incidence, mortality, and prevalence across major tumor types. Such population-level assessments are key to descriptive epidemiology and robust cancer surveillance.


Epidemplot - Global Trends in Epidemiology
Oncology
More Info
Choose Mode:
Incidence
Mortality
Rectangle size by
Color by change
% of total cases
% of group
Number of cases
Normalized to 100k
Male vs Female
Change from 2017 to 2022
Cancers before 50y of age
Choose sex:
All
Settings: (click to open)
Choose age group:
Nomenclature
Short Name
ICD10
ICD10 with Short name
Plot Options: (click to open)
Reset
Save Plot as PDF
Malignant neoplasms of
Melanoma and other skin cancer
C44 n= 60 336 +2.7%
C43 n= 13 095 +11.6%
Ill-defined, secondary and unspecified sites
C78 n= 20 721 +2.1%
C79 n= 17 544 +1.9%
C77 n= 14 050 +27%
C76 n= 2 996 -35.2%
Breast cancer
C50 n= 41 809 +6.7%
Digestive organs
C18 n= 27 839 -1.4%
C25 n= 7 614 +8.2%
C16 n= 4 910 -16.5%
C19 n= 4 784 -17.3%
C20 n= 14 458 -8.2%
C22 n= 3 739 +0.2%
C15 n= 1 775 -15.2%
Respiratory system and intrathoracic organs
C34 n= 29 258 -10.3%
Male genital organs
C61 n= 21 616 +10.9%
Female genital organs
C54 n= 7 779 +8.6%
C56 n= 4 742 -1.3%
C53 n= 4 283 -10.9%
Carcinoma in situ
D04 n= 3 633 -8.7%
D03 n= 3 516 +9.5%
Lymphoid/hematopoietic tissues
C91 n= 5 223 +4.9%
C85 n= 3 199 +1.1%
C90 n= 3 131 +8.5%
C82 n= 3 080 +29.8%
C92 n= 3 398 +0.3%
C83 n= 3 151 +9%
C81 n= 1 535 -11.1%
C96 n= 1 526 +16.4%
Urinary system
C67 n= 12 786 -5.4%
C64 n= 8 929 -6.8%
C71 n= 3 779 -14.1%
C49 n= 3 509 -25.2%
C73 n= 4 374 +13.1%
100.3
0
-92.2
Δ% (2018 → 2024)

Cancer

Colorectal Cancer Screening Initiation at Age 45 Among Texas Medicaid Enrollees, 2018–2021 Ami E. Sedani* Ami Sedani Caitlin Murphy Samuel V. David Bijal A. Balasubramanian Yong-fang Kuo David S. Lopez

Background: In 2018, the American Cancer Society recommended lowering the colorectal cancer (CRC) screening initiation age from 50 to 45 years, preceding Texas Medicaid coverage in 2021. This coverage gap left low-income adults without routine access despite guideline support. We examined CRC screening initiation at age 45 among Texas Medicaid enrollees during this period.

Methods: We conducted a retrospective cohort study using Texas Medicaid T-MSIS Analytic Files (2018–2021). Enrollees who turned 45 years between May 2018 and December 2020 were included if they had ≥6 months continuous enrollment pre-index (45th birthday), and ≥12 months post-index. We excluded those dually eligible for Medicare, or at increased CRC risk per USPSTF criteria. Screening initiation was defined as completion of any recommended CRC test within 12 months post-index, identified using CPT/HCPCS codes. We summarized demographic and clinical characteristics, estimated initiation prevalence, and used multivariable logistic regression to assess adjusted associations between initiation and patient demographics, care utilization, and chronic condition burden.

Results: Of 10,874 enrollees, 3.7% initiated screening within 12 months post-index. Among screening initiators, most underwent direct visualization testing, predominantly colonoscopy (63.5%). Screening prevalence remained low across all years, with a slight increase from <1% in 2018 to 2.0% in 2020. Higher comorbidity burden was the strongest predictor of initiation (OR 4.68, 95% CI 3.32–6.60), while prior primary care visits (OR 1.43, 95% CI 1.14 – 1.79) and female sex (OR 1.39, 95% CI 1.11 – 1.74) showed smaller associations.

Conclusions: CRC screening uptake at age 45 among Texas Medicaid enrollees was extremely low during the coverage gap, even among those with prior primary care engagement. These findings highlight the need for policy alignment and targeted interventions to improve early screening in low-income populations.

LATEBREAKER

Cancer

The Impact of Cardiovascular Diseases on Cancer Screening Utilization: Evidence from a 2016–2024 U.S. National Study Sarala Pandey* Sarala Pandey S. Cristina Oancea

Adults with cardiovascular diseases (CVD) represent a growing U.S. population with complex healthcare needs. While regular cancer screening (CS) is recommended for eligible adults, it is unclear whether the presence of CVD influences engagement in CS. There is limited literature examining CS utilization across specific CVDs, including coronary heart disease (CHD), myocardial infarction (MI), and stroke. Evaluating CS patterns by CVD status at the U.S. national level is essential for informing prevention strategies among high-risk populations. Using nationally representative 2016–2024 BRFSS data, this study examines the association between CVD status (including CHD, MI, and stroke) and CS utilization among U.S. adults, stratified by sex and age-specific CS recommendations. Weighted and adjusted multivariable logistic regression models were used to perform analyses. The weighted and adjusted odds (WAO) of cervical (N= 385,122; 21-65 years old 'YO') CS among females with a history of MI were 18% (95% CI: 0.68, 0.98), significantly smaller than the WAO of corresponding CS among females without MI. The WAO of female colorectal (N= 326,058; 50-75 YO), male colorectal (N= 296,863; 50-75 YO) and male prostate (N= 118,305; 55-69 YO) CS among individuals with CHD were 22% (95% CI: 1.10, 1.36), 30% (95% CI: 1.20, 1.42) and 27% (95% CI: 1.14, 1.42) significantly greater, respectively, than the WAO of corresponding CS among individuals with no CHD. Additionally, marital status significantly modified the association between CHD and CS. Separated or divorced males with CHD had 43% significantly greater WAO (95% CI: 1.23, 1.66) of colorectal CS than their counterparts without CHD. These results demonstrate that specific CVDs are associated with significant differences in CS uptake, highlighting the importance of guideline-based preventive care to reduce health disparities and the risk of complications from comorbid conditions.

LATEBREAKER

Cancer

The role of interpersonal-level sociocultural factors in breast cancer screening in U.S. Hispanic/Latina women: Findings from the Hispanic Community Health Study/Study of Latinos Sociocultural Ancillary Study Vanessa Dávila-Conn* Vanessa Davila Conn Linda C. Gallo Frank J. Penedo Daniela Sotres-Álvarez Christina Cordero En Cheng Krista M. Perreira Amber Pirzada Martha Daviglus Humberto Parada Jr.

Introduction: Compared to non-Hispanic White women, Hispanic/Latina women in the US are more likely to be diagnosed with breast cancer (BC) at later stages, which contributes to disparities in BC outcomes. Interpersonal and sociocultural contexts may impact the utilization of cancer preventive services such as screening, but their roles remain poorly understood. This study assessed whether interpersonal-level sociocultural factors were associated with BC screening among US Hispanic/Latina women.

Methods: This cross-sectional study included 2,414 Hispanic/Latina women aged 40–74 years from the Hispanic Community Health Study/Study of Latinos (HCHS/SOL) Sociocultural Ancillary Study (2010-2012). The primary outcome was self-reported guideline-concordant BC screening, as defined by current U.S. Preventive Services Task Force recommendations. Interpersonal sociocultural constructs were assessed using validated scales, including family relations (9-item Family Environment Scale subscales), perceived social support (12-item Interpersonal Support Evaluation List), acculturation (Short Acculturation Scale for Hispanics), and social networks (20-item Social Network Index). We applied hierarchical structural equation models (SEM) to evaluate the associations between latent interpersonal constructs and screening adherence while accounting for the HCHS/SOL weights and complex survey design.

Results: Most women (75%) adhered to BC screening recommendations. A higher-order latent construct representing family relations—indicated by higher family cohesion and lower family conflict—was associated with greater odds of guideline-concordant BC screening (OR: 5.12; 95% CI: 1.4–18.4).

Conclusion: Interpersonal family dynamics may significantly influence BC screening among Hispanic/Latina women. Family-centered approaches may be relevant for efforts aimed at improving engagement in preventive care and addressing cancer disparities in this population.

LATEBREAKER

Cancer

Reproductive and Exogenous Hormone Exposures and Breast Cancer Among Active-Duty Women in the US Military Caroline Hoffman* Caroline Hoffman Barbara Fuhrman Jennifer Rusiecki Lynsey Lewis Mary Beth Terry Celia Byrne

Reproductive and other hormonal factors have long been associated with an increase in breast cancer rates. It’s unclear whether recent changes in reproductive patterns and use of lower dose exogenous hormones impact the increasing rate of early onset breast cancer in the last two decades. Previous studies also indicated the association between reproductive history and breast cancer risk may differ between white and black women. To better understand hormonal factors related to early onset breast cancer, we conducted a nested case-control study including all breast cancer cases diagnosed among active-duty women in the US military between 2000-2022 (mean diagnosis age of 38). The study includes 711 invasive and 121 DCIS cases with 1711 density sampled controls matched on age and year of diagnosis, race, and year of military enrollment. We evaluated associations with age at last birth and time since last birth with breast cancer among 420 cases and 849 controls who gave birth in the military. Logistic regression models controlling for matching factors estimated the IDR and 95% CI. Any hormonal contraceptive used five or more years increased the rate 42% (95% CI:1.08-1.88) compared to never use. Overall, the breast cancer rate appeared to increase at a later age at last birth. However, this association differed by race; having a last birth at age 35 or older compared to before age 25 increased rates for white women (2.28 (95% CI:1.07-4.99)) but not black women (0.95 (95% CI:0.46-1.92)). Having a birth within ten years of diagnosis was associated with an increased rate (1.22 (95% CI: 0.90-1.65)) after additionally adjusting for number of births. Our findings suggest age and timing of hormonal exposures have an impact on early onset breast cancer rates, though there may be differences by race. Despite the contemporary changes in these hormonal factors, our findings for recent early onset breast cancer parallel those of previous generations.

LATEBREAKER

Cardiovascular

Ferritin-Based Definitions of Iron Deficiency and their Associations with Cardiovascular Disease in Women — National Health and Nutrition Examination Survey, United States, 2003-2018 Domonique Hargrave* Domonique Hargrave Maria Jefferds Laura Hendrickson Yaw Addo

Ferritin-Based Definitions of Iron Deficiency and their Associations with Cardiovascular Disease-mortality in Women – NHANES 2003-2018

Domonique L. Hargrave, MED Jefferds, LP Hendrickson, OY Addo

Background: Iron deficiency (ID) is a major global public health concern, especially among women, and can vary by sociodemographic characteristics. Serum ferritin (SF) measures iron stores. Recently derived physiological SF thresholds (<25 µg/L for women aged <50 years and <33 µg/L for women aged >50 years) identify early treatable ID erythropoiesis. ID is a risk factor for developing cardiovascular disease, and literature suggests ID may be associated with cardiovascular disease (CVD). Our objective was to examine associations between physiological SF thresholds and the risk of CVD in women.

Methods: We conducted longitudinal analyses using National Health and Nutrition Examination Survey (NHANES) data, with linked National Death Index data. We included (N=13,170) non-pregnant women aged ≥20 years who had complete SF and CVD-mortality data, with a mean follow-up time of 8.8 years. We examined associations between ID (physiological SF thresholds) and CVD-mortality using adjusted Cox proportional-hazard models (HRs, 95% Confidence Intervals (CIs). Models were adjusted for age, race/ethnicity, education, and income. Analyses accounted for the complex survey design effects.

Results: The average age of women at baseline was 48.4 years. ID prevalence was 20.2%. There were 1,525 cases of CVD-mortality per 130,684 person-years follow-up. Physiologic ID was associated with CVD-mortality in unadjusted analyses. This association with CVD-mortality was not significant after adjustment for age and sociodemographic factors (aHR: 1.22, 95% CI 0.81-1.86).

Conclusions: Physiological ID thresholds did not predict risk of CVD-mortality in this sample when adjusting for age and sociodemographic factors. Whether screening with non-physiological thresholds might identify individuals with higher risk of CVD-mortality merits further attention.

LATEBREAKER

Cardiovascular

Social drivers of undiagnosed and uncontrolled hypertension in a primary care setting

Karen Schliep* Karen Schliep Sumra Arain Nusrat Emmanuel Adediran Tess Deatley Bernadette Kiraly Kelly Baron Sarang Yoon Camille Moreno Susan Pohl

Introduction

Hypertension is a major contributor to cardiovascular disease and remains disproportionately high among Black adults in the U.S. Despite improvements in awareness and self-monitoring, gaps persist in diagnosis and control, and sex differences may further influence risk. Primary care plays a key role in identifying and treating hypertension, yet the extent to which race/ethnicity and sex disparities continue remains unclear.

Methods

We conducted a retrospective cohort study using University of Utah primary care EHR data from 2015–2025. Adults with ≥2 primary care visits and ≥2 blood pressure measurements were included, excluding those with end-stage renal disease. Hypertension, undiagnosed hypertension, and uncontrolled hypertension were defined using ICD-10 codes, treatments, and blood pressure thresholds (≥140 mmHg or ≥90 mmHg). Sociodemographic and clinical factors were extracted, and Poisson regression with robust error was used to estimate unadjusted and adjusted RR (95% CI).

Results

Among the 301,9322 patients in the study, 213,609 (71%) were hypertensive (diagnosed, undiagnosed, or treated) at some point during follow-up. Among those with hypertension, 118,452 (55%) were undiagnosed, and 54,389 (25%) were uncontrolled. In our adjusted models, we found a lower risk of undiagnosed hypertension but higher risk of uncontrolled hypertension for older vs younger, male vs female, and black/African American or Native Hawaiian/other Pacific Islander vs non-Hispanic white patients. Patients who were Asian, Middle Eastern/North African, or other all had a lower risk of both undiagnosed and uncontrolled hypertension.

Conclusion

Our results highlight the need for primary care and public health systems to strategically apply social risk profiles to guide targeted interventions that improve hypertension detection and control. Further research assessing other social drivers of hypertension control including geographic residence will provide a more complete picture.


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Cardiovascular

Identifying mediators of the effect of cigarette smoking on atrial fibrillation in the Atherosclerosis Risk in Communities (ARIC) Study Oluseye Ogunmoroti* Oluseye Ogunmoroti Alvaro Alonso Olatokunbo Osibogun David Benkeser Ashley I. Naimi

Background: The biological pathways linking cigarette smoking to atrial fibrillation (AF) remain unclear. We quantify AF risk mediation by cigarette smoking-related comorbidities (coronary heart disease [CHD], hypertension [HTN], diabetes mellitus [DM] and obesity) to identify potential intervention targets.

Methods: We analyzed data from 11,580 adults aged 45-64 years at enrollment. Cigarette smoking status was assessed at baseline (1987-1989) by self-report questionnaire and categorized as current, former and never. At visit 3 (1993-1995), the presence of CHD, HTN, DM and obesity was determined using standardized methods. Incident AF was ascertained via ECG, hospital discharge records and death certificates through the end of 2019. Using confounder-adjusted causal mediation analysis, we estimated the risk ratios for the total (TE), natural direct (NDE) and natural indirect (NIE) effects of cigarette smoking on AF, under a no exposure-mediator interaction assumption.

Results: The analytical sample was 44% men and overall mean age (SD) was 54 (6) years at baseline. After a median (IQR) follow-up of 27 (19, 31) years, 2,800 AF cases (24%) were identified. The TE of current smoking (vs. never smoking) on AF was 1.18 (95% CI: 1.08, 1.30) which was similar to the NDE across mediators: CHD 1.18 (1.09, 1.28), HTN 1.19 (1.10, 1.29), DM 1.19 (1.10, 1.28), and obesity 1.19 (1.10, 1.28). The NIE was 1.00 − 1.01 across mediators yielding low proportions mediated: 3% (CHD), 4.8% (HTN), 0.4% (DM), and 0.01% (obesity). The estimates for former smoking were highly imprecise.

Conclusion: The mediation of the effect of cigarette smoking on AF through CHD, HTN, DM, and obesity was minimal. These findings indicate that most of the effect of cigarette smoking on AF is direct, underscoring the importance of smoking cessation. Future research should explore the time-varying nature of these variables along with additional pathways for mediation to identify novel targets for AF prevention.

Cardiovascular

COVID-19 Pandemic-Related Healthcare Disruptions and Risk of Major Adverse Cardiovascular Outcomes Among Older Adults with Multiple Chronic Conditions in New York City, 2020-2024 Lorna Thorpe* Sarah Conderino Rania Kanchi John A. Dodson Yuchen Meng Samrachana Adhikari Jasmin Divers Rajesh Vedanthan Andrea R. Titus Edward Schenck Nichola J. Davis Lorna E. Thorpe

Background: Trends in major adverse cardiac events (MACE) have increased in the years following the COVID-19 pandemic onset. Beyond the direct impacts of COVID-19 infection, healthcare disruptions during the pandemic may have influenced long-term cardiovascular health outcomes. Our objective was to estimate the impact of care disruption on risk of MACE among older adults with multiple chronic conditions (MCC) in New York City (NYC).

Methods: Using electronic health record data from the INSIGHT Clinical Research Network, we established a retrospective cohort of NYC residents aged ≥50 years diagnosed with MCC prior to the pandemic. We monitored their healthcare encounters, diagnoses, and hospitalizations for four years, from March 7, 2020–December 31, 2024. Total care disruption during the acute pandemic was defined as having no ambulatory or telehealth visits for seven months, between March 7, 2020–October 6, 2020. We conducted a survival analysis using accelerated failure time models to assess the association between care disruption and subsequent diagnosis of MACE, defined as hospitalization for acute myocardial infarction, ischemic stroke, heart failure, cardiac arrest, or unstable angina.

Results: Among 271,303 patients in the cohort, 20.3% experienced total care disruption during the acute pandemic phase. On average, adults with disrupted care had lower pre-pandemic healthcare utilization (8.5 vs. 17.1 visits) and fewer comorbidities (3.2 vs. 3.8) than those who received care. A total of 9.4% of patients with disrupted care experienced MACE, compared to 10.2% of those without disrupted care. After adjusting for demographic and pre-pandemic clinical covariates, total care disruption was associated with shorter median time to incident MACE (Time Ratio=0.91; 95% CI: 0.88–0.95).

Conclusion: Total care disruption during the initial months of the pandemic was associated with increased risk of incident MACE in this patient population of NYC older adults with MCC.

Cardiovascular

Coronary Artery Calcium and Incident Atherosclerotic Cardiovascular Disease: An Application of Generalized Heterogeneous Treatment Effect (HTE) Approach Chuyue Wu*
Chuyue Wu Nathan D. Wong Liwei Chen Wenjun Fan Marissa J. Seamans Hua Zhou Roch A. Nianogo

Coronary artery calcium (CAC) is a strong marker of subclinical atherosclerosis, but its prognostic value for atherosclerotic cardiovascular disease (ASCVD) may differ across individual background characteristics. Our objective was to identify baseline factors that meaningfully modify the CAC–ASCVD association and quantify subgroup-specific effects using a generalized heterogeneous treatment effect (HTE) framework. We analyzed 6,784 MESA participants aged 45–84 years free of clinical cardiovascular disease at baseline (2000–2002) and were prospectively followed through 2015. CAC presence was defined by Agatston score >0. Incident ASCVD cases included coronary heart disease, stroke or transient ischemic attack, peripheral vascular disease, and ASCVD-related death. We applied a generalized HTE approach based on parametric g-computation, incorporating stabilized inverse probability of treatment weighting to adjust for baseline confounding and LASSO-regularized logistic models to reduce overfitting and select potential effect modifiers. Counterfactual risk prediction was used to estimate individualized and subgroup-specific conditional average treatment effects (CATEs) on the risk difference scale. A hierarchical clustering approach was then used to identify effect-modifying subgroups. CAC was present in 3,383 participants (49.9%) at baseline, and 1,028 ASCVD events occurred over 15 years. CAC presence was associated with higher ASCVD risk (risk difference 0.10; 95% CI, 0.08–0.12). Greater CAC-attributable excess risk was observed among participants with higher carotid intima-media thickness, older age, higher systolic blood pressure, elevated interleukin-6, larger waist circumference, and a positive family history of cardiovascular disease compared with their counterparts (**Table**). The association between CAC and ASCVD risk is heterogeneous, with stronger effects among individuals with vascular, inflammatory, and metabolic vulnerability. These findings support more selective, context-informed use of CAC testing to guide primary prevention.

Table. Subgroup CATE on the additive (RD) and relative (RR) scale presenting the effect of the presence CAC on incident ASCVD across effect modifiers identified via the generalized HTE approach in the MESA Study, N=6,784

Variable and threshold*	N (%)	CATE (RD, 95%CI)	P for interaction (RD)
Total effect	6784 (100)	0.10 (0.08, 0.12)	-
ICA-IMT (mm)			
<1.07	4518 (66.6)	0.08 (0.06, 0.10)	0.004
>=1.07	2266 (33.4)	0.13 (0.09, 0.17)	
Family history of heart attack or stroke			
No	2943 (43.4)	0.07 (0.04, 0.09)	0.001
Yes	3841 (56.6)	0.12 (0.09, 0.15)	
Systolic blood pressure, mmHg			
<126.12	3692 (54.4)	0.08 (0.05, 0.10)	0.007
>=126.12	3092 (45.6)	0.12 (0.09, 0.15)	
Age at baseline, years			
<62.57	3442 (50.7)	0.06 (0.04, 0.09)	0
>=62.57	3342 (49.3)	0.13 (0.10, 0.16)	
CCA-IMT (mm)			
<0.87	3712 (54.7)	0.05 (0.03, 0.08)	0
>=0.87	3072 (45.3)	0.15 (0.12, 0.18)	
IL-6, pg/mL			
<1.54	4355 (64.2)	0.08 (0.06, 0.10)	0.006
>=1.54	2429 (35.8)	0.13 (0.09, 0.16)	
Waist circumference, cm			
<97.98	3552 (52.4)	0.08 (0.05, 0.10)	0.026
>=97.98	3232 (47.6)	0.12 (0.09, 0.14)	
BMI, kg/m²			
<28.18	3722 (54.9)	0.10 (0.07, 0.12)	0.872
>=28.18	3062 (45.1)	0.10 (0.07, 0.13)	

Notes: *continuous variables were dichotomized at data-driven thresholds identified by the cluster-based cutpoints. Abbreviations: CATE, conditional average treatment effect; CAC, coronary artery calcium; ASCVD, atherosclerotic cardiovascular disease; RD, risk difference; CI, confidence interval; ICA-IMT, internal carotid artery intima–media thickness; CCA-IMT, common carotid artery intima–media thickness; IL-6, I nterleukin-6; BMI, body mass index.

Cardiovascular

Mixture Effects of Adolescent Metabolic Profiles on Serum Uric Acid in Early Adulthood: Evidence from the Ewha Birth and Growth Cohort Seunghee Jun* Seunghee Jun Hyelim Lee Hyeseung Jang Hye Ah Lee Hyesook Park

Background: Higher uric acid levels in young adulthood have been associated with future cardiovascular events, have been correlated with metabolic syndrome components. During adolescence, metabolic disturbances tend to cluster and are highly interrelated, so single-marker approaches may not adequately capture the overall burden of risk. However, prior studies evaluated associations cross-sectionally or focused on individual markers, leaving limited evidence on the joint impact of an overall adolescent metabolic profile on uric acid levels in early adulthood. Therefore, this study aimed to examine the combined effect of an adolescent metabolic profile on uric acid levels in early adulthood.

Methods: The study included 164 participants from the Ewha Birth and Growth Cohort who completed follow-up assessments at ages 13–15 and 19. An adolescent metabolic profiles mixture was defined using waist circumference, BMI, systolic/diastolic blood pressure, fasting glucose, total cholesterol (TC), TG, and HDL-C (reverse-coded so that lower HDL-C indicated higher risk). Serum uric acid (SUA) at age 19 served as the outcome. Mixture effects were estimated using quantile g-computation (qgcomp) and Bayesian kernel machine regression (BKMR).

Results: Mean SUA at age 19 was 5.94±1.51 mg/dL and was higher in boys than girls ($p<0.001$). In qgcomp analyses, a higher adolescent metabolic mixture was associated with higher SUA in crude and adjusted models (adjusted $\beta=0.54$ mg/dL; 95%CI 0.17–0.91). Positive weights were observed for HDL-C, TC, and BMI, whereas DBP and log TG received the largest negative weights. Consistent with the qgcomp findings, BKMR showed a smiliar increasing overall mixture–SUA pattern at higher joint exposure levels.

Conclusions: A higher adolescent metabolic risk profile was prospectively associated with higher SUA at age 19, highlighting adolescence as a potential window for integrated metabolic risk profiling to inform early-adulthood monitoring and prevention.

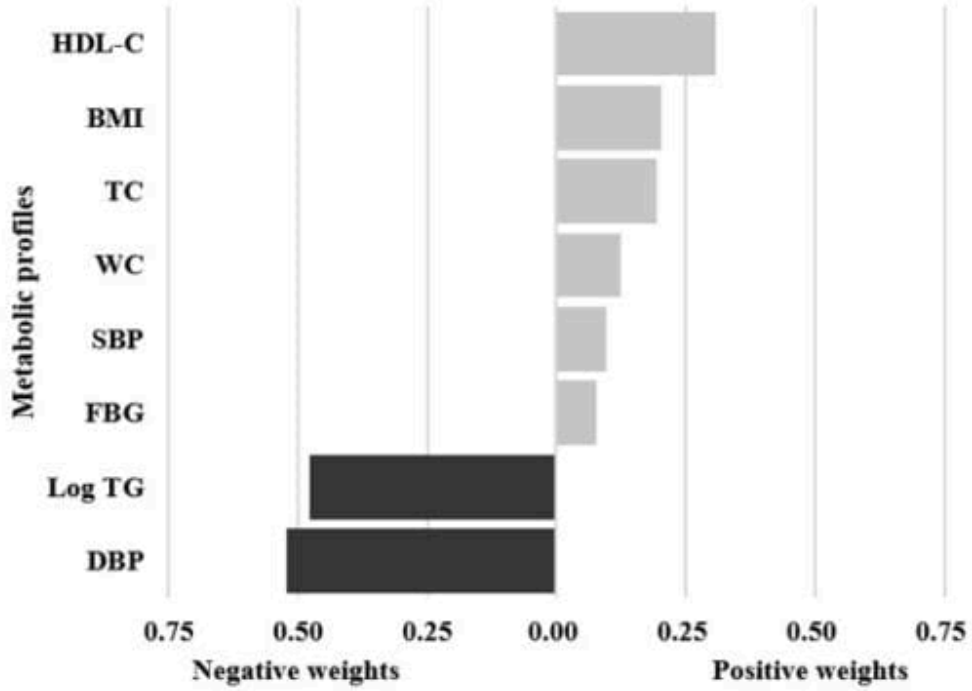


Figure 1. Weights representing the proportion of the positive or negative partial effect in the quantile g-computation models.
Adjusted for sex, age, moderate physical activity, mother's education level, smoking status, and drinking status.
HDL-C, High density lipoprotein cholesterol; BMI, Body mass index; TC, Total cholesterol; WC, Waist circumference; SBP, Systolic blood pressure; FBG, Fasting blood glucose; TG, Triglycerides; DBP, Diastolic blood pressure.

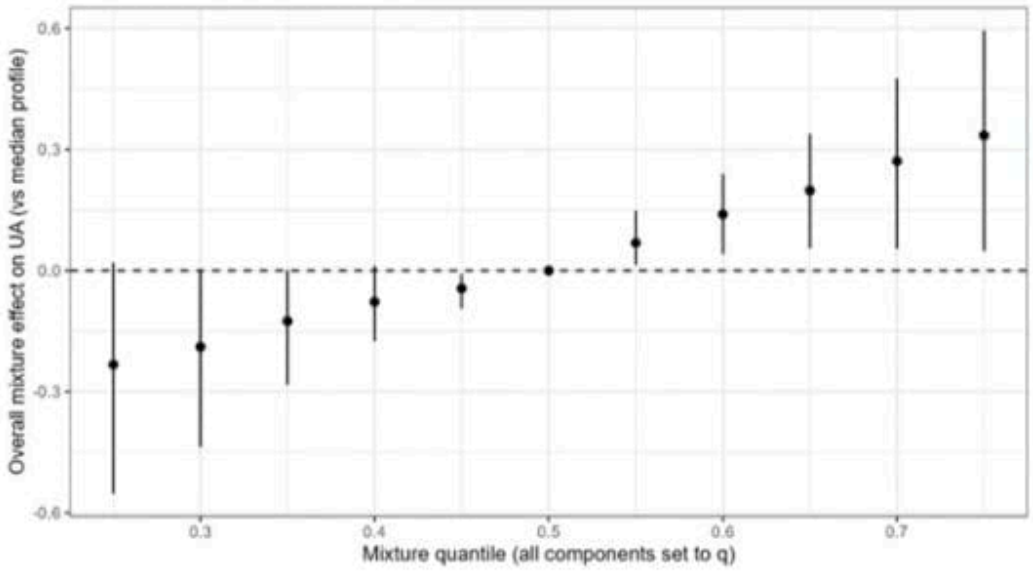


Figure 2. The overall impact of metabolic profiles mixture on SUA based on BKMR models.
Adjusted for sex, age, moderate physical activity, mother's education level, smoking status, and drinking status. The difference indicates the overall effect of all metabolic profile components, defined as the change in the response when all exposures are fixed at the 0.75 or 0.25 quantile.
The plots illustrate the estimated difference in SUA levels when all metabolic profile components are set at specified quatiles compared to their median values (50th percentile, reference level). The x-axis represents the quantiles of all metabolic profile components, and the y-axis shows the change in estimated effect on the SUA. Points represent posterior means with 75% credible intervals indicated by vertical lines.

Cardiovascular

Family Dietary Environments, Sugar-Sweetened Beverage Use, and Metabolic Risk in Adolescents: A Parent–Adolescent Dyad Study Ying-Hua Liao* Ying-Hua Liao Pei-Wen Wu Yu-Ting Chin Sharon Tsai Wei-Ting Lin Chien-Hung Lee

Background: Family dietary environments, including healthy food accessibility and household dietary rules, play a key role in shaping children's dietary behaviors, especially sugar-sweetened beverage (SSB) intake, and may influence early cardiometabolic risk. From a family medicine perspective, these upstream factors may have lasting implications for cardiometabolic health. Using a parent–adolescent dyad design, this study aimed to construct latent factors and risk scores for family dietary environments and examine their associations with adolescents' SSB intake and metabolic syndrome (MetS) risk.

Methods: We analyzed 1,438 parent–adolescent pairs randomly selected from 10 senior high schools in southern Taiwan (2020–2022). Parents reported 6 and 7 family dietary items, which were used to construct latent factors for family food accessibility and dietary rules via confirmatory factor analysis. Adolescents' SSB use disorder (SUD) severity was assessed using summed DSM-5–derived symptoms. MetS was defined according to Taiwan Pediatric Association criteria. Associations of latent factor scores with SUD severity and MetS were examined using linear and logistic regression models adjusted for covariates.

Results: Two factors—healthy and sweetened food accessibility (HFA and SFA)—and one factor, household dietary rule (HDR), were identified from family food accessibility and dietary rule items, respectively. Higher HFA and HDR scores were associated with fewer SUD symptoms (adjusted $\beta=-0.06$ and -0.03, $p<0.05$). Greater SUD severity was linked to higher waist circumference, diastolic blood pressure, triglycerides, and a 1.1-fold increased risk of MetS. Higher HFA scores were also associated with lower MetS risk, partially mediated by reduced SUD symptoms.

Conclusion: HFA and HDR were linked to lower adolescent SUD severity, and high HFA was linked to lower MetS risk, suggesting family dietary environments as modifiable targets for early cardiometabolic prevention.

Cardiovascular

Food Security and Cardiovascular Disease Mortality Among Economically Disadvantaged U.S. Adults: National Health and Nutrition Examination Survey (NHANES) 2011-2018 Jee Won Park* Fadzai Nicola Dube June Pressley Tarang Parekh

Food security is a key social determinant of cardiovascular health, yet evidence on its relationship with cardiovascular disease (CVD) mortality among economically disadvantaged U.S. adults is limited. We examined adult food security and CVD mortality and assessed effect measure modification (EMM) by age, sex, race/ethnicity, and SNAP participation.

Using NHANES 2011-2018 data, linked to the 2019 National Death Index, we analyzed 6,905 non-pregnant adults (age ≥ 20 years) with a poverty-income ratio <2. Adult food security was categorized as high (ref), marginal, low, and very low. Cox proportional hazards models estimated HRs and 95% CIs adjusting for sociodemographic, healthcare use, behaviors, SNAP, and survey cycle. Sensitivity analysis used Fine-Gray sub-distribution hazards models to account for competing risks due to non-CVD deaths.

During a median follow-up of 5.08 person-years (25th-75th percentile: 3.17-6.92 person-years), 164 CVD deaths occurred. The adjusted HRs (95% CIs) for marginal, low and very low versus high food security were 0.91 (0.55-1.51), 1.12 (0.70-1.81), and 1.29 (0.75-2.21), respectively. Fine-Gray analysis showed similar results. In general, there was no strong evidence of EMM. However, positive associations were most compatible with the data among non-Hispanic Black adults; for example, adjusted HR (95% CIs) comparing very low versus high food security was 1.97 (0.81-4.80), while negative associations were most compatible among Hispanic and Other group (0.74 (0.21-2.63)). Similarly, positive associations were most compatible among SNAP recipients and negative associations were observed among non-SNAP recipients.

Our findings were mixed. Some suggestions of differences by race/ethnicity and SNAP participation may indicate certain subgroups of the population that are more affected by lower food security. Future studies should consider other structural and social factors and investigate the causal pathways that may explain these differences.

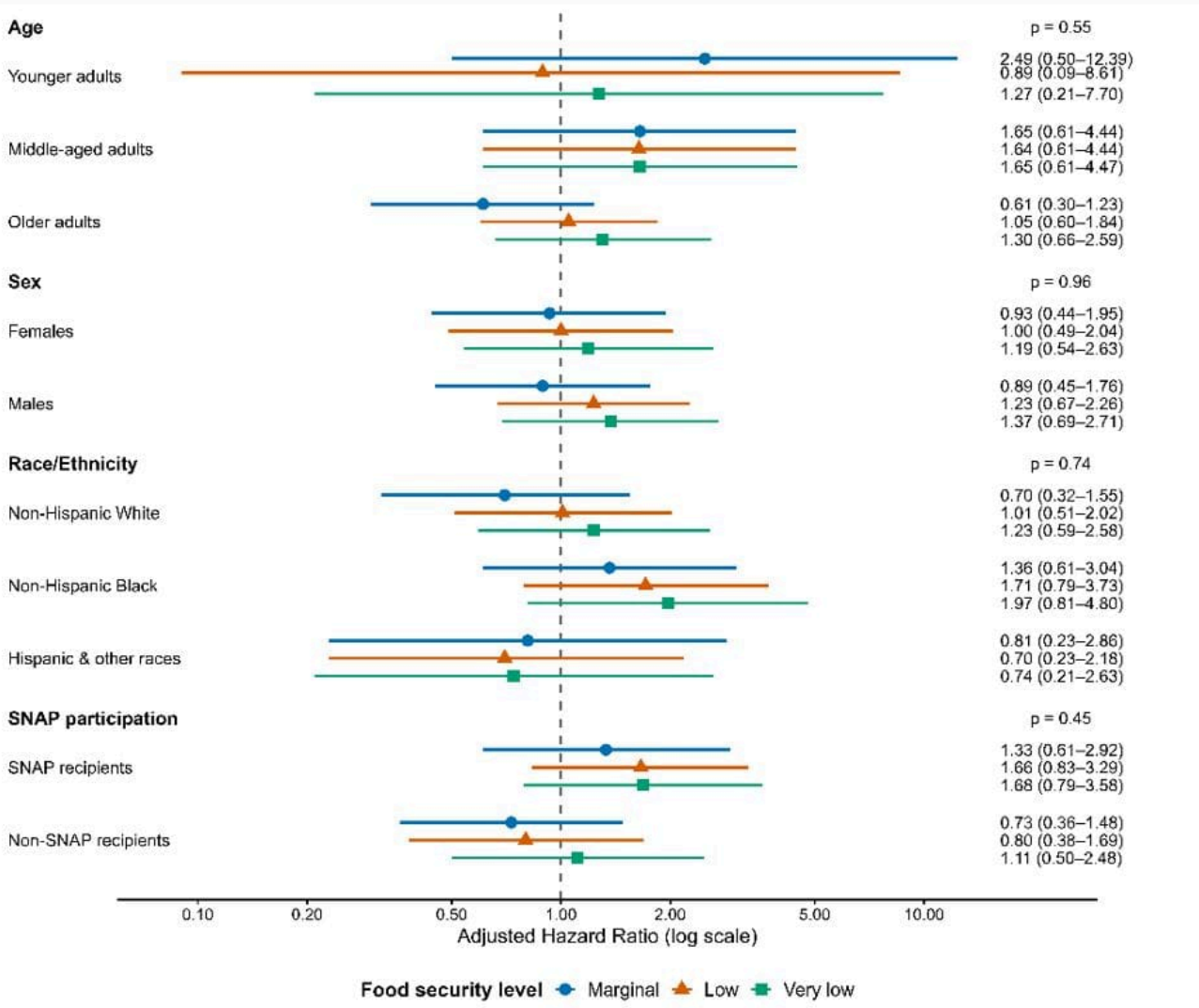


Figure. Adjusted HRs (95% CI) for marginal, low, and very low food security versus high food security and CVD mortality.

Cardiovascular

Alcohol Intake Trend and Patterns Among Adults with Cardiovascular Disease: National Health and Nutrition Examination Survey 1999-2016 Yangbo Sun* Yangbo Sun Qian Yang

Background: The aim of this study is to describe the trend in prevalence and sociodemographic correlates of alcohol consumption among adults with cardiovascular disease (CVD) in US.

Methods: We conducted a cross-sectional analysis in the National Health and Nutrition Examination Survey (NHANES) from 1999 to 2016, a population representative sample of US population. An alcohol use questionnaire was used to collect information about lifetime and current use (past 12 months) of alcohol among participants. Moderate drinking was defined as up to one drink per day for women and up to two drinks per day for men. while heavy drinking was defined as more than one drink per day for women and more than two drinks per day for men.

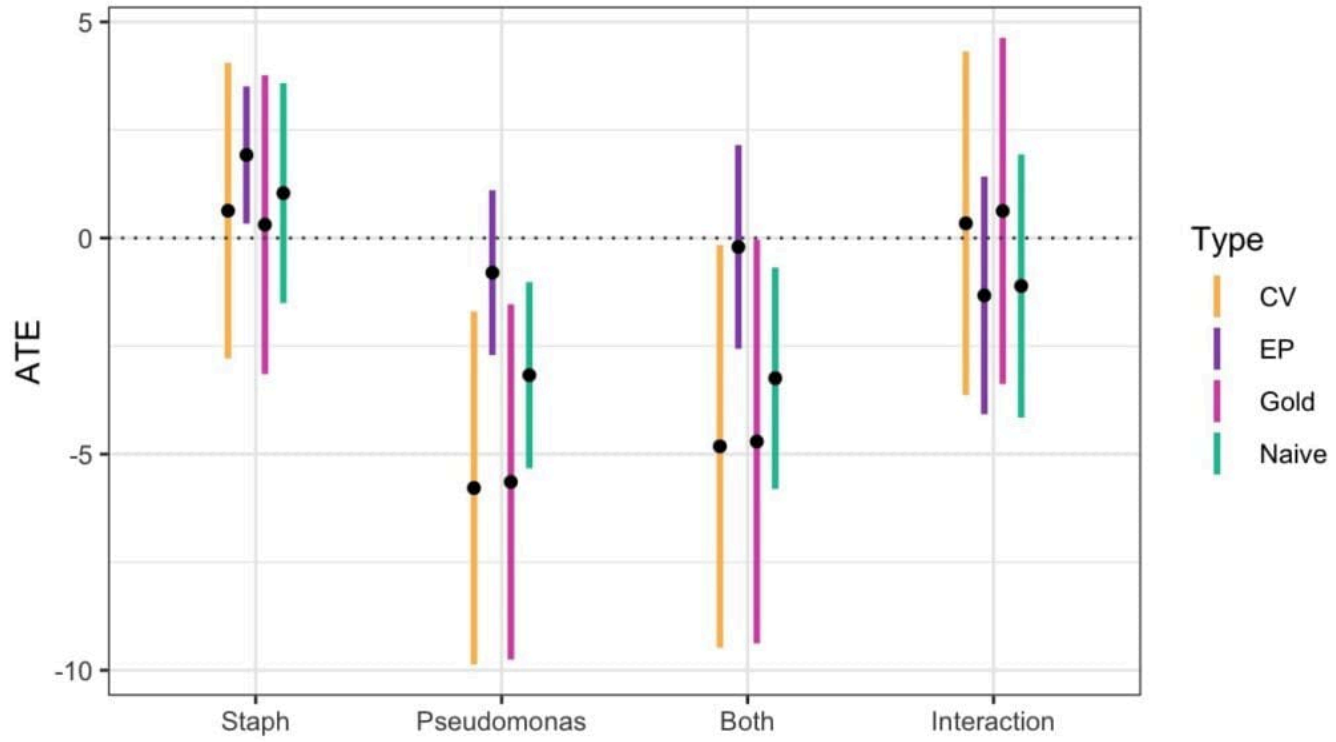
Results: In NHANES from 1999-2016, among adults with CVD, the percentages of moderate and heavy drinking increased from 47.3% to 57.2% and from 6.7% to 7.2%, respectively. Moderate and heavy drinking were associated with older age before 65 years, but inversely associated with age after 65 years. Adults with higher education and household income tended to be moderate drinkers, and current smokers tended to be heavy drinkers.

Conclusions: Most adults with CVD reported current alcohol use in the past 12 months. Our study suggested that cardiovascular care may require holistic risk screening strategies considering alcohol, tobacco and social context concurrently.

Causal Inference

Correcting Exposure Misclassification via Control Variates: Effects of Opportunistic Infections on Lung Function in Children with Cystic Fibrosis Kevin Josey* Kevin Josey Nandini Murali Keith Barnatchez Jordana Hoppe Brandie Wagner

Respiratory cultures from throat swabs or induced sputum guide treatment decisions for lung infections in cystic fibrosis (CF) patients, yet throat swabs exhibit imperfect sensitivity and specificity for detecting Pseudomonas aeruginosa and Staphylococcus aureus. We quantify the bias induced by this misclassification and develop a control variate-adjusted calibration weighting estimator to address multiple misclassified exposures. Our data comprise three disjoint subsamples: patients with only gold-standard sputum cultures; patients with only error-prone throat swabs; and a small validation sample with paired measurements. Using calibration weighting to treat misclassification as a missing data problem, we estimate causal effects in each subsample and demonstrate substantial attenuation bias in swab-based estimates. In our cohort of 550 CF patients ages 6-21, swab-based estimates fail to detect the significant negative effect of P. aeruginosa on lung function (-5.64% FEV, 95% CI: -9.75, -1.53) observed in sputum samples. The validation sample, consisting of 22 participants with paired measurements, reveals 73.7% sensitivity and 95.5% specificity for P. aeruginosa versus 95.8% sensitivity and 64.7% specificity for S. aureus. We show how the validation sample enables a control variate adjustment that integrates information from both estimators, reducing standard errors by 2-5% while preserving consistency. These findings suggest throat swabs may lead to under-treatment of P. aeruginosa infections and provide a methodological framework for causal inference with multiple misclassified exposures.



Causal Inference

Evaluating Comparative Effectiveness Under Real-World Adherence Patterns Nicholas Williams* Nicholas Williams Andrew Mertens Travis Lim Sara Levintow Joy Zora Nakato Carrie Nielson Laura B. Balzer

Deviations from treatment protocols are common in drug studies. For example, persons with HIV may experience interruptions in their antiretroviral therapy (ART), and certain ART regimens may be more robust than others with respect to patients maintaining virologic suppression. Thus, prescribers and patients need to understand the effectiveness of alternative regimens under imperfect adherence, often referred to as “forgiveness.” The standard approach for assessing forgiveness is to compare the outcome across strata of observed adherence levels. For example, this could correspond to comparing the proportion with viral suppression by ART regimen within strata of observed adherence levels. Adherence, however, is often a mediator; it is affected by the treatment regimen (e.g., daily oral regimens may be harder to maintain than long-acting injectables) and influences the outcome, and conditioning on the observed adherence level will generally yield biased estimates of effectiveness. Following the Causal Roadmap, we propose several alternative estimands, including joint stochastic interventions on treatment and adherence. These estimands capture dynamic treatment regimes and the cumulative effects of longitudinal adherence patterns. In simulations, we demonstrate how doubly robust estimators can target these estimands under minimal assumptions and contrast with the standard approach. We first illustrate shortcomings of the standard approaches and then extend to more realistic settings. We conclude with practical recommendations for generating evidence on comparative effectiveness under imperfect adherence.

Causal Inference

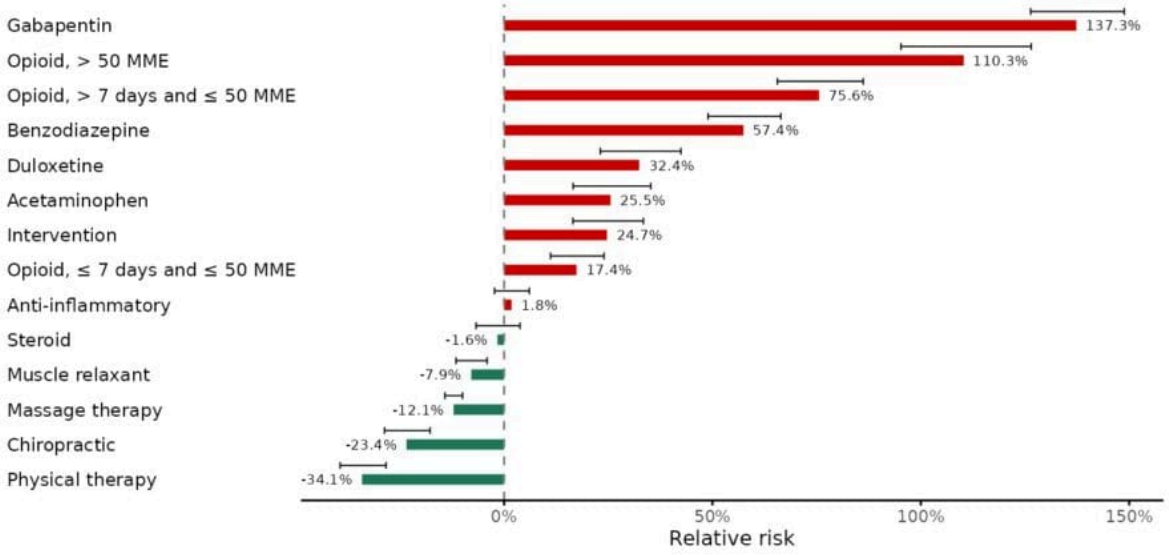
Associations between initial treatments for low-back pain and opioid use disorder risk in Medicaid patients Anton Hung* Anton Hung Kara Rudolph Lisa Doan

Introduction: Acute low back pain is a leading cause of disability worldwide, and despite guidelines cautioning against it, opioid prescribing remains common for this condition. Initial treatment modalities for low back pain range from pharmacologic to non-pharmacologic therapies, each carrying different levels of risk for later developing opioid use disorder (OUD). We studied the incidence of OUD in an opioid-naïve, Medicaid-insured adult population with newly diagnosed acute low back pain and estimated the association between initial treatment modalities and subsequent OUD risk.

Methods: Using Medicaid T-MSIS analytic files from 25 states (2016–2019), we identified opioid-naïve adults with a new diagnosis of acute low back pain who received any pharmacologic or non-pharmacologic treatment within one month. Associations between initial treatment modality and OUD risk were estimated using a non-parametric, doubly robust estimator.

Results: The cohort consisted of 574,196 opioid-naïve adults initiating treatment for low back pain. OUD incidence at the end of 9 and 15 months of follow-up was 1.8% and 3.51%, respectively. Gabapentinoids were associated with the highest increase in OUD risk (137.3%, 95% CI: 126.4%, 148.8%), followed by higher-dose opioids, defined as >50 Morphine Milligram Equivalents (MME) (110.3%, 95% CI: 95.2%, 126.5%). Lower-dose short-duration opioids (≤50 MME, ≤7 days) were also associated with elevated risk, though substantially smaller in magnitude (7.4%, 95% CI: 11.1%, 24.0%). All non-pharmacologic therapies were associated with reduced OUD risk, with physical therapy being associated with the largest risk reduction of 34.1% (95% CI: –39.3%, –28.3%).

Discussion: In opioid-naïve Medicaid patients experiencing low back pain, non-pharmacologic treatment modalities were associated with reduced OUD risk. Gabapentinoids and opioid use were each associated with increased risk; for opioids, the degree of risk increased with higher doses and durations.


Gabapentin
Opioid, > 50 MME
Opioid, > 7 days and ≤ 50 MME
Benzodiazepine
Duloxetine
Acetaminophen
Intervention
Opioid, ≤ 7 days and ≤ 50 MME
Anti-inflammatory
Steroid
Muscle relaxant
Massage therapy
Chiropractic
Physical therapy
137.3%
110.3%
75.6%
57.4%
32.4%
25.5%
24.7%
17.4%
1.8%
-1.6%
-7.9%
-12.1%
-23.4%
-34.1%
0%
50%
100%
150%
Relative risk

LATEBREAKER

Causal Inference

Transporting the effects of statins on cardiovascular disease from a randomized trial to a population of breast cancer survivors Rienna G. Russo* Rienna G. Russo Sarah E. Robertson Miguel A. Hernan Goodarz Danaei Eric B. Rimm Ruth M. Pfeiffer Lene H.S. Veiga Amber N. Hurson Rochelle E. Curtis Erin J. Aiello Bowles Larissa White A. Blythe Ryerson Stacey Honda Veronique L. Roger Ana Barac Gretchen L. Gierach Issa J. Dahabreh Jacqueline B. Vo

Introduction: Long term cardiovascular toxicity of cancer treatments is increasingly recognized, however, data on the effect of statins on CVD prevention among breast cancer survivors are limited. We extended inferences about the effects of statins on the 5-year risk of CVD from the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial–Lipid Lowering Trial (ALLHAT-LLT) to a population of breast cancer survivors.

Methods: We included data from ALLHAT-LLT, which randomized moderately hypercholesterolemic and hypertensive adults aged 55−84 years to pravastatin (use of statins unless contraindicated) or usual care (no use of statins unless indicated), and the National Cancer Institute-Kaiser Permanente Breast Cancer Survivors Cohort, in which we emulated a single arm target trial of usual care among women with non-metastatic breast cancer aged 40−84 years. We estimated intention-to-treat and per-protocol effects among breast cancer survivors using assumptions of partial treatment exchangeability in the target population and transportability of conditional relative effect measures. The outcome was CVD (fatal and non-fatal in-patient myocardial infarction, stroke, heart failure).

Results: There were 9,611 ALLHAT-LLT participants (mean age 66) and 7,602 breast cancer survivors (mean age 65). In intention-to-treat analyses, the estimated 5-year risk difference of CVD comparing pravastatin and usual care was -0.2% (95% confidence interval -2.3%,2.3%) in ALLHAT-LLT and -0.3% (-1.4%,1.0%) among breast cancer survivors. In per-protocol analyses, the estimated 5-year risk difference was -3.1% (-6.3%,-0.1%) in ALLHAT-LLT and -1.7% (-3.3%,-0.01%) among breast cancer survivors.

Conclusions: Adherence to, but not assignment of, pravastatin compared to usual care led to reductions in CVD risk among ALLHAT-LLT participants and breast cancer survivors. Statins may help reduce CVD risk among breast cancer survivors receiving potentially cardiotoxic cancer treatments.

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COVID-19 Pandemic

Effectiveness of COVID-19 mRNA Vaccines by Genetic Match to Circulating SARS-CoV-2 Strains — IVY Network, 26 Hospitals, September 2023–April 2025 Kevin C. Ma* Kevin Ma Diya Surie Emily Bendall Leigh K. Papalambros Alexander Webber Paul W. Blair Cassandra A. Johnson Carlos G. Grijalva Yuwei Zhu Natalie J. Thornburg Clinton R. Paden Wesley H. Self Adam S. Lauring Fatimah S. Dawood

Background: SARS-CoV-2 has evolved through a combination of gradual accumulation of spike protein mutations and infrequent saltation events, such as the transition from Omicron XBB to JN.1 lineages. Saltation has been associated with decreased vaccine effectiveness (VE) of COVID-19 vaccines but less is known about the impact of gradual spike evolution on VE.

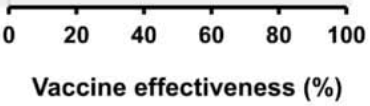
Methods: This multicenter test-negative, case-control VE analysis was conducted using data collected over two seasons (September 13, 2023–April 30, 2025) from 26 hospitals in 20 U.S. states in the IVY Network. Cases in hospitalized adults had COVID-19–like illness and a positive SARS-CoV-2 test with sequencing of clinical specimens; controls in hospitalized adults had COVID-19–like illness but tested negative. Counts of S31 deletions and nonsynonymous mutations in the S1 spike protein domain relative to each season's vaccine strain were tabulated for each case. Multinomial logistic regression was used to estimate VE stratified by S1 mutation count category after adjusting for age, sex, race and ethnicity, admission date, and U.S. Health and Human Services region.

Results: 2,727 COVID-19 cases with sequencing results and 14,870 controls were enrolled September 2023 to April 2025 (median age = 66 years; 51% female; 58% non-Hispanic White). Circulating SARS-CoV-2 viruses diverged from the vaccine strain over time, with an average increase of one S1 mutation approximately every 81 days. VE against COVID-19–associated hospitalizations was 68% (95% CI, 22%–87%) for SARS-CoV-2 viruses with 0–2 mutations, 49% (23%–67%) for 3 mutations, 45% (23%–60%) for 4 mutations, 44% (13%–64%) for 5 mutations, and 38% (1%–62%) for 6–10 mutations.

Conclusions: During 2023–2025, COVID-19 mRNA vaccines provided protection against hospitalization as SARS-CoV-2 viruses accumulated spike mutations, suggesting some robustness of current mRNA COVID-19 vaccine protection against low to moderate antigenic drift.

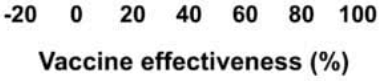
A) Received COVID-19 vaccine dose[a] **≥7 days earlier**

Case-control status and number of spike S1 mutations[b] relative to vaccine strain	No. of vaccinated patients/Total patients, n (%)	Median interval since dose among vaccinated patients, days (IQR)	Vaccine effectiveness[c], % (95% CI)	Standard error[d]
Test-negative control	2623/14,870 (18%)	117 (66–171)	Reference	--
Case, 0–2 mutations[e]	5/257 (2%)	27 (21–54)	68% (22–87)	0.46[d]
Case, 3 mutations	25/531 (5%)	46 (27–67)	49% (23–67)	0.22
Case, 4 mutations	46/520 (9%)	63 (38–84)	45% (23–60)	0.17
Case, 5 mutations	25/227 (11%)	100 (52–136)	44% (13–64)	0.22
Case, 6–10 mutations[f]	22/162 (14%)	144 (125–172)	38% (1–62)	0.24



B) Received COVID-19 vaccine dose[a] **7–89 days earlier**

Case-control status and number of spike S1 mutations[b] relative to vaccine strain	No. of vaccinated patients/Total patients[g], n (%)	Median interval since dose among vaccinated patients, days (IQR)	Vaccine effectiveness[c], % (95% CI)	Standard error[d]
Test-negative control	969/13,216 (7%)	117 (66–171)	Reference	--
Case, 0–2 mutations[e]	5/257 (2%)	27 (21–54)	65% (13-86)	0.46[d]
Case, 3 mutations	24/530 (5%)	45 (24–60)	43% (12–63)	0.22
Case, 4 mutations	37/511 (7%)	54 (33–68)	41% (16–59)	0.18
Case, 5 mutations	10/212 (5%)	44 (36–64)	63% (29–81)	0.33[d]
Case, 6–10 mutations[f]	4/144 (3%)	80 (75–81)	63% (-3 to 86)	0.52[d]



COVID-19 Pandemic

Global changes in life expectancy during the COVID-19 pandemic Hoi Ting (Alexandra) Law* Hoi Ting (Alexandra) LAW Benjamin John Cowling

Background: Different countries experienced varying changes in life expectancy (LE) during the COVID-19 pandemic; the drivers explaining these different trajectories are unexplored.

Methods: We reviewed LE data from 1998-2023 for 183 countries and regions. We classified countries into 12 categories based on their economic levels and which year they had the largest LE reduction. In each category, we conducted principal coordinates analysis to explore similarities between demographic characteristics, COVID-19 vaccination coverage, and public health and social measures (PHSMs) implemented in the COVID-19 pandemic, and regression to investigate significant factors behind LE changes in each year of the pandemic.

Results: The LE of less developed countries, particularly those with a low proportion of older adults, were able to resume the increasing pre-pandemic trend in 2023, while the developed economies could not. The strictness and consistency of PHSMs and the social development level of countries were crucial in affecting the LE in 2020, while COVID-19 vaccination rates became more influential in 2021-2022.

Conclusions: Stringent interventions and COVID-19 vaccination rates play significant roles in influencing LE changes in the pandemic. Targeted PHSMs for vulnerable populations will be essential to restore LE to the increasing trends.

COVID-19 Pandemic

Impact of Border Proximity on COVID-19 Incidence and Mortality along the U.S.-Mexico Border Berenice Arguello* Berenice Arguello Leonides Catarino Dr. Robert Rodriguez Dr. Barbara Martinez Neda Shaokui Ge Janet Reyes

Viral epidemics expose the vulnerabilities of interconnected healthcare systems, especially in regions where borders do not prevent the spread of disease. “Binational health” refers to the health challenges of the U.S.–Mexico border region that stem from social ties, cultural connections, travel, economics, migration, and consumption. In this study we sought to quantify COVID-19 incidence and mortality in U.S. border state counties, compare these indicators between border and non-border counties, and visualize disparities through geographic mapping.

This retrospective cohort study analyzed publicly available, deidentified data from the Centers for Disease Control and Prevention and the U.S. Census Bureau between January 2020 and May 2023 to calculate incidence and mortality for all counties within U.S. border states. Counties situated within 100 km of the U.S.-Mexico border were classified as border counties. Spatial mapping using geographic information system software was conducted to visualize trends and disparities.

Annual incidence and mortality showed higher COVID-19 burden in US–Mexico border counties. In 2020, mean case incidence was 170 vs 120 per 100,000 person-weeks, rising by 2022 to 560 vs 450. Mortality was also higher in border counties (2020: 2.8 vs 2.5; 2022: 8.9 vs 7.5 per 100,000). Relative risk analyses also demonstrated higher weekly case risk in 2020 (RR 1.2, CI 1.15–1.26, $p<0.0001$) and death risk (RR 1.44, CI 1.15–1.80, $p<0.001$) in border counties. Cumulative RR of death ranged 1.44–0.98, significant only in 2020–2021.

Proximity to the U.S.–Mexico border is associated with measurable differences in COVID-19 incidence and mortality. Most apparent was in the year 2020, when new cases and deaths per week RR was highest. The risk of new deaths in border counties reduced by 2022, but incidence of new COVID-19 cases remained significantly higher. Identifying these disparities bring attention to the need for intrastate/interstate preparedness and advocate for equitable resource allocation during future emergencies.

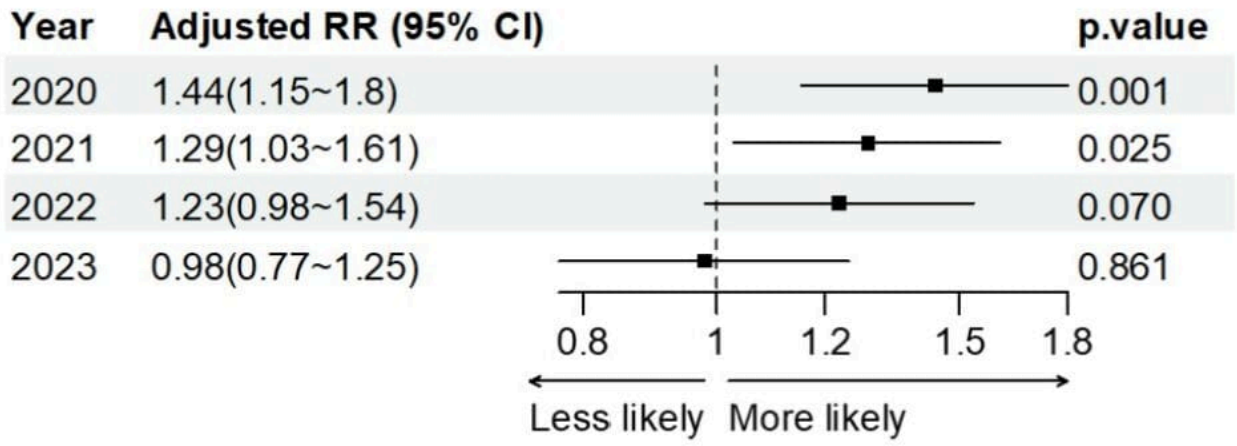


Figure 1. Relative risk of new COVID 19 death, border counties vs. not border counties.

Integrating wastewater-based epidemiology, socio-behavioral, and demographic data to enhance predictive modeling of SARS-CoV-2 spike risk in Virginia Isaiah Omari* Isaiah Omari

Integrating wastewater-based epidemiology, socio-behavioral, and demographic data to enhance predictive modeling of SARS-CoV-2 spike risk in Virginia

Background: Wastewater-based epidemiology (WBE) is an increasingly important tool for monitoring SARS-CoV-2 transmission at the population level. However, models relying solely on viral load trends may inadequately capture spatial heterogeneity in population vulnerability. We evaluated whether integrating longitudinal WBE trends with baseline socio-behavioral and demographic indicators over a multi-year window improves predictive accuracy of SARS-CoV-2 spike risk.

Methods: We constructed a longitudinal panel dataset comprising 10,632 monthly observations across 46 distinct wastewater treatment plant catchments in Virginia over a 5-year period from January 2021 through December 2025. Predictor matrices merged structural demographics from the American Community Survey (ACS) with health indicators from the Behavioral Risk Factor Surveillance System (BRFSS). Spike risk was defined as a binary threshold event (³1.5 x rise above the 2-week trailing mean). To prevent mathematical artifacts from traditional zero-imputation or complete-case deletion, missing values in population covariates were preserved natively within sparsity-aware splitting tree architectures. Predictive discrimination was evaluated on an independent, stratified hold-out test set using multinomial logistic regression, random forests, and extreme gradient boosting (XGBoost). Spatial clustering was assessed via Moran's I; structural drivers were evaluated using a Generalized Linear Mixed Model (GLMM) with random intercepts for location, and temporal forecasting utilized log-transformed seasonal frameworks.

Results: Models integrating WBE, ACS, and BRFSS indicators outperformed models using environmental tracking alone. Accounting for panel clustering revealed honest, non-overfitted predictive power, with the native-NA XGBoost model demonstrating the highest discrimination (Test AUC = 0.6504), closely followed by random forest (AUC = 0.6448) and classification trees (AUC = 0.6253), while multinomial regression performed as a random baseline (Balanced Accuracy = 0.5042). Optimizing the classification cutoff to 0.312 via Youden's J Index successfully mitigated naïve zero-spike estimation bias. In GLMM fixed-effects testing, poor physical health (PHLTH) was identified as the strongest socio-behavioral engine (OR = 1.198, $p < 0.001$), alongside healthcare access constraints (OR = 0.916, $p = 0.008$). Spatial analysis confirmed significant geographic viral clustering ($I = 0.55$, $p < 0.001$), while log-transformed time-series forecasting generated a consensus 3-month upward trajectory across the Commonwealth (ARIMA Month 3: 3.73, Prophet Month 3: 3.61).

Conclusions: Integrating environmental wastewater surveillance with native sparse socio-behavioral and census-derived structural datasets yields an honest, reproducible predictive signal that significantly improves public health risk stratification. Hybrid forecasting structures control for hidden geographic confounding and provide robust 3-month predictive windows to guide localized, targeted intervention infrastructure before clinical surges manifest.

Keywords: wastewater-based epidemiology; SARS-CoV-2; BRFSS; predictive modeling; health

Diabetes

Digital health technologies for self-management of type 2 diabetes in low-resource settings: a scoping review of feasibility, adoption, and equity considerations Edmond Appiah* Edmond Appiah Naa Adorkor Lomotey

Digital health technologies (DHTs)—including apps, SMS, and wearable sensors—hold promise for improving diabetes self-management. However, most evidence originates from high-income countries, and their applicability in low- and middle-income countries (LMICs) and underserved communities is unclear. This scoping review aimed to map the evidence on DHTs for type 2 diabetes in low-resource settings, focusing on feasibility, adoption barriers/facilitators, and reported equity outcomes. We employed the JBI methodology, searching MEDLINE, Global Health, and IEEE Xplore for studies (2015-2025). We defined “low-resource” by either study setting (LMIC) or focus on underserved populations (e.g., rural, low-income) in any country. Of 1,567 screened records, 128 studies were included. Our analysis charted technology type, study design, and key thematic findings. While pilot studies demonstrate technical feasibility, we identified major barriers to sustainable adoption: low digital literacy, data cost burdens, linguistic/cultural misalignment of content, and poor integration into overstretched public health systems. Few studies measured or reported on equity outcomes like narrowing glycemic control disparities. This review maps an innovation landscape that is rapidly expanding but often divorced from the contextual realities of end-users. It underscores the critical need for participatory design, robust equity-focused evaluation, and policy frameworks that address the digital divide to prevent the exacerbation of existing diabetes disparities.

LATEBREAKER

Diabetes

Exploring spatial non-stationarity in modifiable built environment factors and diabetes prevalence in Georgia: a census tract-level analysis Arshya Gurbani* Arshya Gurbani Lia Scott

Introduction: The association between modifiable built environment factors and diabetes prevalence may vary across space. Global regression models may mask underlying relationships occurring at more granular geographic levels. This census tract-level analysis explores such associations, and their potential spatial nonstationarity, in the state of Georgia.

Methods: Spatial autocorrelation in 2022 tract-level diabetes prevalence was tested using Global Moran's I. Using geographically weighted regression (GWR), the association between diabetes prevalence and walkability, park land coverage, retail food environment and average distance to the nearest clinic was estimated, while controlling for several demographic and socioeconomic characteristics. GWR allows for coefficients to vary locally so we can assess whether the significance and magnitude of these associations changed over space.

Results: There is strong evidence of clustering of values in diabetes prevalence in Georgia (Moran's I=0.61, p<0.001). In both the adjusted global and geographically weighted model, walkability was the only statistically significant predictor of interest associated with adult diabetes prevalence (mean [SE] OLS: β = −0.74[S.E. = 0.05], p<0.01; mean [SE] GWR β, -0.57 [SD= 0.23]). Results from the GWR suggest that, on average, a one SD increase (3.4) in national walkability index score is associated with an average 0.57 SD (2.22%) decrease in diabetes prevalence, and that this association is locally significant in 58% of census tracts across the state.

Conclusion: There is evidence that the distribution of diabetes prevalence in Georgia is clustered, and that the association between walkability and diabetes prevalence varies in magnitude and significance across the state. This exploratory study lends evidence to look further into improved neighborhood walkability as a policy intervention to improve the health of Georgians.

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Diabetes

Historical trends in glycated hemoglobin in people living with type-2 diabetes in Mexico between 2012 and 2024 Francisco Canto-Osorio* Francisco Canto-Osorio Alan Reyes-Garcia Ana Basto-Abreu Andrés Catzín Kuhlmann Martha Carnalla Leticia Torres-Ibarrra Carolina Pérez-Ferrer Tonatiuh Barrientos-Gutiérrez Dalia Stern

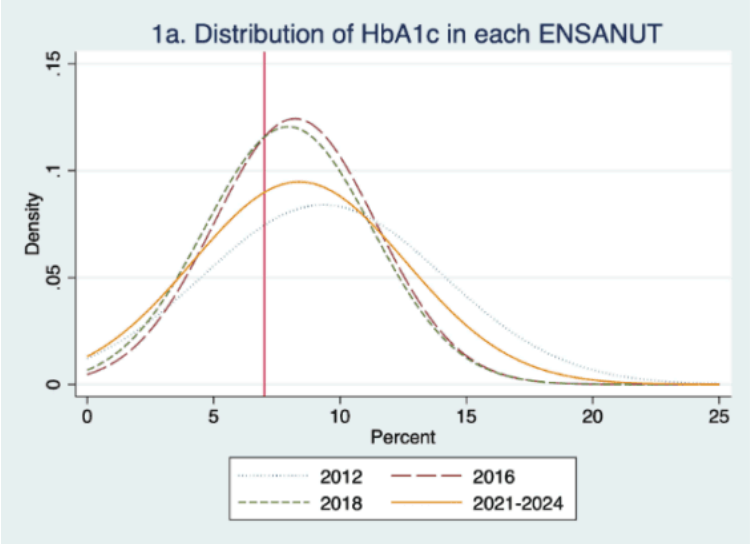
Introduction:

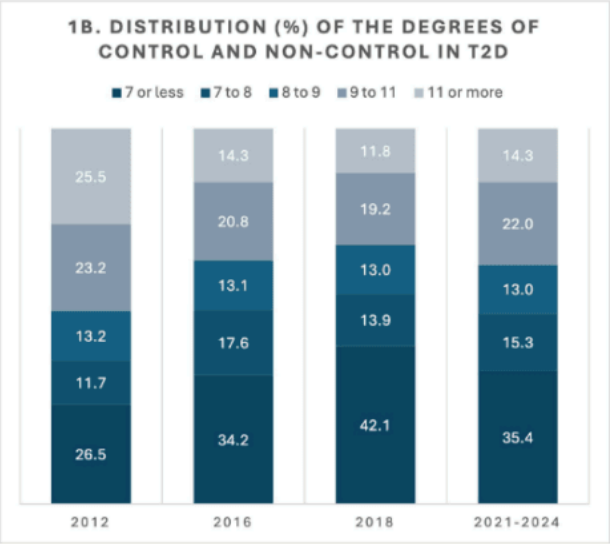
Despite ongoing public health interventions aimed at improving diabetes control in Mexico, the temporal evolution of glycemic control distributions among individuals with type 2 diabetes remains poorly characterized. This is important, as higher glycated hemoglobin (HbA1c) levels are linked to T2D complications and death. Using repeated nationally representative surveys, we characterized the trends of HbA1c among adults with controlled and uncontrolled T2D in Mexico from 2012 to 2024.

Methods: We used data from the National Health and Nutrition Survey (ENSANUT) for 2012, 2016, 2018, and the continuous survey from 2021 through 2024. We included adults aged ≥20 years living with T2D with valid blood samples and an HbA1c determination (n=21,592). For each survey, we examined the HbA1c distribution to assess shifts in the population-level HbA1c over time. We estimated the proportion of individuals under control (HbA1c <7.0%), and across progressively higher HbA1c categories (>7-8, >8-9, >9-11, >11). All estimates were standardized by the age distribution of people living with T2D in 2021-2024.

Results: From 2012 to 2018, the HbA1c distribution shifted towards lower HbA1c levels, suggesting overall improvements in glycemic control in people living with T2D. However, these improvements plateau in 2021–2024 (Figure 1a). The proportion of individuals achieving glycemic control increased from 26.5% in 2012 to 42.1% in 2018, but decreased to 35.4% in 2021–2024. Similarly, the prevalence of poor glycemic control at the highest HbA1c levels (9–11% and >11%) decreased between 2012 and 2018 but showed a slight increase in 2021–2024 (Figure 1b).

Conclusion: Glycemic control in Mexico is low and seems to have stalled in recent years, with evidence of worsening both in the proportion achieving glycemic targets and in the prevalence of severe hyperglycemia.


1a. Distribution of HbA1c in each ENSANUT
Density
0
.05
.1
.15
0
5
10
15
20
25
Percent
2012
2016
2018
2021-2024


1B. DISTRIBUTION (%) OF THE DEGREES OF CONTROL AND NON-CONTROL IN T2D
7 or less
7 to 8
8 to 9
9 to 11
11 or more
25.5
23.2
13.2
11.7
26.5
14.3
20.8
13.1
17.6
34.2
11.8
19.2
13.0
13.9
42.1
14.3
22.0
13.0
15.3
35.4
2012
2016
2018
2021-2024

Diabetes

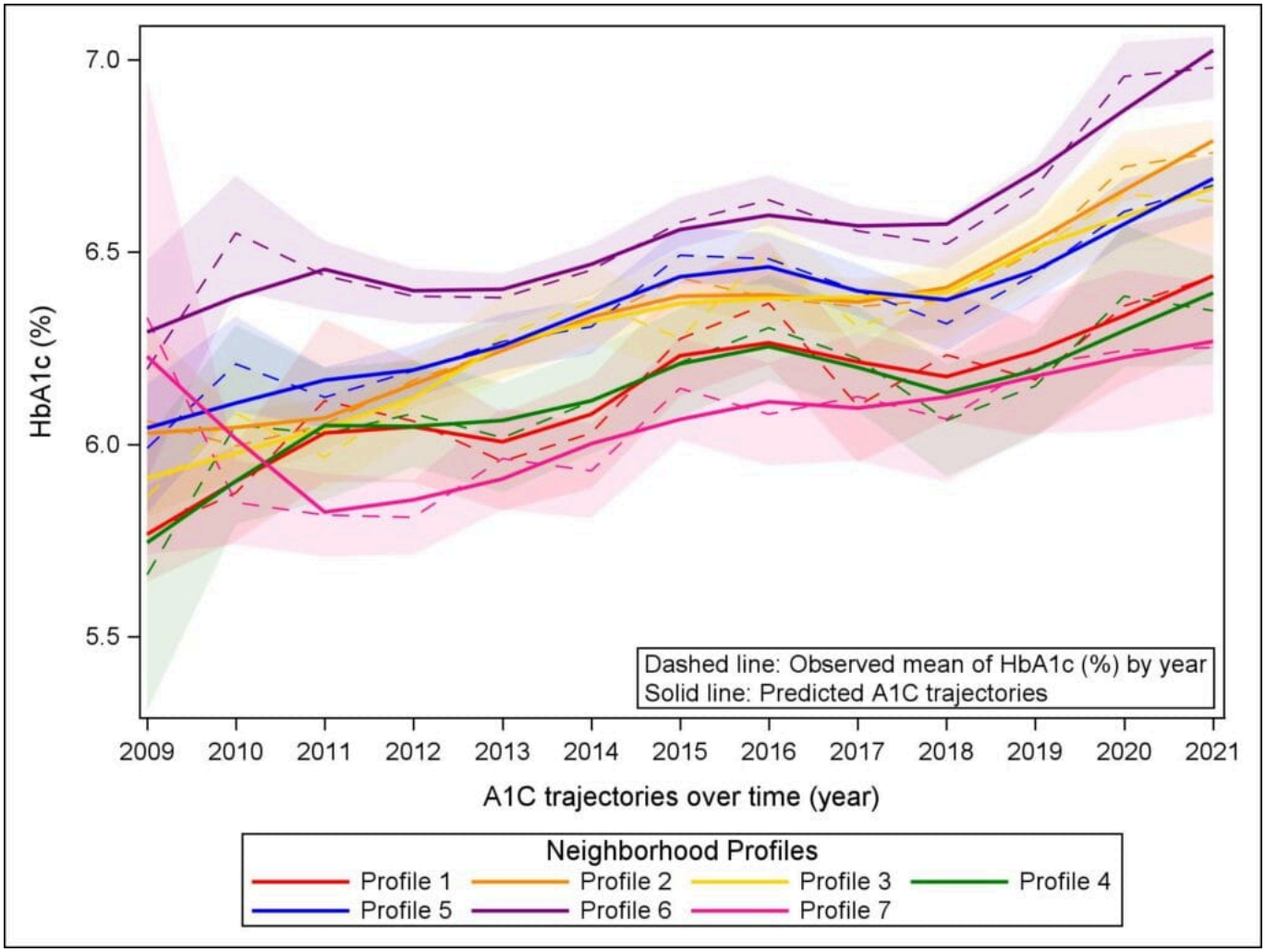
Neighborhood Typology and A1C Trajectories among Women with Gestational Diabetes in New York City: A Longitudinal Study Teresa Janevic* Bohao Wu Natalie Boychuk Shelley Liu Frances M. Howell Andrew G. Rundle Teresa Janevic

Background: Neighborhood environments are associated with type 2 diabetes (T2D), yet prior studies have focused on single neighborhood determinants rather than multidimensional profiles. Women with gestational diabetes (GDM) experience heterogeneous postpartum glycemic trajectories. We used a data-driven approach to classify New York City (NYC) neighborhoods into distinct profiles and examined their associations with postpartum A1C trajectories among women with GDM.

Methods: Using 2009-2021 linked NYC birth, hospital discharge, and NYC A1c Registry data, we identified GDM cases in birth/hospital data. Women with pre-pregnancy diabetes were excluded. We applied latent profile analysis to 10 social and built environment characteristics in 2010 to classify neighborhoods. The profile with the most average neighborhood characteristics was used as the reference. Participants' residential addresses were updated at each A1C test to assign neighborhood profiles as the time-varying exposure. We used linear mixed-effects models with random intercepts at the census block and individual levels to estimate adjusted differences in repeated A1C measurements across neighborhood profiles, adjusting for maternal age, race and ethnicity, educational attainment, nativity, and parity.

Results: Among 13,231 women with GDM at baseline, seven distinct neighborhood profiles were identified. Compared with the Profile 5 neighborhoods (the most average), residence in Profile 1 neighborhoods ("Green and Wealthy", mean difference [β]: -0.11, 95% CI -0.21, -0.01), Profile 4 neighborhoods ("Unhealthy Built Environment and Wealthy", β: -0.11, 95% CI -0.21, -0.02), and Profile 7 neighborhoods ("Affluent Urban", β: -0.16, 95% CI -0.25, -0.07) was associated with lower A1C levels.

Conclusions: Considering multidimensional neighborhood environments revealed distinct A1C trajectories after GDM, underscoring the value of neighborhood-based glycemic control.


7.0
6.5
6.0
5.5
HbA1c (%)
Dashed line: Observed mean of HbA1c (%) by year
Solid line: Predicted A1C trajectories
2009
2010
2011
2012
2013
2014
2015
2016
2017
2018
2019
2020
2021
A1C trajectories over time (year)
Neighborhood Profiles
Profile 1
Profile 2
Profile 3
Profile 4
Profile 5
Profile 6
Profile 7

Diabetes

Maternal Sociodemographic, Pre-Pregnancy, and Pregnancy Factors Associated with Type 2 Diabetes in Adolescents and Young Adults: The PAPAYA Study Saher Daredia* Saher Daredia Sara Aghaee Julia Acker Jennifer Y. Liu Cindy J. Huang Andrew J. Karter Ai Kubo Julianna Deardorff

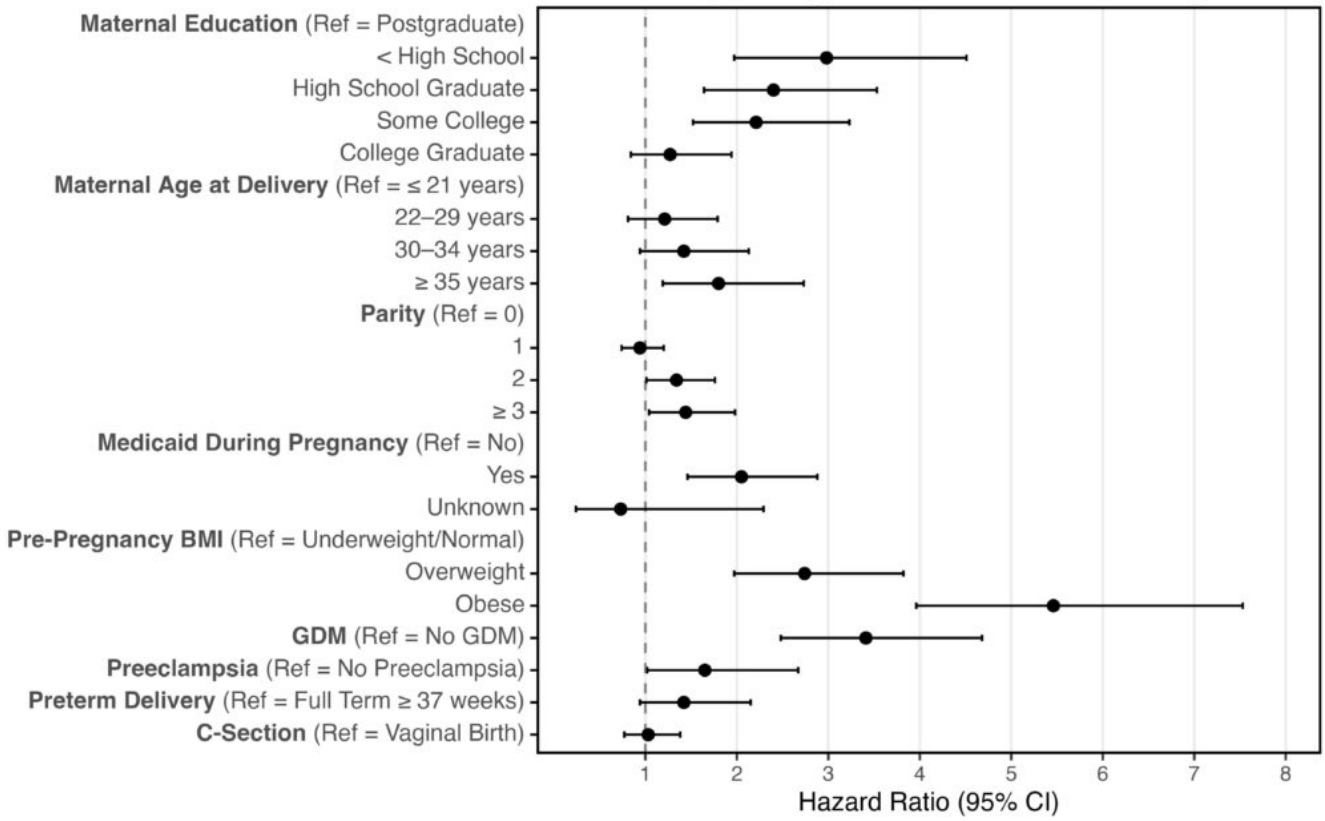
Background: Youth type 2 diabetes (T2D) rates have risen globally. Preconception and pregnancy are sensitive periods for later T2D risk, yet specific exposures contributing to risk remain unclear. We examined associations between maternal and pregnancy factors and early-onset child T2D in the Predictors of Adverse Cardiometabolic Problems in Adolescents and Young Adults (PAPAYA) study at Kaiser Permanente Northern California (KPNC).

Methods: This retrospective cohort included 303,037 racially diverse individuals born at KPNC in 2003-2011. Maternal (education, age, parity, Medicaid coverage, pre-pregnancy BMI and diabetes) and pregnancy (gestational diabetes, preeclampsia, preterm birth, delivery mode) factors were obtained from electronic health records and birth certificates. Early-onset T2D (ages 10–21; N=453) was identified via the KPNC Diabetes Registry. Cox proportional hazards models estimated hazard ratios (HR) adjusting for key confounders.

Results: Lower maternal education was associated with higher hazard of early-onset T2D (HR=2.98; 95% CI: 1.97-4.51 for < high school vs. postgraduate), as were older age at delivery (HR per year=1.04; 95% CI: 1.02-1.06), greater parity (HR per birth=1.11; 95% CI: 1.03-1.20), and Medicaid coverage during pregnancy (HR=2.05; 95% CI: 1.46-2.88). Pre-pregnancy maternal overweight (HR: 2.74; 95% CI: 1.97-3.82) and obesity (HR: 5.46; 95% CI: 3.96-7.53) vs. underweight/normal weight, gestational diabetes (HR: 3.41; 95% CI: 2.48-4.68) and preeclampsia (HR: 1.65; 95% CI: 1.02-2.67) were also associated with higher hazards. Maternal pre-pregnancy diabetes showed time-varying associations, with HRs decreasing from 31.08 (95% CI: 17.85-54.13) at age 10 to 5.99 (95% CI: 2.64-13.56) at age 20. Preterm birth and delivery mode showed no associations.

Conclusion: Several maternal sociodemographic, pre-pregnancy, and pregnancy factors were associated with early-onset T2D, providing potential targets for early-life interventions.

Adjusted Associations between Maternal Sociodemographic, Pre-Pregnancy, and Pregnancy Characteristics and Early-Onset Type 2 Diabetes in the PAPAYA Study



Hazard ratios (HR) and 95% CIs estimated from Cox proportional hazard (PH) models adjusted for minimally sufficient confounders (adjustment sets vary by characteristic). Cox model for maternal pre-pregnancy diabetes did not meet the PH assumption (time-varying HRs reported in abstract text).

Environment/Climate Change

Environmental Metals and Depressive Symptoms among North American Pregnancy Planners: A Novel Application of Volumetric Absorptive Microsamplers (VAMS) for Epidemiologic Research Samantha Schildroth* Samantha Schildroth Krystal E. Kuan Amelia K. Wesselink Eliza Pentz Marco Vinceti Lucas Schmidt Julio Landero Lauren A. Wise

Background: Many metals and metalloids (hereafter, “metals”) are either neurotoxicants (e.g., heavy metals) or essential nutrients required for cellular processes. Exposure to metals can therefore affect health, often non-linearly or in opposing directions. However, less research has focused on psychosocial health outcomes, particularly among women. We assessed associations between capillary blood metal levels and depressive symptoms using volumetric absorptive microsamplers (VAMS) in a prospective preconception cohort.

Methods: We used cross-sectional data from 292 females participating in Pregnancy Study Online (PRESTO), a North American preconception cohort study. At baseline, we measured capillary whole blood concentrations of 22 metals collected in VAMs using a newly developed method and evaluated depressive symptoms using the Major Depression Index (MDI, range=0-50, higher scores reflected greater symptoms). We operationalized metals continuously (per 1-SD increase) or categorically (in tertiles, where there was evidence of non-linearity in splines). We used multivariable linear regression to estimate percent differences (β) in MDI scores with 95% CIs, adjusting for hypothesized confounders.

Results: Most metals were not strongly associated with depressive symptoms, though some heavy metals – e.g., lead, thallium – were weakly associated with higher MDI scores. Several nutrient metals were non-linearly associated with MDI scores: copper, for example, showed an inverted U-shaped association such that there were lower MDI scores for the first (β=-36.6%, 95% CI=-55.1%, -10.4%) and third (β=-27.7%, 95% CI=-48.6%, 1.8%) tertiles compared with the second tertile.

Conclusion: In this study of pregnancy planners, some metals were weakly associated with MDI scores, though the direction and magnitude of association varied by metal. This study represents one of the first to investigate metals and depressive symptoms among females during the sensitive preconception period.

Environment/Climate Change

Spatial patterns of wildfire-related PM2.5 increases and historical redlining during the January 2025 Los Angeles Wildfires Malaika Jade Mason* Malaika Jade Mason

High fine particulate matter (PM2.5) exposure is associated with adverse cardiovascular and pulmonary health outcomes. Wildfire smoke can substantially increase PM2.5 levels in surrounding areas. Although historically redlined neighborhoods experience higher baseline air pollution, less is known about whether this pattern also exists regarding wildfire-related PM2.5 increases. We examined spatial and temporal patterns of PM2.5 across the City of Los Angeles during the January 2025 wildfires, including the spatial overlap between PM2.5 increases and historically redlined areas. Daily PM2.5 data from 11 U.S. Environmental Protection Agency monitors and 86 World Air Quality Index sensors were aggregated into weekly means and spatially interpolated using ordinary kriging to generate PM2.5 surfaces for pre-wildfire, peak wildfire, and post-wildfire periods. Mean PM2.5 concentrations were summarized by Los Angeles Community Planning Areas (CPAs), and changes in PM2.5 were calculated between baseline and peak wildfire weeks. Historical redlining data from the Home Owners' Loan Corporation were intersected with CPAs. HOLC grades range from A ("Best") to D ("Hazardous"), with grades C and D historically assigned to neighborhoods disproportionately inhabited by communities of color and subjected to housing disinvestment. Spatial heterogeneity in PM2.5 was observed during the peak wildfire period, with the largest increases occurring in inland and eastern CPAs. The greatest increases were observed in Boyle Heights (+27.1 µg/m3) and Northeast Los Angeles (+26.4 µg/m3), while western CPAs experienced smaller changes. CPAs predominantly classified as HOLC grade C or D tended to exhibit large wildfire-related increases in PM2.5 compared to those graded A or B. Wildfire-related PM2.5 increases during the January 2025 Los Angeles wildfires were unevenly distributed across the city, with larger increases occurring in historically redlined areas.

Table. Community Planning Areas with the largest observed increases in mean PM2.5 from baseline to peak wildfire week during the January 2025 Los Angeles wildfires, with dominant HOLC grade.

Community Planning Area	HOLC Grade	Change in PM2.5 ($\mu g/m^3$)
Boyle Heights	D	27.1
Northeast Los Angeles	C	26.4
Silver Lake - Echo Park - Elysian Valley	D	20.1
San Pedro	D	19.8
Southeast Los Angeles	D	18.4
Port of Los Angeles	D	17.2
Downtown	D	17.2
South Los Angeles	C	17.1
Westlake	D	16.6
Harbor Gateway	D	15.6

Table includes the 10 Community Planning Areas with the largest observed PM2.5 increases; full results available upon request.

Environment/Climate Change

Perinatal exposure to meteorological-air pollutant mixture and autism spectrum disorders

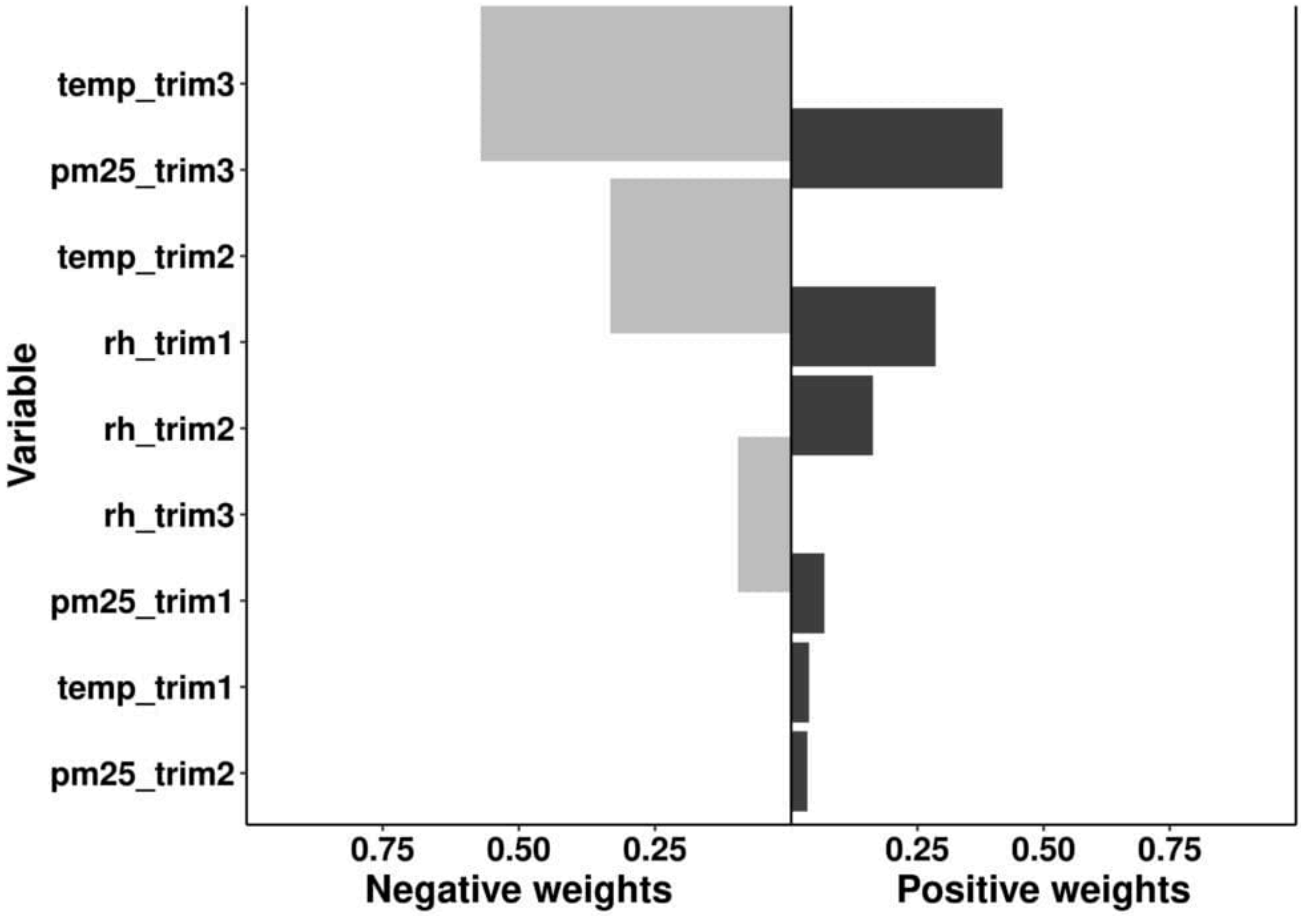
Wanyu Huang* Wanyu Huang Krista Huybrechts Sonia Hernandez-Diaz Matthew Shupler Xinye Qiu Michael Leung Hayon Michelle Choi Yaguang Wei Joel Schwartz Brent Coull Christopher J McDougle Antonella Zanobetti Marc Weisskopf Stefania Papatheodorou

Objective: The prenatal period is critical for brain formation and neurodevelopment. Prenatal exposures to, for example, PM2.5 and extreme weather may increase the risk of neurodevelopmental disorders. Yet few studies have examined the joint effect of air pollutants and meteorological factors with autism spectrum disorder (ASD) in children.

Methods: Daily levels of temperature, relative humidity and fine particulate matter (PM2.5) from spatiotemporal models were linked to a longitudinal cohort of mothers/infants from the Medicaid Analytic eXtract (MAX) database. ASD was identified based on ICD-9/10 codes and modeled as a time-to-event outcome. Weekly levels of each exposure were assigned based on residential zip codes for mothers, then averaged into levels during each trimester. Quantile g-computation models were applied to assess the joint effects of the mixture, adjusting for maternal age, race/ethnicity, socioeconomic factors (area-level), as well as season of delivery.

Results: We included a total of 1,543,129 term births from 2001 to 2013; and observed a cumulative hazard ratio (HR) of 1.05 (95% CI: 0.95 – 1.15) for the mixture per interquartile range (IQR) increase in exposure. Of the factors that were associated with increased ASD, third-trimester PM2.5 contributed the largest share of the positive effect (42%), followed by first- and second trimester relative humidity. Some factors (e.g., 3rd trimester temperature) had an inverse association with ASD (**Fig. 1**).

Conclusion: PM2.5, especially during the third trimester, contributed the most to the increased risk of ASD, with relative humidity in the 1st and 2nd trimesters also contributing to the association. Continuing to mitigate ambient PM2.5 levels is important in potentially alleviating childhood ASD risk among the socioeconomically disadvantaged US population.


temp_trim3
pm25_trim3
temp_trim2
rh_trim1
rh_trim2
rh_trim3
pm25_trim1
temp_trim1
pm25_trim2
Variable
0.75
0.50
0.25
Negative weights
0.25
0.50
0.75
Positive weights

Environment/Climate Change

Dietary predictors of urinary metals concentrations in a cohort of Ugandan adolescent girls and young women Kristen Upson* Kristen Upson Juhee Lee Julio Landero Renee Heffron Andrew Mujugira Flavia Matovu Kenneth Mugwanya Robert Wright Michael Yin Chenxi Li Quaker Harmon

Exposure to toxic metals can adversely affect health. The general population can be exposed through ingestion of contaminated food. To our knowledge, no studies have investigated dietary predictors of metal exposure in Uganda. We conducted a cross-sectional analysis using baseline data from the Kampala Women's Bone Study. Young Ugandan women (n=499) ages 16-25 were enrolled in years 2018-2020. In urine samples, we measured arsenic (As), lead (Pb), mercury (Hg), nickel (Ni), and thallium (Tl) using inductively-coupled plasma-mass spectrometry; metal levels were specific gravity-adjusted to account for urinary dilution. Participants were asked about dietary intake of 22 food groups (both plant and non-plant-based) in the past week. In non-smokers (n=494), we conducted log-binomial regression to estimate the adjusted prevalence ratio (PR) and 95% CI for the associations between daily food intake (vs. none) and urinary metal levels ≥75th percentile, adjusting for age and education. We report aPRs ≥1.3 in magnitude with a confidence limit ratio ≤3. Our data suggested daily root tuber intake and higher Pb (PR 1.6 95%CI: 0.9-2.8) and Tl (PR 1.5 95%CI: 0.8-2.8). With daily rice intake, we observed higher As (PR 1.5 95%CI: 1.0-2.3) and Hg (PR 1.4 95%CI: 0.9- 2.1). Daily intake of sweets and confectionaries were associated with higher Pb (PR 1.5 95%CI: 1.0-2.3) and Hg (1.5 95%CI: 1.0-2.3). Higher Ni (PR 1.6 95%CI: 1.0-2.4) and Tl (PR 1.6 95%CI: 1.0-2.4) were observed with intake of dark greens on most days. As intake of whole grain cereal was low, we evaluated the consumption of any whole grain cereal which was associated with increased As (PR 1.4 95%CI: 1.0-2.0), Hg (PR 1.6 95%CI: 1.1-2.2) and Tl (PR 1.4 95%CI: 1.0-2.0). Our study suggests metal exposure with intake of plant-based foods. Plants can accumulate metals from contaminated soil and water. Further research is warranted to identify individual foods associated with metal exposure in Uganda and contamination sources.

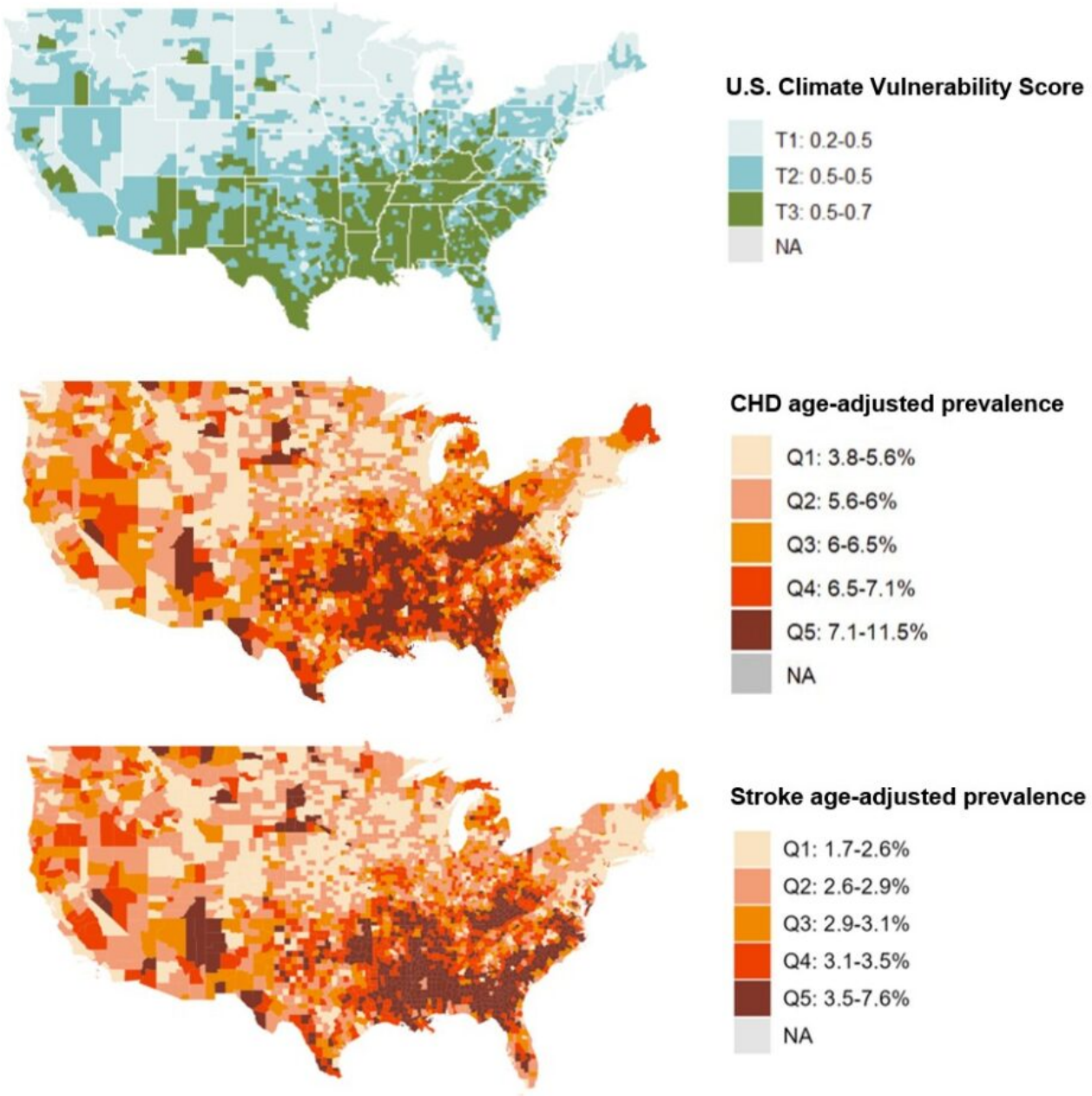
Environment/Climate Change

U.S. Climate Vulnerability Index and Prevalence of Coronary Heart Disease and Stroke

Lindsey M. Russo* Lindsey M. Russo Laura C. Pinheiro Arnab K. Ghosh Azar Abadi Brian W. Whitcomb Jennifer E. Bayly Grace Tee Lewis Emily B. Levitan Sadeer Al-Kindi Monika M. Safford

Introduction: Few studies have examined the relation between climate vulnerability with coronary heart disease (CHD) and stroke in the US using small area estimation methods. Such work is needed to identify high risk counties for targeted intervention. The U.S. Climate Vulnerability Index (CVI) is a novel composite measure of 184 indicators representing county-level vulnerability to climate risks. We sought to determine county-level associations between the CVI and CHD and stroke, hypothesizing that greater CVI would be associated with increased CHD and stroke prevalence.
Methods: Using 2022 CDC Population Level Analysis and Community Estimates data, we conducted geospatial descriptive (Figure) and spatial lag models to estimate associations between county-level CVI (range: 0-1) (2017-2019) and CHD and stroke prevalence, separately. CVI exposure was categorized into tertiles (T1-T3). We used spatial lag regression models to estimate age-adjusted CHD and stroke prevalence and 95% confidence intervals (CI).
Results: Among 3,107 U.S. counties, age-adjusted CHD and stroke prevalence exhibited strong spatial clustering in the Southeastern region. High climate vulnerability tended to cluster in the Southeastern and Southwestern U.S. In spatial lag models accounting for county-level spatial dependence, we observed a 0.83% increase (95% CI: 0.78-0.90) in CHD prevalence, and a 0.61% increase (0.57-0.65) in stroke prevalence (T3 versus T1).
Conclusions: Counties with greater climate vulnerability appear associated with increased age-adjusted CHD and stroke burden, suggesting that communities facing elevated climate risks—particularly in the Southern U.S.—may experience disproportionate cardiovascular impacts. Our small area-level approach can identify counties for targeted support.

Figure. County-level U.S. Climate Vulnerability score (A), age-adjusted (B) CHD and (C) stroke prevalence using CDC PLACES 2022



Environment/Climate Change

Climate signals in the ecology of Naegleria Fowleri Raheleh Mohammadi* Raheleh Mohammadi Yeongjin Gwon Jocelyn J. Herstein Kristina Kintziger Jesse E. Bell

a {
text-decoration: none;
color: #464feb;
}
tr th, tr td {
border: 1px solid #e6e6e6;
}
tr th {
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Background: Naegleria fowleri, the causative agent of Primary Amebic Meningoencephalitis (PAM), is a rare but nearly always fatal infection (95–99% case fatality). Although traditionally linked to warm freshwater, emerging evidence suggests its cysts may persist in cooler, drier conditions, potentially expanding its ecological range. This study explores temporal and spatial patterns of PAM cases in the U.S. and their association with climate-sensitive predictors.

Methods: PAM case data (1962–2023) were obtained from CDC at the county level, including month and year of occurrence. Climate variables—temperature, anomalies, and drought index—were sourced from NOAA datasets, along with regional climate classifications. We compared climate conditions during case-months versus non-case-months and applied generalized estimating equation models to assess associations.

Results: Initially concentrated in southern states (Texas, Florida), PAM cases expanded to western and midwestern regions over time. Decadal trends show increasing frequency, with recent peaks. Case-months exhibited higher temperatures across all regions, even cooler/drier areas. Positive temperature anomalies and drier conditions were more common during case-months. Models indicated temperature anomaly significantly increased PAM incidence (IRR=1.13, CI: 1.11–1.14), while SPI-12 suggested a 12% decrease in incidence per unit increase (IRR=0.88, CI: 0.86–0.90).

Conclusion: Climate variability plays a critical role in PAM emergence. Comparing case-month climate conditions to non-case-months provides insight into pathogen ecology and informs targeted public health interventions.

LATEBREAKER

Environment/Climate Change

Lead and Air Pollution Exposure and Risk of ADHD in Children: Evidence from a Retrospective Cohort in Philadelphia, PA Xuewen Pei* Xuewen Pei Katarzyna Kordas Meng Wang Muwu Xu Jing Nie Amy Hequembourg Adil I. Khan John Turella Marina Oktapodas Feiler

Background

Childhood exposure to lead and urban air pollution remains a significant public health concern, yet evidence linking contemporary low blood lead levels (BLLs) to clinically diagnosed neurobehavioral disorders is limited. In addition, emerging evidence suggests that long-term exposure to ambient air pollution may increase the risk of ADHD. Further, low-income, urban neighbors are disproportionately affected by lead and air pollution exposures.

Methods

This was a clinical retrospective cohort including 14,127 children residing in Philadelphia, PA who visited the Temple University Health System (TUHS) between 2010-2020. Associations between BLLs and ADHD were evaluated using multivariable logistic regression, with BLLs modeled continuously and dichotomized at 3.5 µg/dL; sex-stratified analyses assessed effect modification. Associations between long-term ambient air pollution and ADHD were examined using a matched case-control design matching on age and index time and using conditional logistic regression models. Both models adjusted for individual- and neighborhood-level sociodemographic factors.

Results

Higher continuous BLLs were associated with increased odds of ADHD (adjusted OR 1.51; 95% CI 1.37, 1.67). Children with BLLs ≥3.5 µg/dL had higher odds of ADHD (adjusted OR 1.84; 95% CI 1.56, 2.16) compared with those with BLLs <3.5 µg/dL, with stronger associations observed among males than females. Associations between long-term exposure to PM2.5 or NO2 and ADHD were positive but not statistically significant (PM2.5: adjusted OR 1.19; 95% CI 0.77, 1.83; NO2: adjusted OR 1.02; 95% CI 0.91, 1.15).

Conclusions

Childhood lead exposure, and to a lesser extent long-term ambient air pollution, was associated with increased risk of ADHD in this urban clinical population, underscoring persistent neurodevelopmental risks and the need for continued prevention efforts.

LATEBREAKER

Environment/Climate Change

Wildfires and emergency department visits among children living with sickle cell disease in California: A case-crossover study Zachary Smith* Zachary Smith Jillian Paul Louis Fazen Jaime Madrigano Jhaqueline Valle Kirsten Koehler S. Christy Sadreameli

Background: People living with sickle cell disease (SCD), a rare genetic disorder, may be uniquely vulnerable and susceptible to inflammatory-mediated illnesses from exposure to wildfire smoke. Although the frequency and severity of wildfires are increasing, no studies to our knowledge have looked at associations between wildfire smoke and emergency department (ED) visits among people with SCD.

Methods: We conducted a time-stratified case-crossover study assessing the relationships between wildfire smoke and ED visits among children with SCD living in California from January 2006 to December 2019. Children with SCD and ED visits were identified using California's Sickle Cell Data Collection population-based cohort. Daily mean wildfire and total fine particulate matter (PM2.5) and total ozone (O3) concentrations at lags1-3 were estimated using an ensemble machine learning model and assigned by children's residential ZIP code at time of ED visit. Conditional logistic regression models, adjusted for meteorological factors, were used to quantify the exposure-outcome relationship.

Results: We identified 589 children, 276 children, and 31 children with at least one eligible ED visit for all-causes, pain, and acute chest syndrome (ACS), respectively. Consistent with prior literature, we found PM2.5 at lag3 most predictive of ED visits. A 1 µg/m3 increase in total PM2.5 was associated with higher odds of ED visits for ACS (OR=1.119; 95%CI=1.005, 1.245). Wildfire PM2.5 was also associated with higher odds of ED visits for ACS (OR=1.072; 95%CI=0.968, 1.187), pain (OR=1.004; 95%CI=0.982, 1.028), and all-causes (OR=1.002; 95%CI: 0.991, 1.013) per 1 µg/m3 increase, but these changes were not statistically significant.

Conclusion: Total PM2.5 was associated with increased odds of ED visits for ACS among children with SCD in California from 2006 to 2019. More research is needed to identify patterns of vulnerability and susceptibility to wildfire smoke among children with SCD.

Environment/Climate Change

Examining early gestational susceptibility to ambient air pollutants and risk of pregnancy loss in a time-to-pregnancy cohort Kaniz Rabeya* Kaniz Rabeya Gabrielle Johnson Timothy Canty Karen Schliep Rachael Hemmert Pauline Mendola Neil J Perkins Akanksha Singh Allison Ring Sunni Mumford Carrie Nobles

Background: Early pregnancy is a highly sensitive developmental period in relation to pregnancy loss. We examined air pollution exposure during the earliest gestational weeks encompassing implantation, placentation, and embryogenesis.

Methods: A preconception time-to-pregnancy study (EAGeR trial, 2007-2011) enrolled 1,001 women (18-40 years) from the Intermountain West, with most residing along the Wasatch Front. Residential air pollution exposure was estimated from Air Quality Data for Health-Related Applications (AQDH) & Community Multiscale Air Quality (CMAQ) Models, including ozone (O3), fine particulate matter (PM2.5), & nitrogen dioxide (NO2) and averaged across gestational weeks encompassing pre-ovulation & early embryo development (weeks 1-3), implantation & early loss (4&5), & clinical pregnancy loss (6-9). Pregnancy loss was defined as an observed loss after detection of pregnancy using human chorionic gonadotropin. Generalized linear models estimated relative risk for pregnancy loss per interquartile range increase in pollutants, adjusting for age, income, education, race/ethnicity, and season.

Result: A trend of increasing risk of pregnancy loss was observed during the earliest gestational weeks, including pre-ovulation & early embryo development for both models, although estimates were imprecise. In gestational week 4, PM2.5 was associated with a 29% higher risk of pregnancy loss (RR 1.29, 95% CI 1.00, 1.66 per 2.4 µg/m^3 for CMAQ model) while O3 showed no clear association and NO2 was associated with a non-significant risk decrease. Conversely, during weeks encompassing clinical pregnancy loss, NO2 was associated with an imprecise trend of higher pregnancy loss (RRs ranging from 1.20 to 1.45), while PM2.5 RRs ranged from 0.65 to 0.92.

Conclusion: Exposure to air pollution early in pregnancy may be associated with pregnancy loss, although interdependencies among pollutants may limit inferences. Next steps include evaluating broader air pollution mixtures.

LATEBREAKER

Environment/Climate Change

Co-occurring Exposure to Extreme Heat and Wildfire Smoke During Pregnancy on Preterm Birth Outcomes Aimee Lansdale* Aimee Lansdale Lara Schwarz Dana E. Goin John Boscardin David J. X. González Tarik Benmarhnia Rachel Morello-Frosch Amy M. Padula

Background: Preterm birth (PTB), <37 weeks' gestation, is a leading cause of perinatal mortality and morbidity. Wildfire smoke fine particulate matter (PM2.5) and extreme heat are each associated with increased PTB risk, and co-occurring wildfire-heat events are increasing in California. Yet their joint effects remain understudied.

Methods: In a birth cohort of live singleton births in California conceived between January 1, 2006–December 31, 2020 (N = 4,536,046), we assigned exposures based on maternal residence at birth. Wildfire PM2.5 was estimated using spatiotemporal models; smoke days were defined as ≥5 μg/m³ (2021 air quality guideline for annual PM2.5 by the World Health Organization) with alternative thresholds considered. Extreme heat was defined as days exceeding tract-specific 95th percentile maximum (daytime) or minimum (nighttime) temperatures, calibrated to the warm season to account for regional acclimatization. Smoke and heat waves were defined as 2–4+ consecutive exposure days and assessed individually and jointly. Multivariable logistic regression estimated ORs for PTB, with exposures expressed as percentage of pregnancy days to account for varying gestational length. Interaction was assessed on additive and multiplicative scales. Cox proportional hazards models examined critical exposure windows.

Results: Wildfire smoke days (≥5 μg/m³) were associated with increased PTB risk (OR = 1.02, 95% CI: 1.019, 1.022). Daytime heat showed a slightly stronger association (OR = 1.04, 95% CI: 1.040, 1.042) than nighttime heat (OR = 1.02, 95% CI: 1.023, 1.025). Interaction estimates for joint smoke and heat exposure were positive on both additive and multiplicative scales, indicating synergistic effects of PTB risk.

Conclusion: Wildfire smoke and extreme heat were independently and jointly associated with increased PTB risk. As co-occurring exposures intensify with climate change, mitigating combined exposures during pregnancy is a public health priority.

LATEBREAKER

Environment/Climate Change

Emergency Department Visits for Heat Stroke in the United States, 2016-2021 Tabitha Hardin-Zollo* Tabitha Hardin-Zollo Guohua Li

Despite the knowledge and recognition of increasing frequency and severity of extreme heat events across the United States, there is a remaining gap in the research regarding the demographics of heat stroke mortality and epidemiological trends for ED visits. Using the National Emergency Department Sample, this study investigates the epidemiological patterns of ED visits for heat stroke, defined using ICD-10 codes (T67.0), from 2016 to 2021. Annual incidence rates will be calculated using U.S. Census Bureau data, We hypothesize that heat stroke incidence and mortality rates will increase over the defined time period. Additionally, the highest mortality rates will be in the Northwest and among men, accounting for the lack of population acclimatization due to historically cooler temperatures, and occupational exposures.

Genetics

Genome-wide association study and post-GWAS analysis of serum adiponectin levels in 46,370 Korean individuals SUN HA JEE* SUN HA JEE JiMyoung Kim Wes Spiller Hyungwoo Seo Keum Ji Jung Heejin Kimm

Background:

Adiponectin is an important adipokine involved in lipid metabolism, insulin sensitivity and anti – inflammatory activities. While previous studies have been conducted in populations of European ancestry, there remains a significant lack of large-scale research in non-European cohorts.

Methods:
In this study, we performed a genome wide association study (GWAS) fine-mapping, and GCTA-COJO conditional analyses of plasma adiponectin levels in 46,370 Korean ancestry participants from the Korean Cancer Prevention Study II (KCPS2).

Results:

Among the 1,689 significant SNPs identified ($p < 5e-8$), 627 were mapped to 32 nearest using NCBI37 gene location file. Significant variants were located primarily on chromosome 16 and 3, with the most significant SNP, rs12051272 ($p = 6.12e-440$), residing within the CDH13 gene region. On chromosome 3, the top-associated SNP was rs11711353 ($p = 1.1e-76$), and rs12495941 showed the strongest signal within the ADIPOQ gene region ($p = 4.39e-61$). Further, variant rs12051272 was consistently indicated as having an independent effect on plasma adiponectin levels by fine-mapping and GCTA-COJO analyses. The effect of rs11711353 however appears to be influenced by neighbouring variants.

Conclusions:
The study replicates results from previous genetic studies, and provides a solid foundation for further analyses.The study replicates results from previous genetic studies, and provides a solid foundation for further analyses.

This study was supported by BasgenBio (2021-2026) and the National Cancer Center (HA21C0142).

Genetics

Adjusting for Medication Use in GWAS and its Impact on Mendelian Randomization Analyses: An Example of Systolic Blood Pressure in UK Biobank Aaron Jun Yi Yap* Aaron Jun Yi Yap Aimee L Hanson Gareth J Griffith Eleanor Sanderson

Medication use is common in large-scale population cohorts, and can modify phenotypic traits of interest. This can potentially bias effect estimates in genome-wide association studies (GWAS) and impact downstream analyses such as Mendelian randomization (MR). The best approach to account for medication use in GWAS is unclear. In this study, we compared seven different methods of adjusting for antihypertensive use in a systolic blood pressure (SBP) GWAS of 407,960 White British individuals in the UK Biobank. We found that direct adjustments to measured SBP (adding constants, class-specific constants, censored normal regression) in general yielded a greater number of genome-wide significant variant associations and unmasked stronger GWAS effect estimates than unadjusted measures of SBP. Adjustment for class-specific constants showed the greatest difference relative to unadjusted GWAS. Restriction methods which limit the sample to either untreated individuals or age ranges with low levels of antihypertensive use had less power, due to reduced sample sizes. Effect estimates of treated individuals were deflated relative to untreated individuals, demonstrating the importance of medication adjustment. In MR analyses, we found no substantial differences in inverse-variance weighted (IVW) estimates when using differing exposure GWAS methods in estimation of the effect of SBP on coronary artery disease. Larger variations in IVW estimates were observed for the causal effect of body mass index on SBP across adjustment approaches. In general, the effects of medication use do not substantially affect overall findings. However, bias may arise in MR analyses when the exposure included in the estimation affects the probability of treatment.

LATEBREAKER

Genetics

Disentangling gene-environment correlation and interaction in associations between perceived ethnic discrimination and body mass index in the Hispanic Community Health Study/Study of Latinos (HCHS/SOL) Brooke Mattern* Brooke Mattern Ellyzabeth Morales-Ledesma Misa Graff Kari North Lindsay Fernandez-Rhodes

Obesity risk reflects genetic susceptibility and social exposures. Perceived ethnic-based discrimination is a chronic stressor that may shape body mass index (BMI) through biobehavioral pathways. Polygenic risk scores (PRS) for BMI may correlate with or modify exposure to discrimination, and these associations may differ by sex and female reproductive factors. We estimate associations between a PRS for BMI (11% incremental R2) and perceived ethnic discrimination to evaluate gene-environment correlation (rGE) and gene-environment interaction (GxE), overall and by sex. Data were drawn from 8,593 unrelated adults in the HCHS/SOL baseline examination (2008–11). Perceived ethnic discrimination was assessed via summative score of two questions about its frequency (to self & others) and standardized (mean=3.63, range 2-8). Linear regression models accounted for center, sociodemographics, and genetic ancestry; female-specific models additionally included reproductive factors. The sample's mean age was 47 years (range 18-76); 57% female, and 42% living with obesity. Higher standardized PRS and discrimination scores were independently associated with higher BMI when jointly modeled (β=5.43, 95% CI=5.12-5.74; β=0.36, 95% CI=0.14-0.58). PRS for BMI was significantly associated with perceived discrimination (β=0.11, 95% CI=0.05-0.17), supporting rGE. A PRS x discrimination interaction was not statistically significantly associated with BMI. PRS remained significantly associated with BMI in both males (β=4.68, 95% CI=4.25-5.11) and females (β=5.93, 95% CI=5.5-6.36). PRS was not associated with discrimination among males, but was significant among females (β=0.67, 95% CI=0.38-0.96). In female models including reproductive factors, model fit improved and support for rGE remained. Findings support rGE over GxE, with sex-specific patterning, advancing understanding of how genetic and social processes jointly shape obesity risk in diverse populations.

Global Health

Breastfeeding, Maternal Work Type, and Child Underweight Status Using 2023 Data from the Chitwan Valley Family Study (CVFS) Lena Dang* Lena Dang Emily Treleaven Akina Koju Deepika Bagale Sarah Brauner-Otto

Background: Breastfeeding is generally associated with reduced risk of underweight, and can contribute to optimal growth and development. Underweight remains prevalent in South Asia, where women's labor force participation is rapidly increasing. However, there is little rigorous evidence regarding relationships between maternal work, breastfeeding, and child growth in this region. We analyze these relationships using detailed employment measures to contextualize how women's labor force participation affects child nutrition.

Methods: We used data from 839 children under five years of age (n=784 mothers) from the 2023 Female Labor Force Participation and Child Outcomes data collection of the Chitwan Valley Family Study, a 30-year household panel study in Nepal. We estimated logistic regression models to examine the relationships between maternal work and current underweight status for 832 children with valid maternal work and underweight data. Models adjusted for child age and gender, household wealth quintile, and maternal education, with standard errors clustered by neighborhood. We then estimated the moderating effect of >12 months' duration of any breastfeeding in a sub-sample of 678 children 12+ months with non-missing data.

Results: Over half of children were male (n=450, 54.1%). The overall prevalence of underweight was 10.7% (n=89), and girls tended to be more likely to be underweight (OR=1.43, p=.078). Mothers' work in salaried jobs was associated with lower odds of underweight (OR=0.37, p=.002), while wage labor was significantly associated with higher odds of underweight (OR = 1.78, p = .037). Among children 12+ months, breastfeeding for >12 months tended to reduce the odds of underweight (OR=0.09, p=.107). There was no moderating effect of breastfeeding duration on the relationship between mothers' salary work and underweight.

Conclusions: Longer breastfeeding duration may be protective against underweight among children whose mother engages in wage work.

LATEBREAKER

Global Health

Comparison of antimicrobial resistance among children under 5 in clinic and population-based samples in Niger Angela Cheng* Angela Cheng Ahmed M. Arzika Amza Abdou Sani Ousmane Ramatou Maliki Carolyn Brandt Brittany Peterson Thuy Doan Elodie Lebas Kieran O'Brien Thomas M Lietman

Niger is implementing nationwide mass drug administration (MDA) with azithromycin among children aged 1-59 months to reduce child mortality. Prior trials used population-based samples to monitor antimicrobial resistance (AMR), but clinic-based samples may be more resource-efficient. We leveraged baseline data collection from a cluster-randomized trial to conduct a cross-sectional study to assess whether clinic and population-based samples differ in antibiotic resistance genes (ARGs).

We collected rectal samples from 3 groups of children aged 1-59 months across 39 Centres de Santé Intégrés (CSI, primary health centers). The sick group included 30 children/CSI presenting with diarrheal diseases at the clinics. The healthy group included 30 children/CSI attending routine clinic visits. The population-based group included 10 children randomly selected from 3 villages per CSI.

To account for younger children in the sick group, we age-matched the comparison groups to the sick group by predefined age strata, sampling without replacement. Samples were then pooled by CSI and sequenced. Differential ARG abundance was assessed using DESeq2 with permuted p-values. We also adjusted for antibiotic use in the pairwise comparison between the sick and healthy groups.

After matching, 3,528 children (median age 13 months [IQR: 7–24]; 52.5% male) were included. The abundance of macrolide ARGs was higher in the sick group than in the population-based ($P=0.001$) and healthy groups ($P<0.001$); there was no difference between the population-based and healthy groups ($P=0.38$). The same trend persists for beta-lactams (Figure 1).

Children presenting to clinics with diarrheal disease exhibited higher macrolide and beta-lactam resistance compared to non-sick children, whereas healthy and population-based groups were comparable. Clinic-based AMR has been proposed as a way to monitor MDA, interpretation should include that sick children have higher AMR loads than population-based children.

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Health Disparities

State-Level Socioeconomic Status and Drinking Behavior: An Ecological Analysis Rikki Fan*
Rikki Fan

Introduction: The alcohol harm paradox states that lower socioeconomic groups bear a disproportionate burden of alcohol-related harm despite sometimes reporting lower average consumption than wealthier individuals. This is mainly attributed to differences in drinking patterns (e.g., heavy episodic drinking). This study addresses the gap in ecological, state-level analyses by examining the relationship between state socioeconomic status (SES) and residents' drinking habits.

Methods: This research used a five-year pooled dataset (2019–2023) from the Behavioral Risk Factor Surveillance System (BRFSS). State SES was measured using five-year averages of four metrics from the American Community Survey (ACS): Median Household Income (MHI), educational attainment (proportion of adults over 25 with > high school education), Proportion Under Federal Poverty Line (PFPL), and Unemployment Rate (UER) (age 20–64). Path analysis was employed to examine the associations between these SES factors and various drinking behaviors (e.g., drinking days, binge frequency, Maxdrinks).

Results: The analysis showed complex associations. A higher proportion of educated adults was positively associated with overall drinking in general, but negatively associated with Maxdrinks and binge frequency among current drinkers. A higher MHI was consistently linked to less drinking, showing strong negative associations with binge drinking rate and binge frequency in both the general population and among current drinkers. A higher PFPL was negatively associated with drinking days and binge drinking rate overall, but was positively associated with Maxdrinks and binge drinking rate among current drinkers. A higher UER was associated with less heavy drinking, Maxdrinks, and binge frequency across the population and among current drinkers.

Conclusion: This state-level analysis reveals a complex link between SES and drinking behavior. States with advantageous SES (higher education, higher MHI) may offer some protection against unhealthy drinking patterns. Conversely, while poverty (higher PFPL) may correlate with lower overall drinking rates, it is associated with more intense and potentially dangerous drinking patterns (Maxdrinks, binge drinking rate) among those residents who consume alcohol, providing ecological support for the alcohol harm paradox.

Health Disparities

Association between Shifting Contributions to District-Level Life Expectancy Variation and National Life Expectancy Gains in South Korea, 1999-2022: A Partial Least Squares Analysis Using Repeated Cross-Sectional Data Ikhan Kim* Ikhan Kim Jieun Jeon

Background: Improving overall population health while reducing regional health disparities is a key policy goal in South Korea. However, little is known about how age- and cause-specific contributions to regional life expectancy variation have changed over time or how these changes relate to national life expectancy gains. This study examined trends in district-level life expectancy variation in South Korea from 1999 to 2022, identified age- and cause-specific contributions, and quantified their associations with national life expectancy gains.

Methods: We analyzed sex-, 5-year age group–, district-, and cause-specific population and death data for South Korea from 1999 to 2022. Life expectancy at birth was calculated by sex, year, and district using conventional life table methods. District-level variation was summarized using the mean difference from the national mean. Age- and cause-specific contributions were estimated using a stepwise replacement algorithm, and partial least squares regression was used to assess associations with changes in national life expectancy.

Results: National life expectancy increased from 71.9 to 80.1 years among men and from 79.4 to 86.0 years among women between 1999 and 2022. Over the same period, district-level life expectancy variation declined from 2.35 to 1.27 years among men and from 1.10 to 0.93 years among women. Contributions to regional variation shifted progressively toward older age groups. In addition to neoplasms, cardiovascular diseases, respiratory diseases, and external causes, contributions from neurological and infectious diseases also increased over time. Notably, higher contributions of infectious disease mortality at older ages were associated with smaller national gains in life expectancy.

Conclusions: District-level life expectancy variation followed a convergence pattern among men but a stagnation pattern among women. Reductions in mortality disparities at younger ages were accompanied by a shift in contributions toward older ages. Further decreases in regional life expectancy disparities may require, beyond existing efforts, additional strategies to address geographic inequalities in mortality from infectious and neurological diseases among older populations.

Health Disparities

Rural Medication Disparities for Diabetes, Hypertension and Hyperlipidemia Chia-Lin Chang* CHIA-LIN CHANG

Introduction Health disparities remain a major concern in rural America, where limited healthcare access and socioeconomic challenges lead to higher chronic disease burdens. Prior research on rural medication disparities has focused primarily on opioid prescribing and substance misuse. However, few studies have examined disparities in prescribing practices for chronic diseases, despite their direct implications for treatment optimization, cost-effectiveness, and long-term health outcomes. This study examines rural-urban disparities in chronic medication use to determine whether these disparities reflect actual disease prevalence or inequities in treatment decision-making.**Methods** We analyzed data from the Behavioral Risk Factor Surveillance Survey (BRFSS) 2021–2023 for North Dakota. We compared self-reported prevalence of chronic conditions (diabetes, hypertension, and high cholesterol) and associated medication usage between rural and urban residents. Statistical significance of differences in prevalence and medication adherence between populations was assessed using chi-square tests.**Results** Analysis revealed distinct rural-urban patterns. Insulin use for diabetes was similar between groups. However, rural residents reported significantly higher use of blood pressure medications (81.3% vs. 76.5%, $p=0.056$) and cholesterol medications (29.4% vs. 24.1%, $p<0.001$) compared with urban residents. While higher rates of hypertension explain the increased use of blood pressure medication (36.3% vs. 30.2%, $p<0.001$), the prevalence of hypercholesterolemia was nearly identical between groups (35.6% vs. 33.9%, $p=0.169$).**Conclusion** The finding that rural cholesterol medication use exceeds urban use despite similar disease prevalence suggests that rural-urban differences may reflect variations in prescribing behaviors, treatment thresholds, or access to non-pharmacological preventive care rather than disease burden alone. These patterns raise concerns about possible overprescription or missed opportunities for lifestyle interventions in rural settings. While limited by the self-reported nature of BRFSS data, these preliminary findings highlight a critical gap in rural health management. This study helps future patient-centered care and precision care.

Health Disparities

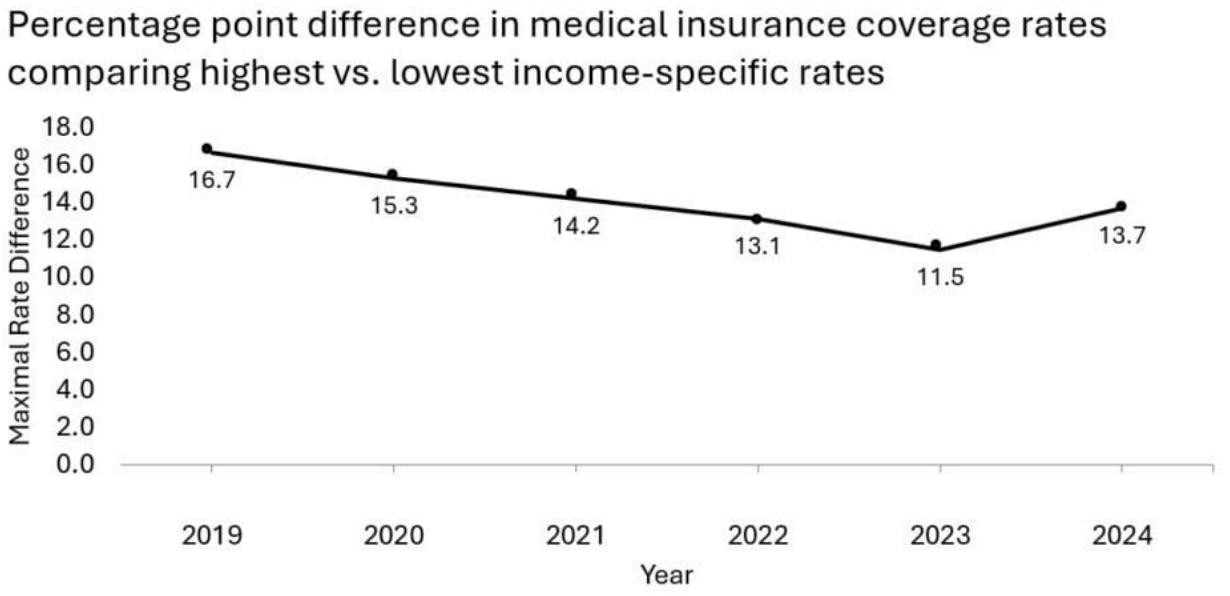
Healthy People 2030: Examining Progress in Medical, Dental, and Prescription Drug Insurance Coverage Christina Fennell* Christina Fennell Jonathan Aram

Background: Healthy People is a national initiative to promote health and reduce disease through the setting and tracking of objectives and targets. Now in its fifth decade, the initiative continues to provide a framework for improving the nation's health. Increasing the percentage of people with medical, dental, and prescription drug insurance are core Healthy People 2030 objectives. This analysis examines progress toward targets and income-specific gaps in these objectives using 2019-2024 National Health Interview Survey data.

Methods: Progress toward targets was measured as the percentage of the targeted change achieved, the change from baseline relative to the difference between baseline and target. Income-specific gaps were measured using the maximal rate difference (MRD), the difference between highest and lowest income-specific rates, and maximal rate ratio (MRR), the ratio of the highest to lowest income-specific rates.

Results: From 2019-2024, the percentage of persons under 65 years with medical insurance improved from 88.0% to 90.1% but did not reach the target of 92.4%. Dental insurance increased from 70.3% to 74.9% but did not reach the target of 75.0%. Prescription drug insurance improved from 82.1% to 84.2% but did not reach the target of 89.1%. The income-specific gaps narrowed over time for some insurance types. For example, the MRD for income groups was 16.7% in 2019 and 13.7% in 2024.

Conclusions: Improvements in total medical, dental, and prescription drug insurance coverage were observed and some income-specific gaps narrowed, but ongoing monitoring is needed.



NOTES: Data are for noninstitutionalized persons under 65 years who reported any type of public or private medical insurance.
Income was measured as family income as a percent of the federal poverty threshold using the following categories: <100, 100-199, 200-399, 400+.
The maximal rate difference represents the difference between the highest and the lowest income-specific rates. For all years, the highest income-specific rate was for the 400+ category. For all years except 2021, the lowest income-specific rate was for the 100-199 category; in 2021 <100 was the lowest rate.
SOURCE: National Health Interview Survey (NHIS), CDC/NCHS.

Health Disparities

Quality of Antenatal Care and Pregnancy Outcomes: Gestational Diabetes and Preeclampsia Analysis in All of Us Participants Sueny Paloma Lima dos Santos* Sueny Paloma Lima dos Santos

Background
The quality of antenatal care (ANC) determines maternal and fetal health outcomes, but researchers have not fully characterized its link to gestational diabetes mellitus (GDM) and preeclampsia. Both conditions significantly affect pregnancy outcomes and long-term maternal health.

Objective
To assess whether the quality of antenatal care (ANC), based on adherence to essential care components, is associated with the risk of gestational diabetes mellitus (GDM) and preeclampsia, overall and by race, among pregnant participants in the All of Us Research Program, Data Release v8.

Methodology

Pregnant participants (N = 900) were identified from electronic health records, procedures, medications, and surveys. Participants ranged in age from 17 to 50 years (mean, 35.0; SD, 6.5). The quality of ANC was defined using six elements: blood pressure measurement, urine protein testing, HbA1c testing, ultrasound exams, iron/folic acid supplementation, and adequacy of visits (≥8 visits, per WHO guidelines). Categories were: **High** — full adherence (≥8 visits and all components), **Intermediate** — missing ≤1 component but ≥4 visits, and **None** — fewer than four visits or missing ≥2 components. Logistic regression estimated odds ratios (ORs) and 95% confidence intervals (CIs) for GDM and preeclampsia, crude and adjusted for race, ethnicity, and maternal age. Interaction terms and stratified models were used to examine race-specific associations.

Results

Blood pressure was measured for all participants. Urine protein tests were performed on 88.2% of participants, HbA1c testing was nearly universal (> 99%), and ultrasounds were also almost universal (>99%). Additionally, 97.4% received iron or folic acid supplementation. However, only 56.4% met the benchmark of eight or more visits. Overall, 55.6% achieved high-quality ANC, 32.3% achieved intermediate quality, and 13.1% achieved low quality. The prevalence of GDM was 51.4% in the high-quality group, 55.7% in the intermediate group, and 57.4% in the low-quality group. The prevalence of preeclampsia was 65.4%, 57.4%, and 52.5%, respectively. Crude models showed no significant association between the quality of ANC and GDM; however, a higher quality of ANC was protective against preeclampsia (Intermediate OR = 0.65, 95% CI: 0.48–0.87, p = 0.005; None OR = 0.56, 95% CI: 0.38–0.84, p = 0.005). After adjustment, results remained consistent: the quality of ANC was not significantly associated with GDM but remained protective for preeclampsia (Intermediate OR = 0.69, 95% CI: 0.50–0.94, p = 0.017; None OR = 0.60, 95% CI: 0.39–0.94, p = 0.024). Importantly, race-stratified analyses revealed heterogeneity: among Black participants, an intermediate quality of ANC was associated with a significantly higher risk of GDM (OR = 3.86, 95% CI: 1.75–8.54, p < 0.001), a pattern not observed in other groups.

Conclusions

The quality of ANC, particularly adherence to recommended visit frequency, shows a protective role against preeclampsia. While no overall association was observed between the quality of ANC and GDM, disparities emerged by race: Black participants showed increased GDM risk with intermediate-quality ANC, which may suggest that ANC effectiveness may vary by racial group, with differential implications for metabolic versus hypertensive outcomes.

Implications

Only half of the participants achieved the benchmark of ≥8 visits, showing persistent gaps in maternal care coverage. Improving the quality of ANC could substantially reduce preeclampsia risk, while targeted strategies may be needed to address elevated GDM risk among Black women. Strengthening equitable access to complete, guideline-based ANC is a critical public health and policy priority to reduce maternal morbidity and disparities across diverse populations.

Health Disparities

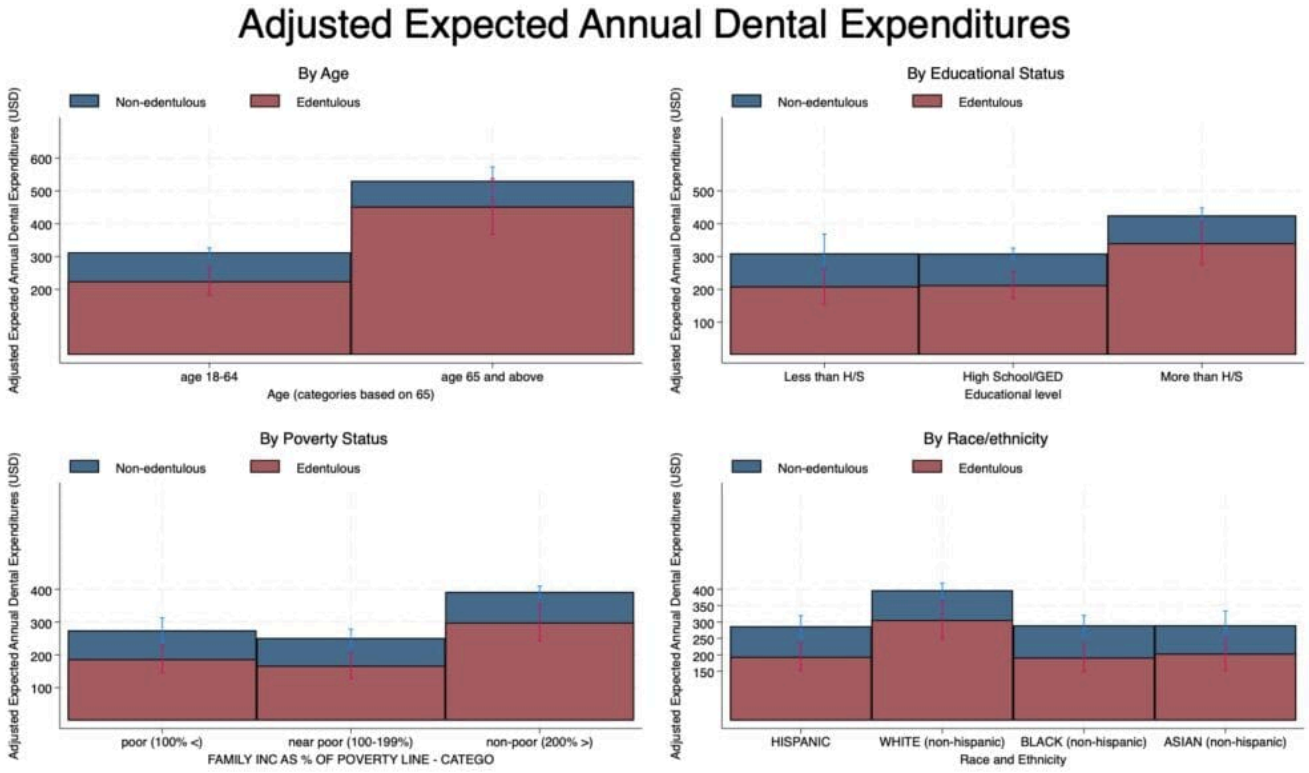
Dentition Status, Dental Visits, And Incremental Costs Among Adults In The U.S. McKing Amedari* McKing Amedari Paul Byers Adejare (Jay) Atanda Ayomide Olatigbe

Objective: Although edentulism may prompt a continued need for professional dental care, patterns of dental service utilization and associated expenditures are not well characterized. We evaluated the association between dentition status (edentulism), dental visits, and incremental costs among adults in the U.S.

Methods: We used data from the 2012-2016 Medical Expenditure Panel Survey, linked with the 2008-2015 National Health Interview Survey, for secondary data analysis. Dental visits were reported as at least one visit (≤12 months), and dentition status was determined as either completely edentulous or dentate. Using multivariable logistic regression, we estimated the association between dentition status and dental visits, controlling for socio-demographic variables and dental insurance. A two-part model was used to determine the incremental costs, adjusted to the 2023 Personal Consumption Expenditure (PCE) healthcare rates. All models were survey-weighted and accounted for complex survey designs.

Results: Our analytical sample was 66,639 adults representing 236 million Americans, of which 6.3% (95%CI: 6.0, 6.7) were completely edentulous, and 56.9% (95% CI: 56.0, 57.8) had no dental visits ≤12 months. Dentate adults had 72% greater odds for dental visits after controlling for covariates, including age, race, income, education, and dental insurance. The total annual expenditure for dental visits for dentate persons was $24.2 million, and $1.2 million for edentate adults. The average change (incremental costs) in expected dental expenditure was $87 greater per capita for dentate adults compared to edentate adults and statistically significant after controlling for covariates ($p < 0.001$).

Conclusion: Edentulism was associated with significantly fewer dental visits and lower dental expenditures. The disparities in dental visits and costs buttress the need to reduce access barriers through integrating oral care with primary care and geriatric care.


Adjusted Expected Annual Dental Expenditures
By Age
Non-edentulous
Edentulous
Adjusted Expected Annual Dental Expenditures (USD)
600
500
400
300
200
age 18-64
age 65 and above
Age (categories based on 65)
By Educational Status
Non-edentulous
Edentulous
Adjusted Expected Annual Dental Expenditures (USD)
500
400
300
200
100
Less than H/S
High School/GED
More than H/S
Educational level
By Poverty Status
Non-edentulous
Edentulous
Adjusted Expected Annual Dental Expenditures (USD)
400
300
200
100
poor (100% <)
near poor (100-199%)
non-poor (200% >)
FAMILY INC AS % OF POVERTY LINE - CATEGO
By Race/ethnicity
Non-edentulous
Edentulous
Adjusted Expected Annual Dental Expenditures (USD)
400
350
300
250
200
150
HISPANIC
WHITE (non-hispanic)
BLACK (non-hispanic)
ASIAN (non-hispanic)
Race and Ethnicity

Health Disparities

Assessing Subjective and Objective Cognitive Function Across Intersectional Identities Using Multilevel Analysis of Individual Heterogeneity and Discriminatory Accuracy (MAIHDA) Nancy Chen* Nancy Chen Miriam T. Ashford L. Paloma Rojas-Saunero Elizabeth Rose Mayeda Alejandra Morlett-Paredes Scott Mackin Erika Cavallone Sarah Tomaszewski Farias Rachel L. Nosheny Kristen M. George

The extent to which intersecting social identities contribute to disparities in subjective and objective cognitive performance remains poorly quantified. We applied an intersectional framework to examine differences in subjective and objective cognition across identities of gender, race/ethnicity, and education.

We analyzed 20,814 participants aged 45+ from the Brain Health Registry. Subjective cognition was measured using the 39-item Everyday Cognition (ECog) Scale, operationalized as the mean score across items. Objective cognition was measured using the Cambridge Cognition Paired Associates Learning test including First Attempt Memory Score (FAMS) and Total Errors Adjusted (TEA). We defined 24 intersectional strata based on gender (men, women), race/ethnicity (Latino, Asian, Black, White), and education (≤2-yr degree, 4-yr degree, Master's/Doctoral/Professional degree). Using the multilevel analysis of individual heterogeneity and discriminatory accuracy (MAIHDA), we fit multilevel linear models with individuals nested within intersectional strata. We estimated age-adjusted null models and main effects models additionally adjusted for gender, race/ethnicity, and education, and quantified between-stratum variance (VPC) and proportional change in variance (PCV).

Mean age was 67±9 years. The most frequent intersectional stratum was White women with a Master's/Doctoral/Professional degree. The variance between intersectional strata accounted for ≤6% of the total variance in ECog, FAMS, and TEA. Most (79-98%) of this between-stratum variance was explained by additive effects of gender, race/ethnicity, and education.

The variance in subjective and objective cognitive performance at the intersectional strata level was small and mostly explained by the additive, not interactive, effects of gender, race/ethnicity, and education. Carefully specified models that adjust for these social factors may adequately capture major disparities in cognitive outcomes.

Table. Multilevel analysis of individual heterogeneity and discriminatory accuracy (MAIHDA) parameter estimates for the Everyday Cognition (ECog) score and Paired Associates Learning (PAL) outcomes, including First Attempt Memory Score (FAMS) and Total Errors Adjusted (TEA).

	ECog Score				PAL FAMS				PAL TEA			
	1A. Null Model		1B. Main-effects model		2A. Null Model		2B. Main-effects model		3A. Null Model		3B. Main-effects model	
Fixed Effects: Regression Coefficients	**Estimate**	**95% CI**	**Estimate**	**95% CI**	**Estimate**	**95% CI**	**Estimate**	**95% CI**	**Estimate**	**95% CI**	**Estimate**	**95% CI**
Intercept	1.43	(1.37, 1.49)	1.33	(1.25, 1.40)	21.53	(20.91, 22.15)	23.19	(22.70, 23.67)	-30.24	(-34.29, -26.19)	-41.06	(-44.48, -37.65)
Age	0.00	(-0.00, 0.00)	0.00	(-0.00, 0.00)	-0.16	(-0.16, -0.15)	-0.16	(-0.16, -0.15)	1.19	(1.15, 1.23)	1.19	(1.15, 1.23)
Gender												
Men			-0.00	(-0.04, 0.04)			-0.80	(-1.01, -0.59)			6.22	(4.76, 8.71)
Women (ref)												
Race/Ethnicity												
Latino			0.08	(0.02, 0.13)			-1.04	(-1.31, -0.77)			6.74	(4.76, 8.71)
Asian			0.12	(0.05, 0.18)			-0.75	(-1.15, -0.36)			3.57	(0.76, 6.38)
Black			0.00	(-0.06, 0.07)			-1.86	(-2.28, -1.45)			12.06	(9.12, 15.01)
Non-Latino White (ref)												
Education												
≤ 2yr degree			0.15	(0.10, 0.20)			-0.82	(-1.07, -0.58)			5.99	(4.13, 7.86)
4yr degree			0.04	(-0.01, 0.10)			-0.23	(-0.47, 0.01)			1.56	(-0.25, 3.37)
Masters/ Doctor/ Professional (ref)												
Random Effects: Variances												
Stratum-level	0.01	(0.00, 0.02)	0.00	(0.00, 0.01)	1.01	(0.54, 2.57)	0.0156	(0.00, 13148)	38.90	(20.77, 97.63)	1.0552	(0.25, 139.64)
Individual-level	0.19	(0.19, 0.20)	0.19	(0.19, 0.20)	15.51	(15.22, 15.82)	15.5209	(15.23, 15.82)	731.42	(717.56, 745.69)	731.43	(717.58, 745.70)
Summary Statistics												
Variance Partition Coefficient (VPC)	3.7%		0.8%		6.1%		0.1%		5.1%		0.1%	
Proportional Change in Variance (PCV)			79.3%				98.5%				97.3%	

Health Disparities

Beyond Average Income: Distinct Life Course Economic Trajectories and Hypertension Risk
Mehrnaz Siavoshi* Mehrnaz Siavoshi

Background
Most research treats income as a static variable, yet economic circumstances fluctuate throughout life. We examined whether distinct patterns of income change over 30+ years differentially impact hypertension risk beyond absolute income level.

Methods
We classified 8,021 PSID participants into five rule-based trajectory groups: stable high income (12.9%), stable low income (19.2%), upward mobility (11.5%), downward mobility (2.3%), and fluctuating income (54.1%). Cox models estimated hypertension hazard ratios adjusted for demographics and time-varying covariates, with additional models controlling for lifetime mean income and volatility.

Results
Unadjusted models showed elevated hypertension risk for stable low income (HR 1.38, 95% CI 1.23-1.54) and downward mobility (HR 1.45, 95% CI 1.17-1.78) compared to stable high income. After demographic adjustment, all trajectory groups showed increased risk, including upward mobility (HR 1.25, 95% CI 1.21-1.29), suggesting lasting effects of early-life disadvantage. However, when lifetime mean income and volatility were included, trajectory groups became protective (stable low HR 0.75, upward mobility HR 0.77), indicating that predictability itself, independent of income level, confers health benefits, potentially through reduced chronic stress.

Conclusion
Economic trajectories have health implications beyond income level alone. The predictability and direction of change matter: early disadvantage leaves biological traces even after economic improvement, while stability appears protective. These findings support life course theory’s concept of biological embedding and suggest that policies promoting income stability may benefit cardiovascular health independent of income supplementation.

Health Disparities

Investigating perceived stress as a partial mediator between race, racial discrimination, and HDP outcomes Autumn Clemons* Autumn Clemons John Pamplin II Lisa Bates Tian Wang Pam Factor-Litvak

Background: Psychosocial stress is a risk factor for hypertensive disorders of pregnancy (HDP), yet its role in contributing to HDP racial disparities remains understudied. We examined whether perceived stress, a measure of psychosocial stress, partially mediated the associations between: 1) race and HDP among the total sample, and 2) racial discrimination and HDP among non-Hispanic (NH) Blacks.

Methods: Included were 6,289 nulliparous individuals with singleton pregnancies who self-identified as NH Black or NH White. Race (a proxy for racism) was the primary exposure. Self-reported racial discrimination (Experiences of Discrimination scale) was the exposure in the subset analysis. Perceived stress (Perceived Stress Scale) was evaluated as a mediator in both analyses. Outcomes, preeclampsia (PE) and new-onset gestational hypertension (GHTN), were analyzed separately. Causal mediation was evaluated using multivariable logistic regression.

Results: NH Black participants had higher rates of PE (12.3% vs. 8.7%, $p < .001$) and higher levels of perceived stress (67.4% vs. 47.6%, p 40% of NH Black participants. Racial discrimination was not associated with each HDP outcome, and no mediation was observed.

Conclusion: This modest mediation finding suggests that pathways beyond perceived stress warrant further investigation and highlight the importance of disaggregating HDP subtypes when evaluating underlying mechanisms.

Health Disparities

The Countereffects of Ethnic Enclaves on Neighborhood Vulnerability: Adiposity Among Mexican American Adults in the Cameron County Hispanic Cohort Ellyzabeth Morales-Ledesma* Lindsay Fernandez-Rhodes Ellyzabeth Morales-Ledesma Miryoung Lee Chelsea Liu Mohanraj Krishnan Cici Bauer Kari E. North Jennifer E. Below Joseph B. McCormick Susan P. Fisher-Hoch Lindsay Fernandez-Rhodes

Missing Data

LATEBREAKER

Health Disparities

Implementation and Evaluation of a Community Health Worker Curriculum to Address Social Determinants of Health Yessica Martinez Mulet* Yessica Martinez Mulet Mike Gonzalez Patricia Rodriguez Espinosa

Community health workers (CHWs) are a growing workforce with demonstrated effectiveness in improving health care access and outcomes for diverse populations. While CHW certification programs exist, due to their broad coverage of many topics, addressing social determinants of health (SDoH) is often overlooked. Using a mixed-methods community-based participatory research design, we co-designed and implemented a 20-hour training curriculum focused on SDoH and resource navigation.

Four community engagement studios (n=60 CHWs) were conducted across the Bay Area to obtain feedback on the content, relevance, and logistics of curriculum implementation. After iterative revisions, we implemented the curriculum with Cohort 1 (N=15, 100% Latino, 87% women, 100% in Santa Clara County). Pre-and post-surveys assessed effectiveness and acceptability. Quantitative data were analyzed using paired-sample t-tests. Qualitative data (open-ended responses) were analyzed using thematic analysis.

Significant increases in SDoH knowledge were noted, with overall knowledge increasing by 48% ($P<.001$). Participants increased their ability to explain the impact of SDoH on families and communities by 42% ($P<.001$) and confidence in their role addressing SDoH by 25% ($P=0.001$). Familiarity with SDoH screening tools increased 45% ($P<.001$) and use of referral models (e.g., closed-loop and no-wrong-door) increased 40% ($P=0.006$). Despite increased knowledge of available resources, CHWs expressed real-world challenges addressing clients' needs, including cumbersome referral processes delaying access. Additional positive outcomes include network building and expansion (100% endorsement).

Findings highlight the need for culturally and linguistically relevant trainings that deepen and complement existing certifications for the CHW workforce. Our mixed-methods evaluation revealed CHWs are highly receptive to curricula designed with their input and focused on topics directly impacting their communities.

LATEBREAKER

Health Services/Policy

Moral Distress Among Providers for Transgender and Gender-Diverse Youth: A National Survey on the Impact of State Legislation and Institutional Policies Laura Stamm* Laura Stamm Ahona Shirin Scott McIntosh Jamie Mehringer

Importance: State bans on gender-affirming care for minors may prevent clinicians from providing care they consider medically necessary, generating moral distress. While qualitative studies have explored provider moral distress, quantitative evidence is limited.

Objective: To assess domain-specific moral distress among clinicians caring for transgender and gender-diverse youth and examine differences by state legislation.

Design, setting, and participants: Cross-sectional electronic survey of U.S. clinicians (2024-2025) practicing in states with varying gender-affirming care legislation (shield law, ban, no legislation, unsure). The analytic sample included 443 respondents.

Main outcomes and measures: Eight moral distress domains rated 0-10. Because distributions were non-normal, medians and interquartile ranges were calculated and compared using Kruskal-Wallis tests with Bonferroni-adjusted pairwise comparisons.

Results: Differences across legislation categories were statistically significant for 7 of 8 domains (all $P<0.05$). Providers in states with bans consistently reported higher distress than those in states with shield laws or no-legislation. Distress related to current legal restrictions was highest in states with bans (median 9 [7-10]) versus shield laws (7 [3-9]) and no-legislation (6 [3-9]; $P<0.001$). Distress regarding anticipated restrictions (median 8 [6-9]), providing care (8 [4-9]), fear for personal or family safety (6 [4-8]), fear of patients being targeted (8 [6-9]), and patient distress due to restrictions (9 [7-10]) were also elevated in states with bans (all $P<0.01$). Distress related to caring for out-of-state patients did not differ by legislation ($P=0.41$).

Conclusions and relevance: Clinicians practicing in states restricting gender-affirming care for minors experience elevated moral distress across legal and patient-centered domains. Restrictive policy environments may constrain clinicians' moral agency and contribute to workforce attrition.


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LATEBREAKER

Health Services/Policy

Is Anyone Listening? Impact of Physical Activity Guidelines on Chronic Disease Prevalence Among U.S. Adults Sarah Melvin* Sarah Melvin

Background: Chronic diseases, including cardiovascular disease, type 2 diabetes, cancer, and obesity, remain leading causes of morbidity and mortality in the United States. Physical activity is a well-established protective factor, and national guidelines introduced as early as 1998 have shifted from performance-based targets to inclusive, health-oriented recommendations. Despite these advances, population-level adherence remains low.

Objective: This systematic review examined the extent to which physical activity guidelines have influenced chronic disease prevalence among U.S. adults aged 18 years and older.

Methods: Following PRISMA procedures, research was conducted in PubMed and Google Scholar for studies published between 1998 and 2025. Eligible studies included observational cohorts, cross-sectional analyses, and randomized trials assessing associations between guideline adherence and chronic disease outcomes. Studies involving pregnant individuals, or mental health outcomes were excluded.

Results: Non-adherence to physical activity guidelines was consistently associated with higher prevalence and earlier onset of chronic disease. In addition to the studies included, national surveillance data were examined to contextualize population-level adherence patterns. Approximately one in four adults meets both aerobic and muscle-strengthening guidelines, with even lower adherence in rural populations and older adults. Data also demonstrates cognitive benefits, including substantially lower dementia risk among adults engaging in moderate-to-vigorous activity. Barriers to adherence persist among individuals with chronic comorbidities, highlighting disparities in implementation.

Conclusions: Although physical activity guidelines have contributed to reductions in chronic disease risk, widespread non-adherence limits the impact. Expanding access, addressing structural barriers, and tailoring interventions to diverse populations are essential for improving health outcomes.

Health Services/Policy

Association between legal access to cannabis and rates of suicide mortality among adults in the United States from 2012 to 2023 Mengni Jing* Mengni Jing Spruha Joshi

Objective

Cannabis legalization is associated with higher rates of suicide among adolescents and increased self-harm among adult males. Little is known the impacts of increased legal access to cannabis through dispensaries on suicide mortality. In this study we examined the associations between legal access to cannabis through both medical and recreational cannabis dispensaries (MCD and RCD, respectively) and and adult suicide death rates in the United States from 2012 to 2023.

Method

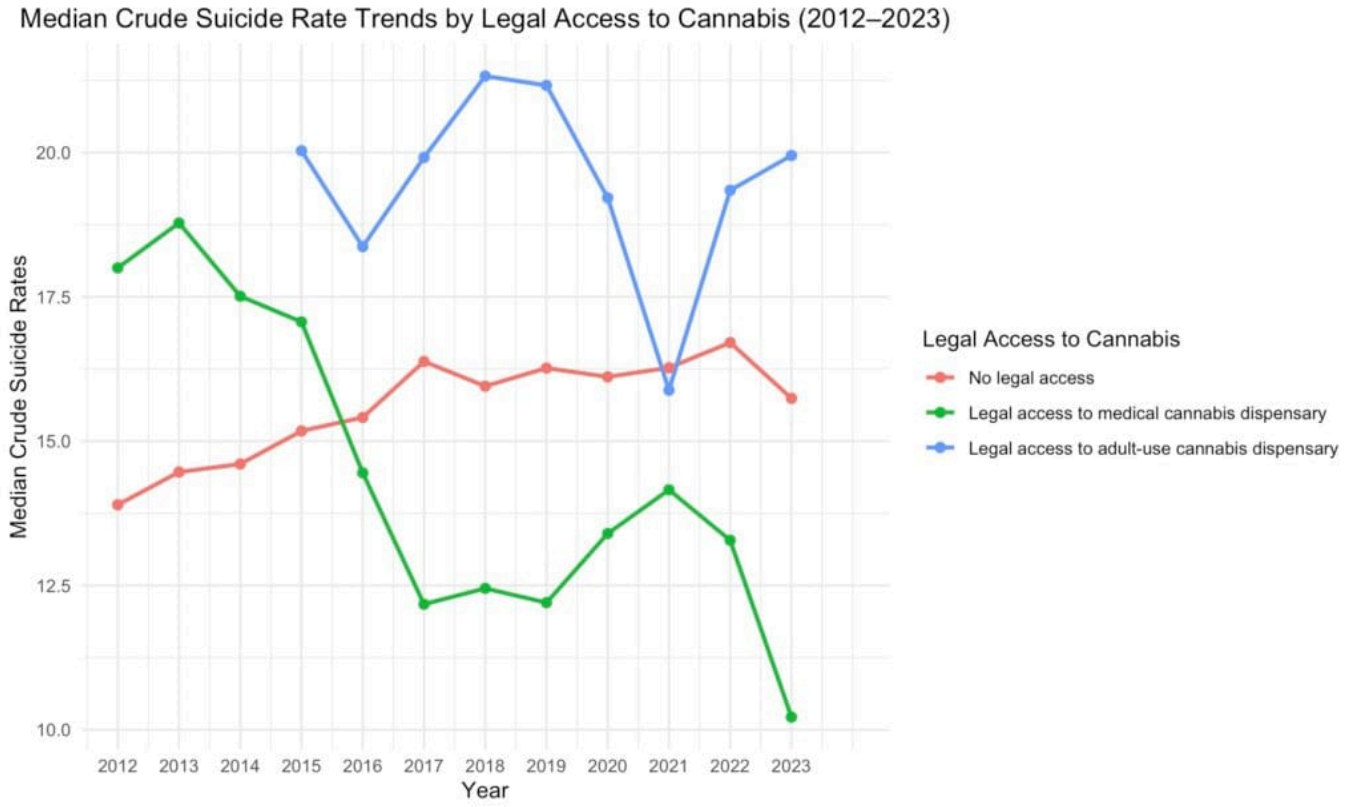
We used monthly adult suicide deaths (N = 528,056) across the 50 states and the District of Columbia from the National Center for Health Statistics Mortality Data during 2012–2023, and linked these to state-month dispensary policy status. We fit Bayesian spatiotemporal models using integrated nested Laplace approximation (INLA) to account for temporal trends and spatial correlation, adjusting for state-level sociodemographic characteristics and other relevant policy statuses. Primary models used a 1-month lag for dispensary policy status, with sensitivity analyses using a 1-year lag.

Results

The average unadjusted monthly adult suicide rate was 1.26 per 100,000 population: 1.25 in state-months without legal dispensary access, 1.16 with MCD, and 1.45 with RCD. In fully adjusted INLA models with a 1-month lag, there was no evidence of an association between MCD and suicide rates (IRR = 1.01; 95% CrI: 0.99–1.03). RCD showed a small, borderline positive association with suicide rates (IRR = 1.02; 95% CrI: 1.00–1.04) compared with no legal dispensary access. Results were similar for the sensitivity analysis of the 1-year time lag of policy status.

Conclusion

Legal access to recreational cannabis dispensaries may be associated with increasing suicide rates among adults, whereas legal access to medical dispensaries was not. Further research should identify which adult subpopulations are most affected and clarify the mechanisms that may explain the relationship between legal cannabis dispensaries and suicide mortality.


Median Crude Suicide Rate Trends by Legal Access to Cannabis (2012–2023)
Median Crude Suicide Rates
20.0
17.5
15.0
12.5
10.0
2012
2013
2014
2015
2016
2017
2018
2019
2020
2021
2022
2023
Year
Legal Access to Cannabis
No legal access
Legal access to medical cannabis dispensary
Legal access to adult-use cannabis dispensary

HIV / STI

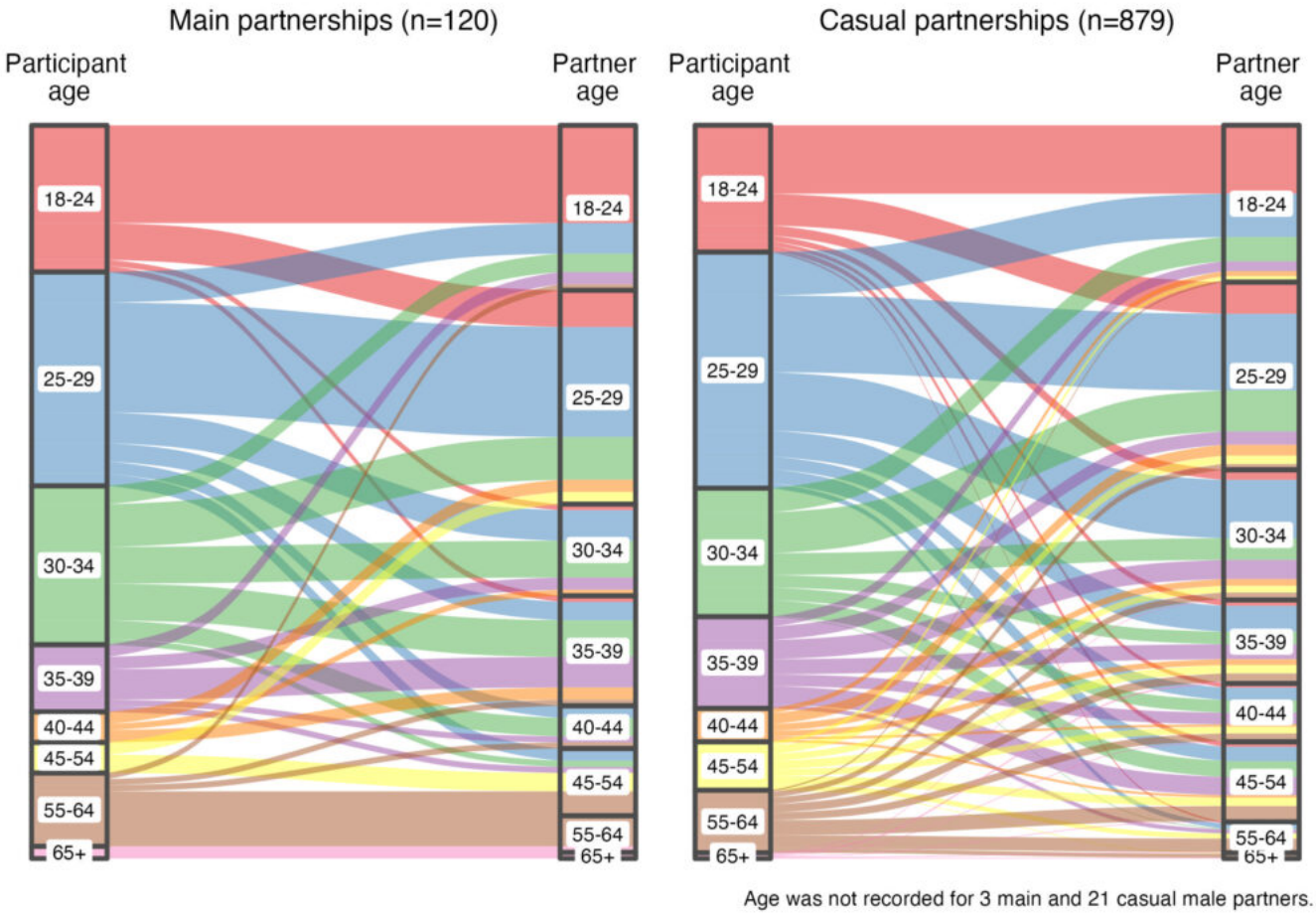
Mixing It Up: Age and Partnership Patterns in MSM Sexual Networks Brittany Liebhard*
Brittany Liebhard Morgan Spahnie William C. Miller Abigail Norris Turner Emily Learner

Background: Syphilis, a sexually transmitted infection (STI) associated with significant morbidity if untreated, is transmitted within sexual networks. Structural characteristics of sexual networks, such as degree and age mixing patterns, are key drivers of transmission, yet are rarely quantified using empirical data. We examined these characteristics among men who have sex with men (MSM) to help understand syphilis transmission patterns.

Methods: We analyzed baseline egocentric sexual networks of men participating in the Network Epidemiology of Syphilis Transmission (NEST) study in Columbus, Ohio (2019-2021). Men reported all sexual partners from the preceding three months; analyses were restricted to male partners. We computed mean degree (average number of sexual partners), the proportion of age-discordant partnerships (partners in different age groups; see figure for groups) and the mean absolute age difference between men and their partners. We examined how network degree and age mixing varied by age and partnership type (main vs casual).

Results: Men (n=241) reported 1,023 male partnerships, for an overall mean of 4.2 partners per person (SD: 4.6, range: 0-25). Men reported substantially more casual (mean: 3.7, SD: 4.6, range: 0-24) than main partners (mean: 0.5, SD: 0.6, range: 0-4). Nearly three-quarters (70%) of all partnerships were age-discordant. The proportion discordant ranged from 44% among men aged 18–24 years up to 93% among men aged 40–44 years. Overall and by each age group, participants were closer in age to their main partners than their casual partners. We observed an age difference of 10 or more years with 16% of main partners and 28% of casual partners.

Conclusion: We observed substantial variation in degree and age mixing patterns by age and partnership type. Recent estimates of sexual network characteristics are essential for understanding current transmission dynamics and designing interventions to curb the syphilis epidemic.



Age was not recorded for 3 main and 21 casual male partners.

HIV / STI

Development and Validation of Two Syphilis Treatment Completion Algorithms Using Routine Surveillance Data in British Columbia, Canada Justin Sorge* Justin Sorge Heather Burgess Doris Chang Venessa Ryan Barbra Arnold Sarah Malleson Rochelle Stimpson Vincent Valdrez Sofia Bartlett Althea Hayden Troy Grennan Kirsty Bobrow

Background British Columbia (BC), Canada, declared a syphilis outbreak in 2019 following sustained increases in infectious and congenital cases. Timely and complete treatment is critical to prevent onward transmission and severe outcomes, particularly during pregnancy. Monitoring treatment completion is therefore a key surveillance activity; however, treatment information is often inconsistently captured in routine public health data. To our knowledge, no studies have described the development of an automated algorithm to identify syphilis treatment completion, and no such algorithm is currently used in Canada.

Objective To develop and validate two independently constructed rule-based algorithms to assign syphilis treatment completion status using routinely collected surveillance data in BC.

Intervention Using the DEVELOP RCD framework, interdisciplinary teams of epidemiologists and clinicians independently designed automated surveillance algorithms based on laboratory, treatment, and case management data. Validation analyses compared algorithm-assigned treatment completion status with clinicians' blinded categorizations, which served as the gold standard.

Outcomes The first algorithm had an overall sensitivity of 53% (95% CI: 45–61) and specificity of 94% (95% CI: 88–97). The second algorithm showed higher sensitivity (71%, 95% CI: 65–77) but lower specificity (78%, 95% CI: 67–86), reflecting different trade-offs in misclassification.

Conclusion Interdisciplinary collaboration was essential to developing automated algorithms for identifying syphilis treatment completion. One algorithm prioritizes specificity and aligns with surveillance definitions, while the other prioritizes sensitivity and aligns with clinical management. These findings provide an evidence-based foundation for scalable, automated monitoring of syphilis treatment completion in public health surveillance.

HIV / STI

Geospatial injection venue attendance dynamics and HIV incidence among people who inject drugs in New Delhi, India from 2017-2025 Griffin Bell* Griffin Bell Steven J Clipman Shobha Mohapatra Aylur K Srikrishnan Muniratnam Suresh Kumar Catherine Lesko Shruti H Mehta Gregory M. Lucas Carl A. Latkin Sunil S Solomon

HIV incidence among people who inject drugs (PWID) in New Delhi, India is among the highest globally. The SARS-CoV-2 pandemic disrupted harm-reduction services and forced relocations, but its effect on HIV transmission is unknown.

To examine spatiotemporal HIV incidence trends, we established a longitudinal cohort of New Delhi PWID. Recruitment, via injection partner referral, occurred in two waves: 2512 participants pre-pandemic (2017–2020) and 988 post-pandemic (2022–2025). Participants underwent rapid HIV testing and completed a behavioral survey at enrollment and up to 10 semi-annual visits. We compared HIV incidence, estimated through Poisson models with generalized estimating equations, over time and across geographic groupings of injection venues, termed “Areas.” Analyses accounting for differential loss to follow-up and death are in progress.

Incidence declined from a pre-pandemic rate of 21 (95% CI: 18-24) cases per 100 person-years (100PY) to a post-pandemic rate of 5 (3-6) per 100PY. Pre-pandemic incidence in a group of venues, “Area 8,” attended by 53% of the cohort was 39 (33-46) per 100PY overall, and 78 (57-107) per 100PY among those reporting needle-sharing. Post-pandemic, Area 8 experienced reduced attendance (53% to 9%), increased saturation of susceptible individuals (40% HIV prevalence pre-pandemic to 65-70% after 2021), and a reduction in incidence to 17 (7-40) per 100PY. Pre-pandemic incidence outside Area 8 was significantly lower at 8 (6-11) per 100PY, declining to 4 (3-6) per 100PY post-pandemic. Surprisingly, needle-sharing at baseline was higher post-pandemic compared to pre-pandemic (54% vs 47%).

HIV acquisition risk depends on individual behaviors, injection networks, and injection venue contexts. Reduced transmission post-pandemic may largely reflect reduced attendance, saturation of susceptible individuals, and behavioral changes at high-incidence venues. High levels of needle-sharing post-pandemic highlight ongoing vulnerability.

HIV / STI

House-Ball Community as a Social Determinant of HIV Outcomes Among Transgender Women of Color Alexander Furuya* Alexander Furuya Cho-Hee Schrader Makella Coudray Asa E. Radix Jenesis Merriman Denton Callander Dustin T. Duncan

Background: The New York City house-ball scene has historically been a community for queer people of color to form chosen families and social networks. We investigated the impact of house-ball participation on HIV care and prevention outcomes among transgender women of color (TWOC) living in New York City.

Methods: We drew data from participants enrolled in the prospective cohort study called the Trying to Understand Relationships, Networks and Neighborhoods Among Transgender Women of Color (TURNNT) Cohort Study. From 2020 to 2022, the research team recruited 179 participants who identified as TWOC and asked them about their participation in the house-ball scene (never, former, current), and their status-neutral HIV care and prevention outcomes, including HIV/STI testing, condom use, Pr1EP use, and HIV viral load suppression. We used Targeted Maximum Likelihood Estimation (TMLE) to estimate the causal relative risk of house-ball participation on these baseline outcomes; we included age, education, income, and US-born nativity as potential confounders.

Results: We found that 6.7% were currently participating in the house-ball scene, 20.7% formerly participated in the scene, and 72.1% never participated. Among TWOC living with HIV (n=94; 52.5%), we found a positive effect of current participation in the house-ball scene on past six-month STI testing compared to never participation (Relative Risk: 1.20, 95% CI: [1.07, 1.33]). Among TWOC not living with HIV (n=85; 45.7%), we found a positive effect of current participation in the house-ball scene on past six-month HIV testing (Relative Risk: 1.27, 95% CI: [1.11, 1.40]).

Conclusions: Community, network connections, and exposure to health campaigns within the house-ball scene may enable and motivate individuals to achieve better HIV care and prevention outcomes.

LATEBREAKER

HIV / STI

Health Status and HIV Risky Behavior in U.S. Adults: The Role of Self-Rated Health and Unhealthy Days–Based HRQOL; results from a 2016-2022 national level study Sarala Pandey* S. Cristina Oancea Ashley Bryant

HIV prevention requires improved identification of individuals at elevated behavioral risk. General health status and health-related quality of life (HRQOL) may reflect physical and mental health burdens linked to HIV risk behavior (HIVRB), but their relative predictive value is unclear. This study examined whether self-reported health and an unhealthy days–based HRQOL category were associated with HIVRB and whether HRQOL was a stronger predictor.

We conducted a cross-sectional analysis of the 2016-2022 Behavioral Risk Factor Surveillance System (BRFSS) data. The outcome HIVRB (yes vs. no) was defined as reporting at least one of the following: injection drug use, treatment for a sexually transmitted disease, or exchange of sex for money or drugs. Exposure 1 was a three-level self-reported health (SRH); Exposure 2 was a three-level unhealthy days–based HRQOL category. Weighted and adjusted logistic regression models were estimated, and effect modification was assessed.

In the overall sample (N=1,337,514), poorer SRH was associated with significantly greater weighted and adjusted odds (WAO) of HIVRB. Compared with excellent/very good health, good health was modestly associated (WAOR=1.10; 95%CI: 1.05–1.14), and fair/poor health showed stronger associations (WAOR=1.30; 95%CI: 1.23–1.37) with HIVRB. The HRQOL measure demonstrated larger, graded associations with HIVRB: moderate (WAOR=1.56; 95%CI: 1.49–1.62) and severe health issues (WAOR=2.15; 95%CI: 2.06–2.25) versus excellent health. Associations were stronger among females, particularly for severe HRQOL impairment (WAOR=2.48; 95%CI: 2.30–2.67), than males (WAOR=1.96; 95%CI: 1.86–2.08), with similar patterns across heavy drinking strata.

Stronger effect sizes for HRQOL suggest cumulative unhealthy days may better capture vulnerability to HIVRB than SRH. Integrating multidimensional health burden measures into HIV screening and prevention strategies may enhance risk identification.

LATEBREAKER

HIV / STI

Timing of Follow-Up Viral Load Testing and Re-Suppression After Virologic Failure Among Patients Prescribed Integrase Inhibitors Lisa Regula* Lisa Regula Jonathan Colasanti Michael Horberg Heidi Crane Peter Rebeiro Vincent Marconi Michael Herce John Gill Jessie K. Edwards

Background: When people with HIV (PWH) on integrase strand transfer inhibitors (INSTIs) have a detectable viral load (VL) after prior viral suppression (VS), a follow-up test within 8 weeks to confirm status is recommended. It is unclear if health system processes for re-testing differ across patient groups.

Objective: Describe timing of follow-up testing and re-suppression after first detectable VL measurement by age, sex, race, region.

Methods: We used data from the North American AIDS Cohort Collaboration on Research and Design, a clinical cohort consortium of adult PWH. Eligible PWH enrolled from 2012 to 2022, engaged in HIV care, initiated an INSTI, achieved VS (VL <200 copies/mL), and had detectable VL (≥200 copies/mL). Index date was first detectable VL, post-VS (median VS: 486 days). Primary outcomes were 6- and 24-mo incidence of follow-up VL testing and virologic re-suppression (<200 copies/mL) estimated using the Aalen–Johansen estimator.

Results: Among 15449 PWH, 74% had a second VL measurement and 66% resuppressed within 6 mo; at 24 mo, estimates were 94% and 88%, respectively. Outcomes were similar by sex and race, but only 68% (95%CI 66-70) of PWH age 25-34 received a follow-up test within 6-mo of index VL, compared to 79% (95%CI 77-80) age >65. At 24 mo, 91% (95%CI 89-92) of PWH age >65 achieved VS compared to only 81% (95%CI 80-83) age 25-34 (Figure). Regions included Canada (<1%) and the US Northeast (32%), South (35%), West (26%), Midwest (7%). In the US, the West had the lowest proportion of second VL test (72%, 95%CI 70-73) or re-suppression (64%, 95%CI 62-66) by 6-mo; at 24-mo, primary outcomes were similar by region. Across all time points, Canadian PWH had the lowest proportion of second VL test and re-suppression, but sample size was limited.

Conclusions: There may be age-based or regional differences in care following a detectable VL in PWH taking INSTIs. Specific groups may benefit from point of care VL testing to minimize time unsuppressed.

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LATEBREAKER

HIV / STI

Implementation of Machine Learning–Based Risk Targeting for HIV Care in Tanzania Huiyu (Joyce) Hu* Huiyu (Joyce) Hu Matilda Mlowe Babuu Joseph Anna Nachbor Amon Sabasaba Jingshen Wang

Background: Machine learning (ML) models have been developed to identify people living with HIV (PLHIV) at risk of disengagement from care and poor treatment outcomes. In Tanzania, the Rudi Kundini, Pamoja Kundini (RKPK) Objective 2 trial tested whether enhanced adherence counseling (EAC) with financial incentives improves viral suppression among PLHIV identified as high-risk using an ML algorithm. We evaluated the clinic-based implementation of this ML-guided strategy by comparing characteristics of individuals enrolled in the trial with those identified as high-risk but not enrolled.

Methods: An ML model was developed using electronic medical record data from HIV care clinics in Tanzania to predict disengagement from care, high viral load, and death. Individual risk scores were generated and a predefined threshold classified individuals as high-risk. High-risk individuals were approached during routine clinic visits for recruitment into the RKPK Objective 2 randomized trial. We compared characteristics of trial-enrolled participants with ML-flagged individuals who were not enrolled. Distributions of ML risk score, age, and time on antiretroviral therapy (ART) were compared using kernel density plots and Wilcoxon rank-sum tests; gender distributions were compared using chi-square tests.

Results: Across four ML risk list rounds, 3,087 individuals were identified as high-risk. Of these, 692 were enrolled and 2,395 were not enrolled. Compared with enrolled participants, ML-flagged individuals not enrolled had higher predicted risk scores (median 0.60 vs 0.57, $p<0.001$) and shorter time on ART (median 52.0 vs 62.2 months, $p<0.001$). The proportion of men was higher among unenrolled individuals (29.7% vs 23.6%, $p=0.002$), while age distributions were similar (median 32 vs 34 years, $p=0.096$).

Conclusions: The ML algorithm identified individuals at elevated risk of poor HIV outcomes, but those at the highest predicted risk were less likely to be reached and enrolled. Individuals most likely to disengage from care may therefore also be the hardest to reach through routine clinic-based recruitment. The large proportion of ML-flagged individuals not enrolled highlights the need for continual updates to outreach lists and improved engagement strategies, including timely EMR data use and proactive follow-up. Differences between enrolled and ML-flagged populations suggest direct trial estimates may not be externally valid. Formal transportability analyses, such as inverse-odds-of-sampling weighting, are a logical next step to estimate population-relevant effects.

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Infectious Disease

Comparative Effectiveness of Three Linezolid Management Strategies for Peripheral Neuropathy During Multidrug- or Rifampicin-Resistant Tuberculosis Treatment: A Target Trial Emulation Matthew Romo* Matthew Romo Malik Adenov Edwin Herrera-Flores Lawrence Oyewusi Andargachew Kumsa Razia Fatima Aga Krisnanda Norbert Ndjeka Alena Skrahina Nino Chumburidze Ofelya Petrosyan Nazgul Samieva Khin Zarli Kyi Lay Allison LaHood Letizia Trevisi Cathy Hewison Kwonjune Seung Palwasha Y. Khan Uzma Khan Carole D. Mitnick Michael L. Rich Helena Huerga Mathieu Bastard Molly F. Franke

Linezolid is a key component of multidrug- or rifampicin-resistant tuberculosis (MDR/RR-TB) regimens, but peripheral neuropathy (PN) is a frequent, treatment-limiting toxicity. Clinicians often suspend linezolid or reduce the dose, but the impact of these changes on treatment success is uncertain. We emulated a target trial using data from the endTB Observational Study, a prospective cohort of people with MDR/RR-TB treated with 18–24-month individualized regimens. Eligible participants had an adverse event of grade 1–2 PN while on linezolid 600 mg daily within 6 months of treatment initiation. We compared three strategies from PN onset (time zero): (1) early linezolid change (suspension or dose reduction) within 0–48 days; (2) late change within 49–181 days; and (3) no change within 0–181 days. Using a clone–censor–weight approach, we estimated the per-protocol effect on end-of-treatment success, standardized for baseline confounders including site, weeks on linezolid at PN onset, and measures of TB disease severity and regimen strength. Among 281 participants from 12 countries, PN occurred a median (IQR) of 13 (6–18) weeks after treatment start. Weighted, standardized probabilities of treatment success were 84% (95% CI: 71%, 93%) for early change, 78% (65%, 87%) for late change, and 85% (79%, 89%) for no change. Compared with no change, treatment success ratios were close to the null value of 1 for both the early change (1.00, 95% CI: 0.83, 1.11) and late change (0.92; 95% CI: 0.75, 1.05) strategies. Modifications to linezolid in the first six months of individualized regimens for MDR/RR-TB were associated with similar probabilities of treatment success compared with continuing linezolid 600 mg daily among people who developed mild or moderate PN. These findings support the clinical practice of cautiously adjusting linezolid when needed to manage PN during MDR/RR-TB treatment.

Infectious Disease

Ambient air pollution and tuberculosis incidence in Brazil: A nationwide panel regression study, 2003-2019 Thi Mui Pham* Thi Mui Pham Thiago Mendonça Derek Mallia Weeberb J. Réquia Katharine Walter

Background: Ambient fine particulate matter (PM2.5) impairs pulmonary immune defenses and may accelerate progression from latent tuberculosis (TB) infection to active disease, yet population-level evidence remains limited.

Methods: We conducted a longitudinal panel analysis using national TB surveillance data from Brazil linked to wildfire-related PM2.5 concentrations across 5,530 municipalities from 2003–2019. Monthly TB notifications were analyzed using Poisson regression with fixed effects for municipalities, state-by-year, and state-by-month to control for time-invariant factors, state-level secular trends, and seasonality. Models adjusted for population size, meteorological conditions, and GeneXpert diagnostic testing. The primary exposure was the monthly number of days with PM2.5 concentrations ≥ 35 µg/m³, the U.S. EPA 24-hour air quality standard commonly used to characterize high-intensity pollution episodes. Sensitivity analyses evaluated alternative thresholds of 25 µg/m³ and 15 µg/m³. To account for TB's prolonged incubation period, we examined lag periods of 6 to 18 months.

Results: Across the study period, 1,505,778 TB cases were reported. Higher PM2.5 exposure was associated with an increased incidence of TB in subsequent months. In the primary analysis, a 14-day increase in days exceeding 35 µg/m³ over the preceding 12 months was associated with a 2.2% increase in TB incidence (95% confidence interval: 1.0%, 3.4%). Associations were stronger at longer lags and attenuated at shorter lags, with estimates including the null at 6 months. Effect estimates were smaller at lower PM2.5 thresholds, with associations including the null at 15 µg/m³.

Conclusions: Elevated wildfire-related PM2.5 exposure was associated with a subsequent increase in TB incidence, consistent with air pollution contributing to the progression to active disease. Ambient air pollution may represent a modifiable risk factor for TB control, particularly in regions with increasing wildfire smoke exposure.

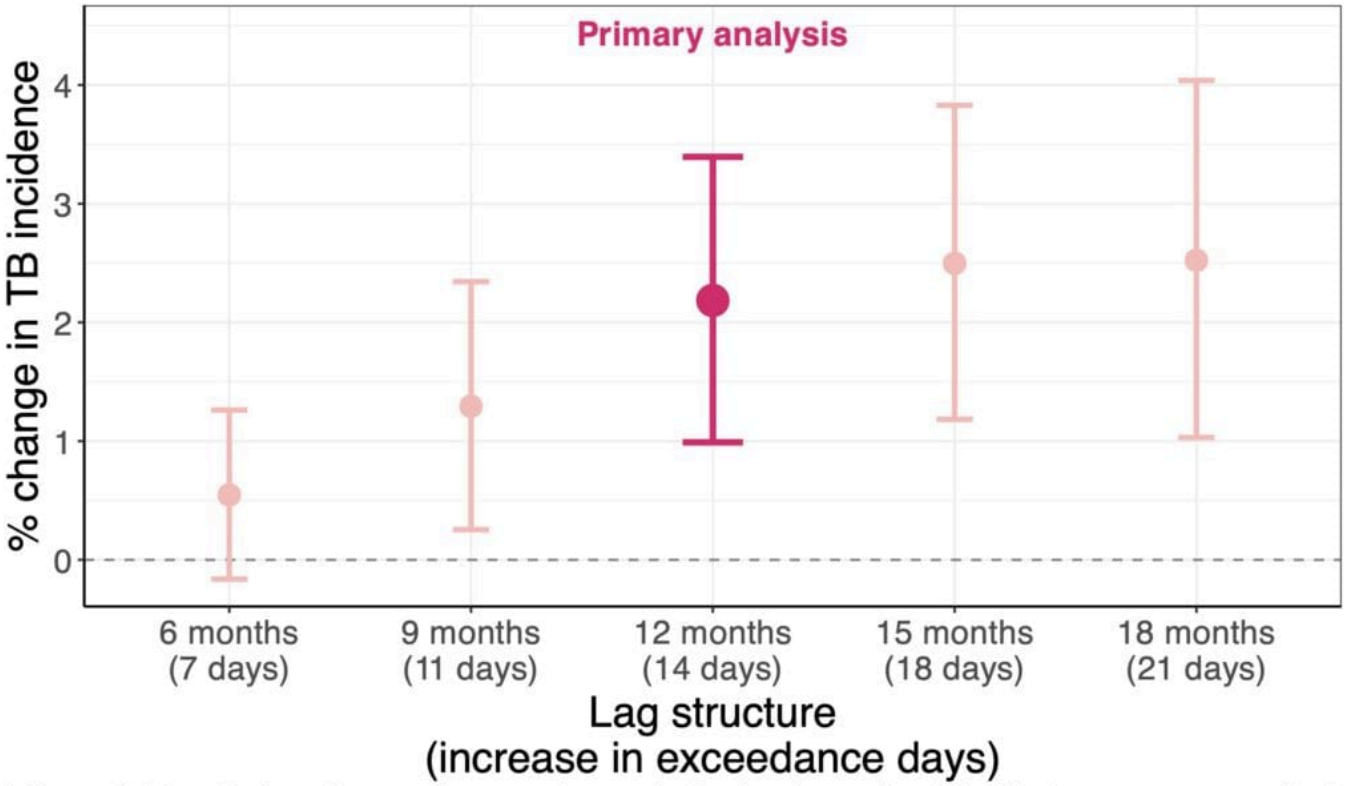


Figure 1. Results from the panel regression analysis showing estimated effects across prespecified lag periods. Points indicate estimated effects, and vertical error bars represent 95% confidence intervals. Lag durations are shown in months, with the corresponding number of $PM_{2.5}$ exceedance days in parentheses. Exceedance days are defined as days on which the average $PM_{2.5}$ concentration exceeded the threshold of 35 μg/m³. The number of exceedance days was selected based on the 95th percentile of exposure within each corresponding lag period, representing an additional high-exposure period. The dashed horizontal line denotes the null effect. The 12-month (14-day) lag is highlighted as the primary analysis.

Infectious Disease

Social margination index and unsuccessful pulmonary tuberculosis treatment outcomes in Sonora, Mexico Gregorio Morales* Gregorio Morales Gerardo Alvarez

Introduction: Pulmonary tuberculosis remains a global public health problem. In Mexico, Sonora in the northwestern of the country, ranks among the highest in incidence and mortality. While individual-level factors have been associated with poor outcomes, the role of contextual factors is still unclear.

Methods: We conducted an ecological study to assess the relation between an Index of Social Marginalization and municipality rates of non-successful treatment outcomes (treatment failure, loss to follow-up, and mortality) among adults with pulmonary tuberculosis susceptible to conventional drug treatment, in Sonora from 2019 to 2023. Poisson regression models were fitted to estimate RR and 95% CI.

Results: Thirty-nine out of 72 municipalities registered pulmonary tuberculosis cases (n=2665) during the study period. Higher rates of non-successful outcomes were observed in municipalities with lower levels of social marginalization. No association was found between the Index of Social Marginalization and treatment failure or loss to follow-up; however, a strong association was observed with pulmonary tuberculosis mortality, with rate ratios ranging from 1.37 (95% CI: 1.23–1.53) in the overall analysis to 1.82 (95% CI: 1.52–2.20) in a sub analysis that include municipalities with the greater rates.

Discussion: The excess mortality observed in less marginalized municipalities suggests that the relationship between social marginalization and pulmonary tuberculosis outcomes is complex and can be influenced by urban dynamics, population concentration, and microcontexts of vulnerability not fully captured at the municipal level. Given the limitations of ecological analyses, these findings highlight the need for more granular geographic analyses and targeted interventions in high-burden areas.

Infectious Disease

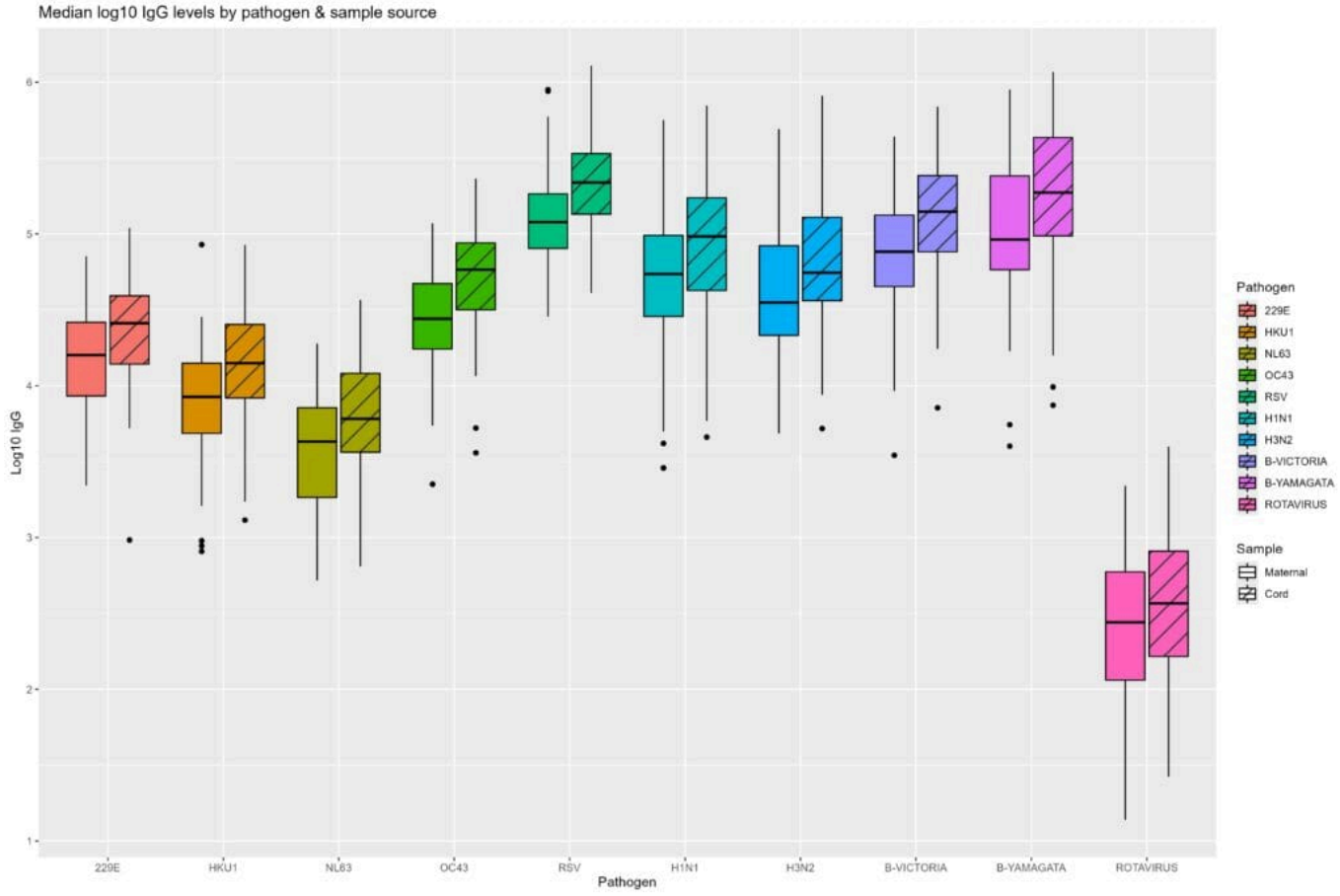
Transplacental transfer of viral IgG antibodies is variable across viral pathogens Shannon C. Conrey* Shannon Conrey Danielle Fayad Monica Epperson Melissa C. Coughlin Allison R. Burrell Claire P. Mattison Rachel M. Burke Julia M. Baker Natalie J. Thornburg Mary Allen Staat Ardythe L. Morrow Daniel C. Payne

Transplacental transfer of maternal antibody provides immune protection to the infant in early life, when the infant's immune system is immature. We examined maternal transfer of antibodies against 10 viral pathogens by comparing IgG concentrations in paired third-trimester maternal to cord sera.

PREVAIL (Cincinnati, OH 2017-2020) collected maternal serum at enrollment (≥34 weeks gestation) and cord serum at birth. Assays quantified IgG antibodies against endemic coronaviruses (OC43, NL63, HKU1, 229E), influenza (H1N1, H3N2, B-Victoria, B-Yamagata), RSV, and rotavirus. Maternal to cord concentration Spearman correlations were calculated. The maternal transfer ratio (MTR) was derived by dividing the cord by the maternal concentration and compared by geometric means (GM) using ANOVA and pairwise t-tests (Holms corrections). The proportion of participants with efficient transfer (MTR >1) by virus were compared using X2. Wilcoxon Rank Sum and Fisher's Exact tests compared demographic and health factors between those we defined as highly efficient (≥8 efficiently transferred) and not highly efficient.

This analysis included 85 dyads with completed IgG assays for all 10 viruses. Maternal to cord correlations ranged from r=0.79 for OC43 to r=0.95 for H1N1 and H3N2 (all p<0.001). The GM MTR for rotavirus (1.44) differed from HKU1 (1.81, p=0.004), OC43 (1.83, p=0.002), B-Victoria (1.75, p=0.04) and B-Yamagata (1.76, p=0.03). Proportion of efficient transfer was ≥92% for all viruses except rotavirus (79%, p<0.001). Most (93%, 79/85) had highly efficient transfer; 65% (55/85) transferred all 10 antibodies efficiently. Child birthweight differed between highly (3.3 (3.1, 3.6) kg) and not highly efficient (2.8 (2.6, 3.1) kg, p=0.02).

Transplacental transfer of IgG antibody is typically efficient but differs by pathogen. Understanding passively acquired immunity should also consider the quality of transferred antibodies and pathogen-specific reasons for differences in efficiency.


Median log10 IgG levels by pathogen & sample source
Log10 IgG
6
5
4
3
2
1
229E
HKU1
NL63
OC43
RSV
H1N1
H3N2
B-VICTORIA
B-YAMAGATA
ROTAVIRUS
Pathogen
Pathogen
229E
HKU1
NL63
OC43
RSV
H1N1
H3N2
B-VICTORIA
B-YAMAGATA
ROTAVIRUS
Sample
Maternal
Cord

Infectious Disease

Spatial Clustering and Multilevel Determinants of Vaccine Misinformation in Angola, Mozambique, São Tomé & Príncipe, and Guinea: Evidence from Demographic and Health Surveys Ahmed Fentaw Ahmed* Ahmed Fentaw Ahmed

Abstract:
Background and aim: Vaccine misinformation, expressed through fear, limited awareness, and sociocultural barriers, remains a major obstacle to immunization in sub-Saharan Africa. Subnational spatial patterns and multilevel determinants of misinformation are not well understood.

Objective: This study aimed to identify spatial distribution and hotspots of vaccine misinformation and to examine individual- and community-level determinants in Angola, Mozambique, São Tomé & Príncipe, and Guinea.

Methods and Analysis: Secondary analyses of the latest Demographic and Health Surveys from Angola (2023–24), Mozambique (2022–23), Guinea (2018), and São Tomé & Príncipe (2008–09) were conducted. Data management and multilevel logistic regression were performed in STATA 17, spatial clustering and hotspots were assessed using ArcGIS (Global Moran's I, LISA), and SaTScan detected purely spatial clusters. Multilevel binary logistic regression identified individual- and community-level determinants. Assumptions included independence within clusters, correct specification of fixed and random effects, and absence of multicollinearity. Statistical significance was set at $p < 0.05$, and associations were reported as adjusted odds ratios (AORs) with 95% confidence intervals (CIs).

Results: Vaccine misinformation exhibited significant spatial clustering in Angola (Moran's I = 0.612, $p < 0.001$). Higher maternal education markedly reduced misinformation (secondary: AOR = 0.55, 95% CI: 0.39–0.78; higher: AOR = 0.04, 95% CI: 0.003–0.55). Attending ≥4 antenatal care visits was protective (AOR = 0.61, 95% CI: 0.47–0.77), whereas higher birth order increased the odds (2–3 children: AOR = 1.81, 95% CI: 1.30–2.51). Spatial heterogeneity was pronounced across provinces, with Cunene (AOR = 6.23, 95% CI: 1.87–20.80), Mexico (AOR = 5.20, 95% CI: 1.56–17.34), and Huambo (AOR = 3.57, 95% CI: 1.12–11.33) identified as hotspots.

Conclusion:
Vaccine misinformation is spatially clustered and shaped by a combination of individual and contextual factors. Targeted interventions in high-risk provinces, along with enhanced maternal education and antenatal care engagement, are essential to mitigate misinformation and improve equitable vaccine coverage. Leveraging spatially informed strategies can optimize resource allocation and maximize public health impact across sub-Saharan Africa.

Keywords: Vaccine Hesitancy; Spatial Epidemiology; Health Geography; Health Communication; Multilevel Modeling; DHS; Sub-Saharan Africa

Infectious Disease

From Hallways to Hotspots: Exploring Residence Hall Risk During COVID-19 Christopher Pierson* Christopher Pierson Julie Casani Edward S. Peters

NC State is a large public university where approximately 21% of more than 35,000 students live on campus in residence halls of four types: hall, suite, hotel, and apartment. Between August 2020 and December 2022, campus officials collected demographic and clinical data to monitor and track students isolated and quarantined on campus as part of the campus's response to COVID-19. Using this data, we examined whether residence hall type influenced community transmission of COVID-19 in dorms. This is vital for managing future outbreaks, including influenza and meningococcal disease.

We constructed epidemic curves, examined geographic case density, and calculated the number of days without positive cases for the campus overall and within each residence style. We conducted multilevel mixed-effects logistic regression to estimate odds ratios of individual residents' infection by hall type, adjusting for semester and accounting for clustering by residence hall. Multilevel mixed-effects Weibull AFT survival analysis for individual students (allowing for multiple events), adjusting for semester and accounting for clustering by residence hall was used to examine dorm style's effect on time to infection. These analyses were also repeated stratifying by semester.

No statistically significant differences among hall types were observed, although semester was associated with infection risk. For example, Spring 2022, which coincided with the Omicron variant, had an OR of 4.27 (CI: 3.74, 4.87) and a time ratio (TR) of 0.06 (CI: 0.05, 0.08) compared with Fall 2020. When stratified by semester, the relationship between hall type and time to infection varied. For example, apartment-style had a TR of 0.20 in Spring 2021, compared to suites, but a TR of 2.53 in Fall 2021. The lack of differences between hall types may be due to robust campus isolation and quarantine procedures, which limited the likelihood of roommate transmission.

Infectious Disease

Double blind randomized controlled trial to evaluate the safety of Lactobacillus rhamnosus GG ATCC 53103 (LGG) vs. placebo in elderly subjects receiving live attenuated influenza vaccine (LAIV) Sam Gebeh* Sam Gebeh Sowmya Rao Patricia Hibberd

Background: Live attenuated influenza vaccine (LAIV) is recommended for healthy non-pregnant persons aged 2-49 years. LAIV has limited effect on vaccine response in the elderly (aged ≥65 years) who are at higher risk due to weakened immune system. Probiotics such as Lactobacillus rhamnosus GG (ATCC 53103) (LGG) may enhance immune response to mucosal vaccines but its effect as a vaccine adjuvant to LAIV is unknown. We conducted a Phase 1 trial of LGG vs. placebo in healthy elderly receiving LAIV, at the end of the 2011-2012 flu season, as it was not ethical to administer LAIV alone during the influenza season.

Objectives: (i) To assess the safety and tolerability of LGG vs. placebo in elderly subjects after LAIV; (ii) To measure anti-influenza systemic immune response (hemagglutinin inhibition (HAI) titers) and anti-influenza mucosal immune response (IgA titers) on Days 21, 28, 56 post LAIV.

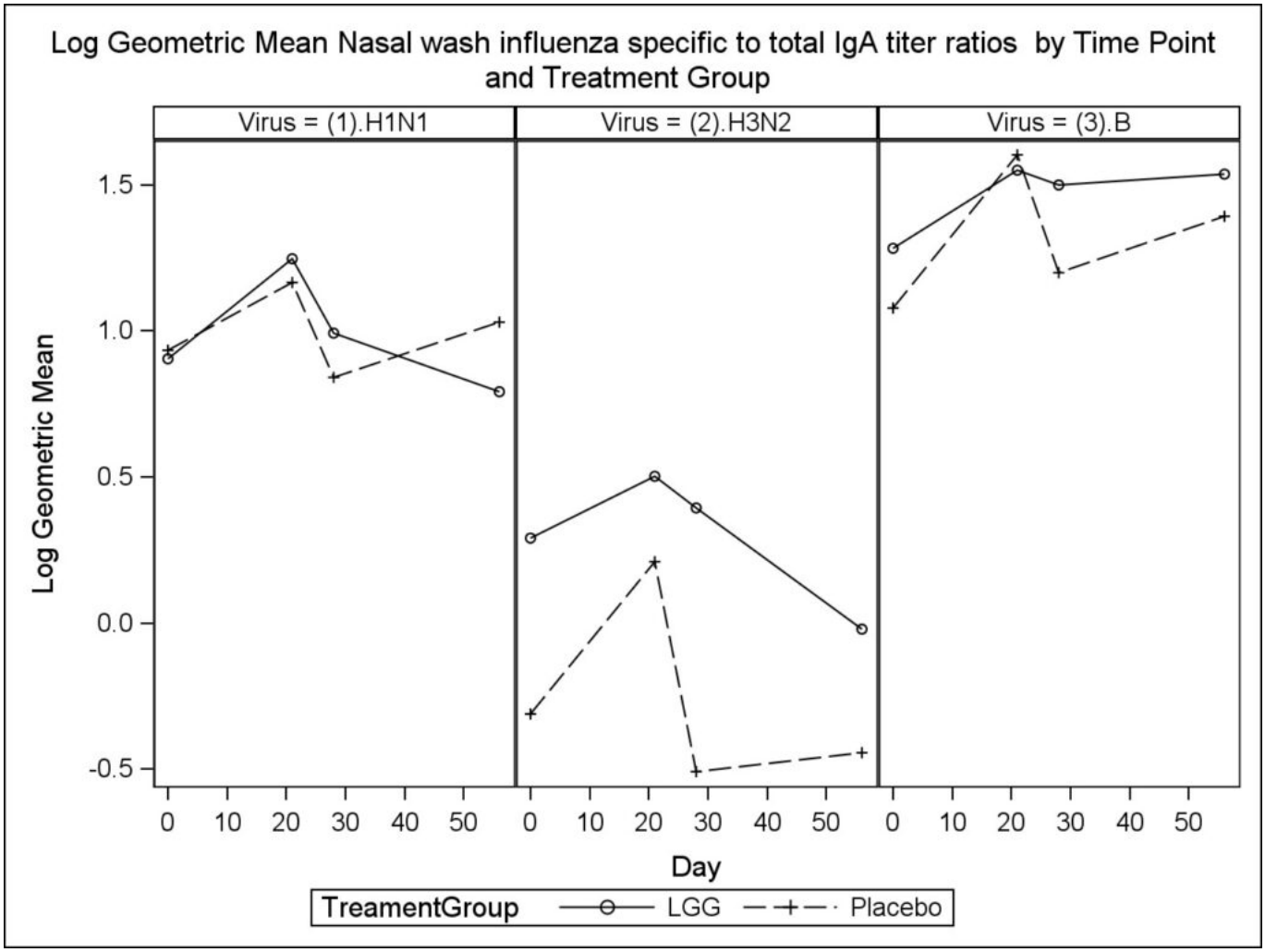
Methods: Elderly subjects aged 65-80 years were randomized to 1×1010 CFU LGG or placebo twice daily for 28 days after receiving LAIV. We assessed subjects and got summary statistics of adverse events from baseline to Day 56. We measured serum HAI titers (H1N1, H3N2, B) and nasal wash influenza specific to total IgA titer ratios at baseline, day 21, 28, and 56 and used 2-sample t-test to compare changes in log geometric mean from baseline to day 28 in LGG vs. placebo group.

Results: Of all 30 subjects, 80% in each group reported treatment-related non-serious adverse events. There were no changes in the log geometric mean serum HAI titers over time in the LGG vs placebo group. Nasal IgA geometric mean fold rise at Day 28 were higher in the LGG group for all antigens, though modest differences between groups.

Conclusion: Administration of LGG with LAIV appears to be safe and well tolerated in elderly, with promising increases in all 3 strain specific nasal IgA fold rises 28 days post-vaccination.

Trial registration: NCT01545349

FDA IND: 14377


Log Geometric Mean Nasal wash influenza specific to total IgA titer ratios by Time Point and Treatment Group
Virus = (1).H1N1
Virus = (2).H3N2
Virus = (3).B
Log Geometric Mean
1.5
1.0
0.5
0.0
-0.5
0 10 20 30 40 50
Day
TreamentGroup
LGG
Placebo

Infectious Disease

An increase in legionellosis cases in the US: An Epidemiological trend assessment before, during, and after the COVID-19 pandemic Katrina Stadler* Katrina Stadler Anthony Elizabeth Alex Hannah

We conducted a preliminary epidemiological assessment of legionellosis cases reported in the United States (US) by evaluating trends before, during, and after the World Health Organization's (WHO) announcement of the end of the COVID-19 pandemic on May 5, 2023. Publicly available data from the Center for Disease Control and Prevention's National Notifiable Diseases Surveillance System (NNDSS) for the years 2016 to 2023 were used in our analyses. T-tests were used to assess differences in the annual number of legionellosis cases before and during the COVID-19 pandemic (2016-2019 and 2020-2022 respectively), as well as for the differences in the monthly number of legionellosis cases before and after the pandemic was declared over (January-April 2023 and May-December 2023 respectively). Overall, the preliminary data show that there was an 8.44% decrease in the average number of legionellosis cases reported during the pandemic (2020 to 2022) compared to prior to the pandemic (2016-2019), however the decrease in the average number of cases was not statistically significant ($p>0.1$). Notably, there was a statistically significant increase (8.63%) in the average number of cases reported per month in 2023 after the WHO declared the end of the pandemic in May 2023 compared to the four months prior ($p<0.001$). This analysis suggests the possible influence of post pandemic conditions or activities (e.g., return to work and/or habitation of previously closed buildings, increased recreational activities, and travel) on the growing trend of legionellosis cases in the US.

Infectious Disease

Spatial, temporal, and space-time trends of reported Shigella spp. outbreaks in the United States, 2009-2022 Muhammad Rashid Bajwa* Muhammad Rashid Bajwa Rebecca Lee Smith

Shigella spp. are the leading cause of acute gastroenteritis posing a public health concern in the United States. This study analyzed surveillance data on Shigella spp. outbreaks reported to the Centers for Disease Control and Prevention via the National Outbreak Reporting System from 2009 to 2022. A total of 1,208 outbreaks were reported across the 48 contiguous states and the District of Columbia, with outbreak incidence varying significantly across time and space. Incidence rates per million population were calculated overall and by age and sex. Descriptive statistics were used to summarize the data, and Joinpoint regression with 95% confidence intervals was used to identify trends. Moran's I was used to identify local clusters and outliers, and Poisson spatial and space–time scan statistics were applied to detect areas and periods of significantly elevated or reduced outbreak rates. Shigella spp. outbreak incidence rates per 1 million population-years increased from 0.27 (95% CI: 0.01–0.84) in 2009 to a peak of 0.74 (95% CI: 0.65–0.84) in 2016, then declined to the lowest rate of 0.03 (95% CI: 0.01–0.05) by 2022. Joinpoint regression trends showed an annual percent change (APC) of 25.12% (95% CI: 11.47 to 53.76, P = 0.001) from 2009 to 2015, followed by a decline with an APC of −38.91% (95% CI: −60.07 to −29.57, P < 0.001) from 2015 to 2022. Persistent high-rate spatial (relative risk, RR = 1.67–5.05) and space–time (RR = 2.28–12.87) clusters were identified in the Midwest, South, and Southwest, including Ohio, Texas, Minnesota, and Arizona. Collectively, these findings demonstrate that Shigella spp. outbreaks in the United States exhibit persistent and regionally distinct spatiotemporal clustering patterns. Identifying areas with sustained elevated outbreak risk can support targeted surveillance, prevention, and response efforts. These findings can guide public health authorities in exposure settings and region-specific Shigella spp. prevention policies across the US.

Infectious Disease

Evaluating the Moving Epidemic Method for establishing seasonal and alert thresholds for influenza-like illness at a single-site university health center setting Carman North* Carman North Michael Mahero

Infectious diseases like influenza like illness (ILI) spread rapidly at institutes of higher education (IHE) thanks to congregate housing, a high level of social interaction in the campus community, and poor uptake of preventive measures like vaccination. Syndromic surveillance may provide an early indicator to student health services at IHEs that ILI season has arrived, allowing IHEs to more effectively deploy influenza intervention strategies and thereby reduce the burden of influenza on all members of the campus community; however, no gold standard for health surveillance currently exists for IHEs. The Moving Epidemic Method (MEM) is a statistical tool that identifies periodicity and intensity of the ILI season, widely used globally for its simplicity and use of standardized data.

In this study, we evaluated the performance of the MEM as a surveillance standard at a single site campus health center. We utilized anonymized electronic health data from a student health center at a large R-1 university in the southeast encompassing ten influenza seasons between 2012 and 2025. Using R, we determined epidemic period, pre- and post-epidemic ILI thresholds, and intensity thresholds based on population-adjusted case counts for each historical season analyzed and calculated standard model performance indicators.

Results showed that seven of ten seasons were classified as medium, two as high, and none as very high. The resulting model demonstrated high specificity (96.01%) and moderate sensitivity (66.08%) in identifying epidemic periods. The findings suggest that MEM is an acceptable surveillance method for ILI at a campus health clinic; however, future research should integrate the use of additional indicators of campus and community impact to improve sensitivity and campus wide response.

This study highlights the potential for MEM to serve as a standardized tool for syndromic surveillance in IHEs, providing actionable insights to reduce the burden of influenza on campus.

LATEBREAKER

Infectious Disease

Infectious Disease Gamal Mohamed* Gamal Mohamed

Modelling Future Outcomes Using Repeatedly Measured Predictors: Prediction of ICU Admission in Patients with COVID-19

Background:
Repeated biomarker measurements are routinely collected in clinical care and provide dynamic information on disease progression. However, epidemiologic applications that explicitly incorporate repeatedly measured predictors to estimate future binary outcomes remain limited.

Objective:
To demonstrate a two-stage modelling framework for incorporating longitudinal predictors into risk prediction of a future binary outcome, using ICU admission among hospitalized COVID-19 patients as an example.

Methods:
We conducted a retrospective cohort study including 372 patients admitted to King Faisal Specialist Hospital and Research Centre (Riyadh, Saudi Arabia) with PCR-confirmed COVID-19 between March and September 2020. Biomarkers were measured every 72 hours. C-reactive protein (CRP) was selected to illustrate the approach.

A linear mixed-effects model was fitted to repeated log(CRP) measurements to estimate patient-specific intercepts and slopes, accounting for within-patient correlation. Estimated random effects were then included in a logistic regression model to assess their association with ICU admission.

Results:
Increasing and persistently elevated CRP trajectories were strongly associated with ICU admission. For each one-unit increase in the CRP slope, the odds of ICU admission increased by 1.98 (95% CI: 1.52–2.58). Model discrimination was good (AUC = 0.79).

Conclusions:
A two-stage approach provides a practical framework for incorporating repeated predictors into dynamic risk prediction and is broadly applicable to binary outcomes beyond COVID-19.

LATEBREAKER

Infectious Disease

A Mixed-Methods Pilot Project to Examine Chagas Disease in the United States Abbey M. Jones* Abbey Jones Marija Zeremski Yiqi Tian Eunice Mak Megha Khatri Arora Manoj Kandpal Jackie Cortez Nancy Jenks Sudha Nagalingam Joel E. Cohen Jonathan N. Tobin

Background: Chagas disease (CD), caused by the parasite Trypanosoma cruzi, results in cardiovascular complications, cardiomyopathy, and death in 30% of people with untreated infections. An estimated 250,000 adults in the USA have CD, but our queries of national databases have found only 4,000 diagnosed individuals. We conducted a mixed-methods investigation to further examine this disparity.

Methods: Data on CD patients were extracted from two electronic health records databases, the Bronx Regional Health Information Organization (Bronx RHIO), covering 5.8 million patients in the Bronx, NY, and TriNetX, a clinical database of 134 million patients in the USA. Univariate statistics were used to describe demographics, clinical characteristics, and cardiac imaging among individuals with CD diagnoses. Bivariate statistics and logistic regression were used to compare CD patients with and without cardiomyopathy. Four focus groups were conducted with community members, clinicians, and staff in NY and AZ to examine barriers and facilitators of screening, diagnosis, and treatment of CD in the USA.

Results: Data were obtained on 61 CD patients (41.0% with cardiomyopathy) in Bronx RHIO and 1,818 CD patients (15.3% with cardiomyopathy) in TriNetX. We found few significant differences among CD patients with and without cardiomyopathy in Bronx RHIO. CD cardiomyopathy patients were more likely to be on antihypertensives, statins, and have received cardiac imaging compared to CD patients without cardiomyopathy in TriNetX. Barriers to CD screening, diagnosis, and treatment include complex testing algorithms, limited awareness, costs, and challenges serving medically underserved patient populations. Facilitators include dedicated staff time, bilingual staff, integrated teams across specialties, and funding mechanisms that will cover testing and treatment costs.

Discussion: CD is underdiagnosed and undertreated in the USA. Improved screening, testing, and treatment programs are needed.

LATEBREAKER

Infectious Disease

Optimal timing for influenza vaccination for adults ≥65 years during the 2023-2024 influenza season Nicola P Klein* Lauren Liao Thomas K Leong Amber Hsiao Kristin Burnett Romain S Neugebauer

Background: Annual influenza infection can cause severe disease, especially among adults ≥65 years of age. Vaccination is an effective prevention strategy recommended annually by the US Advisory Committee on Immunization Practices. While the recommendation is to get vaccinated by October, the optimal vaccination timing may be later if vaccine effectiveness wanes over time.

Methods: We conducted a population-based cohort study within Kaiser Permanente Northern California (KPNC) members aged ≥65 years during the 2023-2024 influenza season to identify optimal timing of vaccination between Sept-Nov before influenza begins to circulate. Using polymerase chain reaction (PCR)-confirmed influenza infection as the outcome, we estimated the risk and relative risk (RR) of infection by April 30, 2024 if everyone in the study population was vaccinated on week 37 (early Sept) or week 46 (mid-Nov). We used longitudinal targeted maximum likelihood estimation (LTMLE) to model time-varying vaccination, censoring, and the outcome, adjusting for baseline demographics and time-varying comorbidities weekly.

Results: Among 736,194 members in the study population, there were 3,389 PCR-confirmed influenza cases (0.46%). Based on preliminary LTMLE analyses which estimated the counterfactual cumulative influenza risk, assuming the full cohort was vaccinated on a particular week, the risk was 0.46% at week 37 and 0.33% at week 46 (Figure 1). When compared with being unvaccinated, the RR of being vaccinated at week 37 was 0.78 (95% CI: 0.62, 0.97) and 0.55 (95% CI: 0.40, 0.74) at week 46. When compared with being vaccinated at week 37, the RR of having influenza if vaccinated at week 46 was 0.70 (95% CI: 0.49, 1.01).

Conclusion: The risk of influenza infection was relatively lower if individuals were vaccinated in November versus in September. The lower risk of influenza infection associated with being vaccinated in November suggests that being vaccinated later during the season may be more protective against influenza.

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Bridging the Gap: Referral Responsiveness Across Support Domains in a Hospital-Based Violence Intervention Program in Arkansas Mofan GU* Mofan Gu Nakita James Nickolas Austin Izah Sydney Sharray Brooklyn Clinton Joshua Joyce

Background/Purpose

Survivors of firearm injury often face a complex web of unmet needs that extend beyond medical care, including housing instability, unemployment, and legal challenges. Hospital-based violence intervention programs (HVIPs) aim to address these social determinants of health through trauma-informed care and connection to community services. Yet, few studies have assessed how well HVIPs identify and act on these needs through formal referral mechanisms. This study evaluates the responsiveness of one HVIP in linking participants to services based on reported needs across multiple life domains.

Methods/Approach

We analyzed data from Project HEAL, Arkansas' first HVIP. At enrollment, participants completed a structured needs assessment spanning ten support domains (e.g., mental health, housing, legal, employment, transportation). Staff encounters were logged throughout the year and categorized by service type. We calculated the number of individuals reporting each need at baseline and the number of unique individuals who received a referral in each corresponding domain. Referral timing was also examined.

Results/Outcome

Mental health was the most frequently reported need (n=55), and 67% of these individuals received a referral—84% of which occurred within the first 3 months. Living support needs were addressed at the highest rate, with 87% of the 30 individuals receiving referrals, primarily early in follow-up. Referrals for legal assistance (80% of 30) were also highly responsive. While smaller in volume, financial education needs (n=7) were met with referrals for 57%. In contrast, healthcare (36%), employment (35%), and education (33%) referrals reached fewer of those who initially reported need. These patterns reflect strong early engagement in core domains and highlight opportunities to enhance linkage in others.

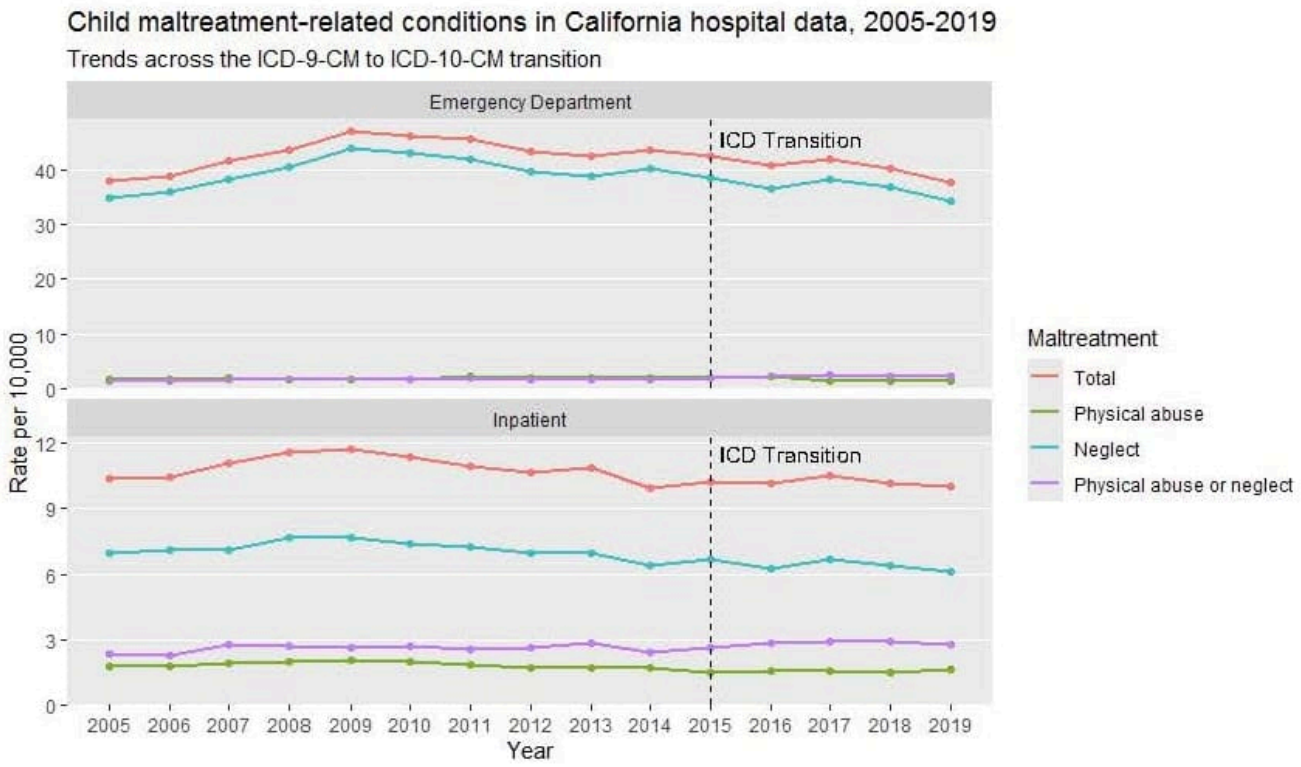
Conclusions/Implications

Project HEAL successfully translated participant-identified needs into timely referrals across multiple life domains. Mental health, legal, and living support showed high alignment between reported needs and service linkage, particularly within the first three months—demonstrating strong case management capacity and early participant engagement. In contrast, lower referral rates for employment, financial education, and healthcare support may reflect persistent, complex needs that are more difficult to address through a single referral event. These domains often require longer-term coordination, workforce opportunities, or systemic resources not always readily accessible. Findings highlight both the strengths and limitations of HVIP-based referrals and underscore the importance of sustained support, flexible service models, and community partnerships to meet evolving participant needs.

Injuries/Violence

easuring child maltreatment-related hospitalizations and emergency room visits across the ICD-9-CM to ICD-10-CM transition: Comparison of three approaches Kriszta Farkas* Kriszta Farkas Sophia Horiuchi Elisabeth Brandstetter Figueroa Corinne A Riddell Jennifer Ahern Patricia G Schnitzer Susan Mason

Child Protective Services reports are a widely used measure of child maltreatment, despite many limitations. Hospital data on conditions indicative of maltreatment may be a complementary surveillance source. International Classifications of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) codes suggestive of maltreatment have been identified; however, the 2015 transition to ICD-10-CM requires crosswalks to capture incidents post-transition. We compared three crosswalk approaches using Centers for Medicare & Medicaid Services General Equivalence Maps: simple forward mapping (“forward”), forward and backward mapping (“forward-backward”), and multi-stage mapping (“multistage”), each varying in comprehensiveness and complexity. Validated ICD-9-CM codes for conditions indicative of child physical abuse and neglect were mapped to ICD-10-CM via each approach. We reviewed ICD-10-CM codes for accuracy, summarized differences across the approaches, and developed a strategy to improve comparability across the transition. We applied the crosswalks to California-wide hospital inpatient and emergency room data from 2005-2019 in children <5 years old and examined trends over the transition. Forward-backward mapping combined with exclusions identified by multistage mapping was the strongest approach. In comparison, forward mapping missed many valid ICD-10-CM codes, often only mapping broad codes. In contrast, multistage mapped many additional ICD-10-CM codes for conditions not of interest but was useful for identifying co-occurring ICD-10-CM exclusion codes needed to isolate the original ICD-9-CM conditions. Application of the final crosswalk resulted in consistent trends in California over the transition. Forward-backward combined with multistage mapping allows for accurate surveillance of child maltreatment in hospital data over the ICD transition; this approach may be useful in other applications.


Child maltreatment-related conditions in California hospital data, 2005-2019
Trends across the ICD-9-CM to ICD-10-CM transition
Emergency Department
Inpatient
ICD Transition
ICD Transition
Rate per 10,000
Year
Maltreatment
Total
Physical abuse
Neglect
Physical abuse or neglect

Injuries/Violence

Child maltreatment, adult partner violence, and age at dementia diagnosis: A sequential causal mediation analysis in the UK Biobank Marie-Céline Schulte* Marie-Céline Schulte Nicholas Magill Karen Devries

Background: Child maltreatment (CM) and adult partner violence correlate with late-onset dementia and a range of established risk factors. However, their associations with age at diagnosis and young-onset dementia (YOD) remain poorly characterized.
Methods: Among 147,938 UK Biobank participants, we identified Alzheimer's-related, vascular, and frontotemporal dementia cases. We examined associations between CM, adult partner violence, age at dementia diagnosis, and dementia diagnosed at age £68 years accounting for diagnostic delays. Weibull accelerated failure time models estimated time from age 18 to diagnosis. Single-mediator and sequential causal mediation models estimated direct effects of CM on dementia diagnosed at or before age 68 years,, indirect effects operating through adult partner violence and 22 established risk factors, as well as proportions mediated, under model assumptions. We calculated E-values for bias quantification.
Results: Of 915 cases, 128 were diagnosed £68 years of age. Individuals CM and partner violence exposed had a dementia diagnosis more than two years younger on average additively than unexposed participants, assuming independent effects. Adult partner violence, socioeconomic deprivation, excessive alcohol consumption, and obesity (body mass index ³30kg/m2) together mediated an estimated 78% of the association between CM and YOD (Adjusted OR: 1.51; 95% CI: 1.01, 2.29), conditional on model assumptions. E-values for indirect effect odds ratios ranged from 1.71 to 2.10, suggesting increasing robustness against unmeasured confounding across the four mediation models.
Discussion: Adult partner violence and midlife risk factors may play a role in associations between CM and younger dementia diagnosis, though interpretations depend on model assumptions.

Mental Health

Associations between food insecurity and mental well-being among US adults: Findings from the 2022-2023 BRFSS Social Determinants module J'Neka Claxton* J'Neka Claxton Guixiang Zhao Machell Town

Background: Food insecurity (FI)—inconsistent access to adequate food—is linked to psychological distress. The Supplemental Nutrition Assistance Program (SNAP) aims to reduce FI.

Objective: Examine the associations of FI with mental health outcomes, including frequent mental distress (FMD), stress, and depression, and explore the role of SNAP in this relationship.

Method: We analyzed data(n=571,053) from the 2022–2023 Behavioral Risk Factor Surveillance System Social Determinants module. FI was defined as responding Always/Usually/Sometimes to the question of food scarcity resulting from insufficient funds. SNAP participation was defined as receiving food stamps. We used Cox regression with robust variance to estimate prevalence ratios, adjusting for sociodemographic variables (age, sex, race/ethnicity, education, marital status, employment status, income, geographic location), household size, and number of chronic conditions.

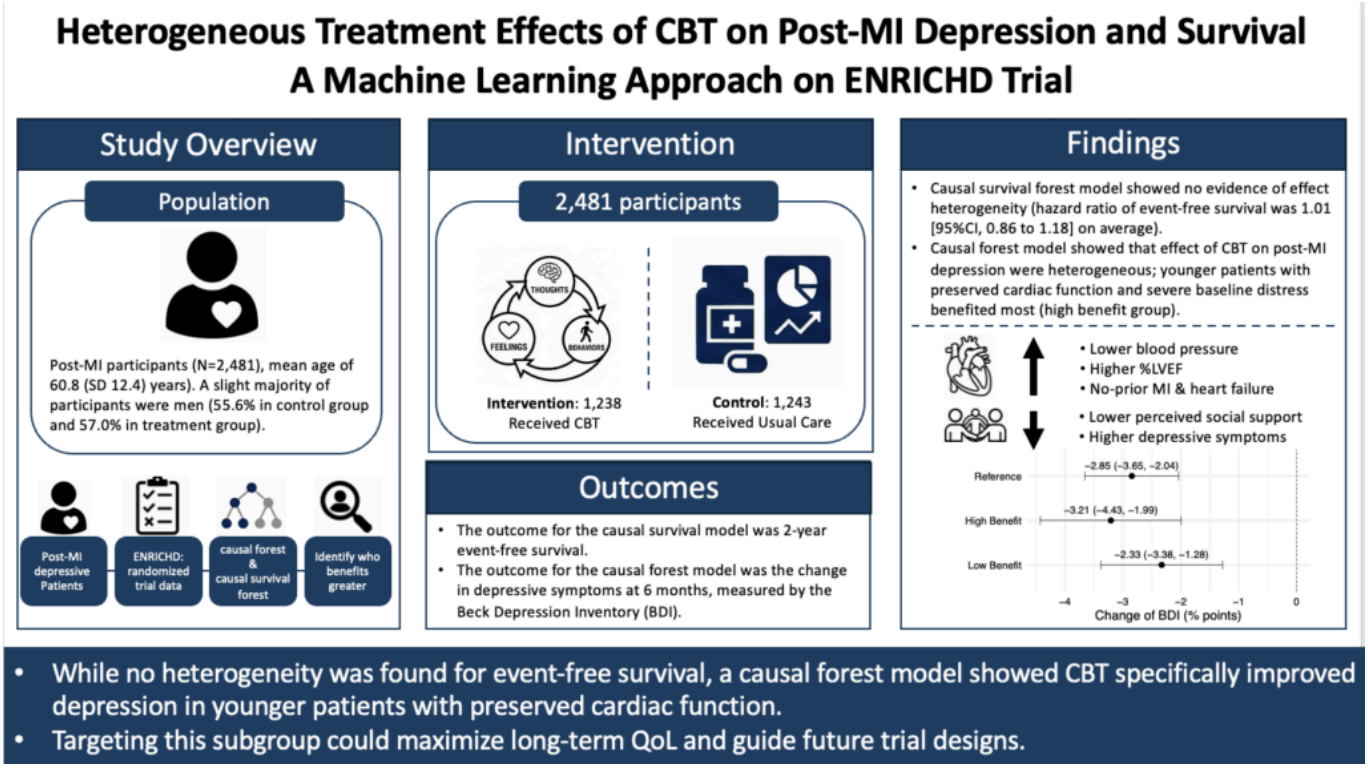
Results: Overall, 14% of adults reported experiencing FI, of whom 38% received SNAP. Prevalence estimates for FMD, stress, and depression were higher among adults experiencing FI than those who did not and were highest among adults experiencing FI with SNAP participation. After multivariate adjustment, prevalences of FMD, stress, and depression were 1.71, 2.13, and 1.42 times higher, respectively, among adults experiencing FI than food-secure adults. Estimates were similar among adults experiencing FI with and without SNAP participation when compared to food-secure adults with no SNAP participation.

Conclusion: The strong associations between FI and impaired mental health suggest public health programs targeting reducing FI may benefit from incorporating mental health support to help improve mental well-being. SNAP participation may not be enough to mitigate the adverse relationship between FI and mental health outcomes.

Mental Health

Heterogeneous Treatment Effects of CBT on Post-MI Depression and Survival: A Machine Learning Approach on ENRICHD Trial Yuta Takemura* Yuta Takemura Ichiro Kawachi Kosuke Inoue

Depression and low perceived social support (LPSS) are associated with poor prognosis after acute myocardial infarction (MI). The ENRICHD trial demonstrated that cognitive behavioral therapy (CBT) improved psychosocial symptoms but failed to reduce all-cause mortality or recurrent MI in the overall population. In this post-hoc analysis of the ENRICHD trial, we investigated the heterogeneous treatment effect (HTE) to determine if specific subgroups derive CBT benefit regarding depressive symptoms or survival. We applied two distinct machine learning algorithms: Causal Survival Forest (CSF) to estimate the conditional average treatment effect (CATE) on event-free survival (all-cause mortality and recurrent MI), and Causal Forest (CF) to estimate CATE on 6-month depressive symptom reduction (Beck Depression Inventory). If HTE was detected, participants were classified into high- or low-benefit groups based on the estimated CATE (defined as



Mental Health

Prevalence and Correlates of Depressive Symptoms Among Ethiopian and Ethiopian-Descent Adults in the Greater Seattle Area: A Cross-Sectional Study Hiwot Weldemariam*
Hiwot Weldemariam Yonathan Dagnew Meron Girma Daniel A. Enquobahrie

Background: Depression is a prevalent mental health condition among immigrants and underserved communities. Community-based estimates of depressive symptoms among Ethiopian and Ethiopian-descendant adults in the United States are limited. **Methods**: We conducted a cross-sectional survey between November and December 2024 among adults (≥18 years) who self-identified as Ethiopian or of Ethiopian descent and resided in the Greater Seattle area. Participants were recruited through social media and community networks. Anonymous surveys were administered via REDCap. Depressive symptoms were assessed using the PHQ-9, with scores ≥10 indicating moderate-to-severe depressive symptoms. Sociodemographic, health, behavioral, and violence-exposure factors were examined. Multivariable logistic regression was used to estimate adjusted ORs and 95% CIs. **Results**: Among 474 participants (mean age 32 years; 51% male; 54% foreign-born), 178 (38%) screened positive for moderate-to-severe depressive symptoms. In adjusted analyses, higher odds of depressive symptoms were associated with increasing age (aOR = 1.05 per year; 95% CI: 1.01–1.09) and part-time employment (vs. full-time; aOR = 5.0; 95% CI: 2.9–8.5). Compared with excellent self-rated physical health, average (aOR = 3.7; 95% CI: 1.1–13.1) and poor health (aOR = 21.2; 95% CI: 6.2–81.9) were strongly associated with depressive symptoms. Additional correlates included prior mental health diagnosis (aOR = 5.0; 95% CI: 2.8–9.8), history of postpartum depression (aOR = 6.7; 95% CI: 3.6–13.6), having more than two children (aOR = 2.9; 95% CI: 1.9–9.1), recreational substance use (aOR = 5.1; 95% CI: 3.2–8.5), and knowing someone injured or killed by a firearm in the past year (aOR = 4.1; 95% CI: 2.6–7.0). Gender, marital status, education, nativity, and years in the U.S. were not significantly associated ($P > 0.05$). **Conclusions:** Depressive symptoms are highly prevalent among Ethiopian and Ethiopian-descendant adults in Greater Seattle. Findings underscore the need for culturally responsive, trauma-informed, and community-based mental health screening and intervention strategies.

LATEBREAKER

Mental Health

Exploring internalized stigma among people living with psychosis and their caregivers: Insights from a community rehabilitation initiative in Malawi Mia Buono* Mia Buono Kazione Kulisewa Brian Pence Bradley Gaynes Abigail Morrison Joshua Chienda Melissa Stockton

In low-resource settings, people living with psychosis (PWLE) experience direct mistreatment (experienced stigma), anticipated mistreatment (anticipated stigma), and acceptance of negative beliefs (internalized stigma). Over time, experienced and anticipated stigma can increase internalized stigma, negatively impacting health. However, predictors and outcomes of internalized stigma among PWLE and their caregivers remain poorly understood.

We analyzed data from PWLE and caregivers participating in a two-arm pilot randomized controlled trial comparing a community-based rehabilitation intervention to enhanced usual care in Blantyre, Malawi (NCT06080477). Sixty PWLE and 118 caregivers who met eligibility criteria were enrolled. Predictor and outcome variables were guided by a conceptual model of internalized stigma. Exploratory factor analysis (EFA) assessed the dimensionality of stigma scales. Bivariate correlations examined associations between predictors and outcomes of internalized stigma.

EFA supported single-factor structures with adequate internal consistency for most stigma scales. Among PWLE, mean internalized stigma, anticipated stigma, and experienced stigma decreased from baseline to 12 months in both arms. Stigma measures were generally comparable between arms except for family-enacted stigma, which was lower at 12 months among those receiving the intervention compared to usual care (mean difference -0.97 (-1.86, -0.07)). At baseline, higher family-enacted stigma was moderately associated with higher internalized stigma scores (correlation coefficient = 0.34; 0.13, 0.53). Greater change in family-enacted and anticipated stigma were weakly associated with a greater change in internalized stigma at 6 and 12 months. Greater internalized stigma was associated with higher depression (0.29; 0.05, 0.50), anxiety (0.27; 0.06, 0.46), and disability (0.25; 0.04, 0.44) at baseline but not over time. Caregivers' internalized stigma decreased over 12 months, with no associated predictors.

These findings highlight that anticipated, experienced, and internalized stigma are prevalent among PWLE in Malawi. Findings suggest the need to continue to explore the mechanisms of internalized stigma to develop strategies to reduce stigma and promote recovery.

LATEBREAKER

Mental Health

Birth cohort differences in depressive symptoms from ages 18 to 30 in the U.S. and mediation by changing social roles Catherine Gimbrone* Catherine Gimbrone Mark Olfson Katherine Keyes John Pamplin

Recent U.S. surveillance studies document rising depressive symptoms among young adults, but less is known about how these symptoms develop across emerging adulthood in different birth cohorts and whether delays in adult social role acquisition contribute to cohort differences.

We analyzed 19 cohorts of Monitoring the Future panel data (born 1971–1989) followed biennially from ages 18 to 30 (1989–2019; N = 7,861). Depressive symptoms were measured using a four-item index (range: 4 – 20). Quadratic latent growth curve models estimated symptom trajectories and cohort effects, including age-by-cohort interactions. Five binary time-varying social roles were evaluated as mediators: full-time college attendance, full-time employment, residential independence from parents, marriage, and parenthood. Models adjusted for sex and race/ethnicity with mediation models further adjusting for lagged depressive symptoms, urbanicity, and parental education.

Results indicated a developmental reversal in cohort effects. Each five-year increase in birth cohort was associated with lower depressive symptoms at age 20 (−0.129; 95% CI: −0.209, −0.048) but higher symptoms at age 30 (0.154; 95% CI: 0.048, 0.259). Social roles partially mediated cohort effects, with modest contributions concentrated after the reversal emerged. Declining marriage explained 11.73% of the total effect at age 30 and declining full-time employment explained 9.8% at age 28. No moderation by sex was observed.

More recent cohorts entered emerging adulthood with lower depressive symptoms than earlier cohorts, but this advantage reversed by age 30. Declining marriage and full time work accounted for a modest portion of cohort differences. Substantial direct cohort effects persisted after accounting for roles, suggesting other unmeasured factors also influence depressive symptom trajectories during emerging adulthood.

Mental Health

The age of anxiety: anti-anxiety medication use among older adults in the United States
Maria Springall De Pablo* Maria Springall De Pablo Don Hedeker Seth Himelhoch Ana W. Capuano Diane S. Lauderdale

National statistics indicate rising rates of anxiety symptoms (e.g., feeling afraid, unable to stop worrying) from 2019 to 2022. For older adults, a treatment challenge is that the most common class of anti-anxiety (AX) medication, benzodiazepines (e.g., Xanax, Valium), are not recommended due to risk of falls and cognitive impairment. Using an ongoing nationally representative cohort of older adults, the National Social Life, Health and Aging Project, we describe AX use among 4,615 older adults by generation ("builders" born 1927-45 vs. "boomers" born 1946-64), measured in 2015/16 (R3) and 2021/23 (R4), and examine sociodemographic correlates. R3 data were collected by interviewers documenting medications in the home, while R4 was multimodal due to the pandemic.

AX use increased by one-third, from 4.1% of participants in R3 to 5.5% in R4. AX use was more common for builders than boomers. In R3, 74.3% of AX use was benzodiazepines and 29.0% other AXs (i.e., buspirone, hydroxyzine); R4 distributions were similar. In both rounds, benzodiazepine use was ~12% more common among builders than boomers. Concomitant use of benzodiazepines plus other AXs increased from R3 to R4, going from 3.3% of users to 4.6%.

Logistic models assessed age, gender, race/ethnicity, education, and logged assets as correlates of cross-sectional AX use. In R3, ORs for Black and Hispanic compared to white participants were 0.18 (95% CI 0.04, 0.74) and 0.27 (95% CI 0.11, 0.69) respectively. Higher education was associated with lower odds of AX use (OR 0.69, 95% CI 0.52, 0.92). In both rounds, higher log assets were associated with lower odds (R3 OR 0.88, 95% CI 0.79, 0.99; R4 OR 0.87, 95% CI 0.80, 0.94), while the odds of AX use were 2.07 (95% CI 1.34, 3.18) and 2.46 (95% CI 1.45, 4.19) higher for females than males.

Despite clinical guidelines, benzodiazepine use remains common for older adults, particularly among builders. Women, those with fewer assets, and less education present higher AX use.

Mental Health

The association between pre-pregnancy weight changes and offspring risks of attention-deficit/hyperactivity disorder Jimin Clara Park* Jimin Park Ketrell L. McWhorter Ruby Charak Megan N. Baber Bong-Seong Kim Ga Eun Nam Kyungdo Han

Background: Pre-pregnancy obesity has been linked to increased risk of attention-deficit/hyperactivity disorder (ADHD) in offspring, but evidence is limited on the association of pre-pregnancy weight and obesity status change with offspring ADHD risk.

Methods: Using nationally representative linked data from South Korea's National Health Insurance Service and the National Disability Registration System(2011-2018), 443,294 offspring of 394,429 mothers aged ≥20 years were followed from birth to first ADHD diagnosis until 2022(mean=6.9 years). Pre-pregnancy weight and obesity status were from two standardized biennial health examinations(within 2 years before pregnancy and about 2 years earlier), and weight change was the percentage difference between them. Obesity status was defined by Asia-Pacific body mass index cutoffs(non-obese, <25 kg/m^2; obese, ≥25 kg/m^2). ADHD diagnosis required specialist-documented diagnoses consistent with the Diagnostic and Statistical Manual of Mental Disorders or International Classification of Diseases criteria with standardized behavioral assessments. Cox proportional hazards models were adjusted for sociodemographic, reproductive, lifestyle, and maternal clinical factors.

Results: Cumulative offspring ADHD incidence was 2.68% among mothers with persistent obesity and 2.64% among mothers who maintained non-obese status. Compared with mothers who maintained non-obese status, persistent maternal obesity was associated with higher offspring ADHD risk(hazard ratio[HR]1.17; 95% confidence interval[CI]1.08-1.26). Compared with weight change within ±5%, ≥10% weight gain was associated with increased risk(HR 1.12; 95% CI 1.05-1.20). In subgroup analyses, the association of persistent maternal obesity with offspring ADHD risk was stronger among mothers with mental disorders(HR 1.75; 95% CI 1.37-2.25;P for interaction=0.011).

Conclusions: Persistent maternal pre-pregnancy obesity and ≥10% weight gain were associated with higher offspring ADHD risk.

Mental Health

Home environment predicts cognitive outcomes in mid-childhood: Evidence from the MAASTHI Cohort, India Giridhara Rathnaiah Babu* Giridhara Rathnaiah Babu Deepa Ravi Debarati Mukherjee

Background

Prenatal exposures can have long-lasting effects on neurodevelopment, yet longitudinal evidence from low- and middle-income countries remains limited. We investigated whether prenatal biological and socioeconomic factors during pregnancy predict cognitive outcomes in mid-childhood in a South Indian birth cohort.

Methods

We used data from the MAASTHI cohort, including children assessed in 2024-25 (5–9 years). The primary outcome was cognitive performance measured using Raven's Colored Progressive Matrices. In the main analysis (n = 955 children), we examined maternal glucose, hemoglobin, birth weight, duration of breastfeeding, and household socioeconomic status. Multivariable linear regression models were adjusted for child age, mother's age, parity, religion, and number of living children.

In a secondary complete-case analysis (n=882 children), we additionally measured home environment characteristics measured in 2023-24 using the Family Care Indicators Tool to explore potential developmental pathways linking early exposures to later cognition.

Results

Prenatal biomarkers, birth weight, and breastfeeding duration were not associated with mid-childhood cognitive scores, while more favourable household socioeconomic conditions during pregnancy were associated with higher cognitive scores. In the complete-case subgroup analysis, poorer home environments were associated with low cognitive scores.

Conclusion

Early socioeconomic conditions and the quality of the home environment were key predictors of cognitive performance in mid-childhood. These findings highlight the importance of improving socioeconomic circumstances and home environments to support optimal child neurodevelopment in low-resource settings.

Keywords: Prenatal exposures; cognition; longitudinal cohort; socioeconomic, home environment; child development; India.

Methods/Statistics

Disease Risk Score Methods for Studying Treatment Effect Heterogeneity in Real-World Data Haedi Thelen* Haedi Thelen Wei Yang Sean Hennessy Jordana Cohen Wensheng Guo Todd Miano

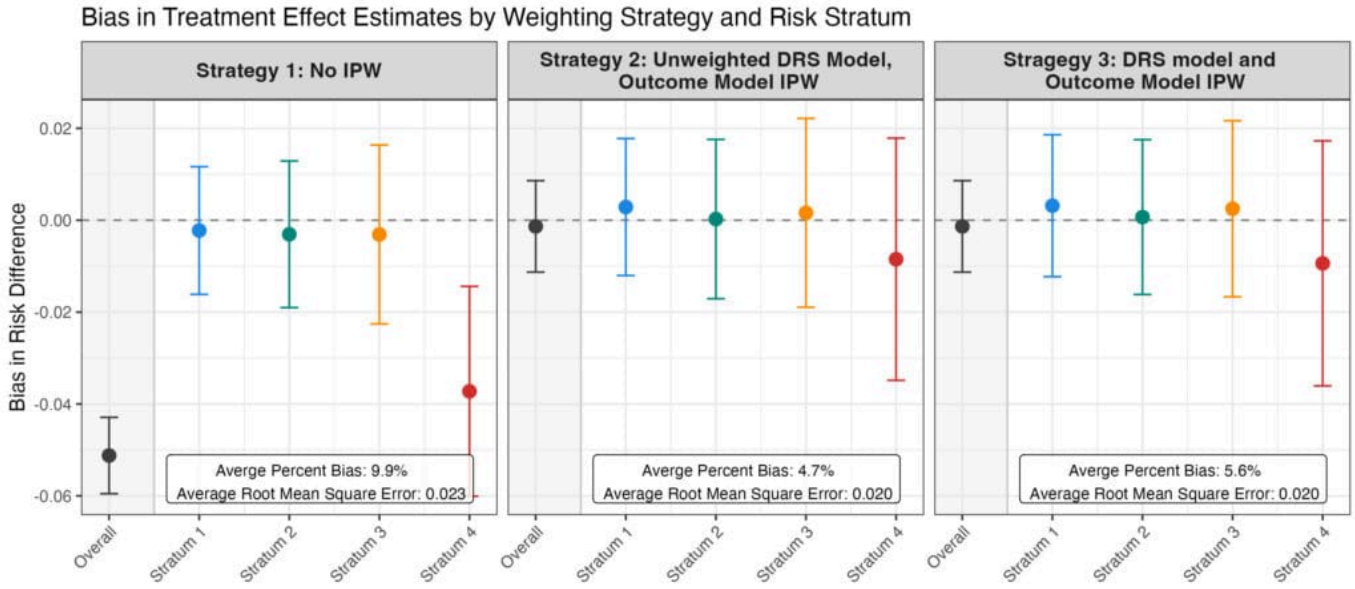
Background: Stratification by an internally derived disease risk score (DRS) can be used to examine heterogeneity of treatment effect (HTE) and to control confounding. However, internal derivation methods developed in randomized trials require adaptation for real-world data, where confounding and DRS model transportability may bias stratum-specific treatment effect estimates.

Objective: To determine whether inverse probability weighting (IPW), when used for DRS score estimation (to address DRS transportability) or outcome modeling (to address confounding) reduces bias and improves efficiency of treatment effects estimated within DRS strata.

Methods: We compared three strategies with increasing IPW use: 1) none, 2) for treatment effect estimation only, 3) for both DRS estimation and treatment effect estimation. We simulated a million individuals with a binary treatment (35% treated), 12 confounding covariates, and a binary outcome (15% incidence in unexposed). The overall treatment effect was a risk difference of 0.08, and the stratum-specific effects ranged from 0.02 in the lowest to 0.18 in the highest risk strata. We repeatedly sampled 10,000 patients, fit a correctly specified DRS model, and compared the bias and root mean square error (RMSE) of the estimated treatment effect within DRS quartiles. To avoid data reuse bias, we used sample splitting to fit DRS models on one half of the unexposed, who were then excluded from effect estimation.

Results: Strategy 1 showed residual confounding (average percent bias across strata was 9.6% with larger bias in the highest risk stratum, see Figure). Strategy 2 reduced the average percent bias to 4.7% and improved RMSE. Strategy 3 did not further reduce bias or RMSE.

Conclusion: DRS stratification alone did not adequately control confounding within strata, whereas IPW of the outcome model substantially reduced bias. Weighting the DRS model did not improve bias or efficiency and may be unnecessary in this setting.



Bias in treatment effect estimates by weighting strategy and disease risk score (DRS) stratum. Strategy 1: DRS stratification without weighting shows residual confounding within strata, "Overall" represents the completely unadjusted estimate (no DRS and no IPW). Strategy 2: Inverse probability weighting (IPW) in the outcome model produces unbiased overall weighted estimate and reduces bias within strata. Strategy 3: Adding IPW to the DRS model fitting step does not provide additional benefit. Average percent bias was calculated as the average of absolute bias across the four strata. Average root mean square error was calculated as the average of root mean square error across the four strata.

Methods/Statistics

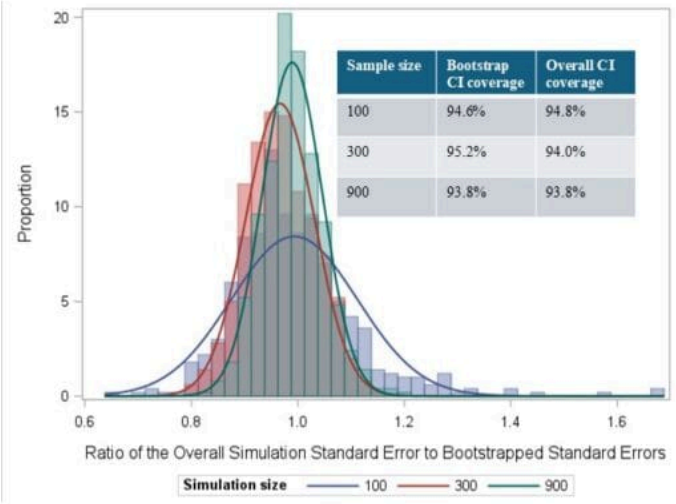
An Alternative to Bootstrapping When Estimating Confidence Interval Coverage in Simulation Studies Michael Webster-Clark* Michael Webster-Clark Claire Su

When contrasting analytic methods or study designs in simulation studies, calculating estimates' mean bias and empirical standard error is straightforward. Confidence interval (CI) coverage (i.e., the proportion of simulation iterations where confidence intervals contain the true value) may also be of interest. While CI coverage is easy to calculate if there is a closed-form solution for the variance of an estimate, obtaining CI coverage when bootstrapping is necessary is time intensive. Even with a relatively low number of simulation iterations (e.g., 500), a small number of bootstrap replicates (e.g., 200) drastically increases computation time.

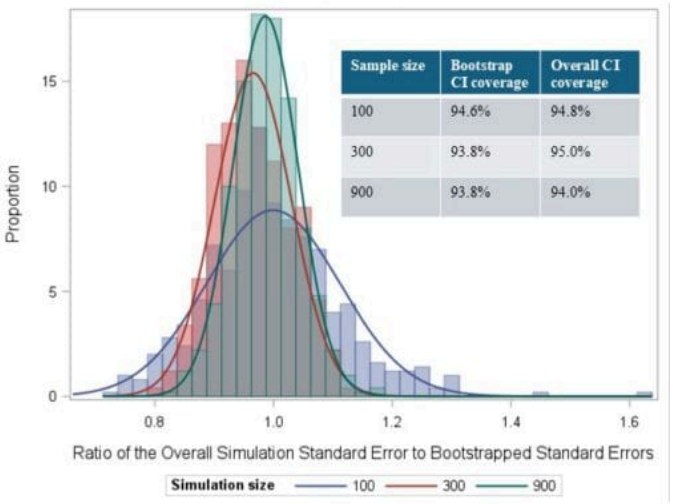
In some cases, using the empirical standard error across simulation iterations to "stand in" for within-iteration standard error to create CIs may allow us to skip bootstrapping. We conducted a simulation study estimating 1) the absolute-scale effect of a binary treatment X on the risk of a binary outcome Y conditional on a confounder C and 2) the marginal effect of X on Y when weighting by C. We examined three simulation scenarios with 100, 300, or 900 individuals per simulation iteration. Within each of 500 simulation iterations we calculated CIs A) obtaining the within-iteration standard error from 200 bootstrap iterations or B) treating the empirical standard error across the simulation iterations as the iteration's standard error.

Figure 1 consists of histograms and density plots of the ratio of the empirical standard error to the iteration-specific bootstrapped standard error for each estimand. Standard errors from the two approaches become more similar as sample size rose and variance decreased, with minor differences in CI coverage between the two except methods. In simulation studies where variance is relatively small and bootstrapping is not feasible (e.g., plasmode simulations), the standard error across iterations may serve as an approximate substitute for within-iteration bootstrapped standard errors.

Panel A: Results estimating a conditional effect via regression



Panel B: Results estimating a marginal effect via IPTW



Methods/Statistics

A Latent Variable Model for Predicting Case Counts Kathryn Shea* Kathryn Shea J. Sunil Rao Lorena Garcia Jiming Jiang

Objective:

Reliable estimation of true disease burden is essential for identifying vulnerable populations, allocating resources, and guiding public health strategies. During the COVID-19 pandemic, reported case counts often incorrectly estimated true infections, with varying reliability across time and space due to factors such as the availability of testing and symptomatic rates of different variants. To address this challenge, we explore a latent-variable modeling approach that uses auxiliary data to improve estimation of true case counts.

Methods:

We propose a Poisson-Gamma model which links reported and true case counts through a latent variable. An empirical best predictor (EBP) is used to estimate the true case counts across geographic areas. Preliminary work includes the development of a baseline model and simulation studies to evaluate the EBP's performance relative to unbiased estimators and the naïve approach of using reported counts directly. Ongoing work extends the model to incorporate spatial autocorrelation to capture relationships between neighboring areas with plans to assess performance under more realistic data-generating processes and a potential application using real COVID-19 data.

Results:

Simulation results suggest that the EBP yields lower mean squared prediction error (MSPE) compared to alternative estimators in simple settings. Further evaluation under more complex and spatially correlated conditions is in progress.

Conclusion:

Early results indicate the potential of a Poisson-Gamma latent-variable framework for improving estimates of true case counts. Future extensions incorporating spatial structure and applied analyses will provide insight into its utility for public health surveillance and epidemic modeling.

Methods/Statistics

Development of an Item Bank to Measure Discrimination and Racism Across Black and Hispanic/Latino Populations: A Modified Delphi approach Nneka Okeke* Nneka Okeke Sara Daniel Zonggui Li Jennifer Contreras Salene Jones Bryce Reeve Ester Villalonga-Olives

Development of an Item Bank to Measure Discrimination and Racism Across Black and Hispanic/Latino Populations: A Modified Delphi approach

Nneka Okeke, Sara Daniel, Zonggui Li, Jennifer Contreras, Salene Jones, Bryce Reeve & Ester Villalonga-Olives

SER Submission Categories: Methods/Statistics, Social

Abstract (Character limit: 2,000 with spaces. Character count: 1,982 with spaces).

Background: Existing measures of discrimination and racism are developed as fixed instruments and do not adequately capture experiences of perceived, structural, and economic discrimination. An item bank is a large collection of psychometrically calibrated items that allows for standardized, flexible, and adaptive testing. We aimed to develop an item bank to assess discrimination and racism that is appropriate for use across Black and Hispanic/Latino populations.

Methods: We used a modified Delphi process to establish content validity and expert consensus. A multidisciplinary panel of subject matter and community experts (n=10) evaluated an initial pool of 226 items drawn from existing measures of racism and discrimination. To strengthen representation of economic discrimination, an additional 97 items were generated from interviews (n=6) and focus groups (n=2) conducted with community advisory board members (n=10) and economic experts(n=4). Items were rated on relevance, clarity, and construct representation using predefined criteria. Based on predetermined consensus thresholds, items were retained, revised, or excluded. Items lacking consensus were revised and reassessed in a subsequent Delphi round until all items were either retained or excluded.

Results: After Round 1, 126 of 226 existing items were retained, 34 were deleted, and 66 existing items plus the 97 new items were re-evaluated. Final consensus-based item selection will be presented at the conference.

Conclusions: The modified Delphi process yielded a refined set of items capturing multi-level sub-domains of racism and discrimination, including structural, community, cultural, and individual-level experiences, with strengthened coverage of economic discrimination. This work advances a comprehensive, evolving item bank for measuring racism and discrimination across Black and Hispanic/Latino populations and supports future psychometric calibration and evaluation of measurement invariance.

Methods/Statistics

Adjusting for unmeasured confounders with validation data using disease risk score calibration: a simulation study Xiaojuan Liu* Xiaojuan Liu Richard Wyss Kueiyu Josh Lin

Background: Leveraging a validation sub-cohort containing confounders unmeasured in the main cohort is increasingly used to reduce bias in observational studies. Existing approaches, such as propensity score (PS) calibration and two-stage calibration, rely on modeling the exposure mechanism and require strong assumptions. We propose an alternative calibration framework using a gold-standard disease risk score (DRS) from the validation cohort.

Methods: We consider a main cohort containing exposure, outcome, and measured confounders X, and a nested validation sub-cohort with an additional confounder U. In the sub-cohort, we defined a gold-standard DRS as the linear predictor of the outcome regression model conditional on X and U. An error-prone DRS constructed from X alone is available in both cohorts. A calibration function mapping the error-prone DRS to the gold-standard DRS is estimated using validation data and applied to the main cohort to obtain predicted values. The exposure effect is then estimated by adjusting for the calibrated DRS. We compared the performance of DRS, PS, and two-stage calibration.

Results: Across 1,000 Monte Carlo replications (main cohort n=10,000; validation n=1,000) under a null scenario with moderate unmeasured confounding, naïve adjustment yielded substantial bias (median odds ratio [OR]=1.61). DRS calibration substantially reduced bias to near null (median OR=0.99) with lower mean squared error (MSE = 0.03) compared with PS calibration (median OR=1.40, MSE = 0.11). Two-stage calibration achieved the lowest bias (median OR=1.00) and MSE (0.01).

Conclusions: PS calibration showed instability and residual bias when strong assumptions required for PS calibration were not met. DRS calibration relaxes some assumptions and provides a more robust alternative, substantially reducing bias, though with greater variability than two-stage calibration. DRS calibration may complement existing methods when assumptions for PS calibration are not met.

Methods/Statistics

An accessible web-based solution for network meta-analysis integrating frequentist and Bayesian methods Janos Tibor Fekete* Janos Tibor Fekete Balazs Gyorffy

Background: Network meta-analysis (NMA) is a methodological framework for comparing multiple interventions in the absence of head-to-head trials. However, conducting NMA often requires advanced statistical expertise and specialized software. The objective of this study was to establish a framework for transparent and reproducible network meta-analysis.

Methods: We established NetMetaEasy, a web-based platform for conducting network meta-analysis of user-provided data using both frequentist and Bayesian methods, enabling both frequentist and Bayesian analytical options within the same analytical environment. As a demonstration use case, aggregated data from phase III trials of cyclin-dependent kinase 4/6 (CDK4/6) inhibitors in hormone receptor–positive early breast cancer were analyzed using a frequentist hazard ratio–based network meta-analysis with disease–free survival (DFS) as the endpoint.

Results: In the CDK4/6 inhibitor demonstration, ribociclib plus endocrine therapy (ET) showed the strongest improvement in DFS compared with ET alone (HR 0.72; 95% CI 0.62–0.83). Our results illustrate that direct and indirect evidence can be rapidly synthesized and compared within a network meta-analysis framework implemented through a web-based analytical environment.

Conclusions: NetMetaEasy provides an accessible, web-based solution for conducting network meta-analysis, integrating frequentist and Bayesian methods within a single inte A Unified Web-Based Environment for Conducting Network Meta-Analysisrface. By lowering technical barriers and supporting transparent, reproducible workflows, the platform facilitates methodological teaching and applied comparative effectiveness research. The new platform is accessible at https://metaanalysisonline.com/netmetaeasy.

LATEBREAKER

Methods/Statistics

Evaluating potential collider bias arising from limiting a sample to VHA utilizers in a prospective cohort study of active servicemembers and veterans Sahra Mohazzab-Hosseinian* Sahra Mohazzab-Hosseinian Mario J. Trejo Claire A. Kolaja Aaron Baraff Erin L. Richard Nicole D. Riedel Lynne Liu Alexandra R. Schmidt Edward J. Boyko Rudolph P. Rull Alyson J. Littman

Introduction: Veterans Health Administration (VHA) electronic health records (EHR) are a rich source of health information, but Veterans who use VHA are systematically different than those who do not. EHR data provides active surveillance on utilizers within that system but may be subject to collider bias if selection is conditioned on the exposure-response function. VHA studies of military-related exposures may be especially prone to collider bias because VHA use is related to both military exposures and health status. This collider bias may be especially inflated in the context of mental health outcomes because veterans with mental health symptoms are more likely to engage in care-seeking behavior at VHA. This project will evaluate the magnitude of collider bias in associations between deployment and post-traumatic stress disorder when limiting the sample to Veterans who receive care from VHA.

Methods: This study used prospective cohort survey data from the Millenium Cohort Study (MCS), a study with up to 24 years of follow up that was designed to evaluate the impact of military service on health outcomes. Active servicemembers are sampled and are prospectively followed through the military separation period, providing self-reported health information among a sample of veterans that includes VHA users and VHA non-users. We estimated relative risk separately in veteran participants and VHA users.

Results: In a cohort of 146,688 veterans, 71,017(48%) used VHA. In unadjusted models, VHA users who experienced deployment with combat were at an increased risk for PTSD (RR 1.4; 95% CI 1.3 to 1.5) compared to non-deployers, and this association persisted in the target population of veterans (RR 1.8; 95% CI 1.7 to 1.9).

Conclusion: Results suggest that magnitude of associations differ between VHA users and veterans. In population-based epidemiologic research of veterans, the utility of VHA EHR may be limited by collider bias.

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Methods/Statistics

Estimating dementia-related outcomes among patients following hospitalization with septic shock Robert Dettmann* Robert Dettmann Jingxuan Wang Robertus van Aalst Michael Flanders Rishi Rai Sarah Ackley

Septic shock (SS) is a leading global cause of morbidity and mortality, yet its long-term cognitive and functional consequences remain underexplored. Emerging evidence suggests an association between SS and an increased risk of dementia, but causal interpretation is limited by the lack of appropriate comparator groups, as SS is not a well-defined exposure and is closely intertwined with hospitalization, comorbidities, and shared vascular risk factors.

Using longitudinal data from NIH's All of Us Research Program, we emulated a series of target trials to compare the hazard of dementia following SS-related hospitalization versus other acute illness-related hospitalizations. Comparator groups included those hospitalized for myocardial infarction (AMI), renal failure (ARF), and pulmonary edema (APE), representing alternative acute illness trajectories sharing features of severe hospitalization but differing in underlying biological mechanisms. Dementia-free adults ≥18 years (N = 52,447) were followed from time of hospitalization, with dementia defined using ICD-9/10 codes. Cox models estimated cause-specific hazard ratios, adjusting for demographic, comorbidity, and SES variables.

SS hospitalization was associated with a higher hazard of dementia compared to non-infectious acute hospitalizations. Sepsis was significantly associated with increased dementia hazard compared to ARF (HR: 1.49, 95% CI: 1.03-2.17). Point estimates suggested notable differences versus APE (HR: 2.13, CI: 0.98-4.55) and AMI (HR: 1.19, CI: 0.97-1.79), though these were not statistically significant. Results were robust to alternative covariate adjustment.

Using an ICD-9/10-based definition of SS and multiple comparator groups, this study clarifies how the hazard of dementia differs after SS compared with other acute hospitalizations. These findings suggest that SS-specific mechanisms, beyond the general effects of critical illness and hospitalization, may contribute to long-term cognitive decline.

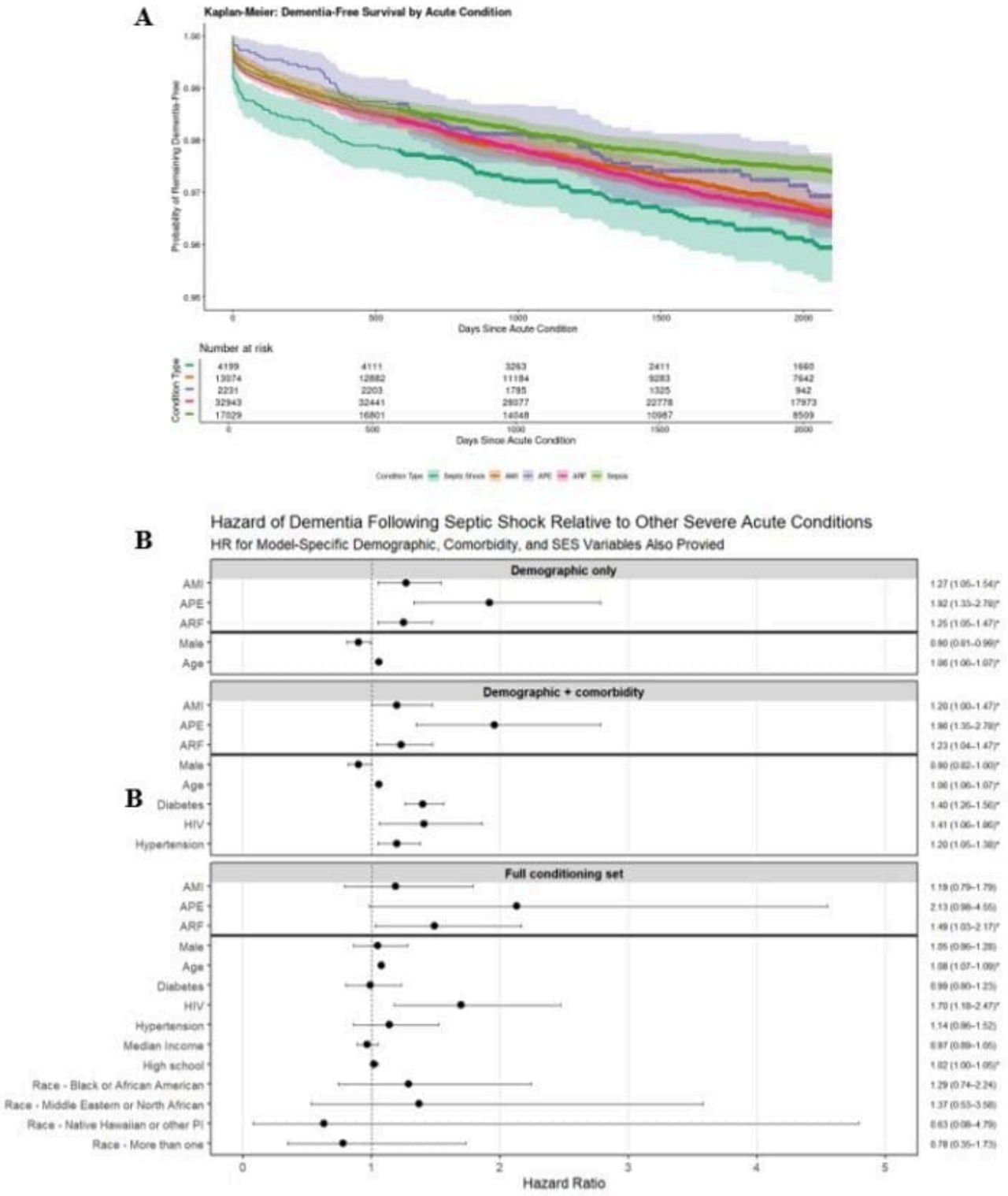


Figure 1. (A) HR of Dementia following hospitalization with septic shock relative to hospitalization with other severe acute conditions. Model 1 (demographic only) adjusts for sex and age at hospitalization, while Model 2 (Demographic + Comorbidity) adjusts for sex and age at hospitalization, as well as history of HIV, diabetes, and hypertension. Model 3 (Full Conditioning Set) adjusts for all prior variables in addition to race and zip code level income and high school status completion proportion; (B) KM curves describing proportion dementia free as a function of time since acute hospitalization event amongst those with septic shock, AMI, APE, ARF, and sepsis.

This study was funded by Sanofi. Robertus van Aalst is a Sanofi employee and may hold shares and/or stock options in the company. The other authors declare no competing interests

Methods/Statistics

Generalizing per protocol estimates of HIV treatment from the ACTG A5202 trial. Timothy Feeney* Timothy Feeney Stephen R Cole

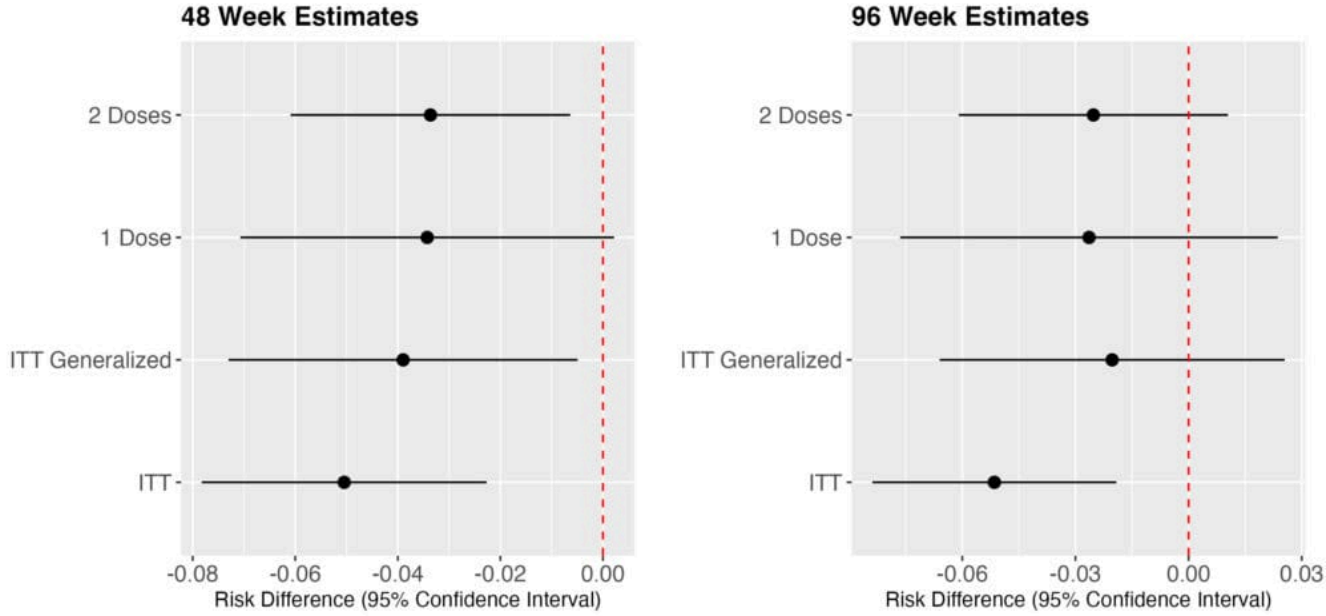
Introduction: In the presence of non-adherence per-protocol estimators are attractive alternatives to intent-to-treat (ITT) estimators, because they can account for non-adherence to assigned treatment. Per protocol analyses typically only estimate treatment effects in the study sample, rather than generalize to a given target population. Our objective was to estimate HIV treatment efficacy in the ACTG A5202 trial generalized to the target population of newly infected HIV persons in the United States in 2008-2009 under multiple definitions of protocol adherence.

Methods: A reanalysis of ACTG A5202 evaluating Tenofovir/Emtricitabine (TDF/FTC) versus Abacavir/Lamivudine (ABC/3TC). Protocols were defined as ITT, and 1 dose missed and 2 dose missed protocols, which censored after missing 1 and 2 doses, respectively. We evaluated the composite risk of viral failure and death at 48 and 96 weeks. Inverse probability weighting was used to evaluate per protocol estimates. CDC data from 2008-2009 and inverse odds of sampling weights were used to generalize to the US population with incident HIV. Weighted Kaplan-Meier estimators were used to estimate risk.

Results: 1857 participants from the A5202 were included. The mean age was 38 [IQR: 31-45], 83% were male, 58% white, and 34% were Black. Estimates are presented in Figure 1. At 48 weeks the ITT risk difference between TDF/FTC v. ABC/3TC was -0.050 (95% CI: -0.08, -0.02), but when generalized to the US population was -0.038 (95%CI: -0.07, -0.004). The generalized 1 dose and 2 dose protocol 48-week risk differences were -0.03 (95%CI: -0.07, 0.003) and -0.03 (95%CI: -0.06, -0.006), respectively. At 96 weeks the ITT risk difference between TDF/FTC v. ABC/3TC was -0.05 (95% CI: -0.08, -0.02). The generalized 1 dose and 2 dose protocol 96-week risk differences were -0.02 (95%CI: -0.07, 0.03) and -0.03 (95%CI: -0.06, 0.01), respectively.

Discussion: Per protocol analyses are infrequently done and very rarely consider multiple definitions of protocol. There were no meaningful differences when comparing risk differences between protocols in the study sample. However, when generalized to the target population with incident HIV, the A5202 risk difference estimates were closer to the null than the non-generalized results. These results may impact decisions about treatment efficacy in clinical care and expectations about subsequent treatment effects.

Figure 1


48 Week Estimates
2 Doses
1 Dose
ITT Generalized
ITT
-0.08
-0.06
-0.04
-0.02
0.00
Risk Difference (95% Confidence Interval)
96 Week Estimates
2 Doses
1 Dose
ITT Generalized
ITT
-0.06
-0.03
0.00
0.03
Risk Difference (95% Confidence Interval)

Neurology

Life Expectancies for Medicaid Beneficiaries with Autism Spectrum Disorder vs. Attention-Deficit/Hyperactivity Disorder, United States, 2000-2020 Guohua Li* Guohua Li Matthew T. Russell Ashley Blanchard Carolyn DiGuiseppi Caleb Ing

Autism spectrum disorder (ASD) and attention-deficit/hyperactivity (ADHD) have been linked to poorer socioeconomic and health outcomes, such as unemployment and premature mortality. Few studies, however, have assessed lifespan issues in ASD and ADHD. The objective of this study was to compare life expectancies for Medicaid beneficiaries with ASD vs. ADHD. Research-identifiable files from Medicaid [i.e., Medicaid Analytic eXtract (MAX) data files and T-MSIS Analytic Files] and the enhanced MAX mortality data (i.e., mortality data through linkage of Medicaid beneficiaries to the National Death Index) from 2000 to 2020 were analyzed to determine age-specific death rates for beneficiaries with ASD and ADHD. The standard life table method was used to calculate life expectancies at birth. Among Medicaid beneficiaries, the prevalence rates of ASD and ADHD were 0.60% and 3.4%, respectively. During the 21-year study period, there were a total of 14,313,693 deaths among Medicaid beneficiaries, including 18,268 with ASD and 118,981 with ADHD. Life expectancies at birth were 64.9 years (64.6 for men and 65.0 for women) for those with ASD, 65.0 years (62.1 for men and 67.9 for women) for those with ADHD, and 70.5 years (66.5 for men and 73.2 for women) for all Medicaid beneficiaries. Life expectancy for Medicaid beneficiaries with ASD is virtually the same as for those with ADHD. Both ASD and ADHD are associated with a substantially reduced life expectancy. The deficit in life expectancy is most pronounced in autistic women.

LATEBREAKER

Neurology

Eviction moratoria and hippocampal development in the Adolescent Brain and Cognitive Development cohort: a difference-in-differences analysis Jeroen van Baar* Jeroen van Baar Mark Hatzenbuehler Mary Willis Marcia Pescador Jimenez Henning Tiemeier Katherine Keyes David Weissman

Adolescence is a sensitive period for brain development. Although hippocampal volume, critical for memory and emotion regulation, is shaped by genetic and cognitive factors, it remains vulnerable to chronic stress. Family stressors such as poverty have been linked to altered adolescent hippocampal development. Threat of eviction is a leading stressor for U.S. families, with almost 7% of renter households facing eviction each year. Between March 13, 2020 and August 15, 2021, temporary eviction bans during the COVD-19 pandemic eased eviction threat. Leveraging state-by-state differences in eviction ban duration, prior work showed that the bans reduced mental distress in adults at risk for eviction, but it is unknown whether the bans also affected adolescent hippocampal development. Using a quasi-experimental study design with a difference-in-differences estimator, we estimated the effect of eviction ban coverage on hippocampal development in the Adolescent Brain and Cognitive Development (ABCD) cohort (N = 11,718 from 21 sites across 17 states, baseline in 2016-2018 at age 9-10). Participants were categorized as a ‘long ban’ group (states with total eviction ban duration >450 days, range 470-518 days) and a ‘short ban’ group (<200 days, range 0-192 days). Hippocampal volume was assessed at 2-year intervals through 2024 (Freesurfer segmentation of T1-weighted magnetic resonance images). We used linear regression models with standard errors clustered at the subject level and adjusted for intracranial volume, age, site, state, and subject (which reduces demographic and socioeconomic confounding). Residing in a long ban state was associated with 44.1 mm3 (95% CI: 32.8, 55.4) greater bilateral hippocampal volume growth compared to the short ban group. Other COVID-era policies, including containment measures and economic support, were not associated with hippocampal volume change. Therefore, social safety net policies may support adolescent brain development.

Neurology

Structural Sexism and Stroke Incidence among Black and White Women and Men: Evidence from the REasons for Geographic And Racial Differences in Stroke (REGARDS) study Chen Chen* Chen Chen Virginia Howard Natalie Colabianchi Debora Kamin-Mukaz Lynda Lisabeth

Background: Individual-level social factors are disproportionately associated with stroke for women. Ecosocial theory suggests that structural determinants, such as structural sexism (SS), could be a stroke risk factor for both sexes, but little empirical evidence exists.

Method: Individuals aged ≥45 years from the nationwide REGARDS study without stroke at baseline (2003-2007) were included (n=27,881) and followed for incident stroke or death until September 30, 2022. A composite measure of SS, operationalized as a sum score of inequalities between women and men across multiple social determinants of health at the county or state level, was calculated using US census and administrative data (**Table 1**) and linked to study participants by FIPS code of home address at baseline. Associations between SS and its subdomains with stroke among women and men, accounting for the competing risk of death and clustering of individuals within counties, were assessed by sex-stratified Fine-Gray models with robust sandwich estimators. Models were adjusted for covariates listed in **Table 2**. Interactions between SSs and sex were added to unstratified models.

Results: Over a median of 12.5 years of follow-up, 1,793 individuals (mean age 64.6 years, 55.5% women) had incident stroke. SS was associated with increased stroke rates (HR=1.05, 95% CI 0.97, 1.13 per one std deviation increase in SS) among women and decreased stroke rates (HR=0.92, 95% CI 0.85, 0.99) among men (interaction p-value=0.01). For subdomains of SS (**Table 2**), only socioeconomic inequality was associated with increased stroke rates (HR=1.14, 95% CI 1.06, 1.23) among women, and only conservative religion was associated with decreased stroke rates (HR=0.88, 95% CI 0.80, 0.97) among men.

Conclusion: Findings suggest the potentially harmful impact of SS, particularly gender inequalities in socioeconomic status, on stroke risk among women. Future studies should aim to unravel the underlying mechanisms of this association.

Table 1 Domains and Indicators for structural sexism for REGARDS participants at baseline (2003-2007)

Domains	Indicators	Level, years available for REGARDS baseline, and data source	Mean (SD)
Political	1) Percentage of men in state legislature	State, 2003, Center for American Women and Politics	0.80 (0.24)
	2) Percentage of a county's vote cast for the Republican Party	County, 2004, IPUMS Contextual Determinants of Health	0.48 (0.14)
Socioeconomic	3) Men to women ratio in percentage of adults age 25+ with a bachelor's degree	County, 2000, Decennial census	1.17 (0.21)
	4) Men to women ratio in median earnings		1.53 (0.20)
	5) Men to women ratio in percentage of adults living above the poverty line		1.05 (0.03)
	6) Men to women ratio in percentage of adults ages 16 and over in the labor force		1.22 (0.07)
	7) Men to women ratio in percentage of adults being employed		1.10 (0.09)
	8) Men to women ratio in percentage of working adults in management or administration positions		1.79 (0.35)
	9) Men to women ratio in percentage of working adults in non-service professional and technical occupations		0.92 (0.44)
	10) Men to women ratio in percentage of working adults who are self-employed		2.56 (0.76)
	11) Men to women ratio in percentage of adults with insurance	County, 2006, Census small area health insurance program	0.94 (0.03)
Reproductive	12) Percentage of women living in counties without an abortion provider	State, 2005, Guttmacher Institute	0.49 (0.24)
Cultural	13) Gender attitude and sexist beliefs	State level, 2003, Project implicit and general social survey	0.42 (0.86)
Religion	14) Percentage of county population composed of religious conservatives	County level, 2000, the Association of Religion Data Archives	0.20 (0.14)

Table 2 Associations between structural sexism and its subdomains with incident stroke among women and men in the REGARDS study

	Women	Men	
One standard deviation increase	Hazard Ratio (95% CI)	Hazard Ratio (95% CI)	P-value for interaction
Structural sexism	1.05 (0.97, 1.13)	0.92 (0.85, 0.99)	0.01
Inequalities in the political domain between women and men	0.98 (0.87, 1.10)	0.91 (0.81, 1.03)	0.21
Inequalities in the socioeconomic status between women and men	1.14 (1.06, 1.23)	1.01 (0.92, 1.11)	<0.001
Women's reproductive rights (access to abortion provider)	1.05 (0.93, 1.19)	1.01 (0.90, 1.13)	0.10
Cultural sexism (gendered attitude and sexist beliefs)	0.98 (0.88, 1.11)	1.09 (0.98, 1.23)	0.18
Sexism in religious institutions (Percentage of county population composed of religious conservatives)	0.95 (0.86, 1.04)	0.88 (0.80, 0.97)	0.67

For the association between the composite measure of structural sexism and incident stroke, the model was adjusted for age, race-ethnicity, education, income, marital status, county-level income inequality, and county population size.
For the associations between the subdomains of structural sexism and incident stroke, the model was mutually adjusted for each subdomain and age, race-ethnicity, education, income, marital status, county-level income inequality, and county population size.

Nutrition/Obesity

Energy-Density Dietary Inflammatory Index (EDII) and Sleep Quality, Duration, and Timing within the Mobile Lifestyle Intervention for Food and Exercise (mLIFE) Study Michael Wirth* Michael Wirth Maryellen Muller Carolina Delgado-Diaz Gabrielle Turner-McGrievy

Background: Previous research has shown that pro-inflammatory changes in diet overtime are associated with worsening sleep characteristics. However, such associations have not been examined within virtually delivered interventions. This study examined whether changes in the Energy-density Dietary Inflammatory Index (E-DII) led to changes in bedtime, wake time, sleep duration, or sleep efficiency in a mobile lifestyle intervention.

Methods: Data derived from the Mobile Lifestyle Intervention for Food and Exercise (mLIFE) study. mLIFE was a 12-month lifestyle intervention via a mobile app with or without a gamification component. Assessments occurred at baseline, month 6 and month 12. Sleep was assessed via Fitbit. Diet was assessed via 3 unannounced 24-hour dietary recalls at each assessment. With adjustment for demographic characteristics, linear mixed models assessed the impact of increases (becoming more pro-inflammatory) in the change in E-DII (ranges from -8 to +8) and baseline E-DII on sleep outcomes. Study arm was also assessed as an effect modifier.

Results: Every one-unit higher baseline E-DII was associated with an 8.1-minute later bedtime ($p<0.01$) and 6.4-minute later wake time ($p=0.02$). Change in E-DII was not associated with changes in any sleep measures. An interaction existed between change in E-DII and study arm for sleep duration ($p=0.05$). Among those without gamification, there was a 3.7-minute increase in sleep duration per increase in E-DII, whereas those with gamification showed a 1.5-minute decrease in duration. Neither of these findings achieved statistical significance.

Conclusions: Previous studies have typically found associations between the change in E-DII scores and sleep quality. Post-hoc analyses revealed little change in E-DII scores (baseline=0.38, month 6 = 0.16, month 12 = 0.03) which may explain the lack of findings. More anti-inflammatory diet changes are likely needed to evince changes in sleep characteristics.

Nutrition/Obesity

Impact of Mandatory Fortification with Folic Acid on Prevalence of Congenital Heart Defects, Neural Tube Defects, and Orofacial Clefts: A Systematic Review and Meta-Analysis

Helena Pachón* Kristin Wu Jessica Parker Amanuel Kisho Amanda Dorsey Lauryn Cravens Mary Ellen Grap Vijaya Kancherla

Fortification of staple grains with folic acid (FA) has been mandated in 73 countries as of 2025. We conducted a systematic review and meta-analysis of population-based studies that evaluated the association between mandatory FA fortification of wheat flour, maize flour, and/or rice and prevalence of critical congenital heart defects (CHDs), neural tube defects (NTDs) and their 3 subtypes, and orofacial clefts (OFCs) and their 2 subtypes, pre- and post-fortification with FA. We searched PubMed and Embase from inception to October 2021, screened records in duplicate, and extracted data using a standardized form. We estimated pooled prevalence odds ratios (ORs) and 95% confidence intervals (CI) using random-effects models. A total of 26 studies across 9 countries met our inclusion criteria. Five studies reported on any critical CHDs, 18 on NTDs or their subtypes, and 11 on OFCs or their subtypes. We found a non-significant 4% reduction in the odds of any critical CHDs following mandatory FA fortification (OR: 0.96, 95% CI: 0.92, 1.01). A strong protective association was noted for total NTDs (OR: 0.64; 95% CI: 0.57, 0.72), spina bifida (OR: 0.63; 95% CI: 0.53, 0.74), anencephaly (OR: 0.59; 95% CI: 0.51, 0.69), and encephalocele (OR: 0.63; 95% CI: 0.46, 0.85). Associations for total OFCs (OR: 0.90; 95% CI: 0.80, 1.00) and cleft palate (CP) (OR: 1.01; 95% CI: 0.85, 1.20) were non-significant. A protective effect of mandatory FA fortification was found for cleft lip with or without cleft palate (CL/CLP) (OR: 0.93; 95% CI: 0.89, 0.97). Consistent with previous literature, our findings support mandatory FA fortification as an effective population-level strategy to reduce NTDs. Meta-analyses of critical CHDs and OFCs were limited by fewer studies and should be further studied in the future.

Nutrition/Obesity

The modifying role of fruit and vegetable intake and physical activity in obesity and chronic disease associations Muskan Ahuja* Muskan Ahuja Sydney Stein Mariah K. Jackson Dana C. Verhoeven Julie M. Petersen

Obesity affects 40% of U.S. adults and is associated with increased risks for a variety of chronic diseases. We examined the relationship between self-reported body mass index (BMI) and chronic diseases and assessed effect modification by fruit and vegetable intake and physical activity. We analyzed cross-sectional data from the Behavioral Risk Factor Surveillance System for 2017, 2019, and 2021 (all U.S. states and DC, n = 1,306,916 adults). BMI was calculated from self-reported height and weight and categorized as underweight, normal weight (reference), overweight, and obesity. Participants reported whether they have ever been diagnosed with certain chronic diseases, including diabetes (type I/II), hypertension, coronary artery disease (CAD), myocardial infarction, stroke, and depression. We created a counter outcome variable (0, 1, or ≥2 diseases) to assess multimorbidity. Risk differences (RDs) were estimated using weighted modified Poisson regression, adjusting for sociodemographic and socioeconomic factors, and key health behaviors such as smoking, alcohol, fruit and vegetable intake, and physical activity. Effect modification was assessed using four strata combining fruit and vegetable intake (≥5 vs <5 servings/day) and physical activity (any vs none). Compared with normal weight, obesity was associated with excess risk for all outcomes, with the strongest associations for hypertension (RD = 181.6 per 1,000), diabetes (RD = 116.3), and depression (RD = 72.4). Obesity was also associated with 345 excess cases of ≥2 chronic diseases per 1,000 adults. In stratified analysis, obesity associations with diabetes, CAD, stroke, depression, and multimorbidity were weaker among adults with high fruit and vegetable intake, any physical activity, or both. These findings add to the existing body of literature suggesting that improved diet and physical activity may reduce chronic disease burden among adults with obesity, though longitudinal and trial studies are needed.

Nutrition/Obesity

Micronutrient Intake, Depression, and Sleep Duration Among U.S. Adults in NHANES 2021–2023 Shilpa Patil* Shilpa Patil RoiSan Nhpang Suruthi Sundarmurugan Malinee Neelamegam Matthew Rossheim

Sleep is a critical determinant of cardiometabolic and mental health, yet the roles of specific micronutrients and depression in shaping sleep duration remain incompletely understood. This study examined whether total intakes of folate, vitamin D, magnesium, and zinc are associated with sleep duration, and whether depression status modifies these relationships among U.S. adults.

Cross-sectional data were analyzed for **4,118 adults** in the **2021–2023 National Health and Nutrition Examination Survey (NHANES).** Sleep duration was self-reported and categorized as short (<7 hours), optimal (7–9 hours), or long (>9 hours) per night. Total daily folate, vitamin D, magnesium, and zinc intakes from foods and supplements were estimated from 24-hour dietary recalls and a dietary supplement questionnaire.

Survey-weighted multinomial logistic regression models, with optimal sleep as the reference, estimated associations between each nutrient and sleep duration, adjusting for sociodemographic characteristics, physical activity, sedentary behavior, alcohol use, multimorbidity, and depression, and tested nutrient–depression interactions. Mean (SD) intakes were 716.7 (731.6) mcg for folate, 32.6 (46.5) mcg for vitamin D, 339.2 (180.9) mg for magnesium, and 16.2 (15.3) mg for zinc. Overall, 20.5% of adults reported short sleep, 69.2% optimal sleep, and 10.3% long sleep. Higher total folate and vitamin D intakes were associated with slightly lower odds of short versus optimal sleep, whereas total magnesium and zinc were not significantly associated with sleep duration.

Clinically significant depression (PHQ-9 ≥10) was strongly related to sleep duration, with higher odds of both short and long sleep compared with no clinically significant depression. Interactions between depression and folate and vitamin D were statistically significant but small in magnitude, indicating limited effect modification. Overall, **depression and sociodemographic factors were more prominent correlates of non-optimal sleep duration than total folate, vitamin D, magnesium, or zinc intake.** Ensuring adequate micronutrient intake may modestly support healthy sleep, but strategies to improve sleep should prioritize mental health and social determinants of health.

Nutrition/Obesity

Food Insecurity and Body Image Concerns in College Students: The Mediating Role of Diet Quality Chidimma Okoli* Chidimma Okoli

Food insecurity (FI) is prevalent among college students and has been associated with poor diet quality and adverse psychosocial outcomes, including body image concerns. However, whether diet quality explains the relationship between FI and body image–related restrictive eating remains unclear. We examined whether diet quality mediates the association between FI and body image–related restrictive eating behaviors among college students. FI was assessed using the 18-item USDA Food Security Survey Module. Diet quality was measured using minimum dietary diversity (MDD), defined as consumption of ≥5 of 10 food groups based on the Diet Quality Questionnaire. Body image concerns were defined as intentionally cutting meal size or skipping meals to lose weight or achieve body image goals. Logistic regression models estimated the total effect of FI on body image concerns, the association between FI and MDD, and the association between MDD and body image concerns, adjusting for FI. Mediation was evaluated using nonparametric bootstrapping with 1,000 iterations. Models adjusted for age, sex, race/ethnicity, BMI, perceived stress, dietary supplements, and meal plan. Among 539 participants, 34.3% were food insecure, 43.2% reported body image–related restrictive eating, and 68.8% met MDD. Food-insecure students were less likely to meet MDD than food-secure students (28.6% vs. 47.0%). After adjustment, FI was associated with lower odds of meeting MDD (OR=0.45; 95% CI=0.28–0.73). Meeting MDD was independently associated with higher odds of body image concerns (OR=1.65; 95% CI=1.05–2.61). The total effect of FI and body image concerns was not statistically significant (OR=1.13; 95% CI=0.72–1.78), and mediation analyses showed no statistically significant indirect effect. Findings suggest diet quality may be an important correlate of body image concerns among food-insecure students. Longitudinal studies are needed to clarify temporal pathways and inform equity-focused interventions.

Occupational

Suicide Mortality in Urban Career Firefighters and Emergency Medical Service Providers Compared with the US and NYC Adult Populations Ankura Singh* Ankura Singh Rachel Zeig-Owens Tyrone Moline David G. Goldfarb David J. Prezant

Background

The evidence regarding whether suicide risk is elevated among first responders is mixed. We investigated whether career firefighters and emergency medical service providers (EMS) had higher suicide rates than the general population.

Methods

Firefighters and EMS from the Fire Department of the City of New York (FDNY) (N=32925) and responders from 3 other city fire departments (N=11917) were included in the study. Participant follow-up started at the later of hire date or 9/11/01 and ended at the earlier of death date or 12/31/23. We obtained death data via the National Death Index and demographic data from the fire departments. Demographic-specific US and NYC (for FDNY analyses only) suicide rates were used to calculate standardized mortality ratios (SMRs) and 95% CIs for suicide. Multivariable logistic regression models assessed associations between select participant characteristics, ascertained from routine health surveys, and suicide in the FDNY cohort.

Results

By 12/31/23 there were 41 and 11 suicide deaths in FDNY firefighters and EMS, respectively, and 52 in non-FDNY responders. FDNY firefighters had lower suicide rates than similar US (SMR=0.35 (0.25-0.48)) and NYC adults (SMR=0.57 (0.41-0.77)). FDNY EMS did not have significantly different suicide rates from the general populations (SMR=0.57 (0.28-1.02) and SMR=0.94 (0.47-1.69) vs US and NYC populations, respectively). The suicide rate in non-FDNY responders was also not different from that of US adults (SMR=0.94 (0.70-1.24)). Risk factors for suicide in the FDNY group were single marital status (OR=5.20 (2.67-10.14)), and screening positive for PTSD (OR=6.13 (3.00-12.52)), depression (OR=6.06 (3.14-11.68)) or alcohol abuse (OR=3.51 (1.53-8.08)).

Conclusion

In the largest cohort study of suicide in career firefighters and EMS to date, we did not find elevated suicide rates compared with general populations. Mental health screening in responder cohorts may help identify those at elevated risk for suicide.

Occupational

Associations of per- and polyfluoroalkyl substances (PFAS) exposures and firefighting experience with microRNA signatures of papillary thyroid cancer Cynthia Porter* Cynthia Porter Jaclyn M Goodrich Shawn C Beitel Brooke A Hawkes Jefferey L Burgess Melissa A Furlong

Background: Papillary thyroid cancer (PTC) is the most commonly diagnosed thyroid cancer. Prior research shows that expression of specific circulating blood microRNAs (miRNAs) differs between individuals with PTC and those without disease, suggesting biomarker relevance. Firefighters may experience an elevated risk of developing PTC due to occupational exposures, including per- and polyfluoroalkyl substances (PFAS).

Methods: This study investigated associations between firefighter-related exposures (serum PFAS, years of firefighting experience, and incumbent versus recruit status) and PTC-relevant miRNA expression. MiRNA expression was quantified from blood collected from 833 firefighters across 15 sites, and 302 firefighters had nine PFAS analytes measured in serum. Thirty PTC-related miRNAs were identified using miRWalk's Disease Ontology. Adjusted linear regression models estimated associations between exposures and miRNA expression while controlling for occupational and demographic covariates. Multiple comparisons were assessed using a False Discovery Rate (FDR) threshold of $p < 0.20$.

Results: Twenty statistically significant ($p < 0.05$) negative associations were observed between five serum PFAS analytes and 10 miRNAs. These included associations between Sb-PFOA and hsa-miR-212-3p; PFHxS and hsa-let-7a-5p, hsa-let-7d-5p, hsa-let-7f-5p; PFNA and hsa-let-7a-5p, hsa-let-7b-5p, hsa-let-7c-5p, and hsa-let-7d-5p; Sm-PFOS and hsa-let-7a-5p, hsa-let-7b-5p, hsa-let-7c-5p, hsa-let-7d-5p, hsa-let-7e-5p, and hsa-miR-760; and n-PFOS and hsa-let-7a-5p, hsa-let-7c-5p, hsa-let-7d-5p, hsa-let-7e-5p, and hsa-let-7f-5p. Twenty-four of 30 miRNAs were associated with incumbent status, and 22 remained significant after FDR correction. Hsa-miR-212-3p and let-7 family miRNAs were negatively associated with PFAS and incumbency.

Conclusion: Associations between PFAS exposure, firefighting status, and PTC-related miRNAs suggest links between occupational exposures and PTC risk overall.

Occupational

Using a standardized interpretation tool and statistical clustering to inform cardiopulmonary exercise testing interpretation and application Lauren Zell-Baran* Lauren Zell-Baran Jeremy Hua Silpa Krefft Michael Mohning Kieran Wohlfarth Camille Moore Cecile Rose

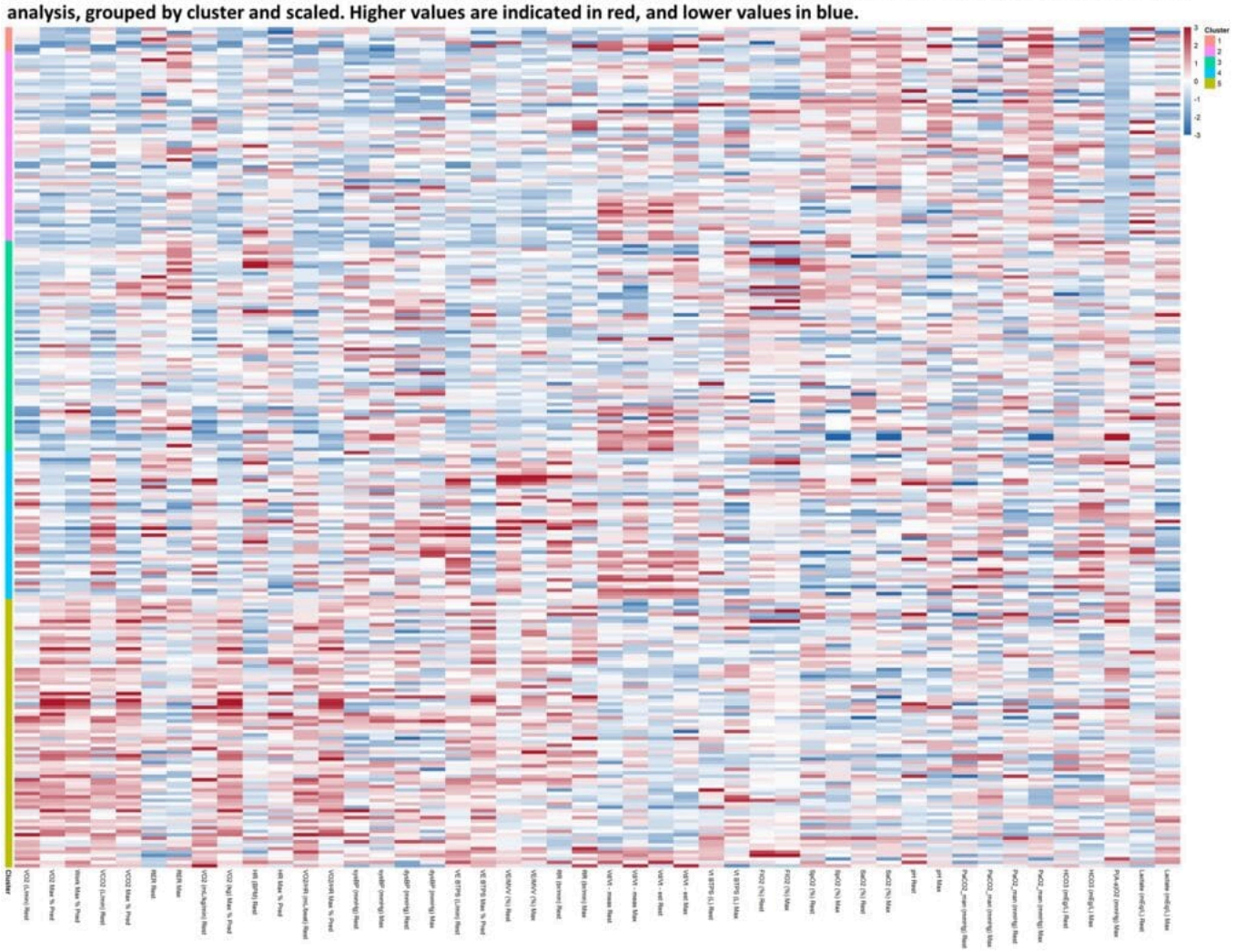
Background: Resting pulmonary function tests underestimate functional impairment in deployed veterans with exertional dyspnea. Cardiopulmonary exercise testing (CPET) is more sensitive for characterizing exercise abnormalities, but interpretation is challenging. We developed a standardized CPET scoring tool to classify primary causes of exercise limitation and compared statistical clustering as an alternative approach that may minimize discordant interpretations.

Methods: Two expert pulmonologists independently scored 280 CPETs from dyspneic veterans as normal or primarily a cardiac, ventilatory, gas exchange or metabolic limitation to exercise, with a third pulmonologist adjudicating disagreements. We standardized 24 rest and exercise variables using inverse hyperbolic sine (Asinh), removed tests with incomplete data (n=36), and applied K-means clustering in R with n=1 to 100 clusters.

Results: The primary exercise limitation by initial expert scoring was discordant in 151/280 (54%). Tiebreak scoring will be compared to the statistical classification method upon completion. Within-cluster variation was minimized near n=5 clusters. Figure 1 shows included variables by cluster. Cluster 1 (n=7) reflects sub-maximal tests. Clusters 2 (n=55) and 3 (n=61) are similar, with reduced maximum oxygen consumption (VO2max), but 2 appears metabolic (deconditioning or mitochondrial dysfunction) while 3 appears cardiac with reduced oxygen pulse (VO2/HR). Cluster 4 (n=43) appears ventilatory-limited with rapid breathing, higher physiologic dead space/tidal volume (Vd/Vt) and maximum ventilation/voluntary ventilation (VE/MVV) at rest, and higher carbon dioxide (PaCO2) at maximum. Cluster 5 (n=78) reflects more normal exercise.

Discussion: A systematic approach is needed to reliably interpret CPET-identified exercise limitations. Efforts to validate this standardized CPET classification system appear promising for enhanced disease phenotyping and management.

Figure 1: Heat map of cardiopulmonary exercise testing (CPET) variables at rest and maximum exercise that were included in the clustering analysis, grouped by cluster and scaled. Higher values are indicated in red, and lower values in blue.



Occupational

The risk of digestive cancers from occupational exposure to ethylene oxide: a preliminary meta-analysis using existing literature Liz Best* Elizabeth Best Tony Cappello Katrina Stadler Alexander Riordan Hannah Mazzotta

We conducted a preliminary literature review and meta-analysis of peer reviewed literature that examined the risk of digestive cancers, including mouth, esophagus, gallbladder, stomach, pancreas, liver, large and small intestines, anus, colon, and rectum, among individuals occupationally exposed to ethylene oxide (EtO). Our literature search was performed in PubMed from inception to 2025. Pooled risk estimates were calculated using DerSimonian and Laird random effects models. The overall meta-relative risk (meta-RR) for digestive cancers was 1.01 (95% CI: 0.69-1.47), mouth cancer was 0.80 (95% CI: 0.34-1.92), esophageal cancer was 1.04 (95% CI: 0.58-1.85), stomach cancer was 1.04 (95% CI: 0.66-1.64), pancreatic cancer was 1.16 (95% CI: 0.87-1.56), liver cancer was 1.08 (95% CI: 0.56-2.09), intestinal cancers were 1.01 (95% CI 0.65-1.55), and anal, colon, and rectal cancers were 0.97 (95% CI: 0.59-1.60). Significant heterogeneity was not observed across the analyses. There were no results for gallbladder cancer. Based on this analysis, there is no evidence to suggest that occupational exposure to EtO is associated with an increased risk of digestive cancers.

LATEBREAKER

Occupational

A Preliminary meta-analysis evaluating risk of digestive cancers from exposure to talc Tony Capppello* Alexander Riordan Elizabeth (Liz) Best Hannah Mazzotta

In 2025, the FDA conducted an expert panel discussion that led to scientific assertions that talc causes inflammation in the digestive tract and thus may increase the risk of colorectal cancer among younger individuals. A systematic literature review and meta-analysis was conducted to examine the risk of digestive cancers, based on currently available literature (including stomach, colorectal cancer (CRC), pancreatic, and hepatic cancers). We followed PRISMA guidelines and searched for all literature pertaining to talc, regardless of talc type, through 2025. Upon inclusion and exclusion criteria, a total of eight cohort studies remained in our final analysis. Meta-analyses were run using Der Simonian and Laird random effects models. CRC yielded a meta-RR of 1.04 (95% CI: 0.68-1.58, n=7), stomach cancer 1.46 (95% CI: 0.68-1.58, n=9), pancreatic cancer 0.85 (95% CI: 0.41-1.73, n=4), and hepatic cancers 1.02 (95% CI: 0.44-2.36, n=2). Moderate heterogeneity was observed for stomach cancer only. When stratified by industrial vs. consumer talc for stomach cancer, the meta-RRs were 1.68 (95% CI: 0.67-4.18, n=5) and 1.05 (95% CI: 0.56-1.95, n=3), respectively. For CRC, the meta-RRs were 0.98 (95% CI: 0.49-1.95, n=3) and 1.08 (95% CI: 0.64-1.93, n=4). Based on these preliminary results, talc does not appear to be statistically associated with digestive cancer. Although industrial talc estimates were observed to be more elevated in magnitude than consumer talc estimates neither reached a level of statistical significance. Further investigation into other confounding factors, such as radiation exposure and high smoking rates among industrial talc miners may contribute to the elevated magnitude of risk, however, consumer talc does not appear to be associated with any digestive malignancy examined.

Perinatal & Pediatric

Residing in a Neighborhood with Historical redlining and stillbirth occurrence in Arkansas

Olabowale Olola* Olabowale Olola Scott Alsbrook Wendy Nembhard Kari Weber

Background: Historical redlining has been associated with disparities in birth outcomes. However, the specific relationship between historical redlining and stillbirth has not been studied, especially in Arkansas, a state with both a history of residential segregation and significant racial health disparities. This study examined the relationship between living in historically redlined neighborhoods and stillbirth occurrence in Arkansas.

Methods: Data were births January 1997 to December 2013 from the Arkansas Reproductive Health Monitoring System. The Homeowners' Loan Corporation (HOLC) Security Maps, developed in the 1930s, assigned neighborhoods one of four grades: green (grade A) "Best," blue (grade B) "Still Desirable," yellow (grade C) "Definitely Declining," and red (grade D) "Hazardous," (redlined). Grade A served as the reference category. Geocoded maternal residential addresses at the time of birth were linked to the HOLC map to assign each address a grade. Logistic regression models were used to estimate unadjusted and adjusted odds ratios and 95% confidence intervals (CIs) for stillbirth outcomes, with grades B, C, and D (redlined) evaluated separately.

Results: This study included 642 stillbirths (cases) and 601 livebirths (controls). Compared with participants residing in grade A neighborhoods, those living in grade B (OR = 5.66; 95% CI: 3.58–8.94), grade C (OR = 4.85; 95% CI: 3.08–7.66), and grade D "redlined" (OR = 5.42; 95% CI: 3.74–7.85) neighborhoods had significantly higher odds of stillbirth.

Conclusion: This study reveals a strong and consistent pattern, indicating that historical redlining is associated with significantly increased odds of having a stillbirth.

KEYWORDS: Historical redlining, stillbirth, HOLC

Perinatal & Pediatric

Acute Otitis Media Treatment Among Children in the US Military Health System Chrystelle Kiang* Chrystelle Kiang Clinton Hall Celeste J. Romano Yixin Chen Anna T. Bukowinski Zeina G. Khodr Gia R. Gumbs Ava Marie S. Conlin Nanda Ramchandar

Background: Approximately 60% of children will experience at least 1 episode of acute otitis media (AOM), a middle ear infection, by age 3. AOM is the most common indication for antibiotic treatment in children and proper usage is necessary to prevent antibiotic resistance and risk of adverse events. We sought to characterize AOM treatment among US military-connected children.

Methods: This retrospective cohort study used Birth and Infant Health Research program data to identify children born between March 2013 and June 2021, with follow-up until age 5 or September 2024. We obtained diagnosis and treatment records from administrative medical encounter data and evaluated concordance with American Academy of Pediatrics guidelines among those treated with antibiotics. Guideline-concordant 1st line treatment was amoxicillin for 10 days for those <2 years and 7 days for ≥2 years. We summarized guideline concordance by child, parental, and provider characteristics.

Results: During the study period, 418,896 children had at least 1 outpatient AOM diagnosis and were prescribed an oral antibiotic. For children ages 6 months–2 years old, 68% were prescribed amoxicillin for 10 days. For children 2–5 years old, only 7% were prescribed amoxicillin for the recommended 7 days while 64% were prescribed amoxicillin for 10 days, and the remaining 29% were prescribed non-guideline concordant antibiotics. There were no meaningful differences by child, parent, and provider characteristics.

Conclusion: While most children in our study were prescribed the guideline-concordant agent of amoxicillin, those aged 2–5 were likely to have a non-concordant duration and receive an oversupply. This inappropriate use of antibiotics may lead to adverse outcomes and antimicrobial resistance.

Perinatal & Pediatric

Neighborhood food environments and perinatal cardiovascular conditions Elleni M Hailu*
Elleni Hailu Irogue Igbinosa Patricia Rodriguez Espinosa Suzan Carmichael

Neighborhood food environments have lasting impacts on various adverse health outcomes. Yet, their influence on risk of perinatal cardiovascular conditions, major drivers of maternal mortality, is understudied. We used hospital discharge data from California births occurring at ≥20 weeks' gestation between 2010-2020 (N= 4,441,281), which was linked with United States Department of Agriculture data and the National Neighborhood Data Archive to characterize food environments. We assessed how limited food access (LFA; based on income, supermarket distance, and vehicle availability) and convenience store and fast-food outlet density per capita (high vs low tertiles) in neighborhoods (i.e. census tracts) may impact risk of hypertensive disorders of pregnancy (HDP; chronic hypertension, gestational hypertension/preeclampsia, eclampsia), HDP subtypes, and non-optimal pre-pregnancy and gestational cardiovascular health (based on hypertension, diabetes, smoking, body mass index, and gestational weight-gain). We used mixed effects modified Poisson regression models with neighborhood random intercepts and robust standard errors adjusting for sociodemographic, pregnancy, and neighborhood factors. Compared to non-LFA neighborhoods, living in LFA neighborhoods was associated with increased risk of all perinatal cardiovascular conditions, with the highest estimates observed for chronic hypertension (Risk Ratio (RR)=1.14, 95% Confidence Interval=1.10-1.18). Living in neighborhoods with high vs low convenience store density was associated with moderately elevated risk of outcomes (RR range: 1.02-1.09), while estimates comparing high vs low fast-food outlet density were attenuated. Estimates were higher when comparing living in LFA neighborhoods with high convenience store or fast-food outlet density than in non-LFA neighborhoods with low convenience store or fast-food outlet density. Findings provide evidence for promoting healthy food access to reduce perinatal cardiovascular risk.

Perinatal & Pediatric

Mid-Pregnancy Extracellular Vesicle Proteomic Signatures Differentiate Preeclampsia and Normotensive Pregnancies Brandie DePaoli Taylor* Brandie DePaoli Taylor Emmanuel Amabebe Akaninyene I Noah Vineet Mahajan Ananth K Kammala Lauren S Richardson Surendra Sharma Ramkumar Menon

Background: Preeclampsia (PE) causes maternal morbidity and mortality, but early detection is limited by its molecular heterogeneity. Extracellular vesicles (EVs) modify key biological processes, and their protein cargo may provide biological insight into PE pathogenesis. However, studies have not extensively examined EVs and their cargo before PE diagnosis.

Methods: We obtained stored plasma (18-20 weeks gestation) from 163 PE cases and 325 normotensive controls in the SCOPE cohort. EVs were isolated by size exclusion chromatography and characterized by size/quantity. Logistic regression estimated associations between EV concentration and PE, adjusting for maternal demographic and behavioral factors. Secondary analyses examined preterm PE, severe PE, and PE with small for gestational age. Proteomic profiling of randomly selected EV samples (50 PE and 50 controls) was performed by DIA mass spectrometry followed by protein-protein interaction and Ingenuity Pathway Analysis (IPA). Differential expression was determined using a log2 fold-change cutoff of ±1.5 with false discovery rate correction.

Results: Higher EV concentrations were associated with preterm PE (OR 1.54, 95%CI 1.10–2.19) and severe PE (OR 1.38, 95%CI 1.05–1.84) (figure 1). Proteomic analyses identified 31 upregulated and 14 downregulated EV proteins in PE compared to controls. IPA revealed dysregulated coagulation and extracellular matrix remodeling pathways consistent with inflammation-induced endothelial injury and hypercoagulability. Downregulated apolipoproteins suggested impaired lipid transport, impacting placental development. Network and canonical pathway analyses further demonstrated dysregulated canonical and non-canonical Wnt signaling, which may drive abnormal placentation.

Conclusions: EVs are elevated in preterm and severe PE as early as 18 weeks gestation. These EVs have unique proteomic signatures but further studies are needed to validate EV-associated dysregulation of Wnt signaling.

Association between EV concentration and preeclampsia adjusted for maternal age, ethnicity, education, smoking, BMI, multivitamin use, employment & alcohol

Group	n	Crude OR, 95% CI	Adjusted OR, 95% CI
Normotensive	325	Reference	Reference
PE	163	1.38, 1.14-1.67	1.33, 1.08-1.64
Term PE	118	1.22, 0.99-1.51	1.16, 0.93-1.45
Preterm PE	45	1.29, 0.92-1.83	1.29, 0.92-1.83
Severe PE	74	1.29, 0.92-1.83	1.29, 0.92-1.83
PE with SGA	43	1.29, 0.92-1.83	1.29, 0.92-1.83

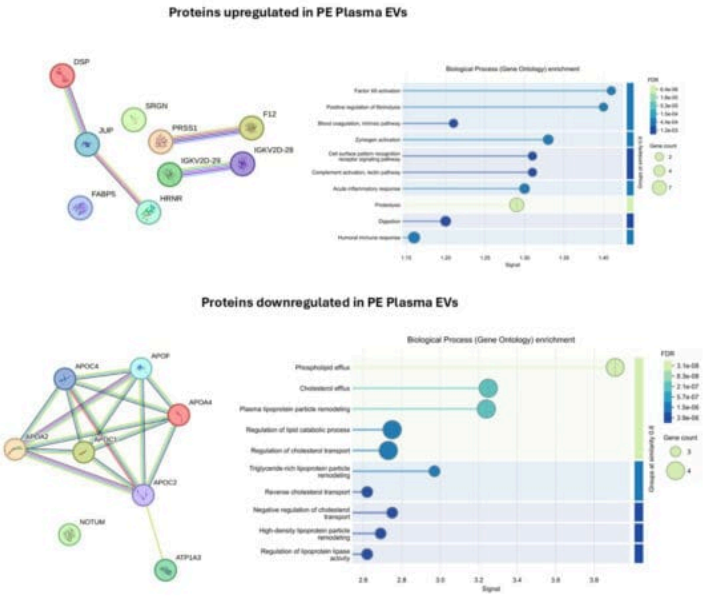


Figure 1. Results from EV isolation and proteomics subgroup analyses. Plasma and data were obtained from the Screening for Pregnancy Endpoints (SCOPE) an international study from UK, Ireland, Australia, and New Zealand. 488 plasma samples at 18-20 weeks gestation were used to determine EV concentration and size. A random subset of EV samples were used for proteomics of EV cargo.

LATEBREAKER

Perinatal & Pediatric

Prenatal polybrominated diphenyl ethers (PBDEs) and kidney function markers in adolescents at age 12 years Amruta Godbole* Amruta Godbole Dr Miguel Fudolig Dr Gabriella Buccini Dr Kim Cecil Dr Kimberly Yolton Dr Joseph Braun Dr Bruce Lanphear Dr Aimin Chen Dr Ann M Vuong

Background: Toxicological studies indicate that polybrominated diphenyl ethers (PBDEs), a class of flame retardants, may impair kidney function through oxidative stress. However, epidemiological evidence, especially for exposure occurring during gestation remains limited.

Objective: To investigate the association between prenatal PBDEs and kidney function in adolescents at age 12 years.

Methods: We used data from the Health Outcomes and Measures of the Environment (HOME) Study, a prospective pregnancy and birth cohort (2003-2006; Cincinnati, OH, USA). We used multivariable linear regression models adjusted for sociodemographic characteristics, pregnancy health behaviors, and reproductive history to estimate associations between log10-transformed PBDE concentrations (ng/g lipid) in maternal serum at 16 weeks' gestation with natural log-transformed adolescent kidney markers, including serum creatinine, cystatin C, urinary albumin, and estimated glomerular filtration rate (eGFR). We used modified Poisson regression to estimate associations between PBDEs with albumin-creatinine ratio (ACR). Effect measure modification by sex was evaluated using interaction terms.

Results: Higher prenatal BDE-28 concentrations were associated with lower ACR (β=-0.52; 95% CI=-0.92, -0.12), lower serum creatinine (β=0.12; 95% CI=-0.22, -0.03), and higher eGFR (β=0.12; 95% CI=0.02, 0.21). BDE-153 was also associated with lower serum creatinine (β=-0.08, 95% CI=-0.16, -0.005), while BDE-47 was associated with higher eGFR (β=0.08, 95% CI=0.004, 0.16). Poisson regression showed inverse associations between several PBDEs and elevated ACR. Evidence of effect measure modification by sex was observed with eGFR for BDE-47(pint=0.061), BDE-99 (pint=0.135), BDE-100 (pint=0.078), and BDE-153 (pint=0.026), with statistically insignificant inverse associations in males and positive associations in females.

Conclusion: Prenatal PBDE exposure was inversely associated with ACR and creatinine but positively associated with eGFR in adolescents. Although these findings indicate better kidney function, they may reflect early subclinical physiological adaptation rather than protection, highlighting the importance of developmental timing and compensatory renal responses.

LATEBREAKER

Perinatal & Pediatric

Language Preference as a Modifier of Prenatal Depression Screening Uptake, 2019-2024

Amanda Luff* Amanda Luff Anne Rivelli Akaninyene Noah Emily Malloy Ravi Mishra Veronica Fitzpatrick

Background: The American College of Obstetricians and Gynecologists issued its first recommendation for universal prenatal depression screening (PDS) in 2015 and reinforced this in 2018. In 2019 the National Committee for Quality Assurance added Prenatal Depression Screening and Follow-up as a quality measure. Language can be a barrier to receipt of recommended screenings. We evaluated how language preference modified uptake of PDS following updated recommendations.

Methods: This retrospective cohort comprised deliveries at or beyond 20 weeks gestation, 2019 to 2024, that initiated prenatal care (PNC) in the first or second trimester. We used logistic generalized estimating equations to account for patients contributing multiple deliveries and calculated marginal probabilities for PDS. An interaction term between language and year assessed if the relationship between preferred language and PDS differed by year of delivery, controlling for maternal age, race/ethnicity, insurance, parity, gestational age, singleton versus multiple gestation, and state of PNC.

Results: Of 91,330 deliveries, patients reported 74 preferred languages: English (94%), Spanish (3%), and Another Language (3%). In 2019, probabilities of PDS were similar across groups: English, 0.50 (95% CI, 0.49–0.51); Spanish, 0.48 (95% CI, 0.40–0.55); and Another Language, 0.50 (95% CI, 0.42–0.58). By 2024, the probability of screening increased to 0.82 (95% CI, 0.82–0.83) for those with English-language preference, 0.69 (95% CI, 0.65–0.74) for Spanish-language preference, and 0.69 (95% CI, 0.64–0.72) for another language preference.

Conclusion: PDS increased from 2019 to 2024, but improvements were not uniform across language groups, resulting in larger screening gaps by 2024 for patients with non-English language preference. Potential contributors include availability of validated instruments in preferred language, interpreter integration at screening, and clinical workflows.

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LATEBREAKER

Perinatal & Pediatric

The Joint Effects of Inflammatory Bowel Disease and Infertility on Preterm Birth Aida Glembocki* Aida Glembocki Hilary K. Brown Maria P. Velez Tanmay Vasa Jun Guan Eric Benchimol Sonia M. Grandi

Background
Inflammatory bowel disease (IBD) and infertility have each been associated with adverse pregnancy outcomes, including preterm birth (PTB). However, the joint effects of IBD and infertility on PTB remain unclear.

Methods
A retrospective, population-based cohort of women aged 15-55 years with a first recorded delivery (≥ 20 weeks' gestation), in Ontario, Canada (2007–2024) was constructed using individual-level health administrative datasets, including MOMBABY (mother-baby linkage) and BORN (perinatal registry). Exposure was defined as a four-level variable: 1) IBD alone; 2) infertility diagnosis and/or treatment alone; 3) joint exposure; 4) neither (comparator). Modified overlap-weighted Poisson models were used to address confounding by indication. Interaction was quantified using the Relative Excess Risk due to Interaction (RERI) and Attributable Proportion (AP).

Results
Among 862,515 women with a first recorded delivery, 4761 had IBD, 122,340 had infertility, and 1276 had both IBD and infertility. Overall, 7.3% of women experienced a PTB, with a higher proportion among women with IBD and infertility (14.7%), with infertility (11.4%), and with IBD (9.7%). Compared with women with neither IBD nor infertility, the risk of PTB was 79% higher among women with both IBD and infertility (RR 1.79, 95% CI 0.92-2.10), 45% higher for women with infertility alone (RR 1.45, 95% CI 1.42-1.48), and 9% higher among women with IBD alone (RR 1.09, 95% CI 0.98-1.21). Joint exposure was found to be associated with a 25% excess risk of PTB, with 14% of the risk of PTB attributable to joint exposure.

Conclusion
IBD and infertility exert a synergistic effect on the risk of PTB. These findings underscore the importance of integrated preconception and prenatal care for individuals experiencing both IBD and infertility and highlight opportunities for risk stratification to improve their clinical management of pregnant women living with these conditions.

Perinatal & Pediatric

Maternal Mental Health and Infant Safe Sleep Practices: A Population-Based Analysis of PRAMS Data Jaksen Perrin* Andrew Williams Jaksen Perrin Taylor Lange Rylie Fode

Background: Despite a 50 percent reduction in sudden unexpected infant death (SUID) attributed to safe sleep campaigns over the past 30 years, approximately 3,500 infants die from SUID in the United States. Maternal mental health factors may be associated with safe sleep environments yet is an underexamined determinant of safe sleep. We examined the association between maternal mental health and safe sleep environments, and if safe sleep recommendations moderate observed association.

Methods: North Dakota 2017-2021 PRAMS participants (weighted n=32,647), self-reported preconception, antenatal, and postpartum depression diagnoses. Participants reported on 8 infant sleep environment factors (e.g. sleep position, toys in crib, sleeping with blanket), and whether a healthcare professional discussed safe sleep recommendations during pregnancy. Logistic regression models estimated odds ratio (OR) and 95% confidence intervals (CIs) for the association between maternal depression and unsafe infant sleep factors for preconception, antenatal, and postpartum depression. Models were adjusted for maternal demographic and health factors and weighted to account for survey design.

Results: Depression during pregnancy was a risk factor for toys in cribs (OR:2.24; CI:1.35-3.73) and placing their infant on a chair to rest (OR:1.78; CI:1.16-2.73). Smoking was a risk factor for use of an infant sleep sack (OR:1.63; CI:1.04-2.54). Postpartum depression was a risk factor for sleeping on a large mattress (OR:1.71; CI:1.19-2.46).

Conclusion: These findings highlight the importance of safe sleep recommendations for mothers with a mental health status to improve infant sleep environments. Healthcare providers should prioritize outreach to mothers with mental health conditions.

Perinatal & Pediatric

Concordance with pediatric urinary tract infection clinical guidelines and short-term outcomes in children in the US Military Health System Yixin Chen* Yixin Chen Clinton Hall Celeste J. Romano Chrystelle Kiang Anna T. Bukowinski Zeina G. Khodr Gia R. Gumbs Ava Marie S. Conlin Nanda Ramchandar

Background: Urinary tract infection (UTI) is a common bacterial infection in early childhood. Inappropriate treatment may lead to adverse short-term outcomes. We assessed concordance with American Academy of Pediatrics guidelines in testing, treatment, and management of UTI, and evaluated the risk of selected adverse outcomes associated with treatment non-concordance in US military-connected children.

Methods: We used Birth and Infant Health Research program data to identify children born January 2012-October 2021 and aged 2-24 months at first UTI diagnosis. Utilizing administrative medical data, we defined testing concordance as having both a urine culture and urinalysis within ± 3 days of diagnosis, treatment concordance as being prescribed proper antibiotics with recommended duration (i.e., 7-14 days) within 5 days of diagnosis, and management concordance as having a renal and bladder ultrasound (RBUS) within 90 days of diagnosis or before a 2nd UTI. Selected adverse health outcomes included antibiotic allergy within 14 days, Clostridium difficile, diarrhea, ER visit, or hospitalization within 30 days of antibiotic dispensation. Adjusted modified Poisson models estimated the risk of any adverse outcome with treatment non-concordance.

Results: A total of 14,112 children with first UTI treated with antibiotics were included. For testing, 8038 (57.0%) infants had both a urine culture and urinalysis done. For treatment, 12,180 (86.3%) infants had proper antibiotics with recommended duration. For management, 3697 (26.2%) had RBUS. We observed 2056 (14.6%) infants with any of the selected adverse outcomes and estimated a null association with treatment non-concordance (RR=1.00, 95% CI: 0.89-1.12).

Conclusion: Many infants with an initial UTI are not receiving recommended diagnostic tests or follow-up imaging, highlighting the need for improved practice guidance. High treatment concordance may limit the power to detect differences in short-term adverse outcomes.

Perinatal & Pediatric

Spatial Variation in Sudden Infant Death Syndrome Across California's San Joaquin Valley, 2019–2022 Elizabeth Amankwah* Elizabeth Amankwah Alec Chan-Golston Sandie Ha Sneha Ghimire

Sudden Infant Death Syndrome (SIDS) remains a leading cause of post-neonatal mortality in the United States and accounts for a large proportion of Sudden Unexpected Infant Deaths (SUID). SIDS is defined as the sudden, unexplained death of an apparently healthy infant under one year of age following a complete investigation. SIDS continues to present persistent regional and sociodemographic disparities. Nationally, SIDS rates increased from 39.8 to 41.7 deaths per 100,000 live births between 2019 and 2022. Although California's overall infant mortality rate is lower than the national average, sudden unexpected infant death (SUID), including SIDS, remains the second leading cause of infant death statewide, with a rate of about 53.4 deaths per 100,000 live births (CDPH, 2023). Within California, parts of the San Joaquin Valley (SJV) exhibit higher SIDS rates, yet fine-scale spatial variation in SIDS risk within this region has not been well characterized.

We conducted a retrospective ecological analysis using California Vital Statistics Birth and Death certificate data from the California Department of Public Health for 2019–2022. The analytic dataset included all live births and infant deaths occurring within the first year of life. SIDS cases were identified using the ICD-10 code R95. ZIP-code–level SIDS rates were calculated per 1,000 live births. Spatial autocorrelation and clustering were assessed using Global Moran's I and Geary's C to evaluate geographic heterogeneity and temporal variability in SIDS risk.

SIDS rates varied across ZIP codes in the SJV, with evidence of spatial clustering and persistent areas of elevated risk over time. These findings highlight meaningful small-area heterogeneity in SIDS risk, which can help identify communities that may benefit from targeted prevention and enhanced surveillance efforts.

Perinatal & Pediatric

Maternal occupational risks and adverse birth outcomes among emergency medical services workers, firefighters, and nurses Paulina Luna Ramirez* Paulina Luna Ramirez Leslie Farland Melissa Furlong Jefferey L. Burgess Michelle Valenti Lisa Labita Woodson Jessica Rainbow Caitlin Clarkson Pereira Stuart Sherman Maia Brown

Emergency service and health care workers face hazardous conditions such as chemical exposure, shift work, stress, and physical strain which may negatively affect pregnancy. Few studies have investigated the impact of occupational exposure as a first responder and adverse pregnancy outcomes. With the use of birth certificates from the state of Arizona (2006-2013), we evaluated adverse birth outcomes among emergency medical services workers without fire exposure (N=414), firefighters(N=376), and nurses(N=13,737) compared to the general population. Using logistic regression, we estimated the association between maternal occupation and risk of low birth weight, preterm birth, cesarean section, low Apgar score, and neonatal intensive care unit (NICU) admission. Models were adjusted for mother’s education and age, as well as birth year. For the outcome of low birth weight, we additionally adjusted for gestational age. We observed higher odds of preterm birth for EMS workers (1.76, 95% CI: 1.34, 2.30), firefighters (1.40, 95% CI: 1.02, 1.88) and nurses (1.22, 95% CI:1.15, 1.30) compared to the general population. Increased odds of cesarean section were observed for EMS workers (1.41, 95% CI: 1.15, 1.72). NICU admission was elevated among emergency medical services workers (2.12, 95% CI: 1.56, 2.89) and firefighters (1.84, 95% CI: 1.30, 2.56) compared to the general population. None of the occupational groups had higher odds of low Apgar score and low birth weight when compared to the general population. These findings suggest associations between maternal occupation in emergency medical services, firefighting, and nursing and select adverse birth outcomes, highlighting the need for future research on implementing workplace protections for pregnant workers.

Perinatal & Pediatric

Congenital heart disease rates and the COVID-19 pandemic: a study in a large integrated health system from 2016-2025 Helena Archer* Helena Archer Ousseny Zerbo Nicola Klein Karen Jacobson Lauren Liao Kristin Burnett John Hansen Julius Timbol

Perinatal & Pediatric

The risk of adverse birth outcomes in mothers with depressive symptoms comorbid with gestational diabetes or hypertension: The Born in Queensland Study Biruk Beletew Abate* Biruk Abate Berihun Assefa Dachew Getinet Ayano Kim Betts Biruk Shalmeno Tusa Rosa Alati

The risk of adverse birth outcomes in mothers with depressive symptoms comorbid with gestational diabetes or hypertension: The Born in Queensland Study

Abstract

Background: Depression, hypertensive disorders of pregnancy (HDP), and gestational diabetes mellitus (GDM) are common pregnancy complications that often co-occur, but their combined effects remain underexplored. In this study, we aimed to assess the joint impact of antenatal depressive symptoms comorbid with either HDP or GDM on adverse birth outcomes.

Methods: In this population-based retrospective cohort study, we analysed 149,025 mother–child pairs in Queensland, Australia. Eligible participants were all women who gave birth between July 2015 and December 2021 and had recorded scores on the Edinburgh Postnatal Depression Scale (EPDS). Logistic regression models estimated adjusted odds ratios (AORs) for adverse outcomes associated with prenatal depressive symptoms alone or in combination with HDP or GDM. We also assessed potential interaction effects.

Results: Depression, HDP, and GDM were each independently associated with increased risks of adverse birth outcomes. Risks were greatest when depression co-occurred with either HDP or GDM. Depression with HDP was strongly associated with preterm birth (AOR 3·08, 2·70–3·53), LBW (AOR 3·05, 2·62–3·53), neonatal resuscitation (AOR 1·55, 1·40–1·73), congenital anomalies (AOR 1·24, 1·05–1·46), low Apgar score (AOR 1·80, 1·41–2·28), and ICN/SCN admission (AOR 1·85, 1·67–2·06), with risks consistently exceeding those for either condition alone. Similarly, depression with GDM was associated with increased risks of preterm birth (AOR 2·60, 2·27–2·98), LBW (AOR 2·44, 2·10–2·83), neonatal resuscitation (AOR 1·51, 1·36–1·68), congenital anomalies (AOR 1·28, 1·09–1·51), low Apgar score (AOR 1·64, 1·29–2·08), and ICN/SCN admission (AOR 1·94, 1·75–2·16).

Conclusions: Antenatal depression comorbid with HDP or GDM is associated with an increased risk of adverse birth outcomes, exceeding the independent additive effects of each condition, underscoring the need for integrated care. Incorporating mental health into routine obstetric practice and evaluating targeted interventions for high-risk women remain key priorities.

Keywords: Depression, Diabetes, Hypertension, Comorbidity, Neonatal Outcomes

Perinatal & Pediatric

Association between Environmental Quality Index and Congenital Heart Defects in Arkansas Jenil Patel* Lydia Famuyide Jenil Patel Wendy N. Nembhard

Introduction: Congenital heart defects (CHDs) occur in 1% of live births in the United States (US) and are the leading cause of death from birth defects. While prior studies have largely focused on isolated environmental exposures, fewer have examined the cumulative influence of multiple environmental domains. This study evaluated whether county-level cumulative environmental quality is associated with the prevalence of CHDs in Arkansas.

Methods: We conducted a retrospective cohort study using births occurring from 2006-2010, linking CHD cases identified through the Arkansas Reproductive Health Monitoring System to county-level Environmental Quality Index (EQI) measures. The overall EQI and five domain-specific indices (air, water, land, sociodemographic, and built environment) were categorized into quartiles. Crude and adjusted prevalence ratios (PR) and 95% Cis were estimated using Poisson regression with cluster-robust standard errors, adjusting for maternal age, smoking during pregnancy, race/ethnicity, rural-urban continuum codes, and maternal education.

Results: Overall environmental quality was not significant associated with CHD prevalence after adjustment (Adjusted PR: 0.85; 95% CI: 0.71, 1.01). No significant associations were observed for the air, land, water, built and sociodemographic domains in the adjusted models. In crude analyses, worse land domain environmental quality was associated with a lower prevalence of CHDs (Crude PR: 0.81; 95% CI: 0.68, 0.97), though this association was attenuated after adjustment.

Conclusion: County-level cumulative environmental quality, as measured by the EQI, was not independently associated with overall CHD prevalence in Arkansas after appropriate adjustment for key maternal and contextual factors. Ongoing analyses will examine associations between EQI domains and specific CHD phenotypes, which may be differentially sensitive to environmental conditions and could be obscured in analyses of CHDs as a heterogenous group.

LATEBREAKER

Pharmacoepidemiology

Acetaminophen use during pregnancy and motor function in offspring at age 5 years

Yuewen Ge* Yuewen Ge Pengfei Guo Katrine Strandberg-Larsen Nis Brix Onyebuchi A. Arah Cecilia Høst Ramlau-Hansen Zeyan Liew

Background
Acetaminophen is the most commonly used analgesic during pregnancy. Epidemiologic studies have raised concerns that prenatal acetaminophen exposure may affect offspring neurodevelopment, but evidence regarding prenatal acetaminophen use and offspring motor function remains limited. Therefore, we investigated whether prenatal acetaminophen exposure affected motor function in offspring.

Methods
We studied 734 mother–child pairs from the Danish National Birth Cohort (1996–2002) who participated in the Lifestyle During Pregnancy Study and completed motor function assessment using the Movement Assessment Battery for Children (MABC) at 5 years of age. The Total Impairment Score (TIS) ranges from 0 to 40, with higher scores indicating greater motor impairment. TIS was categorized using the 5th and 15th percentile cutoffs to define levels of motor impairment. We estimated odds ratios (ORs) across categories of motor function using multinomial logistic regression models. We estimated mean differences in continuous motor scores using multivariable linear regression. Models were adjusted for maternal socioeconomic and lifestyle factors, and the main indications for acetaminophen use.

Results
Prenatal acetaminophen use was not associated with motor function assessed by the MABC at age 5. Compared with never use, ever use was associated with an adjusted OR of 1.32 (95% CI: 0.90, 1.92) for abnormal motor function and 1.08 (95% CI: 0.65, 1.79) for borderline motor function. Results were similar when motor function was analyzed continuously ($\beta = 0.54$; 95% CI: -0.38, 1.46). Neither increasing duration nor cumulative exposure to acetaminophen during pregnancy demonstrated any consistent dose–response patterns. Findings were also null across sex-stratified analyses.

Conclusions
These findings did not support an association between prenatal acetaminophen exposure and the impairments of motor function measured at age 5.

Pharmacoepidemiology

Incidence of potential prescribing cascades involving overactive bladder medications among US older nursing home residents Lexie R. Grove* Lexie Grove Andrew R. Zullo Richa Joshi Kelsey L. Corcoran Arman Oganisian Preeti Chachlani Kaleen N. Hayes

Background: Medications for overactive bladder (OAB) can cause severe adverse events among older nursing home (NH) residents, including cognitive impairment and injurious falls. Prescribing cascades, wherein side effects caused by one drug are managed by prescription of a second drug, may contribute to unnecessary OAB drug use. A recent expert panel identified four potentially inappropriate prescribing cascades involving OAB drugs, but little is known about the epidemiology of these cascades in the NH setting.

Objective: To estimate the 90-day incidence of potential OAB prescribing cascade events, defined as OAB drug initiation after initiation of a loop diuretic (LD), cholinesterase inhibitor (ChEI), selective serotonin reuptake inhibitor (SSRI)/serotonin-norepinephrine reuptake inhibitor (SNRI), or tricyclic antidepressant (TCA), among older NH residents.

Methods: We used 2013-2023 Medicare claims linked to Minimum Dataset clinical assessments to identify long-stay NH residents aged 66 or older with 12 prior months of continuous enrollment in Medicare Parts A, B, and D. The study index date was the first dispensing date (i.e., initiation) of a precipitant drug (i.e., a LD, ChEI, SSRI/SNRI, or TCA). We excluded individuals with any use of a precipitant drug (separately for each drug class) or OAB drug in the 180 days prior to the index date.

Results: We identified 108,249 LD initiators; n=37,100 ChEI initiators; n=95,379 SSRI/SNRI initiators; and n=7,685 TCA initiators (mean age=83 years [SD=8]; 70% female). The 90-day incidence of OAB drug initiation was 0.55% (LD), 0.73% (ChEI), 0.70% (SSRI/SNRI), and 1.16% (TCA). The median time to OAB drug initiation was between 30 and 40 days for all precipitant drug classes.

Conclusions: OAB drug prescribing cascades appear to be uncommon among older NH residents. Clinicians may rely on non-pharmacological strategies to manage urinary symptoms that arise after initiation of drugs known to cause these side effects.

Pharmacoepidemiology

Characterizing the Epidemiology of Antimicrobial Use in a Large U.S. Municipal Companion Animal Shelter Paulina Colombo* Paulina Colombo Jennifer Wishnie Timothy Ojodare Kevin Olson Jennifer Wilcox Katherine Ellingson

Background: Responsible antimicrobial use (AMU) in animals is essential to optimize care and minimize antimicrobial resistance (AMR). While AMU guidelines exist in animal production and small animal clinics, gaps remain for animal shelters. The University of Minnesota (UMN) and World Health Organization (WHO) have proposed AMR frameworks to classify animal antibiotics by AMR and public health risk. This study aimed to (1) characterize AMU in a large, municipal shelter; (2) calculate species-specific days of therapy (DOT); and (3) determine differences in prescribing of high-risk antibiotics by species. **Method:** Electronic records (Jan 2022–Jun 2025) were analyzed to calculate AMU per 1,000 shelter-days for dogs and cats. Prescriptions were categorized by UMN clinical tiers and by public health importance per the 2024 WHO framework. GEE models accounting for non-independence of prescribing events by animal were used to model prescription of “Second-line” (UMN) and “Critically Important” (WHO) AMU by species. **Result:** Over 3.5-years, 26,509 antibiotic prescribing events occurred for 15,784 unique animals. 30% of cats and 34% of dogs received antibiotics. Cats had shorter average courses than dogs (4.8 vs 6.1 days). Penicillins, tetracyclines, and cephalosporins were the most frequently prescribed classes. AMU was 249.5 DOT/1,000 shelter-days for cats and 173.0 for dogs. Under UMN tiers, 29.3% of canine and 10.9% of feline prescriptions were “Second-line” therapies (culture/sensitivity needed). Under the WHO framework, 29.3% of canine and 10.6% of feline prescriptions were “Critically Important” antimicrobials. Dogs had higher odds of receiving “Second-line” (OR 3.70; 95% CI: 3.37-4.07) and “Critically Important” (OR 3.90; 95% CI: 3.52-4.29) antibiotics ($p<0.001$). **Conclusion:** Compared to dogs, cats had 44% higher overall antibiotic DOT/1000 shelter-days. In contrast, dogs had over 3 times the rate of WHO “Critically Important” prescriptions (to humans) compared to cats.

Psychosocial factors

Changes in Life Satisfaction and Receipt of Social and Emotional Support among Adults Residing in 7 States: 2015-2017 to 2022-2024 Guixiang Zhao* Guixiang Zhao Machell Town J'Neka S. Claxton

Background Psychosocial factors play important roles in promoting health behaviors and overall health. This study assessed how psychosocial factors changed across the COVID-19 pandemic period among US adults.

Methods During the periods of 2015-2017 (pre-COVID period) and 2022-2024 (post-COVID period), 7 states† collected data via BRFSS‡ on 2 psychosocial factors-life satisfaction and receipt of social and emotional support (SoES). Age-standardized prevalence estimates for the 2 psychosocial factors were estimated to measure changes across the 2 periods, overall and by sociodemographic characteristic.

Results During 2022-2024, the age-standardized prevalence was 92.9% (95% CI: 92.6-93.2%) for life satisfaction and 75.4% (74.9-75.9%) for receipt of SoES among adults, which were significantly lower than those for the period of 2015-2017 [93.9% (93.5-94.4%) and 79.2% (78.4-79.9%), respectively]. The changes persisted across most sociodemographic characteristics. The largest decrease in life satisfaction (relative change ≥2.5%) was seen among adults aged 18-34 years; non-Hispanic (NH) American Indian/Alaska Native (AI/AN), Asian, and other races; never married; unemployed or retired; and with household income below $50,000. The largest decrease in receipt of SoES (relative change ≥5.0%) was seen among adults aged 18-49 years; male; NH AI/AN and other races; with educational level of high school or above; divorced/widowed/separated or never married; unemployed, retired, or other (homemakers, students, or those unable to work); with household income below $75,000; and resided in Louisiana, Minnesota, or Oklahoma.

Conclusions The findings of this study highlight exacerbated psychosocial factors during the post-COVID period. Although causality cannot be inferred and generalizability of the results is limited because data are from only 7 states, future research may focus on whether improving psychosocial factors could help promote population health at nationwide level.

Key Words: BRFSS, Life Satisfaction, Social and Emotional Support.

†7 states include Louisiana, Minnesota, Ohio, Oklahoma, Rhode Island, Tennessee, and Wisconsin.

‡ BRFSS: Behavioral Risk Factor Surveillance System

Reproductive

Substance Use and Pregnancy Attempts in the Apple Women's Health Study Michelle Klawans* Michelle Klawans Nathaniel MacNell Donna Baird Allen Wilcox Anne Marie Jukic

Background: Use of alcohol, electronic nicotine devices (ENDs), and cannabis is common and increasing among women of reproductive age. However, little is known about patterns of use when starting an attempt to conceive a pregnancy.

Methods: We analyzed data from Apple Women's Health Study (AWHS) participants aged 18-44 years who consented and enrolled between November 2019 and July 2025 and began a pregnancy attempt after enrollment. Substance use was reported on a monthly questionnaire along with whether a participant was trying to become pregnant that month. We calculated the overall prevalence of tobacco, alcohol, and cannabis use in the first study cycle. We also calculated first study-cycle prevalence of use for those who started a pregnancy attempt at any time during follow-up and compared this with the prevalence of use among those who did not start a pregnancy attempt within 6 months of enrollment.

Results: A total of 104,368 participants were included, of whom 6,549 reported starting a pregnancy attempt during follow-up. In the first study cycle from all participants, the prevalence of alcohol use was 61% (n=63,418), cigarettes, 3.4% (n=3,596), ENDs, 16% (n=17,401), and cannabis, 28% (n=29,250). In the first month of attempting pregnancy, the prevalence of current cannabis use was 20% (n=329/1,647) which was similar to use among those not attempting pregnancy, 21% (n=396/1,910). Those in the first month of attempting to conceive were slightly less likely to report current alcohol use than those who were not attempting to conceive (n=994/1,654; 60.0% vs. n=1285/1921; 66.9%).

Conclusion: In this sample of AWHS participants, those who started attempting to conceive a pregnancy had a similar prevalence of current cannabis use as those who did not start a pregnancy attempt. Use of alcohol and cannabis were common in those beginning a pregnancy attempt.

Reproductive

Severity-Graded Obstetric Trauma and Postpartum Mental Health Diagnoses in a Hospital-Based Birth Cohort Shashi Sarnaik* Shashi Sarnaik Farah Qureshi Celia Karp

Background: Obstetric trauma (e.g., severe physical harm during labor and delivery) may increase risk of postpartum mental health conditions, yet prior research has largely relied on self-reported data on childbirth experiences and/or mental health screening instruments. Less is known about the mental health sequelae of clinically documented obstetric trauma within hospital cohorts. This study examined whether severity-graded obstetric trauma may help identify populations at elevated risk for postpartum mental health diagnosis.

Methods: Data were from 2,442 mothers in the Boston Birth Cohort, a preterm birth cohort based at the Boston Medical Center. Obstetric trauma was defined using delivery-related diagnoses of severe maternal morbidity, postpartum hemorrhage, obstetric anal sphincter injuries obtained from participants' medical records. Diagnoses were categorized as severe if life-threatening and non-severe if non-life threatening. Postpartum mental health cases were also extracted from medical records, and included new diagnoses of stress or adjustment disorders, depression, anxiety, or other mental health disorders obtained within one year postpartum. Associations were evaluated via logistic regression models adjusted for sociodemographic and pregnancy-related clinical covariates.

Results: 17% of participants experienced obstetric trauma (12% severe; 5% non-severe), and 20.9% received a postpartum mental health diagnosis. In adjusted analyses, severe obstetric trauma was associated with higher odds of postpartum mental health diagnosis (aOR = 1.25, 95% CI: 0.92–1.70) while associations with non-severe trauma were not apparent (aOR = 1.04, 95% CI: 0.66–1.69).

Conclusions: Severity-graded obstetric trauma showed patterns consistent with higher postpartum mental health risk, particularly for severe events. Findings suggest that obstetric trauma severity may be a clinically observable signal for postpartum mental health surveillance within healthcare systems.

LATEBREAKER

Reproductive

Human Parvovirus B19 Pregnancy-Related Complications Across the COVID-19 Pandemic Period: A National Electronic Health Records Study—United States 2018–2025 Christopher Luthers* Christopher Luthers Alfonso Hernandez-Romieu Emily Carter Emily Koumans Olivia Almendares Jason Block

Background. Human parvovirus B19 activity increased following the COVID-19 pandemic, triggering a U.S. Health Alert Network advisory reminding public health partners and clinicians that B19 infection during pregnancy can result in serious complications. We investigated the risk of fetal complications before, during, and after the pandemic.

Methods. We used data from PCORNet, a U.S. dataset linking standardized electronic health records. Pregnant women and fetal complications including anemia, blood transfusion, growth problem, and hydrops fetalis, were identified using ICD-10 codes. Women with B19 were identified using ICD-10 codes, positive B19 IgM, or PCR laboratory testing. Complications among B19 pregnant mothers were evaluated in 2018–19, 2021–22, and 2024–25. Risk ratios (RRs) and 95% confidence intervals (CIs) were calculated to compare complications between pregnant women with and without B19 infection within each period.

Results. The risk of pregnancy complications among pregnant women with B19 increased across periods: 5.59% (95% CI: 3.8–7.4) in 2018–19, 7.10% (4.30–9.90) in 2021–22, and 14.45% (11.83–17.07) in 2024–25. In comparison, complication risk among women without B19 was 2.36% (2.32–2.41), 1.43% (1.40–1.46), and 1.59% (1.56–1.62), across similar periods respectively. The relative risk of complications associated with B19 infection increased substantially over time: RR 2.37 (1.71–3.28), 4.97 (3.35–7.38), and 9.08 (7.56–10.89) across similar periods respectively.

Conclusions. In 2024 –2025, B19 infection during pregnancy was associated with a substantially increased risk of fetal complications. Relative risk was nearly fourfold higher than pre-pandemic levels, suggesting a stronger observed association between B19 infection and adverse pregnancy outcomes in the post-pandemic period. Although absolute complication risk remains low, clinicians should remain vigilant and closely monitor pregnant women with confirmed or suspected B19 infection.


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Respiratory

Adherence to Positive End-Expiratory Pressure Protocols Across Sepsis Phenotypes among Ventilated Critically Ill Children Lucia Petito* Ngoc Duong L. Nelson Sanchez-Pinto, MD, MBI Lucia Petito, PhD

Background: Pediatric sepsis is clinically heterogeneous, and emerging evidence suggests that treatment responses may differ by clinical phenotype. We evaluated 7-day risks of multiple organ dysfunction syndrome (MODS) or death under varying adherence to Acute Respiratory Distress Syndrome (ARDSNet) Positive End-Expiratory Pressure (PEEP)-to-FiO_2 targets and whether these varied based on high- vs. low-risk Pheonix Sepsis phenotype defined at admission.

Methods: We analyzed harmonized data from 13 U.S. pediatric intensive care units (2012–2018). The outcome was persistent multiple organ dysfunction syndrome (MODS) on day 7 or death within 7 days. Patients discharged before day 7 were assumed outcome negative. We compared risk under a hypothetical “always adherent” strategy (PEEP within ARDSNet target range >80% of hours per 12-hours when FiO_2>0.21) versus the natural course risk. We adjusted for baseline and time-varying confounders using the parametric g-formula; nonparametric bootstrap (B=200) was used to generate 95% confidence intervals.

Results: Of 13,728 patients (observed for 79,556 person-days) with suspected infection requiring mechanical ventilation within the first 12 hours of PICU admission, 9,675 (70.5%) and 4,053 (29.5%) belonged to the high- vs low-risk phenotype. Of these, 52.8% met PEEP target at PICU admission, increasing to 80% on day 7. Estimated 7-day risk of MODS or death was 33.1% under the natural course versus 29.5% under the “always adherent” strategy (risk difference [RD] -3.6%; 95% CI: -4.8% to -2.5%). This effect varied by Phoenix Sepsis phenotype (high risk RD -5.1%; 95% CI: -6.7% to -2.8%; low risk phenotype RD -0.2%; 95% CI: -0.7% to 0.2%).

Conclusions: Adherence to ARDSNet PEEP/FiO_2 targets was associated with lower day-7 persistent MODS or death compared to natural course risk, with heterogeneity by Phoenix Sepsis phenotype underscoring the particular importance of adherence to ventilation targets among the highest risk phenotype.

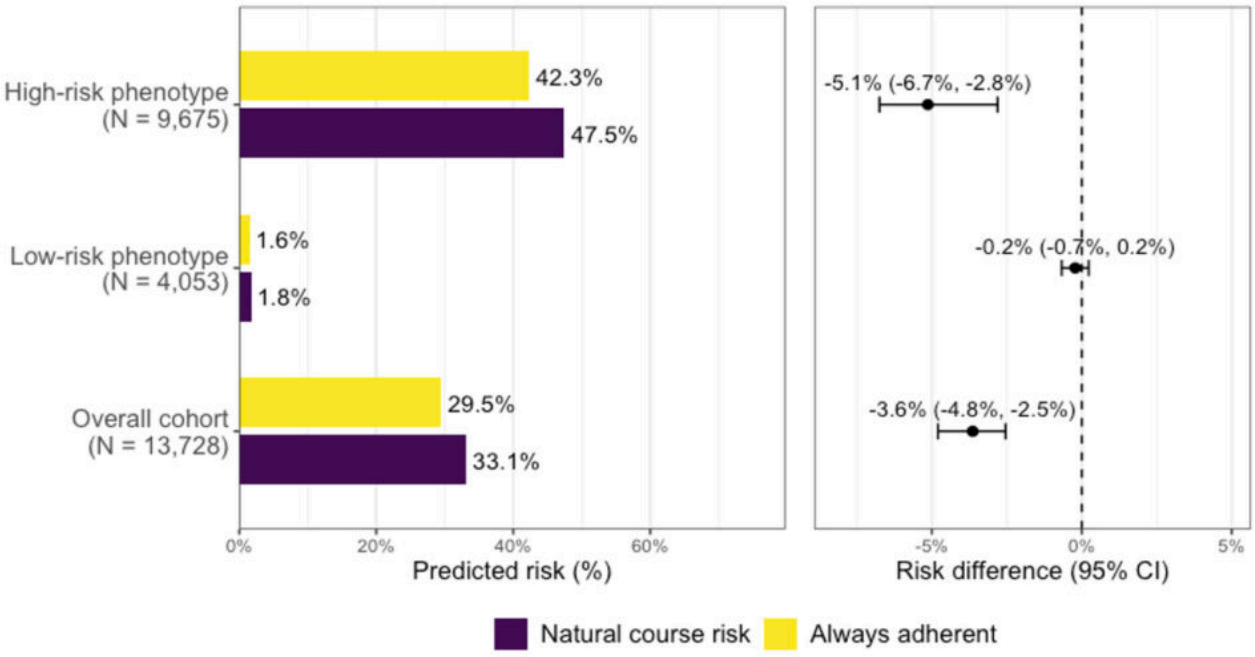


Figure. (Left) Estimated 7-day risk of MODS or all-cause death if all ventilated children were always adherent to ARDSNet PEEP-to-FiO_2 targets (yellow) versus the natural course (purple), stratified by Phoenix-score based risk phenotype. The left panel displays predicted risk under each strategy. (Right) Corresponding risk differences with nonparametric bootstrap-based 95% confidence intervals.

Science Communication & Media

Evaluating Health Promotion and Communication Strategies for Mosquito-Borne Disease Control in the United States: A Scoping Review Protocol Jordan Robinson* Jordan Robinson Skyler Finucane Sarah Yeo Mary Hayden Kacey Ernst

Mosquito-borne diseases (MBD) continue to bring evolving challenges across the Unites States (US). Endemic transmission and periodic outbreaks of West Nile Virus occur throughout much of the country, while expanding Aedes aegypti and Aedes albopictus populations increase risks of transmitting new MBDs. Public support and engagement are vital aspects of integrated MBD control. However, previous work has shown significant gaps in public knowledge between vector presence and taking action to limit disease exposure. This scoping review aims to identify existing research on measuring the effectiveness of health promotion, health messaging, and communication strategies for mosquito-borne diseases in the United States by evaluating interventions and their assessments. Using the JBI Manual for Evidence Synthesis and the Preferred Reporting Items for Systematic Reviews and Meta-analysis extension for Scoping Reviews (PRISMA-ScR), we screened 17,686 studies. Eligible studies were experimental trials conducted in the US that tested public education interventions focused on endemic MBDs. Screening occurred in two phases: first by title and abstract review then full text screening. Final selected studies will go through text extraction following a standardized form to gather paper details, intervention type, methodology, outcomes, and key findings. Descriptive and narrative synthesis will summarize these papers under the following categories: disease occurrence and distribution, types of interventions, primary group disseminating messages, assessment and evaluation of interventions, impacts of intervention on MBDs, and study designs utilized. Results from this scoping review will identify any gaps in MBD education and inform future research and outreach priorities.

Screening

Factors Associated With Positive Mammography Intentions Among African American College Students in Mississippi Dinan Noor* Dinan Noor NAK Mujahidul Islam Noverra Mahmud Azad R Bhuiyan Sandra Melvin Tanya Funchess

Introduction: Breast cancer remains a major public health concern in the United States, with pronounced age-specific disparities. Although overall incidence is comparable between African American and White women, African American women under 40–45 years' experience substantially higher early-onset incidence, with rate ratios ranging from 2.0 (ages 0–24) to 1.1 (ages 35–39). Young African American women also face more aggressive disease and nearly twice the mortality of young White women. Although recommended age is 40 in Mississippi, persistent mortality disparities suggest gaps in screening access, uptake, and awareness among younger women who may benefit from earlier risk assessment. No prior research has examined breast cancer screening knowledge, intentions, and perceived barriers among African American college students aged 18–39 years in the state.

Purpose: To examine the association of breast cancer knowledge and perceived barriers with positive intentions to obtain mammography among female college students aged 18–39 years in Mississippi.

Methods: A cross-sectional, self-reported survey using convenience sampling assessed knowledge of risk factors, early symptoms, screening procedures, and perceived barriers. A scoring system measured knowledge of risk factors and early symptoms. Chi-square tests and t-tests were conducted, and p-values recorded.

Results: Among 383 participants (mean age 26.29 ± 6.3), 87.4% were unmarried, 37.1% had children, 46.9% worked full-time, and 78.9% reported household income below $50,000. Positive intention to undergo mammography was significantly associated with age (<.001), higher class standing (<.001), marital status (.014), having children (<.001), insurance status (<.001), having heard about mammography (<.001), perceiving mammography as painful (.022), positive family history (.03), and higher knowledge scores for risk factors and early symptoms (.048).

Conclusion: Positive intentions toward mammography among young African American college women are shaped by sociodemographic factors, prior exposure to information, perceived barriers, and breast cancer knowledge. These findings highlight the need for targeted education and early awareness initiatives to support informed screening intentions in this underserved population.

Screening

Evaluation of noninvasive markers for metabolic dysfunction-associated steatotic liver disease among high-risk populations Christian S. Alvarez* Christian S. Alvarez Aika Wojt Alvaro Rivera-Andrade Maria F. Kroker-Lobos Manuel Ramírez-Zea Eduardo Gharzouzi John D. Groopman Barry I. Graubard Katherine A. McGlynn

Metabolic dysfunction-associated steatotic liver disease (MASLD) is a major public health concern, with Hispanic populations experiencing a disproportionately high prevalence in the United States. Although transient elastography (TE) provides a reliable, noninvasive measure of hepatic steatosis, its use in population-based studies is limited by cost and logistics. As a result, steatotic liver indices are increasingly used; however, their agreement with TE has not been fully characterized in high-risk populations across different geographic settings.

Agreement between TE-derived controlled attenuation parameter (CAP) and steatotic liver indices was evaluated among Hispanic adults aged ≥40 years from the National Health and Nutrition Examination Survey (NHANES, 2017-2020) and the North American Liver Cancer Study (NALCS) conducted in Guatemala. MASLD was defined as CAP ≥263 dB/m. Indices included the fatty liver index (FLI), hepatic steatosis index (HSI), liver fat score (LFS), triglyceride-glucose waist-to-height ratio (TyG-WtHR), and lipid accumulation product (LAP). Concordance was assessed using weighted percent agreement. Accuracy in identifying CAP-defined MASLD was evaluated using area under the receiver operating characteristics curve (AUC). Analyses were stratified by sex.

The analytical sample included 592 participants from NHANES and 500 from NALCS. CAP-defined MASLD prevalence ranged from 57.9% (NHANES) to 59.2% (NALCS). Percent agreement between CAP and steatotic indices ranged from 60.2% to 74.1% with the highest agreement observed for LFS (74.1%) in NHANES and for FLI (71.4%) in NALCS. Overall accuracy for identifying CAP-defined MASLD was moderate, with AUC values ranging from 0.67 to 0.77 across indices and datasets. Results were broadly similar by sex.

Noninvasive steatotic liver indices demonstrated acceptable agreement with CAP-defined MASLD, supporting their use in population-based studies among high-risk groups across different geographic settings.

Social

Impacts of Quebec's Minimum Legal Age for Cannabis Use: A Difference-in-Discontinuities Approach Sarah Windle* Sarah Windle José Ignacio Nazif-Munoz Sam Harper Arijit Nandi

Background: While countries worldwide are liberalizing access to cannabis, few studies have examined the impact of the cannabis minimum legal age (MLA) on the initiation, prevalence, and frequency of substance use among youth and young adults. In Canada, non-medical cannabis use was legalized in 2018, with varying MLAs (18 in Quebec and Alberta, 19 in other provinces). Quebec is the only province to have changed its MLA since legalization, increasing from 18 to 21 in 2020.

Methods: We will use annual cross-sectional Quebec Cannabis Survey data (2018-2014) to examine the impact of new legal access to cannabis (at age 18 or 21), as well as responsiveness to changes in the MLA (e.g., losing and regaining access to legal cannabis), on cannabis use among youth and young adults, using a difference-in-discontinuities approach (i.e., differenced regression discontinuities). This approach identifies a "treated" discontinuity (e.g., the difference in cannabis use between 17- and 18-year-olds in 2019) and a "control" discontinuity (e.g., the difference in cannabis use between 17- and 18-year-olds in 2018 [pre-legalization]). By differencing these discontinuities (similar to a difference-in-differences approach), we remove the increase in cannabis use that would be expected due to secular trends and legal access to alcohol. Each survey year will be analysed separately, providing different information concerning policy impacts (e.g., new/losing/regaining access to legal cannabis). We will apply sampling and bootstrap weights, and consider heterogeneity by sociodemographic characteristics.

Significance: Quebec's unique cannabis MLA changes offer the opportunity to consider the impacts of MLA selection, providing evidence for whether the cannabis MLA is effective in delaying cannabis use for some youth and young adults, and whether these individuals reduce cannabis consumption in response to an increase in MLA. Lessons learned are relevant to global cannabis policy decision-making.

Social

Attending Historically Black Colleges or Universities and all-mortality in US Black adults

M. Maria Glymour* Marilyn Thomas Carol Wei Jennifer Manly Suzanne Judd Virginia Howard Christina Mangurian Justin White Rita Hamad

INTRODUCTION

Higher education strongly predicts reduced risk of mortality yet evidence suggests heterogeneity in health returns to education. Black adults may derive long-term health benefits from attendance at an Historically Black College or University (HBCU) compared to attending a Predominantly White Institution (PWI). No prior study has evaluated all-cause mortality in a nationwide sample.

METHODS

The REasons for Geographic and Racial Differences in Stroke (REGARDS) prospective study recruited Black and White US adults aged 45 and older during 2003-2007. The analytic sample included Black college-goers who attended high school in a state with an HBCU (N=1,960). In 2012, data collection was initiated on childhood, adult, and family factors. Participants retrospectively reported each college ever attended, which was classified as a PWI (reference) or HBCU. Every 6 months, interviews collected mortality information from next of kin or proxies. Adjusting for participant characteristics (e.g., age, gender) and early-life predictors (e.g., childhood health, school support), Cox proportional hazard models estimated adjusted mortality ratios (2012–2023) and effect modification by whether participants were college-aged before 1955 (during legal racial segregation), 1955-1964 (before the Civil Rights Act), or after 1964.

RESULTS

Mean age was 62 years (SD±8.2) and 35% attended an HBCU. HBCU versus PWI attendees had negligibly lower all-cause mortality (HR 0.99; CI 0.88, 1.12). Although CIs were wide, those college-aged during 1955-1964 had lower mortality (HR 0.87; CI 0.87, 1.06) but elevated mortality for those college-aged before 1955 (HR 1.03; CI 0.85, 1.24) and after 1964 (HR 1.46; CI 0.91, 2.33).

CONCLUSION

We found little evidence that HBCU attendance was associated with lower mortality yet could not rule out substantial protective or harmful effect modification by college-aged years. These results are inconsistent with prior findings related to other health outcomes.

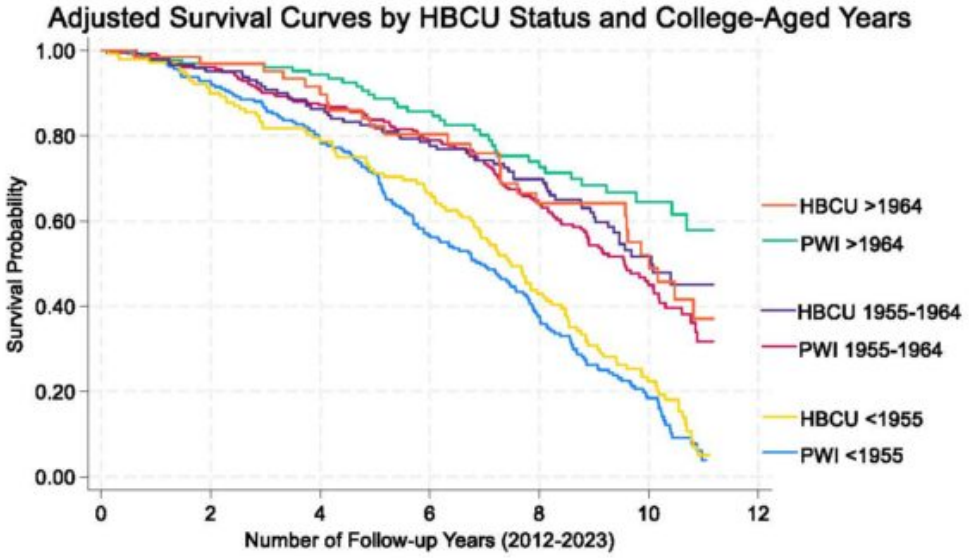
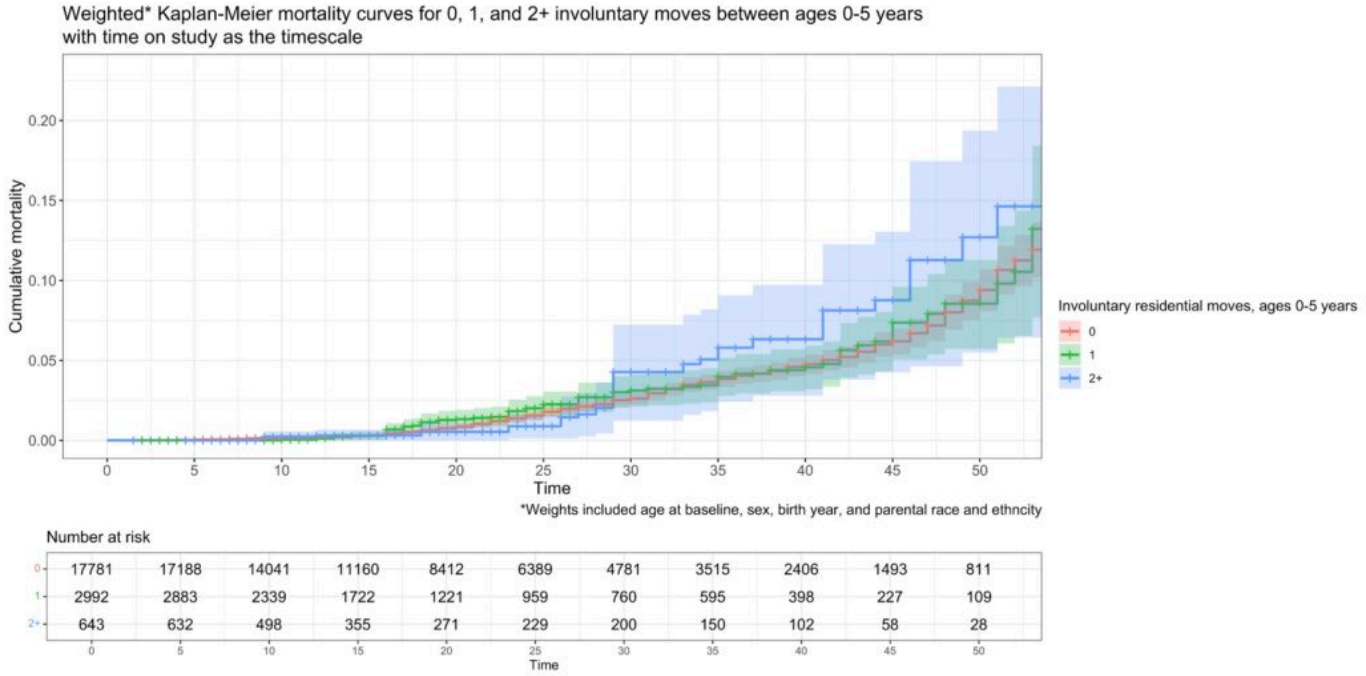


Figure. Kaplan Meier survival curves among Black adults in the REasons for Geographic and Racial Differences in Stroke (REGARDS) study who attended high school in an state with an historically Black college or university (HBCU) and attended an HBCU versus a predominantly White institution (PWI), stratified by years when college-aged prior to the *Brown vs Board of Education* court decision ending legal racial segregation of schools (<1955), prior to the Civil Rights Act (CRA) prohibiting racial discrimination in education (1955-1964), or after the adoption of the CRA (>1964).

Social

Examining the relationship between involuntary residential moves from ages 0 to 5 years and mortality through adulthood in a national, population-based cohort study Taylor M. Mobley* Taylor Mobley L. Paloma Rojas-Saunero Onyebuchi A. Arah Kathryn M. Leifheit Elizabeth Rose Mayeda

Although many studies document negative health effects of involuntary residential moves in childhood, few studies have examined their lifecourse health consequences. We examined the relationship between involuntary moves between ages 0-5 years and mortality from childhood into adulthood in a national population-based sample. This analysis included children of Panel Study of Income Dynamics (PSID) families who entered the study between 1969-2021. Additionally, we required that children were between ages 0-5 at baseline and remained in the study at age 6 (N = 21,416). Involuntary moves between ages 0-5 (e.g., evictions, parental divorce, etc.) were defined by the PSID research team based on the head of household's self-reported primary reason for moving between waves, measured annually from 1968-1997, and biennially thereafter, and categorized as 0, 1, or 2+. Year of death up to 2023 was obtained from PSID staff, family members, and death certificates. We estimated 5-year interval risk ratios (RRs) and differences for death after 10 years of follow-up from inverse probability of treatment-weighted (IPTW) Kaplan-Meier curves using time on study as the timescale. IPTWs included age at baseline, sex, birth year, and parental race and ethnicity. We estimated 95% confidence intervals (CIs) with 500 bootstraps. A total of 453 deaths were observed over a mean follow-up of 22 years. About 83% of the sample experienced 0, 14% experienced 1, and 3% experienced 2+ involuntary moves between ages 0-5. Risk of mortality at 30 and 50 years of follow-up was higher for participants who experienced 2+ vs. 0 involuntary moves on both scales, but estimates were imprecise (RR (95% CI): 1.6 (0.5-2.9) at 30 years and 1.3 (0.7-2.2) at 50 years). In future work, we plan to measure time-varying effects of involuntary moves on mortality across the lifecourse.



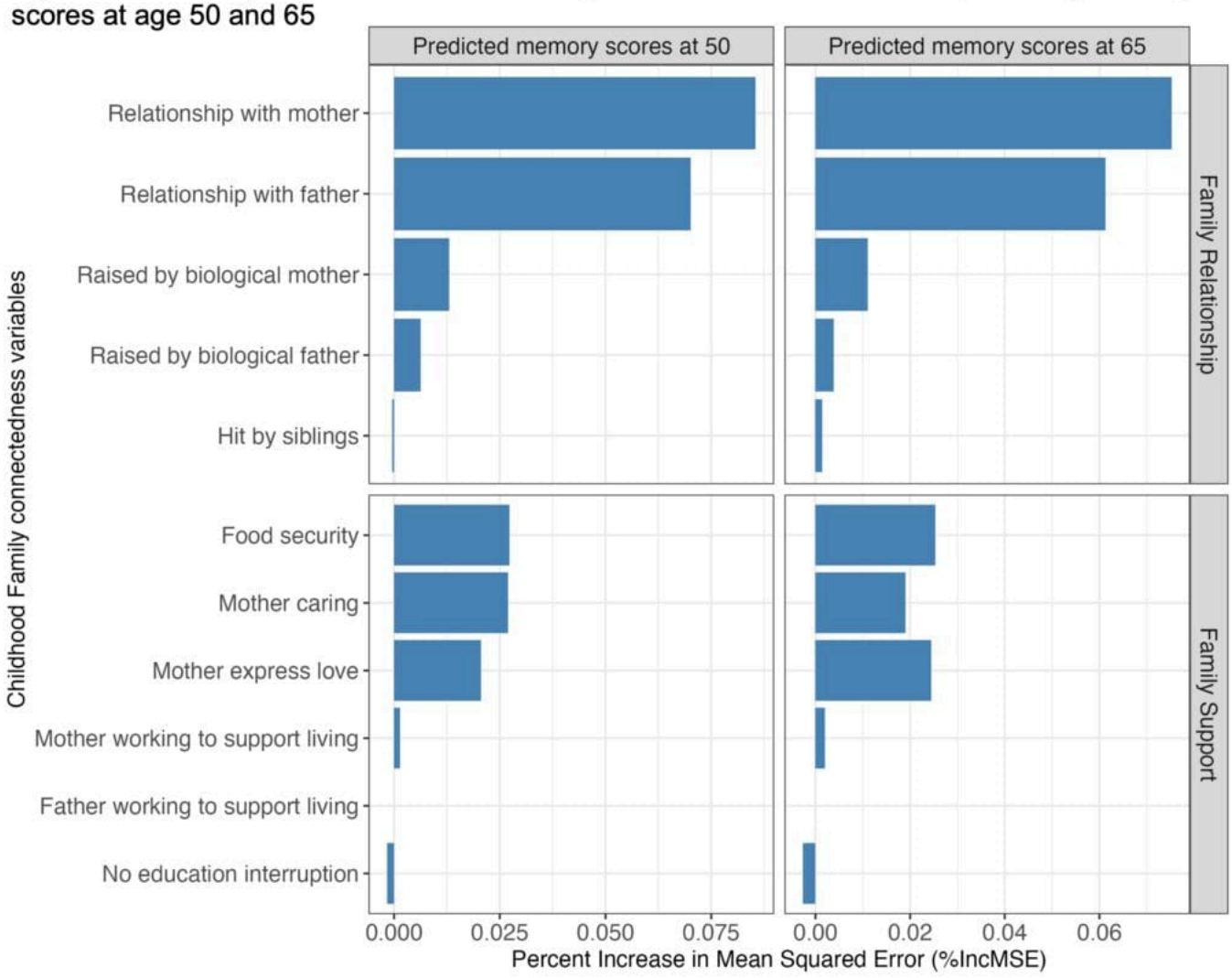
Social

The association of childhood family connectedness and life-course memory function

Yingyan Wu* Yingyan Wu Lingzhi Chu

Childhood family connectedness is linked to better later-life cognition, yet its multidimensional nature makes it unclear which components matter most in shaping cognitive aging. This study aims to identify key aspects of childhood family connectedness and quantify their associations with later-life cognition. We used data from the China Health and Retirement Longitudinal Study (CHARLS). Childhood family connectedness was defined using self-reported relationship variables [relationships with parents (good versus fair/poor), being raised by biological parents, history of being hit by siblings] and support variables [childhood food security, maternal care or expression of love, parents working to support the family, and childhood education interruption]. Cognitive outcomes were predicted episodic memory scores (average of immediate and delayed word recall scores; range: 0-10) at ages 50 and 65. We adjusted for age, sex, childhood rural/urban residence, childhood residential region, and birth order (first or not) as confounders. We ranked relative variable importance based on percent increase in mean squared error (%IncMSE) using random forest models, followed by estimated associations for the most influential factors with memory scores using linear regression. We included 16,396 participants (mean age=61.2 years, 51.3% women) with interquartile ranges of 4.64-6.27 and 3.14-4.84 for memory scores at ages 50 and 65, respectively. Relationships with parents emerged as the most influential factors (Figure). Good relationships with mother were associated with higher memory scores at ages 50 (b=0.17, 95% CI 0.08, 0.26) and 65 (b=0.15, 0.07, 0.23). Similarly, good relationships with father were associated with higher memory scores at ages 50 (b=0.12, 95% CI 0.04, 0.20) and 65 (b=0.13, 95% CI 0.05, 0.20) higher scores at ages 50 and 65, respectively. These findings highlight that perceived relationships with parents may be a key pathway shaping cognitive health later in life.

Figure. Variable importance of childhood family connectedness variables in predicting memory scores at age 50 and 65



Social

The Association Between Early Life Social Determinants and Adult Morbidity in a Jamaican Sickle Cell Disease Cohort Alphanso Lorenzo Blake* Alphanso Blake Trevor Ferguson Seeromanie Harding Novie Younger-Coleman Keri-Ann Blake Monika Parshad-Asnani

Genotype plays a major role in Sickle Cell Disease (SCD) severity; however, the role of early-life exposures remains unclear. This study evaluates the association between early-life exposures and adult complications in Jamaicans living with SCD.

Retrospective data on newborns with SCD in the 1973 – 1981 Jamaica Sickle Cell Cohort Study were analysed. Early life exposures including birth weight, household structure, social amenities scores (SAS) and parental occupation classification (by the International Standard Occupational Classification), were evaluated against physician-diagnosed leg ulcers, acute chest syndrome (ACS) and chronic kidney disease (CKD). Using Stata 19, binary logistic regression models assessed the strength and direction of associations and ROC curves and Hosmer-Lemeshow tests assessed the goodness of fit. Complete case analysis handled missing data. Ethical approval was granted by the Mona Campus Research Ethics Committee.

In a sample of 535 persons (52% males), haemoglobin (Hb) SS (56.5%) and HbSC (31.4%) were the dominant genotypes. No sex differences between SCD genotypes and early life exposure groups were seen. Leg ulcers (25.1%) were more common (p=0.01) in males (30.0%) vs females (19.8%), while ACS (23.5%) and CKD (9.5%) showed no sex differences. In multivariable models, CKD showed no association with exposures; however, persons with higher birthweight had 23% reduced odds of ACS (OR(95%CI)=0.77(0.61 – 0.96), p=0.019). Leg ulcers were 44% less likely in females (OR(95%CI)=0.56(0.33 – 0.92), p=0.024), 57% less likely in persons in SAS tertile 3 vs 1 (OR(95%CI)=0.43(0.22 – 0.83), p=0.013) and 77% more likely in those with parental occupation skill level 2 (OR(95%CI)=1.77(1.01 – 3.10), p=0.046) vs 1.

Birthweight, sex and SAS are non-clinical factors which significantly influence adult SCD complications. Early interventions targeting vulnerable groups may help reduce long-term morbidity and improve outcomes in SCD populations

Social

Racial and Ethnic Inequalities in Hypertension and Cardiovascular Diseases in the Latin American and Caribbean Region, 2000-2023: A Scoping Review Diana Higuera-Mendieta* Diana Higuera-Mendieta Khardjatou Marianne Djigo Yazmin Sanchez Pardo Arjumand Siddiqui Diego I Lucumi John Jackson Andrea Ferreira Sharrelle Barber

The Latin American and Caribbean region has a unique history of racialization rooted in the transatlantic slave trade, colonization, and the enduring legacy of racism, resulting in racial hierarchies that shape the unequal social, economic, and political reality of Afro-descendant and Indigenous people. This reality, in turn, shapes racial and ethnic inequalities in health, including hypertension and cardiovascular diseases (CVD). Yet, our understanding of these inequalities remains fragmented in the region due, in large part, to the lack of quality, reliable data, as well as competing conceptualizations of race and ethnicity and the underlying mechanisms that produce racial and ethnic inequalities in health. To better understand these challenges within the context of epidemiologic studies of hypertension and cardio vascular outcomes, we conducted a scoping review of the literature to: 1) describe how race and ethnicity are conceptualized and measured in studies of hypertension and CVD in Latin American and Caribbean countries; 2) describe observed patterns of racial and ethnic inequalities and the mechanisms used to explain them; and 3) identify the main data sources on race and ethnicity variables. We followed the Joanna Briggs Institute framework and PRISMA-ScR guidelines. We searched Seven databases for empirical studies reporting on racial or ethnic disparities in hypertension and CVD in 22 Latin American countries. Two reviewers independently screened, and four extracted data. A narrative synthesis was supported by tables and maps. We identified 43 studies published between January 1, 2000 and June 30, 2023, across seven countries in the region. While research on racial inequalities in these outcomes has increased over time, the conceptual and methodological rigor of epidemiologic studies should be improved to adequately document and address racial inequalities in hypertension and CVD and the underlying mechanisms rooted in racism that exacerbate them.

Social

Effects of dialog-based museum viewing on emotional well-being among older adults: a quasi-experimental study Hiroshi Habu* Hiroshi Habu Yukiko Honda Yuki Arakawa Yoko Kanahama Yusuke Komuta Hayato Fujioka Anri Makino Kazumi Kumagai Sawako Inaniwa Tatsuya Ito Naoki Kondo

Background
Rapid population aging in Japan has intensified concerns about social isolation among older adults. Museums have implemented programs to promote social engagement and well-being, but quantitative evidence on their health impacts remains limited.
Objective
To examine the effects of dialog-based museum viewing programs on emotional well-being among older adults.
Methods
We conducted a quasi-experimental study among adults aged 65 years and older in Tokyo, Japan. Participants were allocated using a program-embedded random allocation to a dialog-based viewing group or a video-based viewing group. The 60-minute program was conducted at the University Art Museum, Tokyo University of the Arts. Emotional well-being was assessed before and after the program using the Generic Wellbeing Questionnaire (12-item version). Pre–post changes were analyzed using linear regression models, with and without adjustment for age, sex, and usual museum visitation. Multiple testing was addressed using the false discovery rate. Analyses were conducted using R (ver. 4.5.2). Ethical approval and written informed consent were obtained.
Results
Twenty-six older adults participated (15 dialog-based), as implemented, with a mean age of 71.9 years. For all positive emotion items, adjusted point estimates favored the dialog-based viewing group. In particular, enthusiasm showed the largest improvement (adjusted coefficient 0.93, 95% CI 0.42 to 1.44). For negative emotional items, irritability showed a relatively large improvement (adjusted coefficient −0.81, 95% CI −2.02 to 0.40), while other negative items also showed point estimates favoring improvement, although CIs were wide.
Conclusions
Dialog-based museum viewing facilitated by art communicators was associated with enhancement of positive emotions among older adults and suggested improvements in some negative emotional states. This study provides quantitative evidence to inform future research on the health impacts of arts-based programs.

LATEBREAKER

Social

Reversal in the health literacy–anxiety association from 2020 to 2025: repeated panel surveys and free-text content shifts in Japan Yujiro Kuroda* Yujiro Kuroda Aya Goto Rei Wakayama Masahiro Sano Kohta Suzuki

Background: During the early phase of the COVID-19 pandemic, higher health literacy may have intensified anxiety because active information seeking occurred under profound uncertainty. Whether this association persisted in later phases remains unclear.

Methods: We analyzed two repeated panel surveys of Japanese adults conducted in 2020 (n=3,486) and December 2025 (n=2,965) using comparable questionnaires. Anxiety was classified as no/low, high, or fear. Health literacy was divided into communicative (items 1–3) and critical (items 4–5) domains. Primary analyses applied baseline-anchored tertiles defined by the 2020 distribution. Covariate-adjusted multinomial logistic regression models (sex, age, education, employment, and area) tested wave-by-health literacy interactions. Free-text responses were coded using a refined rule-based dictionary, incorporating common spelling variants, to quantify thematic mentions. Adjusted wave effects on category presence were estimated.

Results: Overall anxiety declined substantially in 2025 compared with 2020. In adjusted models, in 2020, higher communicative health literacy was associated with greater likelihood of high anxiety and fear. In 2025, this pattern attenuated and shifted toward lower anxiety, most clearly for fear. Free-text content also changed, with decreased emphasis on uncertainty, policy and healthcare strain, and daily-life disruption, and increased references to vaccination and normalization, including comparisons with seasonal infections; however, uncertainty remained as prevalent as the newly increased topics.

Conclusions: The association between communicative health literacy and anxiety reversed between 2020 and 2025, paralleling marked shifts in narrative content. Risk communication strategies should reflect the evolving information environment and pandemic phase, promoting constructive information appraisal rather than anxiety amplification.

One sentence summary of the abstract
Across repeated surveys in 2020 and 2025, the association between communicative health literacy and COVID-19 anxiety reversed, while free-text narratives shifted from uncertainty and system strain toward vaccination and normalization, highlighting the importance of phase-specific risk communication that supports constructive information appraisal.

Structural

Intersecting socio-structural determinants of depression among men who have sex with men in the United States: A multilevel analysis of individual heterogeneity and discriminatory accuracy (MAIHDA) Jason M. Lo Hog Tian* Jason Lo Hog Tian Katrina S. Kennedy Irah L. Lucas Michael Smith Jr. Mariah Valentine-Graves Cristian Acero Martinez Travis Sanchez Stefan Baral Amrita Rao

Depression remains a driver of poor health and wellbeing among cisgender gay, bisexual, and other men who have sex with men (MSM). However, the way that socio-structural determinants interact to shape depression is currently unknown in this population. This study used multilevel analysis of individual heterogeneity and discriminatory accuracy (MAIHDA) to quantify variation in depression risk across strata defined by key socio-structural determinants.

We analyzed cross-sectional data from 15,362 cisgender MSM aged 15+ from across the United States as part of the American Men's Internet Survey (AMIS) collected between 2021 – 2024. Strata were defined by socio-structural determinants: age, race, region, past-year homelessness, and past-year illicit drug use. A PHQ-9 score ≥10 was used as a cutoff for significant depression symptoms. MAIHDA was used to quantify joint and individual contributions of intersecting socio-structural determinants on predicted probability of depression.

Overall, 20% (n=3,080) of participants had significant depression. In the null model, 13% of total variance was attributable to between-stratum differences; however, this was reduced by 99.6% after inclusion of the socio-structural variables, indicating that differences in depression risk were primarily due to additive effects. Homelessness accounted for the largest percentage of stratum-level variance (50%), followed by age (45%), drug use (24%), region (4%) and race (2%). Predicted depression prevalence ranged from under 10% among older, stably housed individuals without drug use to over 65% among younger individuals (<25 years old) experiencing homelessness and drug use.

There was substantial heterogeneity in predicted depression with the greatest probability characterized by people experiencing homelessness, younger individuals, and people who use drugs. Interventions prioritizing housing stability and substance use services for young MSM are likely to yield the greatest impact.

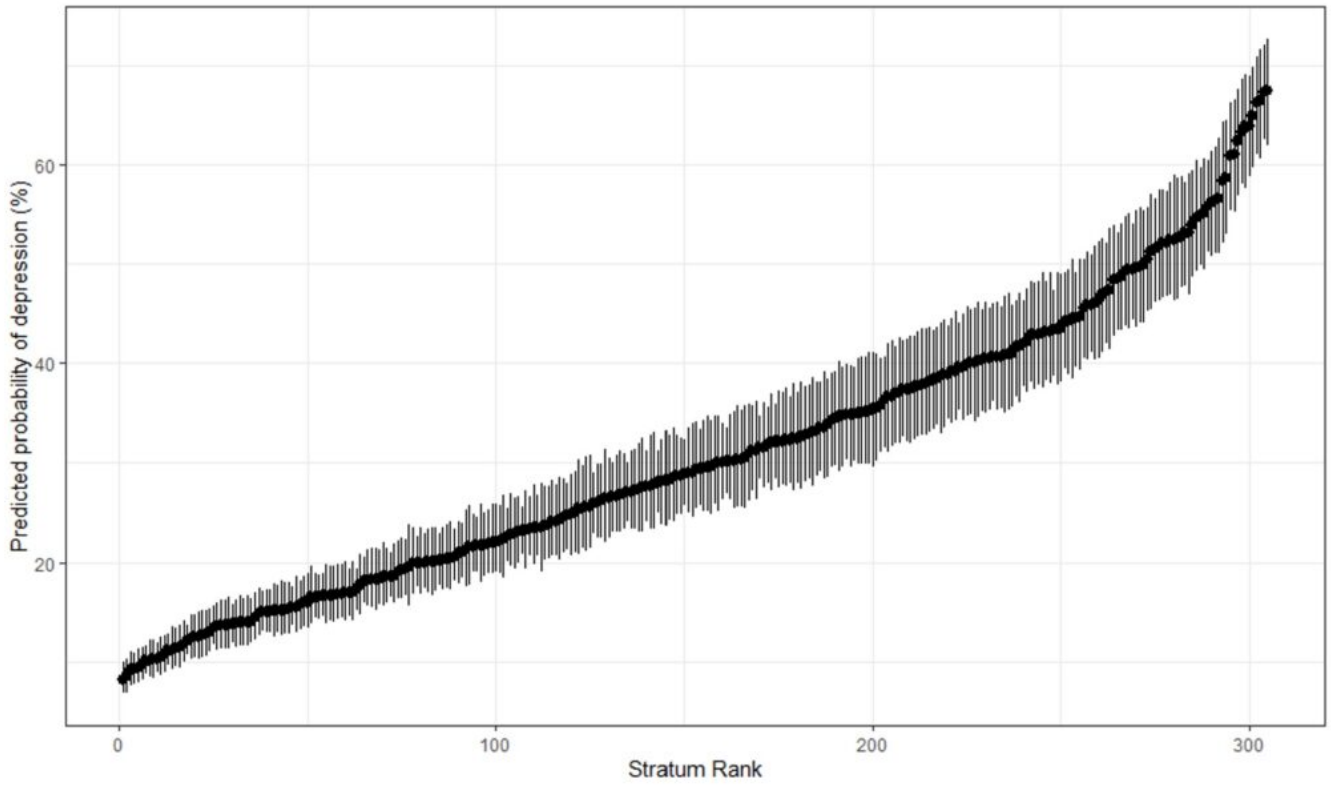


Figure 1 Predicted values by stratum ranked low to high. Markers indicate predicted value for each stratum. Spikes indicate approximate 95% CIs.

LATEBREAKER

Structural

The Association Between Latino Ethnic Enclaves and Air Pollution in California Valerie Martinez* Valerie Martinez Asa Bradman Maria-Elena Young Andrew Williams

Background: Air quality in California ranks among the worst in the United States (US), with many areas failing to meet National Ambient Air Quality Standards for fine particulate matter (PM2.5) and ozone (O3). Exposure contributes to substantial morbidity and mortality and disproportionately affects communities of color. On the other hand, ethnic enclaves, areas where an ethnic group is densely concentrated and socially distinct, have been shown to be favorable for many health endpoints through social support mechanisms. However, evidence on whether ambient pollutant concentration within enclaves are different from other areas is limited.

Objective: To examine associations between Latino ethnic enclaves and ambient air pollution concentrations.

Methods: This ecological study consists of 2,590 California ZIP code tabulation areas (ZCTAs). Enclaves were defined using the American Community Survey 5-year estimates (2009–2013; 2014–2018): population density, dissimilarity index, and isolation index. Each metric was classified into tertiles and ZCTAs in the highest tertile for all three metrics were considered enclaves. Daily PM2.5 and O3 concentrations, derived from US Environmental Protection Agency monitoring data, were linked to ZCTAs and aggregated to weekly averages. Generalized linear mixed models estimated percent differences in pollutant concentrations between enclave and non-enclave and 95% confidence intervals (CI) while adjusting for temporal autocorrelation and confounders.

Results: Compared with non-enclaves, ZCTAs classified as Latino enclaves and Mexican enclaves were associated with 3.50% (95% CI: 2.37, 4.65) and 7.16% (95% CI: 4.54, 9.85) higher weekly PM2.5 concentration, respectively. No significant associations were observed for O3.

Conclusion: Latino and Mexican enclaves in California experience higher PM2.5 concentrations than non-enclaves, highlighting the need for equity-focused air pollution exposure mitigation efforts.

Study Design

Immortal time considerations in linked data Amarnath Marthi* Amarnath Marthi Michael Webster-Clark Richard Wyss Jennifer Lund Til Stürmer Michele Jonsson-Funk

Linking data sources, such as electronic health records (EHRs) to administrative claims, may address incomplete capture of exposures, covariates, and outcomes needed for robust epidemiological analyses. While offering advantages, linkages can introduce selection bias and misclassification. One less-studied threat to internal validity is immortal time bias resulting from linkage.

We discuss how immortal time can be introduced by misalignment of the start of follow-up relative to (1) the data source linkage period (the years of data being linked) and/or (2) the specific date when a person is linked based on the recording, in all data sources**,** of individual-level data elements required for linking (individual linkage date). We illustrate this bias by comparing 90-day mortality after claims-defined hip fracture in adults ≥65 from a random sample of Medicare fee-for-service (FFS) beneficiaries (random cohort) to FFS beneficiaries linked to University of North Carolina health system EHR (linked cohort).

In analyses ignoring the data source linkage period, 90-day mortality post hip fracture was 14.3% (95%CI 14.1-14.5) in the random cohort (N=138816) compared to 11.3% (95%CI 10.6-12.0) in the linked cohort (N=8600). After accounting for the data source linkage period (N=7865), this risk increased to 12.4% (95%CI 11.6-13.1). Among hip fractures that occur after the individual linkage date (N=6210), 90-day mortality rose to 14.6% (95%CI 13.7-15.4) in the linked cohort. Results were similar after using standardized mortality weighting to balance the linked and random cohorts on age, sex, and race. We show how linkage-related immortal time bias may cause these differences.

When designing, conducting and reviewing research in linked datasets, researchers should consider not only if the correct linkages were generated but also ensure the start of follow-up does not occur before the data source linkage period or the individual’s linkage date to avoid immortal time bias.

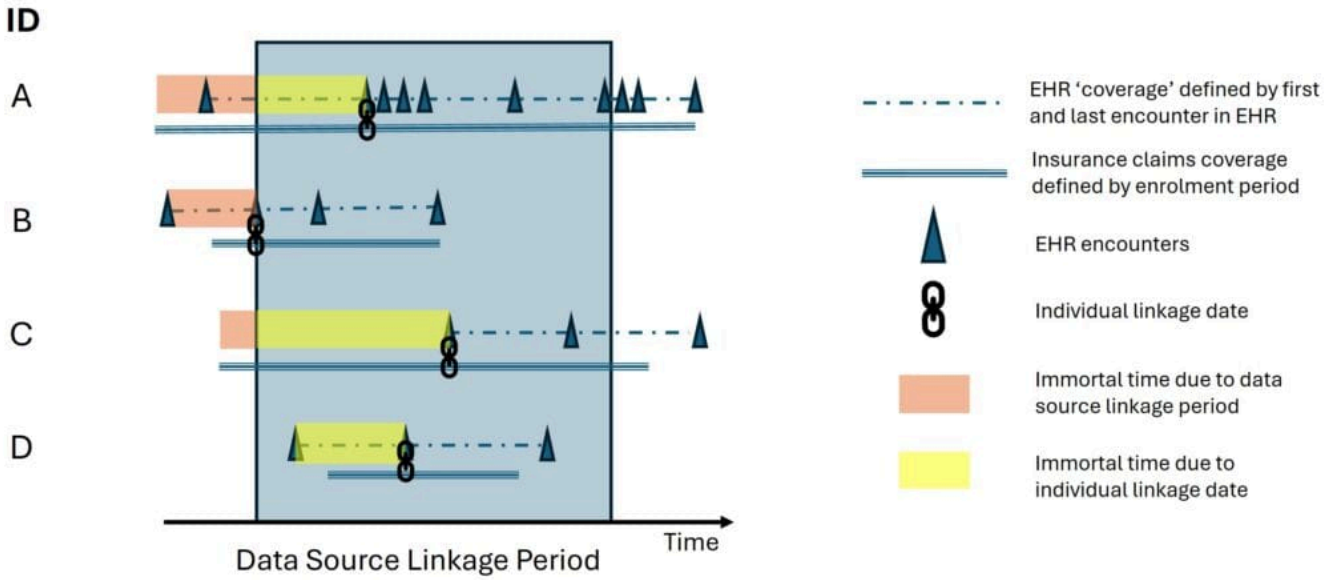


Illustration of immortal time resulting from linking administrative claims data with electronic health records. Individuals are immortal until data elements required for linkage (Medicare beneficiary number, date of birth and sex in the empirical example) are recorded in both data sources. Additional considerations apply when time varying and time-explicit data elements are required for linkage.

Substance Use

Evaluation of the Raising the Bar campaign: changing social norms of parental drinking behaviors in Marin County, CA Michaela George* Michaela George Marina Mendia Gianna D'Arezzo Margaux Grey Kelly McDermott

Given high levels of drinking and substance use among adults in Marin County, CA, it is imperative to find evidence-based interventions and community supported solutions. Negative parent modeling has driven youth drinking and substance use higher in Marin County than all other counties in California. Using a mixed methods approach, we aimed to understand the impact of a community-based organization designed to promote substance free behaviors on parents of school aged children in Marin with a holistic program evaluation.

Methods

In partnership with the community organization Raising the Bar (RTB), the research methodology consisted of quantitative and qualitative data collection through key informant interviews, parent leader focus groups, and a community-wide survey in Marin County to better understand the awareness, knowledge, and behaviors of the target population.

Results

Preliminary results include knowledge of increased substance use in Marin County by parents and youth, general awareness of the RTB program goals, and differences in personal behaviors and observed behaviors at community events. Quantitative data show differences between younger and older adults, Hispanic and non-Hispanic adults, and the four geographical regions of the county ($p<0.001$). Significant gaps in awareness and understanding provide opportunities to target audiences.

Conclusions

Based on these findings, our recommendations to the RTB program are to segment the audience for more targeted intervention, clarify the messaging, enlist local champions to support the campaign at the school level throughout the school year, and partner with enforcement agencies to implement existing policy.

Substance Use

Parsing the Prairie: Rurality Metrics and Their Association with Smoking in Nebraska

James Buckley* James Buckley Daisy Dai

Objective: To evaluate the effect of different rural-urban classification schemes on the association between rurality and increased smoking prevalence at the census-tract level.

Background: Smoking prevalence is well established by literature as linked to rurality. However, there is no one accepted measure of rurality in the United States. Government agencies currently utilize several different methods of determining rurality and urbanicity at varying levels of geography. Common classification schemes include Rural-Urban Commuting Areas (RUCA / Census Tract), Rural Urban Continuum Codes (RUCC / County), Urban Influence Codes (UIC / County), and Core-Based Statistical Areas (CBSA / County). All these metrics broadly categorize geographical units into metropolitan, small metro/micropolitan, and rural areas and many build from similar core assumptions, usually the Office of Management and Budget's (OMB) Metropolitan/Micropolitan system.

Methods: Smoking prevalence was obtained from the CDC Places dataset. RUCA, RUCC, and UIC were obtained from the USDA's Economic Research Service. County-level metrics were disaggregated down to constituent census tracts. CBSAs were obtained from the OMB. ANOVA was used to compare mean cigarette smoking prevalence with post-hoc pairwise comparisons using Tukey's adjustment.

Results: All assessed rurality metrics reported mean smoking prevalence for the most rural areas as between 14.59 and 14.77 percent. All assessed rurality metrics reported mean smoking prevalence for the most urban classification ranged from 13.45 to 13.71 percent. The mean difference in cigarette smoking prevalence between the most urban classification and most rural classification ranged from 0.96 to 1.31 percentage points. All mean differences were significant at 0.05 significance level.

Conclusions: Smoking prevalence was consistently higher in rural areas than in urban areas, regardless of the rural-urban classification scheme used.

Substance Use

Realized causal effect of non-specific psychological distress on substance use outcomes among transgender women of color in New York, NY Adam Whalen* Adam Whalen Alexander Furuya Jenesis Merriman Miho Kawanami Sahnah Lim Chau Trinh-Shevrin Jeremy Kidd Denton Callander Asa E. Radix Dustin T. Duncan

Transgender women of color (TWOC) may be particularly vulnerable to the adverse health effects of substance use. Substance use is associated with psychological distress, and TWOC experience higher rates of psychological distress than the general population, partly due to discrimination. We sought to determine the realized causal effect of psychological distress on substance use behaviors in TWOC. We used baseline and 6-month follow-up data from the Trying to Understand Relationships, Networks, and Neighborhoods among Transgender women of color (TURNNT) Study, a 1-year prospective cohort in New York, NY. Exposure and covariate data were taken from baseline and outcome data were taken from 6-month follow-up to ensure temporality. Our exposure was non-specific psychological distress (NSPD) measured as a Kessler-10 score ≥20. We explored two substance use outcomes separately: past 6-month hazardous drinking, defined as at least a few times weekly, and any past 6-month substance use other than alcohol or cannabis. We established positivity using theoretical confounders: age, annual income, HIV serostatus, experience of everyday discrimination, and baseline outcome for each analysis. Analyses used targeted maximum likelihood estimation, a non-parametric doubly robust estimator, via ensemble SuperLearner. We included 168 participants with complete data; at baseline, 63% reported NSPD, 15% reported hazardous drinking, and 19% reported other substance use; at follow-up, 13% reported hazardous drinking and 20% reported other substance use. We found a causal risk ratio of 4.52 for the effect of NSPD on hazardous drinking (95% CI: 1.22–16.74), and a causal risk ratio of 1.44 for other substance use (95% CI: 0.76–2.73). In a population of TWOC, the risk of hazardous drinking would be over 4 times higher if everyone had NSPD compared to if no one had NSPD. Interventions should target psychological distress in TWOC to reduce problematic alcohol consumption and improve health.

Substance Use

Trends in the association between cannabis use disorder and suicidal ideation in the United States, 2014–2023 Tosin Oyetunji* Tosin Oyetunji Alec M. Chan-Golston Sandie Ha Sidra Goldman-Mellor

Amid rising cannabis use, declining perceived harm, and policy liberalization over the past 15 years, we examined whether the association between cannabis use disorder (CUD) and past-year suicidal ideation among U.S. adults changed from 2014–2023 and varied by sex, age, and race/ethnicity. Using data from 415,861 adults in the 2014–2023 National Surveys on Drug Use and Health, we examined temporal association change between past-year CUD (≥2 of 9 harmonized DSM-5 criteria) and suicidal ideation. Logistic regression models, adjusted for demographic, social, clinical, and geographic covariates, tested whether survey year moderated the CUD–suicidal ideation association overall and in strata by sex, age, and race/ethnicity. Adults with cannabis use disorder had 57% higher odds of past-year suicidal ideation than those without (OR, 1.57; 95% CI, 1.44–1.72) across years. Adjusted models including interaction terms for CUD and survey year showed elevated odds in certain years, such as 2016 (OR, 1.71; 95% CI, 1.23–2.36). Among males, similar elevations occurred in 2016 (OR, 2.11; 95% CI, 1.34–3.30) and 2021 (OR, 1.77; 95% CI, 1.12–2.80). However, none of these interactions reached Bonferroni-adjusted statistical significance. Results suggested that the strength of the association between cannabis use disorder and suicidal ideation remained stable from 2014–2023 and did not differ significantly across sex, age, or racial/ethnic groups despite widespread legalization, increased potency, and shifting norms. Additional research is needed to examine longitudinal CUD-suicidal ideation associations, and to incorporate potency-specific exposure (THC concentration, product type, concentrate use) measurements to clarify potential dose-response relationships.

Substance Use

Multilevel predictors of telehealth and integrated primary care within behavioral health services, US, 2024 George Pro* George Pro Mofan Gu Corey Hayes

Background

Integrated primary care (IPC) within behavioral health services helps address comorbidities that complicate treatment. Most behavioral health patients who need IPC don’t receive it. Telehealth has been shown to improve behavioral health access and outcomes, and telehealth combined with IPC is the next step in providing comprehensive behavioral healthcare. To date, no epidemiologic studies have assessed the prevalence of combined telehealth and IPC, or multilevel factors that promote its adoption.

Methods

We used the Mental Health and Addiction Treatment Tracking Repository to identify all known licensed substance use disorder and mental health outpatient treatment facilities in the US (2024; N=17,599 facilities). We used multilevel logistic regression to predict telehealth and IPC, using facility-level characteristics (owner type), census-tract-level characteristics (rurality, social vulnerability), county-level characteristics (broadband coverage), and state telehealth policies (modality-neutral, in-person requirements, state-line barriers, and nurse-independent practice). We included interactions between state policies, underserved communities, and treatment service type. State was defined as a random effect.

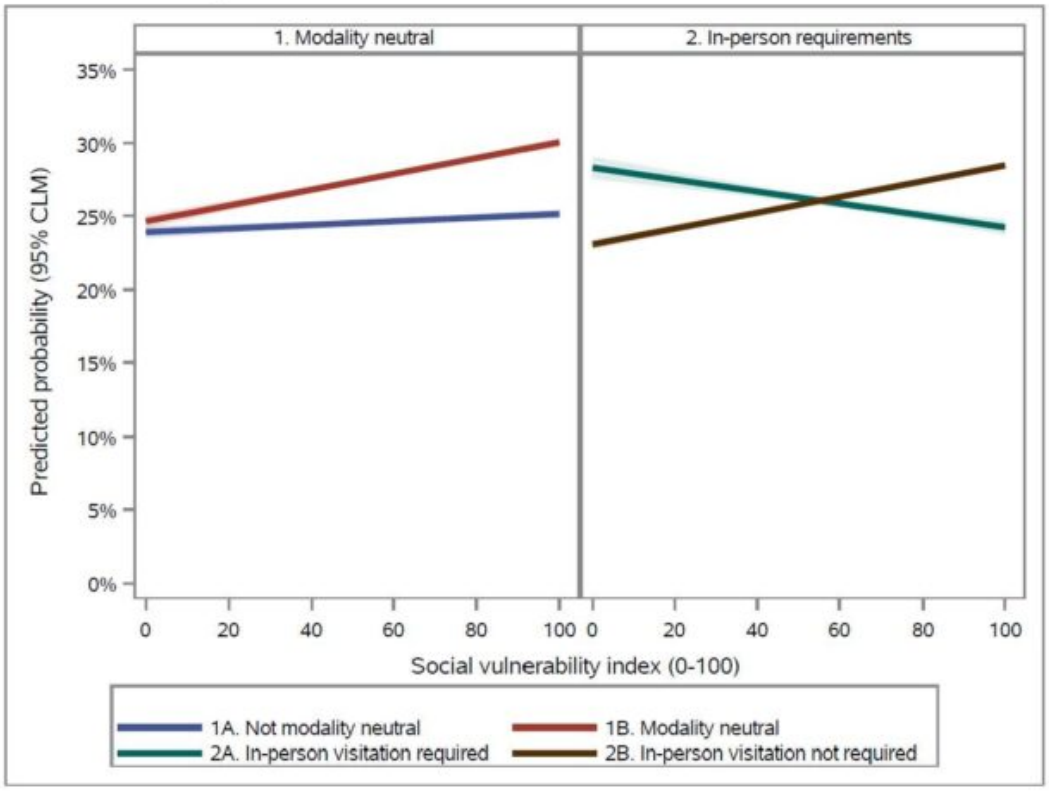
Results

A quarter of treatment facilities offered telehealth and IPC. Facilities located in underserved communities were more likely to provide telehealth and IPC when their state had policies that allowed modality neutrality (interaction $p=0.06$) and allowed patients to start telehealth without an initial in-person visitation (interaction $p<0.01$; Figure 1).

Conclusion

State telehealth policies do not affect all communities within a state equally, as some policies are more advantageous to facilities serving more vulnerable populations. Policies that allow a range of telehealth modalities and do not require an initial in-person visit were more effective at improving access to telehealth and IPC among communities with higher vulnerability.

Figure 1: Model-based predicted probability of telehealth and IPC, by social vulnerability index and state telehealth policies



Substance Use

Patterns of heroin overdose deaths: Evidence from Kentucky hospitalization data Venetia Aranha* Venetia Aranha Seyed Karimi Jovita Murillo Kira Taylor

Background: Kentucky ranked fourth nationally in drug overdose deaths during 2016-2021. Our study examined patterns of heroin overdose deaths among hospitalized patients with heroin involvement during this period, which coincided with the implementation of harm reduction services and the COVID-19 pandemic in Kentucky. Methods: We analyzed inpatient hospitalizations from the Kentucky Health Facilities and Services (KHFS) database from 2016 to 2021 using ICD-10-CM codes for heroin overdose (T40.1). Adjusted odds ratios and 95% confidence intervals for heroin overdose mortality were estimated relative to 2019 using interrupted time series analysis (ITS), controlling for demographics, admission type, and the Charlson Comorbidity Index (CCI, adapted from Glasheen et al.). Heroin involvement was identified in any of the first 25 diagnosis fields. Results: Among hospitalized patients with heroin involvement, 8.75% died, indicating high in-hospital mortality. Deaths declined from 11.56% in 2016 and 11.08% in 2017 to 8.69% in 2018, followed by a post-pandemic rise from 5.56% in 2020 to 8.26% in 2021. Black patients had significantly lower odds of heroin-related deaths compared with White patients (OR = 0.40, 95% CI: 0.20–0.80). Overdose deaths were highest among patients with mild (10.68%) and severe (10.09%) CCI scores. Heroin overdose deaths were higher in 2017 (OR = 2.33, 95% CI: 1.44–3.98), declined in 2018 (OR = 1.71, 95% CI: 0.98–2.99), and then increased again after 2019, (2020 OR=1.08; 95% CI: 0.60–1.95) (2021 OR=1.70 95% CI: 0.97–2.98). Adjusted ITS model indicated the odds of heroin overdose deaths were elevated during the pre-intervention period (2016–2017) and decreased in the post-intervention period (2018–2021). Additionally, heroin overdose deaths were not affected by the COVID-19 pandemic. Conclusion: Our findings support the notion that harm reduction services should be continued and strengthened in order to combat the drug epidemic.

Substance Use

Unmet Subsistence Needs, Substance Use Patterns and Mental Health Among Women Experiencing Homelessness: A Longitudinal Analysis Anna Krasnova* Anna Krasnova Martha Shumway Morgan M. Philbin Abigail W. Batchelder Elise D. Riley

Women who experience homelessness and unstable housing (WHUH) disproportionately experience mental health challenges and substance use, including methamphetamine use. Most women who use methamphetamine engage in polysubstance use, but the effects of substance combinations on mental health are poorly understood. We examined how sociodemographic factors and polysubstance use are associated with mental health among WHUH from San Francisco community venues in 2016-2019 and followed monthly for 6 months. Substance use was assessed via self-report and toxicology. Overall mental health status was assessed using the SF-12 Mental Health Component Summary (MCS-12) score, which ranges from 0-100; a 3-5 point difference is considered clinically meaningful. We used longitudinal mixed effects models and LASSO regression to identify the substances and related combinations most strongly associated with overall mental health. We adjusted for social and structural factors, HIV status, and menopause status. Among 245 WHUH (median age 53.2 years, IQR: 45.3-59.2), 39.3% were Black; MCS-12 scores averaged 40.2 at baseline (general population average=50). Substances used during follow-up included tobacco (82.9%), opioids (62.8%), crack/cocaine (69.7%), methamphetamine (47.0%), cannabis (75.6%), and alcohol (74.8%); 83.3% reported polysubstance use. Factors with the most influence on MCS-12 scores included: having ≥1 unmet subsistence need (housing/food/clothing) was associated with -3.6 points (CI: -5.3, -1.9), and methamphetamine use -2.4 points (CI: -4.1, -0.7). Polysubstance use was not significantly associated with MCS-12 scores. Beyond unmet subsistence needs, methamphetamine use stands out from other substances as a particularly strong contributor to poor overall mental health among WHUH. This highlights the need to address methamphetamine use alongside services that support social determinants of health and unmet subsistence needs to maximize mental health outcomes for WHUH.

Substance Use

Interpersonal Dynamics and Drug Injection Behaviors: A Longitudinal Study of Injecting Dyads Maia Scarpetta* Maia Scarpetta Neia Prata Menezes Tiffany Nguyen Claire C. McDonell Kimberly Page Torsten B. Neilands Meghan Morris

Background: High-risk injecting behaviors often occur within ongoing injecting partnerships, yet longitudinal evidence on how within-partnership changes in interpersonal dynamics shape subsequent equipment sharing is limited. We examined whether month-to-month changes in partnership-level relationship factors predict later injecting risk.

Methods: We used longitudinal dyadic data from the UFO Partnership Study, in which verified injecting dyads were followed monthly for up to six months. The analytic sample included 92 individuals in 85 injecting partnerships, restricted to dyad-level visits. The primary outcome was dyad-mean recent sharing of needles and ancillary equipment. Interpersonal dynamics were measured using the Interpersonal Dynamics in Injecting Partnerships scale, with dyad-level exposures defined as the mean of partners' scores for trust, intimacy, cooperation, risk perception, and power. Analyses used dyad-level repeated measures with cross-classified random effects for partnerships and individuals. Time-varying interpersonal dynamics were lagged to predict subsequent injecting risk, adjusting for baseline and time-varying covariates.

Results: Dyad-level trust varied over time and was positively associated with subsequent injecting risk (β = 0.40, 95% CI: 0.21–0.68). Power (β = 3.95, 95% CI: 2.24–5.64) and intimacy (β = −2.45, 95% CI: −4.38 to −0.51) showed nonmonotonic associations, with higher risk at intermediate power and at low and high levels of intimacy. Random-effects estimates indicated meaningful between-partnership heterogeneity. Cooperation and risk perception were not significantly associated with outcomes.

Conclusions: Changes in trust, power, and intimacy within injecting partnerships predict subsequent injecting risk. These findings underscore relationship dynamics as time-varying determinants of harm and potential targets for partnership-centered harm reduction and hepatitis C prevention.

LATEBREAKER

Substance Use

Prevalence of Current Substance Use by Disability Status and Disability Type among Adults in the United States and Territories: BRFSS 2020–2023 Precious Patrick Edet* Precious Patrick Edet Hannah Allen-King

Background: Adults with disabilities in the United States (U.S.) experience disproportionately higher rates of substance use than those without disabilities, with 41% reporting past-month use in 2021 compared to 25% of adults without disabilities. Despite this disparity, little research has examined how current substance use varies by disability status and type across U.S. states, regions, and territories, particularly during the COVID-19 pandemic—a period of disrupted healthcare access and increased substance use.

Methods: Data were drawn from the 2020–2023 Behavioral Risk Factor Surveillance System (BRFSS), a nationally representative survey of non-institutionalized adults. The analytic sample included 1,719,106 adults across all 50 U.S. states, District of Columbia, and three territories (Guam, Puerto Rico, and the U.S. Virgin Islands). Descriptive statistics were used to assess the prevalence of current substance use (cigarettes, e-cigarettes, alcohol, and marijuana) across regions, states, and territories. Bivariate analyses using Chi-square tests examined differences in current substance use by disability status (any vs. none) and by disability type (hearing, vision, cognitive, mobility, self-care, and independent living). Analyses accounted for the BRFSS complex sampling design and were conducted using the procsurvey freq procedure in SAS v.9.4.

Results: Substantial geographic variation emerged between 2020–2023. Among adults with disabilities, cigarette use was highest in Tennessee (49.7%) and Guam (51.2%), e-cigarette use in Kentucky (50.7%) and Guam (41.6%), alcohol use in Wisconsin (52.9%) and the U.S. Virgin Islands (41.6%), and marijuana use in Alaska (27.6%) and the U.S. Virgin Islands (27.1%). Across all states and territories, adults with disabilities reported significantly higher prevalence of cigarette, e-cigarette, and marijuana use compared to those without disabilities, but significantly lower prevalence of alcohol use. People with cognitive disabilities had significantly higher prevalence of all substance use compared to those without cognitive disabilities, while people with hearing and self-care disabilities had the lowest.

Conclusions: Current substance use varies significantly across the U.S. and its territories by disability status and type. These findings highlight the importance of tailored, evidence-based prevention and treatment strategies that consider local policy and contextual factors to reduce disparities in substance use among adults with disabilities, particularly cigarette, e-cigarette, and marijuana use during public health emergencies.

LATEBREAKER

Substance Use

Integrating EHR and Survey Data via Machine Learning to Dissect the Rare Genetic Architecture of Alcohol Use Disorder: Findings from All of Us Biobank Mingzhou Fu*
Mingzhou Fu Pedro Lazcano Priya Maddhesiya Sophia Gunn Fion Shiau Dong Wang Kelly Jakubiak Carina Pizzano Tarjinder Singh

Background: Alcohol use disorder (AUD) etiology involves complex social (SDOH) and genetic factors. Traditional studies overlook the phenotypic spectrum of AUD with simplified definitions. We used the *All of Us* (AoU) biobank to integrate multi-modal data and identify genetic variations for AUD via a machine learning (ML)-derived risk score.

Methods: We identified 19k AUD cases and 190k controls in AoU. A CatBoost ML model was deployed to generate continuous individual-level liability scores as AUD risk scores across 7k features from EHR, SDOH, prescription and survey data. This score was then used as the primary trait in genetic analysis, including meta-analyzed GWAS and rare variant (RV) burden analysis for constrained geneset (pLI>0.9) and individual genes.

Results: The ML model achieved high validity (AUC = 0.94), separating cases (score=2.8±1.77) from controls (score= -0.29±1.02). ML model highlights top features of self-reported alcohol use, smoking, sex/gender, specific SDOH, and substance prescriptions, captured across EHR and survey data. Genetic analysis (N = 126,730) successfully recapitulated the known *ADH1B* variant (rs1229984; β=0.10, P=2.5×10-20). RV geneset analysis revealed increased AUD risk with rare deleterious variants (β ~0.05, P < 2.2 x10-6). Gene-based analysis identified more than 20 significant risk genes (P < 2.5×10-6) including known AUD genes such as *POMC*. Interestingly, it also discovered several novel genes such as *CHRNA4*, previously reported in other substance use traits, and are critical in brain neuronal and cognitive functions. These genes may explain a cross-trait addiction vulnerability.

Conclusion: Transforming binary diagnoses into an ML-based liability risk spectrum enhances the power to detect rare genetic contributors. This “deep phenotyping” reveals novel biological drivers hidden in traditional frameworks.

LATEBREAKER

Substance Use

Validation of a Novel Systematic Social Observation for Assessing Public Disorder in Neighborhoods Surrounding Community-Based Overdose Prevention Programs in New York City and Rhode Island Laura C. Chambers* Laura C. Chambers Yu Li Maxwell S. Krieger Bennett Allen Alex H. Kral Mercedes Guzman Herrera William C. Goedel Brandon D.L. Marshall Magdalena Cerdá

Background: Systematic social observation (SSO) can objectively measure changes in the social and built environment, but its application in evaluating the effects of overdose prevention programs (OPPs) on public disorder is limited.

Methods: We developed, implemented, and validated an SSO instrument in New York City (NYC) and Rhode Island (RI). Research assistants (RAs) assessed neighborhoods surrounding OPPs from 4/19/2023-6/22/2023 in NYC and 11/4/2024-12/20/2024 in RI. We used a novel randomization schedule to control for temporal fluctuations in public disorder. Among paired observations with simultaneous assessments by two RAs in NYC, we used Gwet's AC1 to assess inter-rater reliability (IRR). Among independent observations by a single RA, we used exploratory factor analysis (EFA) and Bayesian multi-level item response theory (IRT) models to derive separate latent measures of public disorder for NYC and RI and externally validated the measures against local arrest data.

Results: Among 19 paired observations, IRR was suitable or near perfect (Gwet's AC1 ≥60%) for 80% of categorical items (n=43/54). Separate EFA among independent observations from NYC (n=564) and RI (n=463) each identified three factors assessed with the instrument: drug litter, people, and built environment. IRT-based latent measures of public disorder (estimated from the three identified factors) exhibited positive spatial autocorrelation (NYC Moran's I=0.393, P<0.001; RI Moran's I=0.068, P<0.001). In NYC, item severity and discrimination were highest for the drug litter factor (Table). In RI, item parameters were relatively uniform across factors. The NYC latent measure was associated with total arrests (incidence rate ratio=1.42, 95% confidence interval [CI]=1.04-1.95) and drug-related arrests (incidence rate ratio=1.60, 95% CI=1.10-2.32). The latent measure was not associated with total arrests or any arrest subtype in RI.

Conclusion: The SSO instrument had strong psychometric properties. The latent measures of public disorder may be useful outcomes in future studies on neighborhood effects of OPPs. External validation suggests the NYC latent measure successfully captured variation in drug-related public disorder. The RI measure may capture variation in the environment that is less related to policing patterns.

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Women’s Health

Vitamin D deficiency and the odds of bacterial vaginosis among US women: Results from NHANES 2001-2004 Yinglin Dai* Yinglin Dai Nicole Talge Kristen Upson

Bacterial Vaginosis (BV), a vaginal microbiome dysbiosis marked by depletion of protective Lactobacillus species and overgrowth of anerobic bacteria, affects about 30% of US premenopausal women. Vitamin D may support a healthy vaginal microbiome through glycogen synthesis used by Lactobacillus species to produce lactic acid, lower vaginal pH, and reduce BV risk. Thus, vitamin D deficiency could plausibly increase BV risk. However, studies among non-pregnant women have yielded discrepant results. We conducted a cross-sectional analysis using data from the National Health and Nutrition Examination Survey cycles 2001-2004. The study population comprised premenopausal, non-pregnant, non-breastfeeding women ages 20-49 years (unweighted N=1380). Serum 25-hydroxyvitamin D (25(OH)D) levels were categorized as <20, 20-30, and ≥30 ng/ml to define deficient, insufficient, and sufficient vitamin D status, respectively. Gram-stained slides of vaginal samples were examined by microscopy and scored using Nugent’s criteria for negative, intermediate, and positive BV. We conducted multinomial logistic regression to estimate the adjusted (aOR) and 95%CIs for the associations between vitamin D status and intermediate and positive BV. The weighted prevalence of intermediate and positive BV was 29% and 28%, respectively. Our data suggested that deficient (vs. sufficient) vitamin D was associated with increased odds of intermediate BV (aOR 1.31, 95%CI: 0.84-2.04) and positive BV (aOR 2.36 95%CI: 1.53-3.64). No association was observed with insufficient vitamin D. To explore the mechanism, we evaluated the outcome of higher vaginal pH (>4.5) using log-binomial regression. Deficient vitamin D was associated with higher vaginal pH (adjusted prevalence ratio 1.42, 95%CI: 1.39-1.45). In this US non-pregnant population, our results suggest that deficient vitamin D status is associated with BV. Further research is warranted in a prospective setting to understand the underlying mechanisms.

LATEBREAKER

Women’s Health

Prevalence of chronic pain during the first year postpartum among TRICARE beneficiaries, 2013-2022 Jackielyn Lanning* Jackielyn Lanning Celeste J. Romano Clinton Hall Ava Marie S. Conlin Marissa J. Seamans

Introduction: Persistent pain is a common yet underrecognized issue in the postpartum period, with particular relevance for military service members given strenuous occupational demands. This work aimed to address research gaps by estimating the prevalence of chronic pain during the first postpartum year among US military families and assessing differences by patient military status.

Methods: TRICARE patients with a live delivery from 2013–2022 were identified using Birth and Infant Health Research program data. Live births were ascertained via diagnostic/procedure codes in medical encounter records and confirmed by linkage to enrollment data. Patients were required to have at least 6 months of observation (i.e., enrollment) throughout the first year postpartum. Chronic pain was defined as either one chronic pain diagnosis ≥30 days post-delivery or two non-chronic pain diagnoses ≥30 days apart. Prevalence was calculated overall and by pain site and military status. Timing of diagnoses in the first year was assessed. Crude prevalence ratios (PRs) for demographics were estimated by Poisson regression with robust error variance; models for occupational characteristics were adjusted for maternal age and birth facility type (military or civilian).

Results: Among 889,321 patients, 9.2% had indication of chronic pain within the first year postpartum. Back (4.6%), abdominal (2.1%), and pelvic/perineal (2.0%) were the most common pain sites. Back pain diagnoses rose from 1.5% to 2.0% between months 2-5 postpartum while other sites remained steady. Maternal age <25 years, unmarried status, military birth facility, and multiple birth were associated with higher prevalence. Prevalence among military patients was nearly triple that of non-military patients (aPR 2.83, 95% CI 2.79-2.87), with Army and mid/senior enlisted patients having the highest aPRs.

Conclusions: Chronic pain was relatively common in the first postpartum year and disproportionately affected military patients.

Women’s Health

The effectiveness of perineorrhaphy during vaginal pelvic organ prolapse surgery to reduce the risk of reoperation Beth MacLean* Beth MacLean Susanne Ehn Mats Pihlsgård Claudia Bruss Simon Timpka

Background: In the US alone, at least 140,000 women undergo pelvic organ prolapse surgery annually. Reconstruction of the perineal body between the anus and vagina through concomitant perineorrhaphy is frequently performed, despite uncertain benefit.

Methods: In a pre-registered observational registry-based cohort study, we sought to emulate a pragmatic target trial where patients undergoing pelvic organ prolapse surgery were perioperatively randomized to perineorrhaphy or not if the clinical relevance of performing the procedure was uncertain. Eligible patients were identified from the comprehensive Swedish National Quality Register of Gynecological Surgery, whereby they received primary vaginal pelvic organ prolapse surgery with native tissue repair between January 1st 2007 to June 30th 2021. The primary outcome was absolute cumulative risk difference in reoperation by 5 years, estimated as the average treatment effect following Stürmer trimming to exclude patients less likely to be included in a trial. Secondary patient-reported outcomes included subjective recurrence (feeling a vaginal bulge) or dissatisfaction with results by 1 year. Missing data were addressed through multiple imputations by chained equations and outcome estimates were pooled from 20 imputed datasets.

Results: In total, 40,607 eligible patients (10,634 [26.2%] with perineorrhaphy) were included, of which 21,206 patients contributed data to the target trial emulations. The estimated risk of reoperation per 100 patients was 11.5 (95%CI 10.5; 12.6) following surgery with perineorrhaphy and 13.5 (95%CI 12.9;14.1) without, equating to an absolute risk reduction of 2.0 reoperations per 100 patients (95%CI -3.2; -0.8). Perineorrhaphy also improved patient-reported secondary outcomes.

Conclusion: Among patients with uncertain benefit of having a perineorrhaphy during pelvic organ prolapse surgery, this additional procedure reduced the risk of reoperation and improved patient-reported secondary outcomes.

Women’s Health

Beyond Diagnosis: Migraine and Depressive Symptoms in Young Women in the Growing Up Today Study Holly Crowe* Holly Crowe Kathryn Rexrode Janet Rich-Edwards Alyssa Lebel Hadine Joffe

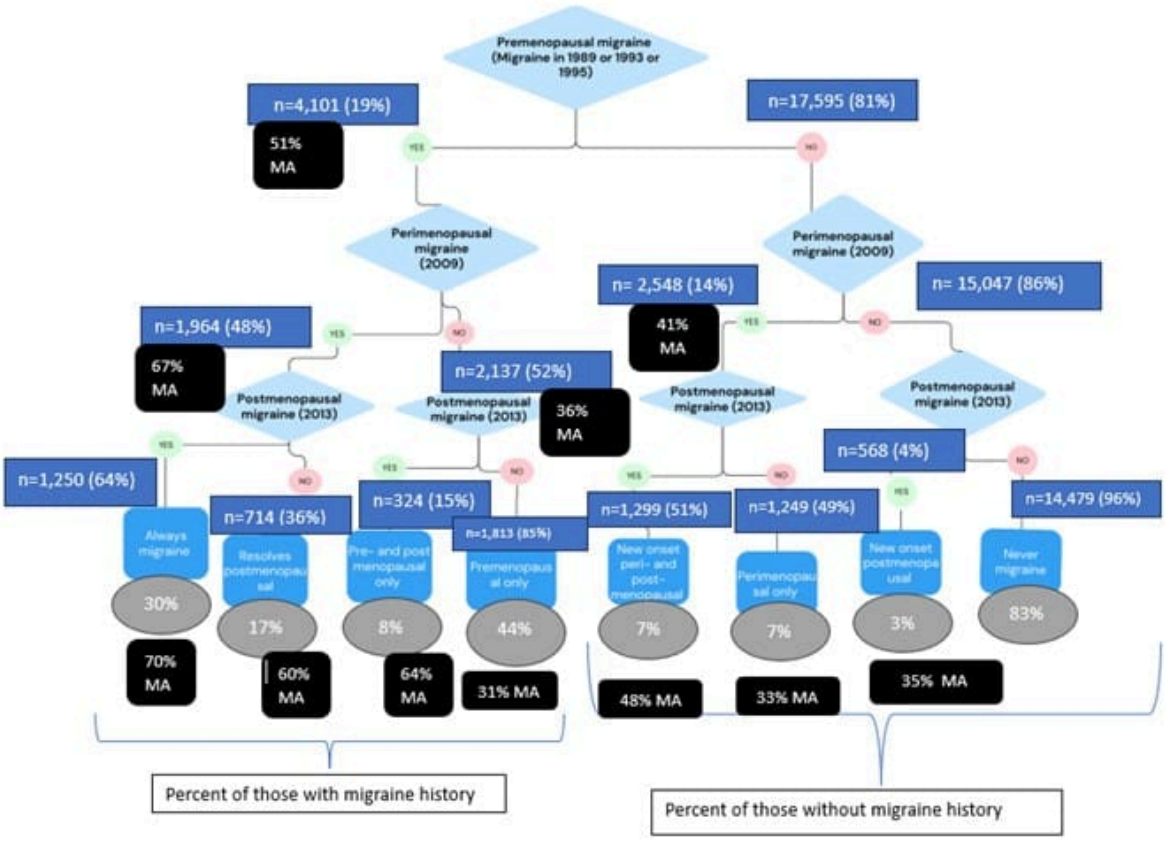
Half of people with migraine or depression are diagnosed before age 18. Adolescence and young adulthood are characterized by neurodevelopmental changes and increased risk of declining mental health, especially among young people with chronic health conditions. However, the link between adolescent-onset migraine and depression is understudied, and research tends to focus on diagnosed depression and migraine, which likely underestimates the true burden. To quantify the association between migraine and depression in young adults, we used data from 15,031 female participants in the ongoing Growing Up Today Study (age 9-17 at enrollment). We used self-reported physician diagnoses, as well as ICHD-3 criteria to categorize headache symptoms as migraine (yes/no) and a CESD-10 ≥10 cutoff to categorize mild depression symptoms during multiple time points from 2007-2016 (ages 11-29). We found that 28% of young adults reported experiencing migraine symptoms (21%) or diagnosis (19%)and 43% reported ever experiencing probable depression (CESD≥10; 33%) or a diagnosis of depression (23%). We used multivariable logistic regression to quantify the association between migraine and depression, adjusting for age at enrollment and menarche, race and ethnicity, diet score, physical activity, and history of trauma and abuse. We found a strong cross-sectional association between any migraine and depression (OR= 3.30, 95 CI: 2.99-3.64). The estimates for migraine and depression symptoms, regardless of diagnoses, were 1.80 (95% CI: 1.51-.2.15). These results indicate that migraine and depression symptoms commonly co-occur in young people, whether subthreshold or diagnosed. Young adulthood is a critical period for mental health screening, particularly among individuals with migraine, who are especially vulnerable.

Women’s Health

Migraine Trajectories Across the Menopausal Transition by Aura Status in the Nurses’ Health Study 2 Holly Crowe* Holly Crowe Janet Rich-Edwards Kathryn Rexrode Pamela Rist Hadine Joffe

Nearly 25% of women experience migraine as they approach the menopausal transition. Although migraine prevalence seems to increase during perimenopause and decline after menopause, epidemiologic evidence is inconsistent and distinctions for migraine aura status are unknown. We used data from 21,696 participants in the Nurses’ Health Study II to characterize migraine trajectories overall and by migraine type (with and without aura). Self-reported physician-diagnosed migraine was assessed serially over 28 years. We used participant-reported final menstrual period (FMP) date to identify migraine before perimenopause (>2 years before FMP), during perimenopause (±2 years from FMP), and after menopause (>2 years after FMP). We calculated frequencies for eight possible migraine trajectories across the transition by aura status. Nineteen percent of participants reported premenopausal migraine (N=4,101), of whom 51% had migraine with aura. Nearly half also reported perimenopausal migraine (N=1,964), and two-thirds of these had migraine with aura. Nearly 16% of women overall experienced post-menopausal migraine, including 64% of women with both pre- and perimenopausal migraine (N=1,250). Among those with migraine at all time points, 70% had migraine with aura, compared with 31% of those with premenopausal migraine only. Among participants without premenopausal migraine (N=17,595), 83% never experienced migraine across the transition, 14% had new-onset perimenopausal migraine, and 3% had new-onset postmenopausal migraine. Approximately half of those with new onset perimenopausal migraine continued to experience migraine after menopause and 41% had migraine with aura. Migraine trajectories across the menopausal transition are heterogeneous, and migraine with aura is more common among those with enduring migraine. These findings parallel evidence of greater persistence of migraine with aura during pregnancy and highlight etiologic differences by migraine subtype.

Migraine Trajectories across Menopause for 21,696 NHS2 Participants with a Final Menstrual Period 2007-2010



Women’s Health

The Association Between Period Pain and Pain Catastrophizing on Academic and Daily Life Disruptions in Undergraduate Students Madalynn Gilpin* Madalynn Gilpin Tara Cortez Farideh Bahlouli Amy Shafrir

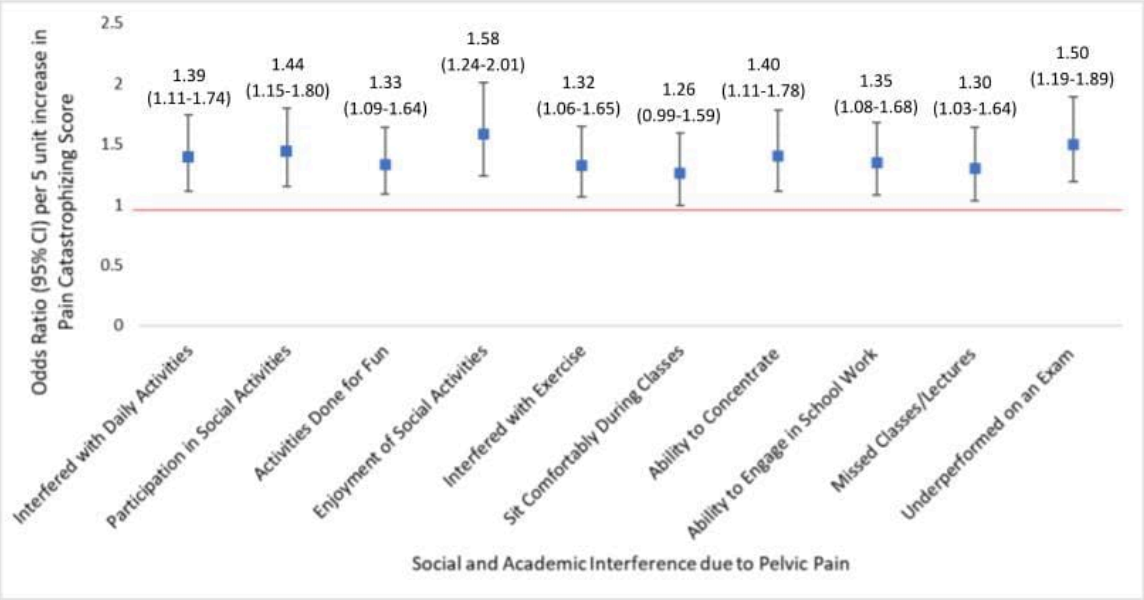
Background & Objective-Studies consistently report high rates of period pain among undergraduate women (63–80%), underscoring its burden. Pain catastrophizing (PCS) is linked to greater pain intensity, distress, and functional impairment in conditions such as menstrual pain. This study examined the association between pain catastrophizing and its impact on daily and academic functioning.

Methods- In this cross-sectional study, we recruited college undergraduate students aged 18–25 who reported menstrual periods and moderate or severe pelvic pain in the past six months. Between February and May 2025, participants completed a questionnaire on demographics, pelvic pain, and medication use. PCS was measured using the 13-item Pain Catastrophizing Scale and summed to create a total score between 0 and 52. We assessed daily life and academic interference due to period pain, categorized as somewhat/quite a bit/very much vs. never/a little bit. We used logistic regression to assess associations between academic and daily life interference due to pelvic pain and PCS scores, adjusting for age, period pain severity, and pain and hormone medication use.

Results– Among 100 participants, the mean age was 20.2 years (standard deviation: 1.24), and the majority were of the white race (87.6%). Higher PCS scores were associated with reduced enjoyment of social activities (OR: 1.58; 95%CI: 1.24-2.01 per 5 unit increase in PCS), suboptimal exam performance (OR: 1.50; 95% CI: 1.19-1.89 per 5 unit increase in PCS), and reduced participation in social activities (OR: 1.44; 95%CI: 1.15-1.80 per 5 unit increase in PCS). Results for all daily life and academic interference are shown in Figure 1.

Conclusion– Higher pain catastrophizing was associated with greater period pain-related interference across daily life and academic domains, independent of period pain severity, highlighting the need to address psychological factors to reduce pain interference.

Figure 1: Social and Academic Interference due to Pelvic Pain and Associations With Pain Catastrophizing: Odds Ratios With 95% Confidence Intervals.



Women’s Health

Patterns of depot medroxyprogesterone acetate (DMPA) injectable contraceptive use and predictors of discontinuation in young Ugandan women ages 16-25 years Kristen Upson*
Kristen Upson Juhee Lee Renee Heffron Andrew Mujugira Flavia Matovu Kenneth Mugwanya Michael Yin Chenxi Li Robert Wright Julio Landero Quaker Harmon

The injectable contraceptive depot medroxyprogesterone acetate (DMPA) is the leading hormonal contraceptive in Uganda. Yet, data on DMPA use patterns and predictors of discontinuation in Ugandan adolescent and young women are sparse. Thus, we used data from the Kampala Women’s Bone Study, a cohort of 499 young Ugandans ages 16-25 initiating DMPA or condom use. Participants were enrolled in years 2018-2020 and followed for 2 years with quarterly study visits. Among 268 DMPA initiators, we estimated the probability of DMPA continuation using Kaplan-Meier survival curves. We conducted Cox proportional hazard regression to estimate the adjusted hazard ratios (HR) and 95% CIs for associations between predictors and time to DMPA discontinuation. Predictors included baseline age, education, and travel time to study clinic and time varying factors of COVID-19 lockdown, vaginal sex frequency, menstrual bleeding, weight change (from baseline), and DMPA type (IM or SQ). Probability of DMPA continuation at 3-, 6-, 12-, and 24-months were 63%, 39%, 15%, and 2%, respectively. However, among those who discontinued, 32% restarted DMPA use. Factors associated with increased DMPA discontinuation risk included being age 20 (vs. age 19; HR 1.5, 95%CI: 1.0-2.3), COVID-19 lockdown (HR 2.9 95%CI: 1.9-4.2) and no vaginal sex in past 3 months (vs. 13-35 times; HR 1.6, 95%CI: 0.9-3.0). In contrast, vaginal sex >45 times in past 3 months was associated with decreased DMPA discontinuation risk (HR 0.7, 95%CI: 0.5-1.1) as well as having ≤7 years of education (vs. 12-16 years; HR 0.7, 95%CI:0.5-1.1), no menstrual bleeding (vs. regular bleeding; HR 0.6, 95%CI: 0.4-0.9) and only spotting (HR 0.4, 95%CI: 0.2-0.9). No associations were observed with travel time, weight change, or DMPA type. To our knowledge, this is the first study of DMPA use patterns and predictors of discontinuation in adolescent and young Ugandan women. Our results can inform efforts to reduce unintended pregnancy.

Women’s Health

Female cancer risks and infertility diagnosis: an analysis based on Taiwanese national data
Tingju Hsu* Tingju Hsu Tsung Yu

Introduction: Infertility affects approximately 17.5% of women globally and 15% in Taiwan. Associations between infertility and hormone-sensitive cancers remain inconclusive from prior studies. Using national data, we examined the association between the infertility diagnosis and subsequent risk of breast, endometrial, and ovarian cancers among Taiwanese women. **Methods:** From Taiwan’s National Health Insurance Research Database (1990–2021), we identified 65,860 women aged 18 to 60 years with incident infertility diagnosis and matched them individually by birth year to three controls. Incident breast, endometrial, and ovarian cancers were identified through registry linkage. Cox proportional hazards models adjusted for income levels and urbanicity for the cancer outcomes were evaluated. The models were further stratified by age at the first infertility diagnosis to five groups, less than 30, 30 to 34, 35 to 39, 40 to 44, and 45 years or older, for strata-specific HR. **Results:** Infertility diagnosis was not associated with overall breast cancer risk (HR=1.07 with 95% CI [0.99–1.15]). However, women first diagnosed at age 40 to 44 showed a significantly higher risk (HR=1.29 with 95%CI [1.05–1.60]). Infertility diagnosis was associated with increased endometrial cancer risk overall (HR=1.63 with 95%CI [1.38-1.92]) and also in less than 30 (HR=1.99 with 95%CI [1.45–2.73]), 30–34 (HR=1.49 with 95%CI [1.12–1.99]) and 35–39 (HR=1.70 with 95%CI [1.19–2.42]) age groups. No significant association for infertility diagnosis and ovarian cancer risk overall (HR=1.06 with 95%CI [0.86–1.31]) or in any age groups. **Conclusion:** Infertility diagnosis was associated with increased endometrial cancer risk, especially when diagnosed before age 40, and with increased breast cancer risk when first diagnosed at ages 40 to 44. The findings suggest that age at infertility diagnosis may identify subgroups with distinct hormone-related cancer risks and inform risk stratification in future studies.

LATEBREAKER

Women’s Health

Genital herpes: Gender comparisons in the development of cardiovascular disease May Baydoun* Sri Banerjee Jagdish Khubchandani Alva Daniels Latissa Hall Corey Sloan Heather Esnaola

Genital herpes, or HSV-2, is a serious public health problem with about half a billion people worldwide between the ages of 15-49 having this type of virus. Within the United States, nearly 20% in have this viral infection. While genital herpes can be caused by two types of viruses and can potentially lead to cervical cancer, we assume that genital herpes is solely caused by HSV-2. In this study, we explored the relationship between HSV-2, angina pectoris, and gender differences to gain an improved understanding of health equity. The 2003-2018 National Health and Nutrition Examination Survey is a nationally representative survey among the non-institutionalized population that is published in two-year cycles. Inclusion criteria for this study were individuals who were 20 to 59 years or older. Diagnosis of genital herpes was determined from self-reported data. Logistic regression was utilized to determine the connections between HSV-2 and angina pectoris, as it pertains to male versus female patients. For angina pectoris, the crude odds ratio (OR) for HSV-2 was 3.59 (95% confidence interval [CI], 1.34-9.60, $p< 0.01$). The adjusted OR was statistically significant 3.58 (CI 1.02-12.59, $p< 0.05$), among female patients with HSV-2, but not statistically significant (3.18 CI 0.45-22.2, $p=0.24$) among male patients with HSV-2, after adjusting for medical (obesity and congestive heart failure) and demographic variables (age, education level, insurance, and poverty). According to our findings, female patients with HSV-2 are approximately four times more likely to experience angina pectoris than male patients. Clinicians should encourage patients to consistently use condoms or dental dams during all sexual activity, including oral, anal, and vaginal sex, especially among female patients. Consistent screening through swab tests or blood tests can be used to screen for HSV-2. Also, female patients particularly must be monitored as this can allow for herpes to indirectly lead to cardiovascular disease.

LATEBREAKER

Aging

Kidney Function and Cognitive Performance in Early Midlife: Findings from the National Longitudinal Study of Adolescent to Adult Health Aanya Bahl* Kamaryn Tanner Dana Goin Eric A. Whitsel Jennifer Momkus Farizah Rob Aanya Bahl Allison E. Aiello

Background: Chronic kidney disease is associated with cognitive impairment and increased Alzheimer's disease (AD) risk in older adults. However, most studies focus on adults aged 65 and older or those with diagnosed kidney disease. We examined whether kidney function in early to midlife is associated with cognitive performance.

Methods: We analyzed Wave V (ages 33–43) and Wave VI (ages 39–51) data from the National Longitudinal Study of Adolescent to Adult Health. Kidney function was assessed with estimated glomerular filtration rate, using 2021 CKD-EPI equations with creatinine and cystatin C (eGFRCr-Cys) and creatinine alone (eGFRCr). Cognitive performance at Waves V and VI included immediate and delayed recall, backward digit span, and a principal components–derived summary score (PC Score Cognition). Survey-weighted linear regression was adjusted for age, sex, race, education, BMI, high cholesterol, diabetes, hypertension, smoking, alcohol use, and pregnancy.

Results: In cross-sectional Wave V analyses (n=589), eGFRCr-Cys was positively associated with all cognitive measures (Figure 1). Fully adjusted associations were slightly reduced and were statistically significant for PC Score Cognition and Immediate Recall. Corresponding associations with eGFRCr were positive, but confidence intervals included the null. Restricting analyses to participants with normal to mildly impaired kidney function (n=491) attenuated effect estimates, suggesting lower kidney function drove observed relationships. Wave V eGFR was associated with Wave VI cognitive performance (PC Score Cognition β=0.03; 95%CI: -0.06, 0.12).

Conclusions: eGFRCr-Cys was strongly associated with cognitive performance in early midlife; a 10 ml/min/1.73m2 lower eGFR corresponded to a 0.07 SD lower cognitive score. These findings suggest that reduced kidney function, even without clinical disease, is linked to cognitive performance in early midlife and may represent a novel early biomarker for future risk of AD.

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LATEBREAKER

Aging

Immune Aging Biomarkers of Immune Cell Composition and Their Association with Cognitive and Physical Aging Beyond Inflammation Markers: A Longitudinal Analysis in the Health and Retirement Study Mingyin Wang* Mingyin Wang

This longitudinal study in the Health and Retirement Study investigated how immune cell composition and aging biomarkers relate to cognitive and physical decline beyond standard inflammation markers. While it is known that inflammation influences aging, the specific impact of different immune cells on the brain versus the body over time has remained unclear due to a lack of long-term data. Analyzing data from over 7,500 participants tracked from 2016 through 2020, researchers found that cognitive and physical aging follow distinct biological paths. Higher albumin levels were associated with better outcomes for both, but other markers were more specialized: high NLR and certain “naive” CD8+ T-cells specifically predicted lower cognitive scores, whereas physical disability was primarily linked to the accumulation of “memory” CD8+ T-cells. These findings suggest that because the brain and body have different immune drivers, clinicians may need to monitor specific cell types rather than general inflammation to accurately assess a patient’s unique health risks during aging.

Aging

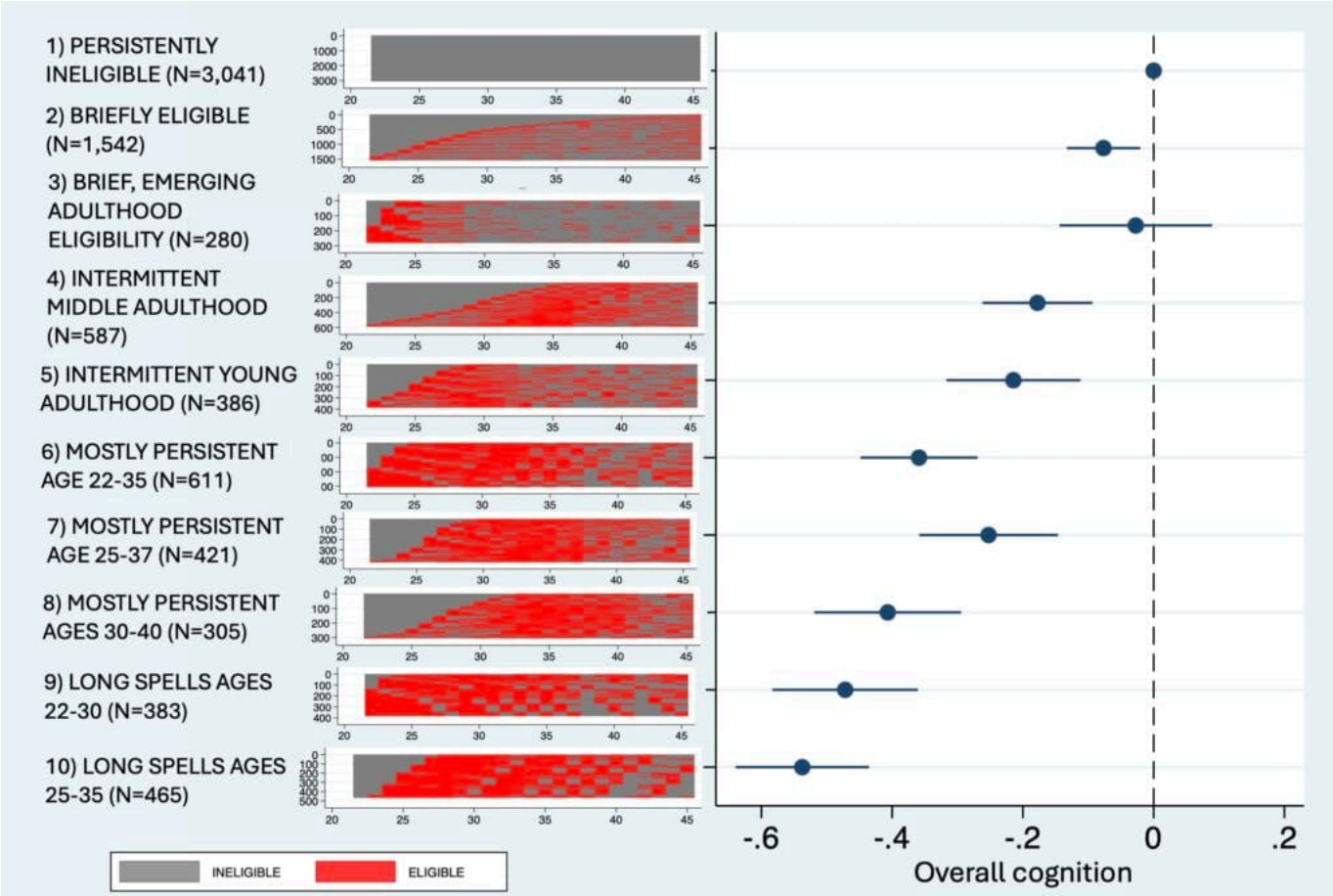
Food insecurity patterns in early adulthood to midlife and cognition: a sequence analysis approach Lucia Pacca* Lucia Pacca Amanda M Irish Suzanna M Martinez Anusha M Vable

Dementia is the 6th leading cause of death in the U.S., with marked disparities by socioeconomic status. Prior cross-sectional studies have found that food insecurity predicts lower cognition, but little research has evaluated lifecourse food insecurity. This study evaluates the association between food insecurity trajectories in emerging to middle adulthood, indicated by SNAP eligibility, and cognition.

Using a sample of 8,021 participants from the National Longitudinal Survey of Youth 1979, we determined SNAP eligibility status (yes/no) annually from age 22-45, according to 2008 USDA criteria based on income and assets. We calculated the similarity between SNAP eligibility trajectories using sequence analysis and grouped similar trajectories using cluster analysis. We then examined the association of SNAP eligibility clusters with overall cognition (z-score) around age 48, using linear regressions adjusted for individual-level socio-demographic characteristics.

We identified 10 clusters based on the timing and duration of SNAP eligibility. We found one cluster of persistently ineligible, two clusters of briefly eligible, two of intermittent eligibility, three of mostly persistent eligibility and two with long spells of eligibility (Figure 1). Compared to “persistently ineligible”, all clusters except for “brief, emerging adulthood eligibility” were associated with lower cognition. The association was stronger for individuals with longer periods of SNAP eligibility (e.g., “long spells of eligibility from age 25-35”: b=-0.53, 95% CI= -0.63, -0.43) than for those with intermittent eligibility (e.g., “intermittent middle adulthood eligibility”: b= -0.17, 95% CI: -.26, -.088).

Results suggest that food insecurity between in young and middle adulthood predicts lower cognitive functioning, especially when persistent. Given limited treatment options for dementia, targeting modifiable risk factors, such as expanding anti-hunger federal programs, may improve cognitive health.


1) PERSISTENTLY INELIGIBLE (N=3,041)
2) BRIEFLY ELIGIBLE (N=1,542)
3) BRIEF, EMERGING ADULTHOOD ELIGIBILITY (N=280)
4) INTERMITTENT MIDDLE ADULTHOOD (N=587)
5) INTERMITTENT YOUNG ADULTHOOD (N=386)
6) MOSTLY PERSISTENT AGE 22-35 (N=611)
7) MOSTLY PERSISTENT AGE 25-37 (N=421)
8) MOSTLY PERSISTENT AGES 30-40 (N=305)
9) LONG SPELLS AGES 22-30 (N=383)
10) LONG SPELLS AGES 25-35 (N=465)
INELIGIBLE
ELIGIBLE
-.6
-.4
-.2
0
.2
Overall cognition

LATEBREAKER

Aging

PM2.5 Metal Components and Cognitive Decline in the Adult Changes in Thought Study

Ting Zhang* Ting Zhang Yayi Zhu Paola Sebastiani Adam A. Szpiro Paul Crane Trenton Honda Helen Suh

Objective: Prior evidence linking fine particulate matter (PM2.5) and cognitive decline is mixed, possibly due to incomplete assessment of follow-up exposure and PM2.5 metal components. We examined associations of baseline and cumulative follow-up PM2.5 mass and metal components with cognitive decline in the Adult Changes in Thought (ACT) cohort.

Methods: This analysis included 5,673 adults aged ≥65 years in the Greater Seattle area, with a median of 5 cognitive assessment over 8 years of follow-up. Spatiotemporal estimates of PM2.5 mass and metal components were linked to residential histories. Linear mixed-effects models with inverse probability of censoring weighting (IPCW) included either baseline exposure × time or cumulative follow-up exposure × time to model rate of change in the outcome. Models were adjusted for baseline age, gender, race/ethnicity, marital status, education, enrollment cohort, neighborhood SES, baseline smoking, natural splines for calendar year, and time interactions for all covariates.

Results: Preliminary results showed PM2.5 mass had largely null associations with cognitive decline, although there was evidence of a small decrease in rate of decline for executive function in the pre-baseline 2-year exposure window (β=0.002, 95% CI: 0.000, 0.004). In contrast, several metal components were associated with domain-specific decline. Sulfur was associated with accelerated decline in executive function (β = −0.033, 95% CI: −0.064 to −0.001) and language (β = −0.041, 95% CI: −0.075 to −0.008). Vanadium was associated with faster decline in visuospatial function (β = −3.652, 95% CI: −6.688 to −0.616). We also observed faster memory decline associated with lead, and accelerated visuospatial decline associated with zinc, silicon, sulfur, and bromine. Copper, in contrast, was associated with a slower rate of memory decline.

Conclusion: Specific PM2.5 metal components, rather than total PM2.5 mass, were associated with accelerated domain-specific cognitive decline. These findings highlight the importance of considering pollutant composition when evaluating the neurodegenerative risk of air pollution.

LATEBREAKER

Aging

Clinically Documented Social Adversity (Z55–Z65 Codes) and Brain Structure: A Cross-Sectional Neuroimaging Study in UK Biobank May A. Beydoun* May Beydoun Hind A. Beydoun Indira C. Turney Jack Tsai Zhiguang Li Osorio Meirelles Minkyo Song Mustapha Bouhrara Nicole Noren Hooten Michele K. Evans Alan B. Zonderman

Social adversity is linked to poor health outcomes, yet clinically documented social hardship captured by ICD-10 Z55–Z65 codes has rarely been examined in relation to brain imaging markers. We investigated associations between documented social adversity and structural and microstructural brain measures in UK Biobank.

In this cross-sectional study of up to 37,184 participants with linked Hospital Episode Statistics and multimodal MRI data, exposure was defined as any Z55–Z65 code recorded between 2010 and 2020 prior to imaging. Outcomes included standardized structural MRI measures (gray matter, white matter, hippocampal volume, white matter hyperintensity burden) and diffusion MRI markers (fractional anisotropy, mean diffusivity, intracellular and isotropic volume fraction, orientation dispersion). Multivariable linear regression, propensity score matching (1:1–1:3), and inverse probability weighting were applied.

Before matching, exposed participants had lower income, higher comorbidity, poorer self-rated health, and greater medication use; covariate balance was achieved after matching. Z55–Z65 exposure was not associated with volumetric measures ($|\beta| < 0.03$ SD). In contrast, exposure was consistently associated with altered white matter microstructure, including lower fractional anisotropy ($\beta \approx -0.11$ to -0.15 SD), higher mean diffusivity ($\beta \approx 0.08$ to 0.11 SD), and lower intracellular volume fraction ($\beta \approx -0.11$ to -0.15 SD), largely driven by psychosocial codes (Z60–Z65).

Clinically documented social adversity was linked to widespread microstructural alterations but not volumetric differences, suggesting diffusion MRI may be a sensitive marker of social stress–related brain aging.

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Aging

Gendered Pathways of Pleasure, Satisfaction, and Health: A Longitudinal Study of Older U.S. Adults from 2005 to 2023 Caitlin* Caitlin Flouton Blanco Hongjie Liu

Objective: This gender-stratified study aims to disentangle the independent effects of age, period, and birth cohort on sexual relationship quality among older U.S. adults, and to examine the longitudinal associations between sexual quality and self-rated physical and mental health.

Methods: We analyzed four waves (2005–2023) of data from the National Social Life, Health, and Aging Project (NSHAP), comprising 6,068 adults aged 57+. Hierarchical age-period-cohort (HAPC) models quantified temporal effects on physical pleasure and emotional satisfaction. Longitudinal mixed-effects models then assessed how these dimensions predicted health trajectories among 4,113 participants with repeated measures, testing for interactions and adjusting for key sociodemographic confounders.

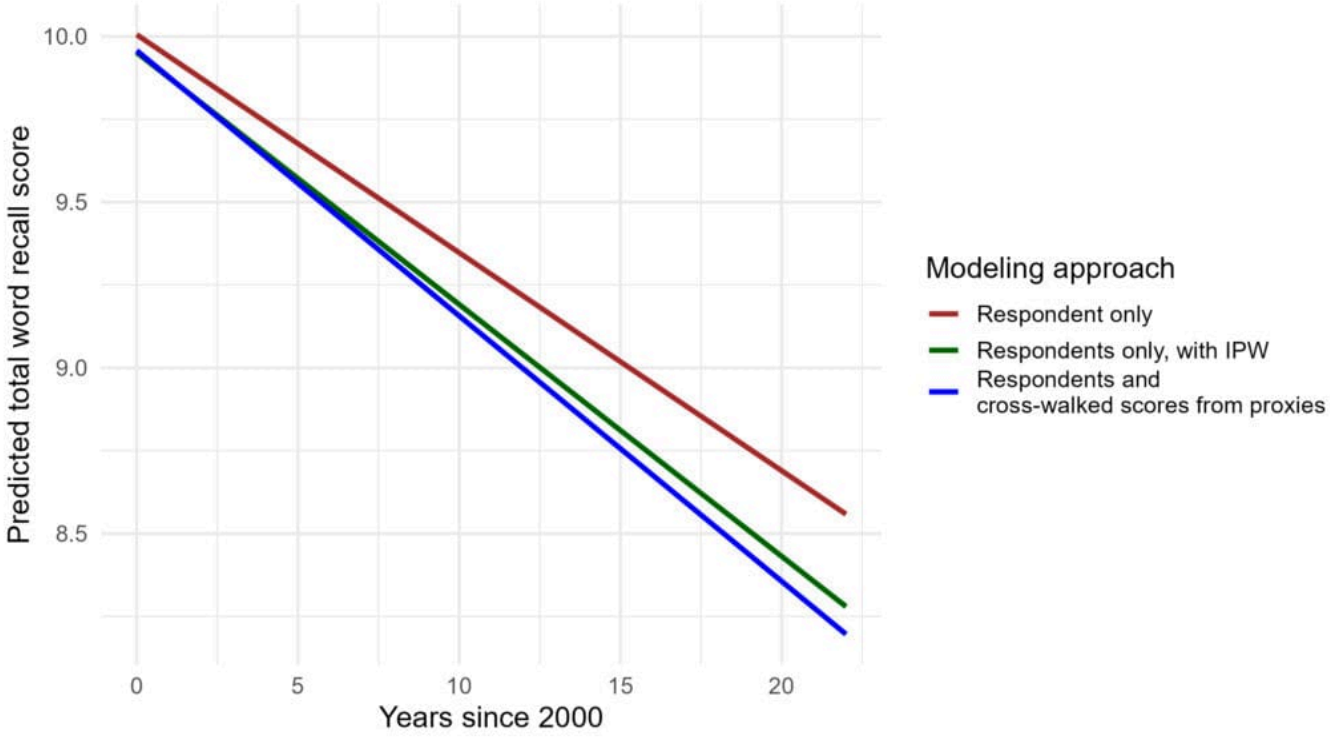
Results: APC analysis revealed a U-shaped age effect for emotional satisfaction in both genders, with a nadir around age 69. A pronounced gender gap emerged in cohort effects, where men reported consistently higher propensities for “extremely” pleasurable relationships (range: 23.6–32.7%) compared to women (9.0–13.7%). Longitudinally, both physical pleasure (females: aOR=1.48, 95% CI: 1.36-1.61; males: aOR=1.55, 95% CI: 1.42-1.69) and emotional satisfaction (females: aOR=1.52, 95% CI: 1.39-1.66; males: aOR=1.68, 95% CI: 1.52-1.85) were associated with better mental health. A key finding was a significant synergistic interaction among men for both health outcomes, where the protective effect of physical pleasure increased with higher emotional satisfaction.

Discussion: Sexual relationship quality is a dynamic determinant of health in later life, shaped by gendered experiences across age, historical period, and cohort. Findings underscore the importance of integrating multidimensional, gender-sensitive approaches to sexual well-being into geriatric care and health promotion.

Aging

Cross-walking proxy reports and direct episodic memory assessments to reduce selective attrition in dementia studies Eleanor Hayes-Larson* Eleanor Hayes-Larson Junxian Liu Emma Nichols Katrina L Kezios

In dementia research, bias due to selective attrition can arise when cognitively impaired participants are unable to complete cognitive assessments. Proxy respondents can provide alternative cognitive assessments, but proxy-rated cognition is not directly comparable to respondent-based memory test scores. Using data from the 2016 Health and Retirement Study (HRS) Harmonized Cognitive Assessment Protocol (HCAP), we developed and validated a cross-walking approach to convert proxy-rated cognition scores to directly-assessed episodic memory scores in the HRS. Among 3,029 HCAP participants with both direct (immediate and delayed 10-word recall) and proxy cognitive assessments (IQCODE), we cross-validated prediction models to estimate total (sum of immediate and delayed) word recall scores from proxy-reported IQCODE scores, evaluating 16 model specifications (including linear or spline IQCODE, respondent age, proxy relationship, and interactions) and selecting the best-performing model based on RMSE. We applied the final model to construct longitudinal memory trajectories for the HRS cohort followed 2000-2022using generalized estimating equations (GEE), restricted to individuals aged ≥50 who were self-respondents in 2000 (N=15,456). We used respondent word recall scores when available, and predicted scores based on the final model when only proxy cognitive assessments were available. For comparison, we implemented inverse probability weighting (IPW) to account for differential likelihood of proxy vs self-response over time. GEE models (**Figure**) confirmed that analyses of only respondent direct assessments underestimated the rate of memory decline over time due to selective attrition; cross-walking and IPW produced similar and steeper trajectories. The cross-walking approach retains cognitively impaired participants using a simple conversion formula, offering a flexible alternative to weighting methods that can be complex to implement longitudinally.


Predicted total word recall score
10.0
9.5
9.0
8.5
0
5
10
15
20
Years since 2000
Modeling approach
Respondent only
Respondents only, with IPW
Respondents and
cross-walked scores from proxies

Aging

Antidepressant and Anti-Anxiety Medication Use and Longitudinal Cognitive Function in Older Adults Maria Springall De Pablo* Maria Springall De Pablo Don Hedeker Seth Himelhoch Ana Capuano Diane S. Lauderdale

Antidepressant and anti-anxiety (anxiolytic) use has increased. For older adults, there have been concerns about side effects including cognitive decline, especially for benzodiazepines. We examined medication use and cognitive function over time in a national cohort of older adults (National Social Life, Health and Aging Project), overall and by drug class based on known mechanism of action (MOA).

4,100 older adults (born 1927-65) were interviewed up to 3 times at home every ~5 years (2010/1, 2015/6, 2021/3). Interviewers recorded medications by label into a database. Cognitive function was measured using the Montreal Cognitive Assessment Survey Adaptation (MOCA-SA, score 0-20). Multivariable linear mixed models simultaneously examined associations between antidepressant and anxiolytic counts (0, 1, >1) and MOCA-SA, adjusting for age, gender, race/ethnicity, education, depression and anxiety symptoms, and tobacco and alcohol use. Gender effect modification was assessed. MOA models used these categories: anticholinergic antidepressants, benzodiazepines, other antidepressants, and other anxiolytics.

Use of 1 antidepressant was associated with a 0.28 decrease in MOCA-SA scores (95% CI: -0.46, -0.11), and >1 was associated with a 0.45 decrease (95% CI: -0.80, -0.09). The association was stronger among men (-0.52, 95% CI: -0.79, -0.24) than women (-0.20, 95% CI: -0.40, 0.01), but the interaction term was not significant. Anxiolytics were not significantly associated with MOCA-SA. MOA models showed lower scores for anticholinergic antidepressant users (-0.53, 95% CI: -0.88, -0.18) and other antidepressant users (-0.23, 95% CI: -0.40, -0.05), but not for benzodiazepines or other anxiolytics.

Across time, antidepressant use is associated with lower cognitive scores. This association is stronger with >1 antidepressant, among men, and among anticholinergic antidepressant users. Anxiolytics, including benzodiazepines, showed no significant association with cognitive function.

Aging

Social vulnerability and incidence of all-cause dementia and Alzheimer's disease in the United States Laura Arboleda Merino* Laura Arboleda Merino Erika Walker Spruha Joshi Wei Hao J Scott Roberts Kelly M. Bakulski Sung Kyun Park

Introduction: Dementia is a growing global public health concern. Lifestyle and environmental risks for dementia operate within wider social and structural contexts, where increased social vulnerability can amplify obstacles to prevention, early detection, and care. We evaluated the association between social vulnerability and the incidence of Alzheimer's disease (AD) and all-cause dementia among U.S. adults.

Methods: We linked data from the National Health and Nutrition Examination Survey (NHANES, 1999-2016) with Medicare claims to identify incident AD and all-cause dementia cases through 2018. A modified Social Vulnerability Index (SVI) was constructed by summing seven individual-level indicators: income, education, health insurance, race/ethnicity, employment, housing tenure, and food security, yielding a score from 0 (least) to 7 (most vulnerable). High SVI was defined as quartile 4, while low SVI as quartiles 1–3. Adjusted hazard ratios were estimated using survey-weighted Cox proportional hazards models with age as the time scale.

Results: Participants (N=9,190) had a mean baseline age of 64.8 years and an average SVI of 1.53. Over a mean follow-up of 9.06 years for AD and 8.86 years for all-cause dementia, 641 developed AD and 1,393 individuals developed dementia. Higher social vulnerability was consistently associated with elevated dementia risk. Compared with individuals in the low-SVI group, the high-SVI group had a 32% higher risk of AD (HR: 1.32, 95% CI: 1.08-1.62) and a 66% higher risk of all-cause dementia (HR: 1.66, 95% CI: 1.45-1.89). Modeled continuously, a one-unit increase in SVI corresponded to an 11% higher risk of AD (HR: 1.11, 95% CI: 1.05-1.17) and a 19% higher risk of all-cause dementia (HR: 1.19, 95% CI: 1.15-1.23).

Conclusion: Higher social vulnerability was strongly associated with increased risk of incident dementia. Addressing social and structural determinants of health may be critical to reducing this growing public-health burden.

Aging

Estimating the causal effect of hearing impairment on risk of dementia over 18 years in US older adults: A target trial emulation Yixun Ke* Yixun Ke Muxi Zheng Scott C. Zimmerman Anna M.Pederson Paige D. Wartko Yulin Hswen Phillip Hwang Marcia Pescador Jimenez M. Maria Glymour Willa D. Brenowitz Roch A. Nianogo

Hearing impairment is a potential modifiable risk factor for dementia. However, the long-term effects using rigorous methods have remained understudied. We estimated the effect of baseline hearing impairment on the risk of developing dementia among older adults in the United States using a target trial framework over up to 18 years of follow-up. We used data from the Health and Retirement Study (HRS) 1998-2016, including adults aged ≥50 years without dementia at baseline. We considered individuals to have hearing impairment if they rated their hearing quality as fair or poor at baseline, and to not have hearing impairment if they rated it as excellent, very good, or good. Incident dementia was derived using the Langa-Weir classification algorithm. We used pooled logistic regression and the parametric g-formula with time since baseline as a discrete-time scale to estimate adjusted survival and adjusted effects on dementia had all participants started with vs without the hearing impairment at baseline, accounting for censoring. We adjusted for demographics, health and lifestyle covariates. We used multiple imputation to address missingness in exposure and covariates and bootstrapping was used to estimate the 95% CIs. On average, if everyone in the population had baseline hearing impairment, there would be 2.02 (95% CI: 1.16, 2.88) excess dementia cases out of 100 individuals compared to if everyone did not have baseline hearing impairment. Similarly, the average risk of dementia if everyone in the population had baseline hearing impairment would be 1.38 (95% CI: 1.19, 1.56) times that if everyone did not have baseline hearing impairment. In this study, we found that baseline hearing impairment increased the risk of dementia over 18 years of follow-up. These findings support early intervention on hearing impairment as a potentially important population-level strategy for dementia prevention.

Table1. Baseline Effect of Hearing Impairment on Dementia		
Years Since Baseline	**Risk Difference (%) (RD, 95% CI)**	**Risk Ratio (RR, 95% CI)**
5	2.03 (1.22, 2.84)	1.46 (1.26, 1.67)
10	2.45 (1.52, 3.37)	1.31 (1.18, 1.43)
15	2.31 (1.21, 3.40)	1.19 (1.10, 1.29)
18 (End of follow-up)	2.16 (0.98, 3.34)	1.16 (1.07, 1.25)
Average	2.02 (1.16, 2.88)	1.38 (1.19, 1.56)

*Adjusted for age, sex, race/ethnicity, APOE ε4 carrier status, current marital status, household income, health insurance coverage, smoking status, depressive symptoms (CES-D), self-rated health, and history of stroke, cancer, lung disease, heart disease, and diabetes.
**Missing covariate data were handled using multiple imputation. Effect estimates were obtained using the parametric g-formula. 95% confidence intervals were quantified using 200 nonparametric bootstrap resamples of the imputed data.

Aging

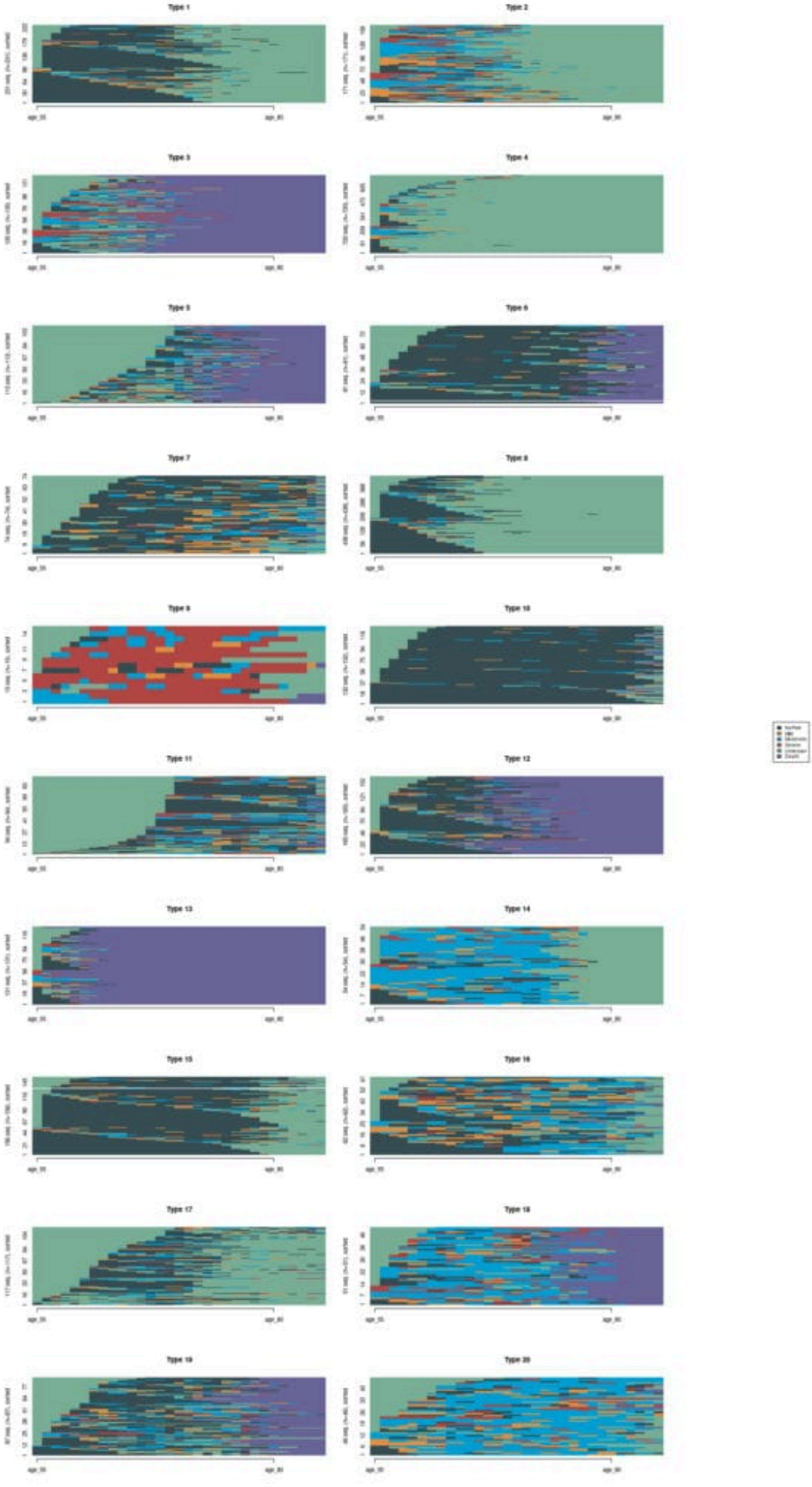
Mapping Thirty–Year Pain Trajectories in Later Life: Sequence Analysis of U.S. Middle-aged and Older Adults in the Health and Retirement Study Muxi Zheng* Yulin Yang Muxi Zheng Ulrike Muench Paola Gilsanz M. Maria Glymour Cynthia I. Campbell Catherine A Schaefer Scott Zimmerman Jacqueline M Torres Lucia Pacca

Pain is highly dynamic, yet little is known about how its timing, order, and duration vary across the life course. This study uses sequence analysis to identify longitudinal patterns of pain over 30 years among middle-aged and older adults.

We analyzed data from 30,728 participants aged 55-85 in the US Health and Retirement Study (HRS, 1992-2022). Pain status and severity were self-reported at each survey wave, operationalized as no pain, mild pain, moderate pain, severe pain, unknown, and deceased. We carried forward pain categories between wave years. We used sequence analysis to quantitatively compare individual pain trajectories, and hierarchical agglomerative clustering to group similar trajectories.

We identified 20 distinct pain trajectory clusters (Figure 1) over 30 years across 16 waves. These trajectories varied substantially in timing of onset, pain persistence, severity progression, and stability of pain over time. To enhance interpretability, the 20 types were collapsed into five meta-groups: persistently low or no pain (49.5%; Types 1, 4, 8,13), early-onset persistent pain (14.4%; Types 6, 7, 10, 15), late-onset pain (14.9%; Types 3, 5, 11, 17), intermittent pain (11.3%; Types 2, 9, 14, 16, 20), and progressively worsening pain (9.9%; Types 12, 18, 19). While mild and severe pain patterns were largely intermittent, a greater number of individuals experienced moderate pain for extended durations.

Middle-aged and older adults report a diverse experience of pain patterns over time, including age when pain begins, duration and severity, and whether it worsens, improves, or is intermittent. By tracing comprehensive pain histories rather than relying on snapshots, sequence analysis makes this diversity visible. Determinants and consequences of these trajectories may vary widely, and understanding which trajectory an individual is experiencing may inform pain prevention and care.


Type 1
Type 2
Type 3
Type 4
Type 5
Type 6
Type 7
Type 8
Type 9
Type 10
Type 11
Type 12
Type 13
Type 14
Type 15
Type 16
Type 17
Type 18
Type 19
Type 20

Aging

Subjective cognitive decline reflects brain pathology independent of depressive symptoms

Nancy Chen* Nancy Chen Sarah Tomaszewski Farias Paola Gilsanz Batool Rizvi Elizabeth Rose Mayeda Maria Corrada Rachel A. Whitmer

Subjective cognitive decline (SCD) may reflect neurodegenerative processes but is also closely linked to depressive symptoms, which itself is a risk for dementia. We examined whether depressive symptoms mediate associations between SCD and imaging biomarkers of neurodegeneration, cerebrovascular injury, and amyloid burden.

We analyzed an ethnoracially-diverse sample of adults aged 50-101 from harmonized KHANDLE, LA90, and STAR. SCD was measured using the 12-item Everyday Cognition (ECog) (range:1-4; higher=greater SCD). Hippocampal volume and white matter hyperintensities (WMH) were measured using 3T MRI, normalized to intracranial volume and z-standardized. Amyloid burden was assessed using florbetapir PET among a random subset of KHANDLE and LA90 and quantified using standard uptake value ratios (SUVR). The potential mediator, depressive symptoms, was measured by the NIH PROMIS depression toolbox. All measures were assessed at the same or proximate visit. Mediation analyses estimated total, natural direct, and natural indirect effects, adjusted for sex, race/ethnicity, age at scan, education, and cohort.

Participants' (N=724) mean±SD age was 81.1±10.7, 58% were women, 52% had less than a college education, and 20% identified as Asian, 33% as Black, 19% as Latino, and 25% as White. Mean ECog was 1.38±0.41 and mean amyloid SUVR was 1.10±0.19. Higher (worse) ECog was associated with higher odds of having depressive symptoms (OR=2.69,95%CI=1.77,4.07), and smaller hippocampal volume (bTotalEffect=-0.26,95%CI=-0.43,-0.10;Table 1) with no evidence of mediation by depressive symptoms. Higher ECog was also modestly associated with greater WMH and higher amyloid-SUVR, and neither association showed evidence of mediation.

Greater SCD was associated with neurodegeneration and, to a lesser extent, cerebrovascular injury and amyloid burden. Depressive symptoms did not mediate these associations, suggesting that SCD may reflect underlying brain pathology independent of depression.

Table. Mediation Analyses: Total effects, natural direct effects, natural indirect effects, and percentage mediated were estimated separately for imaging measures of neurodegeneration (hippocampal volume), cerebrovascular injury (log-white matter hyperintensities volume), and amyloid (SUVR) with depressive symptoms as the potential mediator and ECog score as the exposure.

Model*	N	(Outcome) Neuroimaging biomarker	Total Effect Estimate (95% CI)	Natural Direct Effect Estimate (95% CI)	Natural Indirect Effect Estimate (95% CI)	Percentage Mediated Estimate (95% CI)
Model 1	681	Hippocampus	**-0.26 (-0.43, -0.10)**	**-0.26 (-0.44, -0.09)**	0.00 (-0.04, 0.04)	-0.9 (-15.8, 13.9)
Model 2	676	Log-WMH	0.16 (-0.01, 0.33)	0.15 (-0.04, 0.33)	0.01 (-0.03, 0.05)	8.8 (-20.0, 37.6)
Model 3**	485	Amyloid-SUVR	0.04 (-0.00, 0.08)	0.04 (-0.00, 0.08)	-0.00 (-0.01, 0.00)	-13.8 (-39.6, 12.1)

*All models adjusting for age at scan, gender (men vs women), race/ethnicity (Asian, Black, Latino, Other vs White), education (≥ College vs < College), and cohort study (LA90, STAR vs KHANDLE).
**Only in KHANDLE and LA90

Aging

Who Do These Estimates Really Represent? An Application of Pre-Enrollment Inverse Probability Selection Weighting to a Late-Life Aging Cohort Sirena Gutierrez* Sirena Gutierrez Claire C Meunier Joseph Roscoe Liliana Paloma Rojas-Saunero Eleanor Hayes-Larson Jacqueline M Torres Dan M Mungas M Maria Glymour Rachel A Whitmer Paola Gilsanz Elizabeth Rose Mayeda

Studies of older adults are shaped by multiple socially patterned selection processes prior to enrollment, including survival, retention within health systems, and self-selection into study participation. These processes challenge the estimation and interpretation of causal effects of earlier life determinants of healthy aging. Inverse probability weighting (IPW) is commonly used to address post-enrollment attrition, but studies rarely account for pre-enrollment selection due to limited pre-enrollment data. We developed a composite IPW for the Kaiser Healthy Aging and Different Life Experiences (KHANDLE) study, a multi-ethnic cohort of long-term Kaiser Permanente Northern California (KPNC) members, to account for selection into the cohort along 3 selection processes: dementia-free survival, health system membership, and enrollment. KHANDLE participants were current KPNC members on 1/1/2017, born before 1952, who participated in at least one Kaiser Permanente Multiphasic Health Checkup (MHC) exam between 1964 and 1985. The target population was all MHC participants born before 1952, regardless of survival or membership status as of 1/1/2017. Using midlife health covariates measured in the MHCs and sociodemographic covariates measured from electronic health records, we estimated: 1) dementia-free survival to 1/1/2017; 2) KPNC membership on 1/1/2017 conditional on survival; and 3) KHANDLE participation conditional on survival and membership. We will compare estimated effects of midlife hypertension on late-life dementia risk in KHANDLE participants and after extending estimates to the MHC target population. Our framework is applicable to other studies of lifecourse determinants of health among older adults by enabling correction for survival bias, selective enrollment, and unmeasured structural processes that may otherwise bias late-life estimates.

Aging

Mobile Phlebotomy to Enhance Diversity in Alzheimer's Disease Biomarker Research: The California Blood Biomarker Study Yodit Goshu* Yodit Goshu Joseph Fong Miriam T. Ashford Alejandra Morlett-Paredes Erika Cavallone Kristen M George R. Scott Mackin Chengshi Jin Anna Aaronson Rachel Nosheny Elizabeth Rose Mayeda

Ongoing advances in biomarker research have led to development of plasma biomarkers for Alzheimer's disease and related dementias (AD/ADRD), offering a minimally invasive, cost-effective, and scalable alternative to neuroimaging and cerebrospinal fluid biomarkers, typically limited to major medical centers. Mobile phlebotomy, where phlebotomists travel to participants' homes for blood draws, may facilitate broader participation in biomarker research. The California Blood Biomarker Study (CABBS) evaluated the feasibility of participant enrollment and completion of mobile phlebotomy for plasma AD/ADRD biomarkers and genetic analysis in a racially and ethnically diverse sample of participants aged 55+ in the California Brain Health Registry (CAL-BHR), a web-based AD/ADRD research registry. Out of 7,379 CAL-BHR participants invited, 498 (6.7%) enrolled in CABBS and 407 (5.5%) completed a blood draw. CABBS participants who completed a blood draw were demographically similar to CAL-BHR participants who did not complete a blood draw. Compared to the California population aged 55+ represented by the 2022 Behavioral Risk Factor Surveillance System, CABBS participants who completed a blood draw tended to be younger, included a higher proportion of women, displayed greater racial and ethnic diversity, had higher average levels of education, and reported a higher prevalence of memory concerns. Some CABBS participants reported scheduling and communication challenges with the mobile phlebotomy company; however, they remained interested in participating in this study and future research. Our study team resolved these issues as the study progressed. Among CABBS participants with a blood draw, 10% had biomarker values consistent with preclinical Alzheimer's disease. Our findings support mobile phlebotomy as a feasible strategy for enhancing diversity in AD/ADRD biomarker research, while highlighting the importance of pilot testing and logistical infrastructure in future studies.

Aging

Associations of alcohol consumption with memory loss in European middle-aged and older adults: evaluating time-varying confounding, lagged effects, and “sick quitter” effects

Shelli Vodovozov* Shelli Vodovozov Sherry Shu-Yeu Hou Annie Pederson Scott C. Zimmerman David Kapaon Rebecca E. Graff Catherine Schaefer Hélène Choquet Laura. A. Schmidt Yvette Cozier Yvette Cozier

Estimating effects of alcohol consumption and cessation on dementia incidence is complicated by reverse causation as declines in cognition or health lead individuals to reduce or stop drinking.

Participants (n=68,379) from 20 countries in the Survey of Health, Ageing and Retirement in Europe reported alcohol consumption up to 8 times (mean=1.98, SD = 0.95). Alcohol use was categorized per sex-specific NIAAA guidelines (none, low/moderate, heavy). Memory (immediate and delayed 10-word recall; z-scored) was assessed 1–3 waves after each alcohol report.

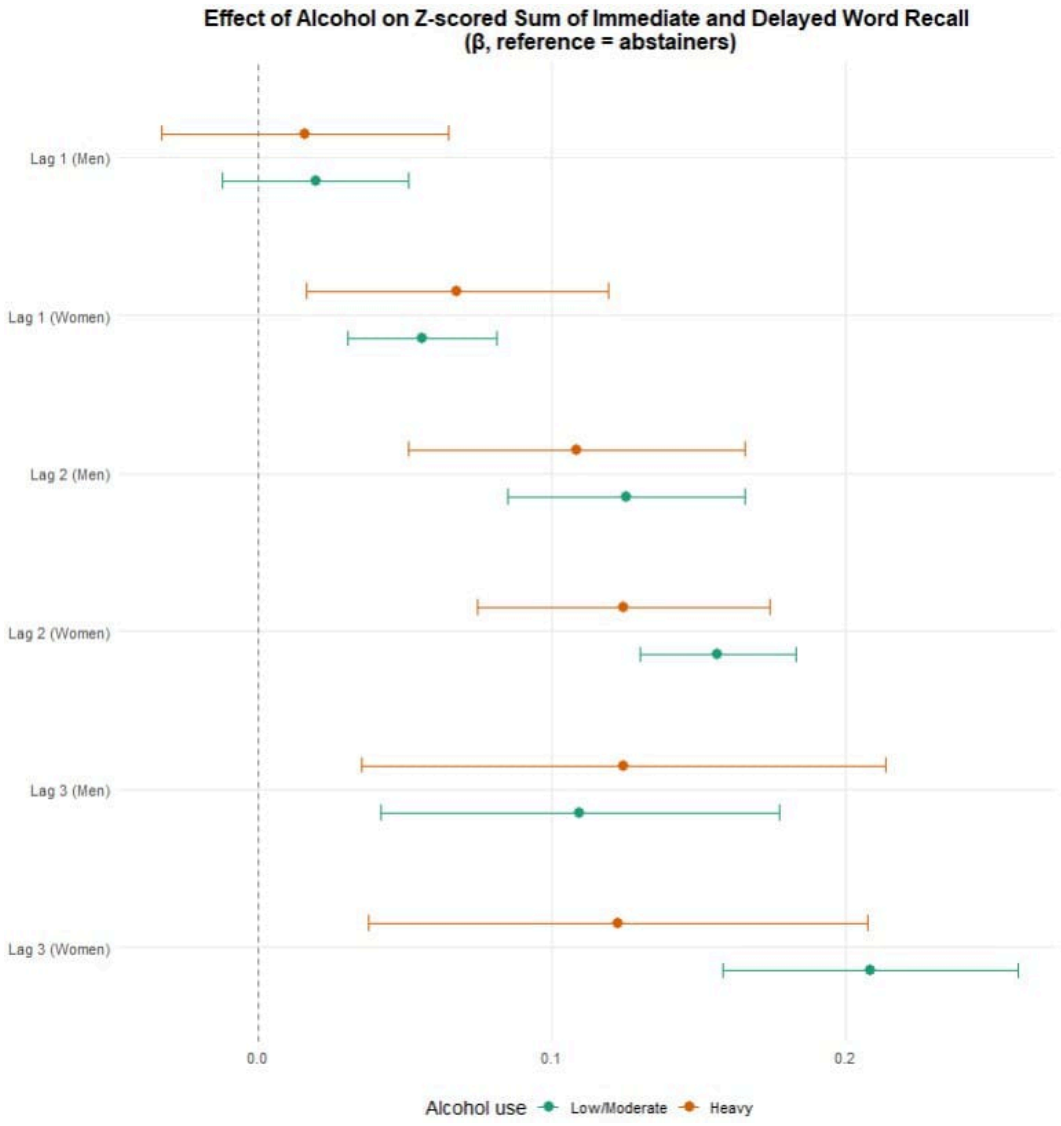
We estimated stabilized inverse probability weights for treatment and censoring and applied generalized estimating equations to weighted data. Covariates included sociodemographics, prior cognition, health behaviors, diagnoses, and self-rated health (1 = poor to 5 = excellent). Analyses were stratified by sex. E-values assessed sensitivity to unmeasured confounding, and pooled logistic regression examined predictors of alcohol cessation to quantify reverse causation.

Memory was better among heavy drinkers (vs non-drinkers) reported one (βheavy=0.07[0.01, 0.12], two (βheavy=0.12[0.07, 0.17], or three waves prior to memory (βheavy=0.21[0.04, 0.21]. Among men, estimates were (βheavy=0.10 [0.05, 0.16] at lag one and βheavy=0.12[0.04, 0.21] at waves two and three.

E-values ranged from 1.32-1.48 among women and 1.43-1.49 among men.

Higher past cognition was associated with lower odds of alcohol cessation among women (OR=0.93[0.90, 0.96]), and each unit increase in self-rated health was associated with greater cessation among women (OR=0.79[0.76, 0.82]) and men (OR=0.78[0.75, 0.82]).

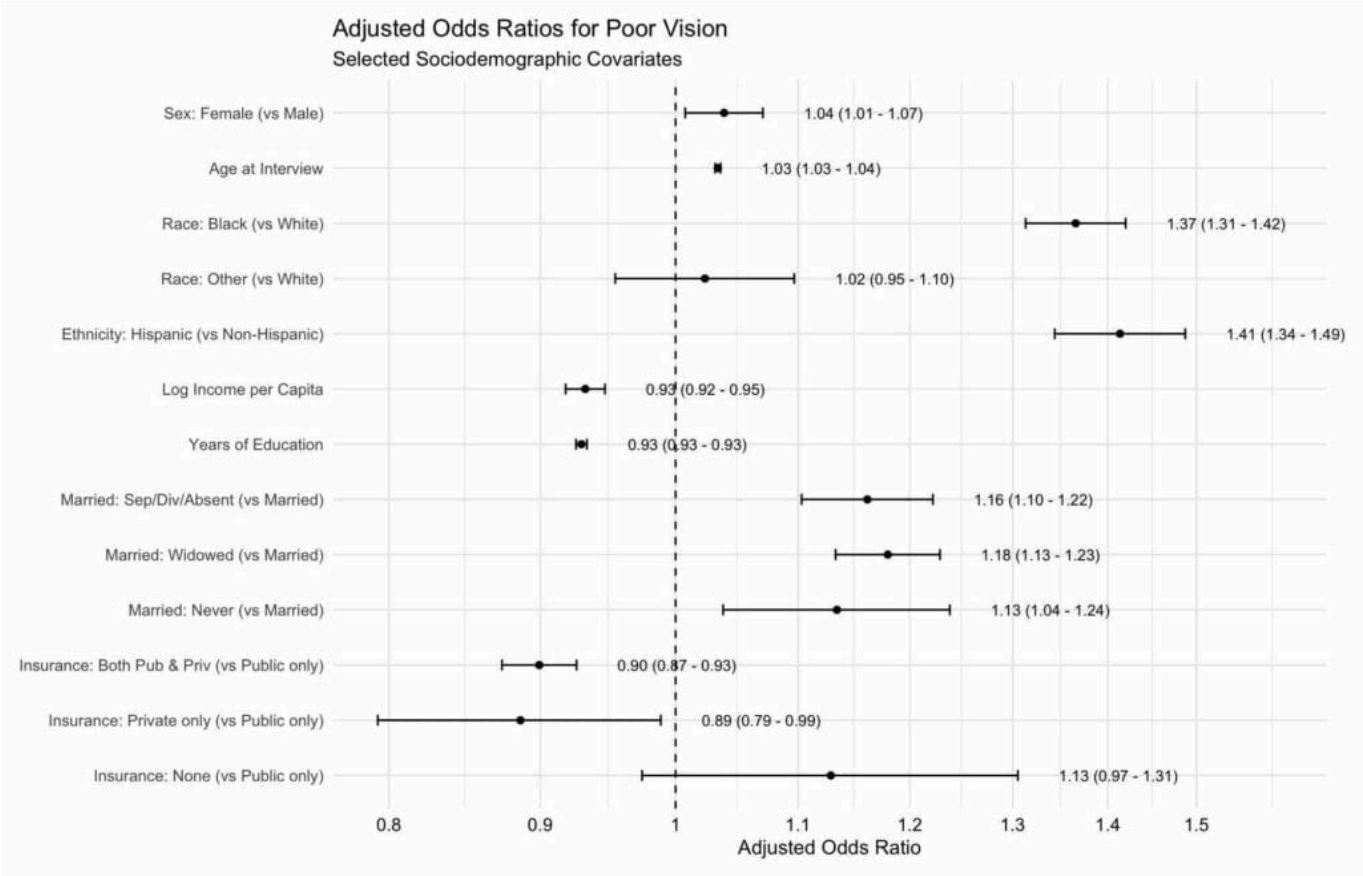
Heavy alcohol use was associated with better memory in this large European cohort. Evidence of reverse causation suggests this association reflects health and cognition-related selection into continued drinking, underscoring limitations of conventional observational designs and the need for methods that better address dynamic exposure changes.


Effect of Alcohol on Z-scored Sum of Immediate and Delayed Word Recall
(β, reference = abstainers)
Lag 1 (Men)
Lag 1 (Women)
Lag 2 (Men)
Lag 2 (Women)
Lag 3 (Men)
Lag 3 (Women)
0.0
0.1
0.2
Alcohol use
Low/Moderate
Heavy

Aging

Sociodemographic Predictors of Poor Vision Among Older Adults: Evidence from the Health and Retirement Study Muxi Zheng* Muxi Zheng Yixun Ke Scott C. Zimmerman Anna M. Pederson Roch Nianogo Paige D Wartko Hélène Choquet M. Maria Glymour Willa D. Brenowitz

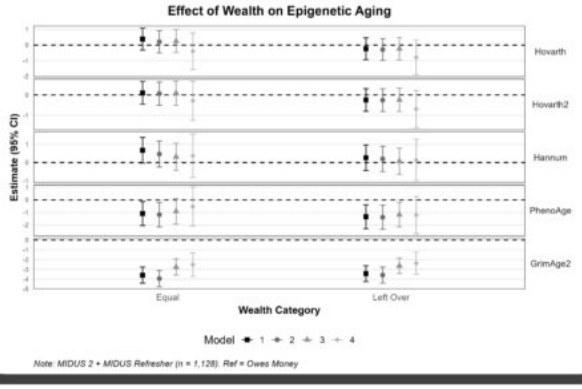
Understanding how sociodemographic factors are associated with poor vision is important for informing interventions. Among adults aged 65+ enrolled in the Health and Retirement Study between 1994-2020 (N=25,992), we evaluated associations between sociodemographic characteristics and poor vision. Participants self-reported eyesight (with glasses if they normally use glasses) at biennial interviews; poor vision was defined as self-rated fair or poor including with glasses use. Logistic regression models were used to estimate associations of sociodemographic characteristics (sex, race and ethnicity, education, age, marital status, income, and insurance type) with odds of poor vision. To determine if social factors predict vision accounting for health status, models were adjusted for lifestyle and health conditions variables from the prior interview. Participants had a mean age of 74.6 years. Females had higher odds of poor vision than males (OR=1.04, 95% CI: 1.01-1.07). Older age was associated with higher odds of poor vision (OR=1.03, 95% CI: 1.03-1.04). Black participants had higher odds of poor vision (OR=1.36, 95% CI: 1.31-1.41) compared to White participants, and Hispanic participants had higher odds than Non-Hispanic participants (OR=1.41, 95%CI: 1.34-1.48). Higher education (OR=0.93, 95%CI: 0.92-0.95) and higher income (OR=0.93, 95% CI: 0.93-0.93) were associated with lower odds of poor vision. Separated/divorced (OR=1.15, 95%CI: 1.09-1.21), widowed (OR=1.17, 95%CI: 1.12-1.21), and never married (OR=1.12, 95%CI: 1.03-1.23) individuals had higher odds of poor vision than married individuals. Those with both public and private insurance (OR=0.90, 95%CI: 0.87-0.93) and with only private insurance (OR=0.86, 95% CI: 0.77-0.96) had lower odds of poor vision than those with public insurance only.
Sociodemographics were associated with poor vision. This suggests the need for targeted efforts to improve access to vision care among disadvantaged older adults.

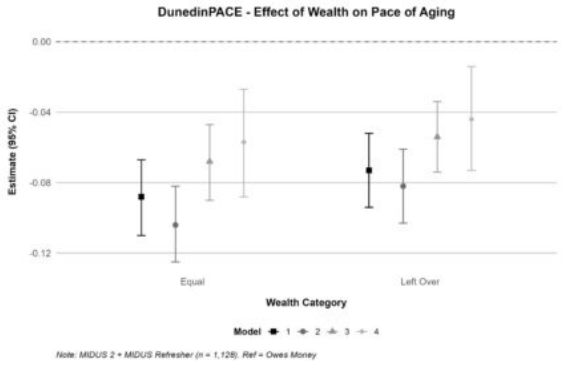

Adjusted Odds Ratios for Poor Vision
Selected Sociodemographic Covariates
Sex: Female (vs Male)
1.04 (1.01 - 1.07)
Age at Interview
1.03 (1.03 - 1.04)
Race: Black (vs White)
1.37 (1.31 - 1.42)
Race: Other (vs White)
1.02 (0.95 - 1.10)
Ethnicity: Hispanic (vs Non-Hispanic)
1.41 (1.34 - 1.49)
Log Income per Capita
0.93 (0.92 - 0.95)
Years of Education
0.93 (0.93 - 0.93)
Married: Sep/Div/Absent (vs Married)
1.16 (1.10 - 1.22)
Married: Widowed (vs Married)
1.18 (1.13 - 1.23)
Married: Never (vs Married)
1.13 (1.04 - 1.24)
Insurance: Both Pub & Priv (vs Public only)
0.90 (0.87 - 0.93)
Insurance: Private only (vs Public only)
0.89 (0.79 - 0.99)
Insurance: None (vs Public only)
1.13 (0.97 - 1.31)
0.8
0.9
1
1.1
1.2
1.3
1.4
1.5
Adjusted Odds Ratio

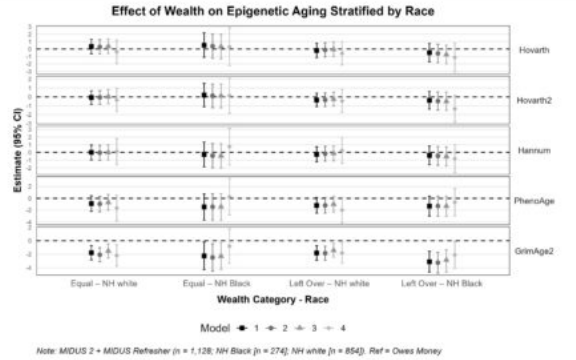
Aging

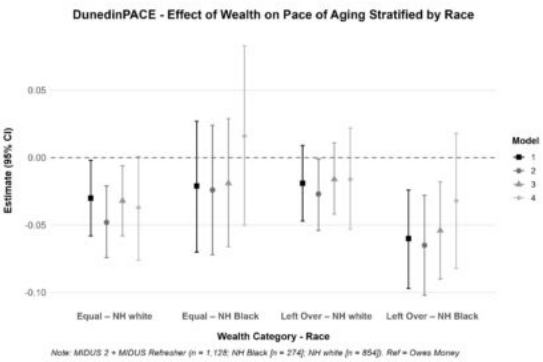
Self-reported wealth is associated with epigenetic aging in the Midlife in the United States (MIDUS) Study Koichi Sakakibara* Jourdyn Lawwrence Koichi Sakakibara A. Tai Simpson Stephanie M. Hernandez Agus Surachman Yanping Jiang Jourdyn A. Lawrence

Introduction: Recent literature has linked wealth to morbidity and mortality, but its biological embodiment remains understudied. This study examined the relationship between self-reported wealth and epigenetic aging (EA), a critical biological predictor of age-related chronic health conditions. Method: We used pooled cross-sectional data from 274 non-Hispanic Black and 854 non-Hispanic white participants in the Midlife in the United States (MIDUS) Study Wave 2 and Refresher (mean age=54, 55% female). EA was assessed using five epigenetic clocks (Hovarth, Hovarth2, Hannum, PhenoAge, and GrimAge) and one pace-of-aging measure (DuendinPACE). Self-reported wealth reflected an assessment of whether the participant's household would break even, have money remaining, or still owe after liquidating assets and paying any debts. Linear regression models were fit to assess relationships between self-reported wealth and EA. Models were also stratified by self-identified race. Results: Adjusted for age and sex, individuals reporting"debts would just about equal assets" showed significantly slower aging compared to those who reported they "would still owe money" using PhenoAge, GrimAge2, and DunedinPACE. Associations remained after adjusting for sociodemographic and health-related variables. Participants who reported they "would have money left over" also had a slower aging trend compared to those who reported "would still owe money", but the 95% CIs overlap with those of "just about equal" (B: -0.044 CI: -0.073, -0.014, and B: -0.057 CI:-0.088, -0.027, respectively in DunedinPACE). The stratified analyses presented overlapping 95% CIs between non-Hispanic Black and non-Hispanic white adults across EA. Conclusion: This study highlights the role of individuals' perception of their wealth status in health and aging. These findings demonstrate how wealth and wealth inequality can be embodied through biopsychosocial processes.


Effect of Wealth on Epigenetic Aging
Hovarth
Hovarth2
Hannum
PhenoAge
GrimAge2
Estimate (95% CI)
Equal
Left Over
Wealth Category
Model 1 2 3 4
Note: MIDUS 2 + MIDUS Refresher (n = 1,128). Ref = Owes Money


DunedinPACE - Effect of Wealth on Pace of Aging
0.00
-0.04
-0.08
-0.12
Estimate (95% CI)
Equal
Left Over
Wealth Category
Model 1 2 3 4
Note: MIDUS 2 + MIDUS Refresher (n = 1,128). Ref = Owes Money


Effect of Wealth on Epigenetic Aging Stratified by Race
Hovarth
Hovarth2
Hannum
PhenoAge
GrimAge2
Estimate (95% CI)
Equal – NH white
Equal – NH Black
Left Over – NH white
Left Over – NH Black
Wealth Category - Race
Model 1 2 3 4
Note: MIDUS 2 + MIDUS Refresher (n = 1,128; NH Black [n = 274]; NH white [n = 854]). Ref = Owes Money


DunedinPACE - Effect of Wealth on Pace of Aging Stratified by Race
0.05
0.00
-0.05
-0.10
Estimate (95% CI)
Equal – NH white
Equal – NH Black
Left Over – NH white
Left Over – NH Black
Wealth Category - Race
Model
1
2
3
4
Note: MIDUS 2 + MIDUS Refresher (n = 1,128; NH Black [n = 274]; NH white [n = 854]). Ref = Owes Money

Aging

Cancer History and Risk of Alzheimer's Disease in Women: A Nested Case–Control Study in the NYU Women's Health Study Xiaolan Zhao* Xiaolan Zhao Fen Wu Karen L. Koenig Alan A. Arslan Yelena Afanasyeva Anne Zeleniuch-Jacquotte Yu Chen

Abstract

Background: Previous observational studies have reported an inverse association between cancer and Alzheimer's disease (AD). However, important knowledge gaps remain, including whether this inverse relationship is consistent across cancer subtypes.

Methods: The New York University Women's Health Study (NYUWHS) enrolled 14,273 AD-free women aged 35–65 years between 1985 and 1991 and followed them for over 30 years. Incident cancer diagnoses were ascertained through self-completed mailed questionnaires verified by medical records and tumor registries. AD diagnoses were ascertained through linkage with the Centers for Medicare & Medicaid Services (CMS). We conducted a nested case-control study of 1,632 AD cases identified through Medicare claims linkage and 2,911 controls selected using risk-set sampling matching on age, race/ethnicity, and Medicare coverage. We used conditional logistic regression to estimate odds ratios (ORs) and 95% confidence intervals (CIs) for the association between cancer and AD, adjusting for potential confounders. Inverse probability weights based on selection predictors were applied in weighted conditional logistic regression models.

Results: Overall, a history of any cancer prior to AD was associated with lower odds of subsequent AD during follow-up compared with no cancer history (OR = 0.80, 95% CI = 0.70–0.92). In IPW-weighted analyses, the 95% CI was slightly narrower (OR = 0.80, 95% CI = 0.75–0.87). When assessing associations for each specific cancer, the inverse association was more pronounced for breast cancer (OR = 0.80, 95% CI = 0.73–0.88), endometrial cancer (OR = 0.73, 95% CI = 0.55–0.95), and melanoma (OR = 0.60, 95% CI = 0.49–0.74).

Conclusions: Among women in a long-term prospective cohort, cancer history was associated with reduced odds of developing AD, particularly hormone-related cancers.

Keywords: Alzheimer's disease, cancer, breast cancer, midlife risk factors, women's health, prospective nested case-control study

Aging

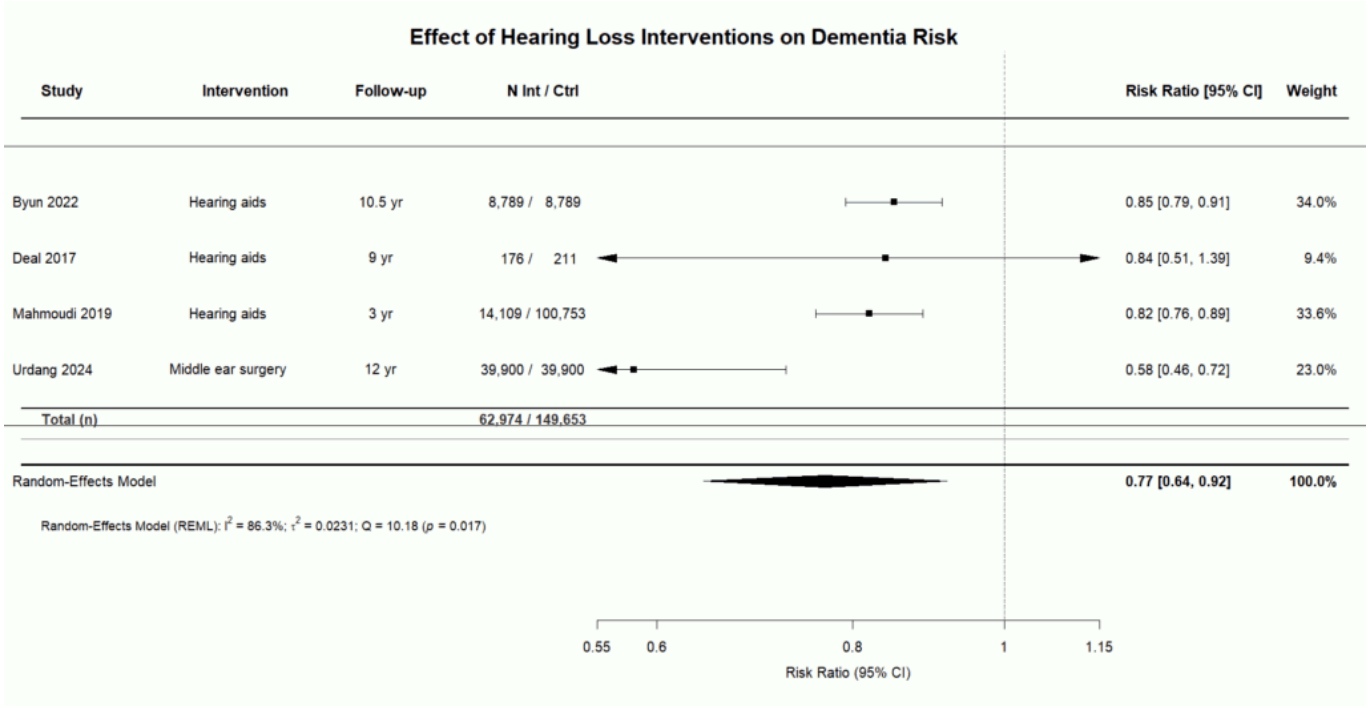
Impact of Hearing Interventions on Dementia Risk and Cognitive Decline in Older Adults with Hearing Loss Rhea Dcunha* Rhea Dcunha Shelli Vodovozov Christina Sheppler Carrie Patnode Melinda Davies Scott C. Zimmerman M. Maria Glymour Willa D. Brenowitz

Background: Hearing loss affects over 430 million people globally and is associated with dementia, but it is unclear whether hearing loss interventions are associated with dementia incidence.

Methods: We conducted a systematic review and meta-analysis of randomized and non-randomized controlled trials, cohort studies, and pre-post single arm studies evaluating the impact of hearing loss interventions on cognitive outcomes in adults aged ≥ 45 years with confirmed hearing loss. Studies among individuals with prevalent cognitive impairment, dementia, psychiatric disorders, HIV/AIDS, Down syndrome, Parkinson's disease, or non-dementia related conditions were excluded. Interventions included hearing aids, cochlear implants, and aural rehabilitation, compared with usual care or no intervention. The outcome was incident dementia. We searched MEDLINE and PsycInfo from inception through July 2025. Two reviewers independently screened studies. Results were pooled using random-effects meta-analysis, and publication bias was assessed via Egger's regression.

Results: Four studies reporting incident dementia (N = 212,627) were included. Studies were conducted in the US, South Korea, and multinational cohorts, with follow-up ranging from 3-12 years. All 4 studies were observational cohorts that used propensity score matching or multivariable adjustments to control for confounding. The pooled risk ratio was 0.77 (95% CI: 0.64–0.92), indicating receiving hearing interventions was associated with a 23% lower dementia risk (Figure 1). Substantial heterogeneity was observed (I^2 = 86.3%). No evidence of publication bias was detected (p = 0.61).

Conclusions: Our findings suggest treating hearing loss may be an important approach toward reducing the incidence of dementia. However, all included studies were observational, and residual confounding by health-seeking behavior and socioeconomic factors cannot be ruled out.


Effect of Hearing Loss Interventions on Dementia Risk
Study
Intervention
Follow-up
N Int / Ctrl
Risk Ratio [95% CI]
Weight
Byun 2022
Hearing aids
10.5 yr
8,789 / 8,789
0.85 [0.79, 0.91]
34.0%
Deal 2017
Hearing aids
9 yr
176 / 211
0.84 [0.51, 1.39]
9.4%
Mahmoudi 2019
Hearing aids
3 yr
14,109 / 100,753
0.82 [0.76, 0.89]
33.6%
Urdang 2024
Middle ear surgery
12 yr
39,900 / 39,900
0.58 [0.46, 0.72]
23.0%
Total (n)
62,974 / 149,653
Random-Effects Model
0.77 [0.64, 0.92]
100.0%
Random-Effects Model (REML): I² = 86.3%; τ² = 0.0231; Q = 10.18 (p = 0.017)
0.55
0.6
0.8
1
1.15
Risk Ratio (95% CI)

Aging

Evaluating individual socioeconomic status as a mediator for the effect of residential segregation and late-life cognition Yi Lor* Yi Lor Rachel L. Peterson Peter James Michelle J. Ko Kristen M. George Chinomnso Okorie Paola Gilsanz M. Maria Glymour Rachel A. Whitmer

Introduction: Possible mechanisms linking residential segregation to cognition remain unclear. We examined whether late-life socioeconomic status (SES) mediates the associations between midlife segregation and late-life cognition.

Methods: The KHANDLE and STAR cohorts include 2,476 ethnoracially diverse older adults (40% Black, 20% White, 17% Asian, 14% Latinx) with self-reported midlife (age 40) residence linked to census tract data (1970–2010). City-level residential segregation was assessed using dissimilarity (uneven distribution of ethnoracial groups across tracts within a city) and isolation (likelihood of interacting with same-group members in a city). Executive function (EF), verbal episodic memory (VEM), and semantic memory (SM) were assessed at baseline (2017-2018). Late-life SES (low vs. high) was defined using self-reported income, public assistance, and financial concerns. Regression-based mediation analysis decomposed the total effect (TE) of segregation on domain-specific cognition into the natural direct effect (NDE) and natural indirect effect (NIE) via SES for each race/ethnicity.

Results: Participants (mean age 73.9±8.5 years) were 62% female and 89% had a college/trade education or more. Among Asian participants, higher isolation was associated with worse EF (βTE=–0.76[95%CI:–1.35, –0.14], βNDE=–0.78[–1.35, –0.14]) but was not mediated by late-life SES (βNIE=0.02[–0.08, 0.09]); higher dissimilarity was associated with worse VEM (βTE=–0.42[–0.90, –0.03], βNDE=–0.42[–0.90, –0.03]) but was not mediated by SES (βNIE=0.02[–0.02, 0.05]). Among Latinx participants, higher isolation was associated with worse SM (βTE=–0.90[–1.73, –0.19], βNDE=–0.89[–1.74, –0.17]) but was not mediated by SES (βNIE=–0.01[–0.09, 0.06]); higher dissimilarity was not associated with late life cognition. No TE, NDE, or NIE were observed among Black participants.

Discussion: Late-life SES did not mediate the association between residential segregation and late-life cognition.

Table 1: The direct, indirect and total effect of midlife city-level racial residential segregation on late-life cognition through late-life socioeconomic status (SES)

	Executive Function	Semantic Memory	Verbal Episodic memory
	β (95% CI)	β (95% CI)	β (95% CI)
Asian-White Dissimilarity among Asian Participants			
Direct Effect	-0.13 (-0.52, 0.24)	-0.21 (-0.67, 0.29)	-0.44 (-0.91, -0.04)
Indirect Effect	0.01 (-0.04, 0.08)	0.03 (-0.03, 0.11)	0.02 (-0.02, 0.05)
Total Effect	-0.12 (-0.48, 0.25)	-0.18 (-0.64, 0.28)	-0.42 (-0.90, -0.03)
Black-White Dissimilarity among Black Participants			
Direct Effect	-0.16 (-0.50, 0.16)	0.12 (-0.24, 0.44)	-0.20 (-0.50, 0.14)
Indirect Effect	0.01 (-0.02, 0.04)	0.01 (-0.03, 0.05)	0.01 (-0.02, 0.04)
Total Effect	-0.15 (-0.48, 0.17)	0.12 (-0.24, 0.44)	-0.19 (-0.49, 0.15)
Latinx-White Dissimilarity among Latinx Participants			
Direct Effect	-0.27 (-0.81, 0.23)	0.24 (-0.40, 0.78)	-0.57 (-1.01, -0.06)
Indirect Effect	0.00 (-0.06, 0.05)	-0.01 (-0.08, 0.09)	0.00 (-0.04, 0.04)
Total Effect	-0.28 (-0.81, 0.22)	0.23 (-0.39, 0.79)	-0.57 (-1.02, -0.06)
Asian Isolation among Asian Participants			
Direct Effect	-0.78 (-1.35, -0.14)	-0.30 (-1.12, 0.50)	0.24 (-0.53, 1.05)
Indirect Effect	0.02 (-0.08, 0.09)	0.02 (-0.13, 0.12)	0.01 (-0.05, 0.07)
Total Effect	-0.76 (-1.35, -0.14)	-0.28 (-1.15, 0.53)	0.25 (-0.55, 1.05)
Black Isolation among Black Participants			
Direct Effect	-0.20 (-0.44, 0.07)	-0.03 (-0.28, 0.27)	-0.23 (-0.52, 0.06)
Indirect Effect	0.01 (-0.02, 0.03)	0.00 (-0.02, 0.04)	0.01 (-0.02, 0.04)
Total Effect	-0.19 (-0.44, 0.07)	-0.03 (-0.27, 0.28)	-0.23 (-0.51, 0.07)
Hispanic Isolation among Hispanic Participants			
Direct Effect	-0.59 (-1.54, 0.29)	-0.89 (-1.74, -0.17)	1.03 (-0.09, 2.13)
Indirect Effect	-0.02 (-0.12, 0.06)	-0.01 (-0.09, 0.06)	-0.05 (-0.20, 0.08)
Total Effect	-0.61 (-1.53, 0.24)	-0.90 (-1.73, -0.19)	0.98 (-0.12, 2.05)

*Models adjusted for age, gender/sex, education, parent education, midlife neighborhood SES, late-life

Aging

Examining the Joint Effects of Positive Spousal Social Support and Closeness on Dementia Risk using Causal Survival Analysis Nicola Churchill* Nicola Churchill Jacqueline Torres Roch Nianogo

Little is known about how different sources of social support work together to modify dementia risk, or how the quality of spousal relationships may amplify or constrain the cognitive benefits of broader social networks. Aspects of spousal relationship quality may help protect against dementia risk, including via mental health-related mechanisms. We evaluated the individual and joint effects of two measures of spousal relationship quality – perceived positive support and closeness – in association with dementia risk. We used data on respondents 50 years+ and their spouses to the U.S. Health and Retirement Survey (HRS), 2006-2020, focusing on those dementia/cognitively impaired but no dementia (CIND)-free and who were married or partnered at analytic baseline. Reporting closeness with spouse was associated with a greater risk of dementia (RR:1.07 95% CI:1.01, 1.14) and reporting positive support from a spouse was associated with a lower risk of dementia RR:0.87 95% CI:0.71, 1.06), with no meaningful variation by sex/gender. Among men, reporting both positive social support from and closeness with their spouse was associated with a greater risk of dementia (RR:1.06 95%CI:0.94, 1.19). Conversely, among women, reporting both positive social support from and closeness with their spouse was associated with a *lower* risk of dementia (RR:0.93 95%CI:0.84, 1.02). Our results suggest nuanced links between aspects of the spousal relationship with dementia risk, including by sex/gender and consideration of individual vs. joint exposures. Findings of association between spousal support and greater dementia risk could be influenced by reverse causation, whereby greater spousal closeness reflects caregiving dynamics in the context of early cognitive decline. Further research should address additional sources of bias (e.g. marital selection) and evaluate potential mechanisms to interrogate plausibility of observed associations.

Aging

Sex Differences in Dementia Prevenance in China and Taiwan: A Comparative Decomposition Analysis Yan-Jhu Su* Yan-Jhu Su Liying Luo

Background: Women have higher dementia risk than men across countries, yet the biopsychosocial factors underlying this sex gap remain unclear.
Methods: We analyzed nationally representative samples of adults aged ≥60 years from the 2018 China Health and Retirement Longitudinal Study (n=8,364) and the 2019 Taiwan Longitudinal Study of Aging (n=4,753). Population-level dementia prevalence was defined as the proportion of participants scoring ≤12 on Mini-Mental State Examination in China or ≤10 on the Montreal Cognitive Assessment in Taiwan. We considered biopsychological risk factors including education, cardiovascular problems, and health behaviors. Blinder–Oaxaca decomposition method was used to partition the male–female gap into differences due to endowment (population composition) and coefficient (association with dementia).
Results: In China, dementia prevalence was 3.9% among men and 13.9% among women (10.0 percentage-point [pp] difference, 95% CI: 11.4 to 8.6 pp). This sex difference was largely explained by endowments, particularly lower educational (6.2 pp) and higher IADL limitations (0.5 pp) among women, whereas coefficient changes played a small counterproductive role (4.5 pp). In Taiwan, dementia prevalence was 4.0% in men and 12.7% in women (8.7 pp difference, 95% CI: 10.2 to 7.1 pp). Similarly, most of the sex gap was attributable to endowments (8.0 pp), including lower education (5.0 pp), higher nonmarriage (0.8 pp), and more IADL limitations (0.8 pp), while coefficient effects were modest and nonsignificant.
Conclusions: Women in both China and Taiwan exhibit substantially higher dementia prevalence when using literature-based thresholds. In both datasets, sex differences are driven primarily by lower education and functional disadvantage rather than differential cardiovascular vulnerability or health behaviors, highlighting education and functional health as intervention opportunities for reducing sex difference in dementia prevalence cross populations.

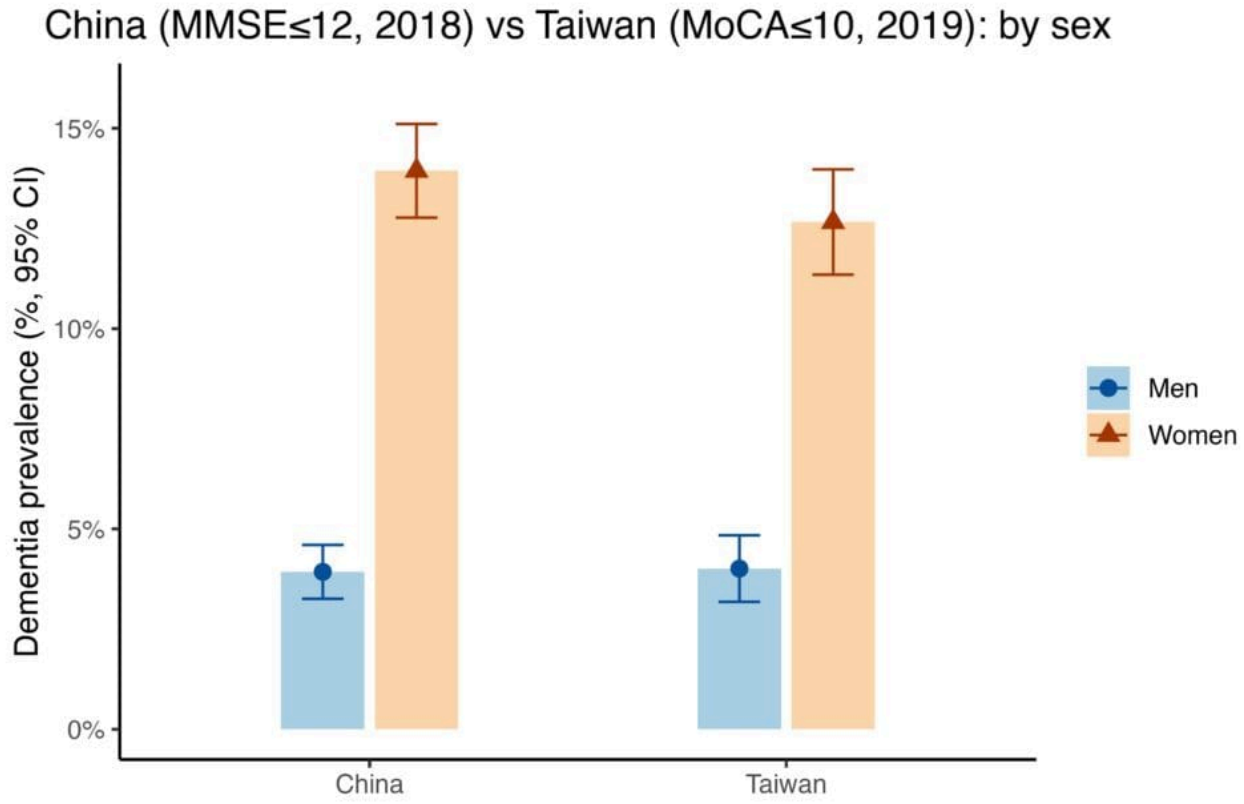


Figure 1. Dementia Prevalence by Sex in China (MMSE ≤12, 2018) and Taiwan (MoCA ≤10, 2019)

Aging

Evaluating time-varying pain status and memory: Evidence from the Health and Retirement Study Yulin Yang* Yulin Yang Anna M Pederson Scott C Zimmerman Paola Gilsanz Cynthia I Campbell Catherine A Shaefer M. Maria Glymour Ulrike Muench

The relationship between pain and cognitive decline is unclear, in part because of the fluctuating nature of pain. We evaluated time-varying high impact pain (HIP) on cognitive, accounting for time-varying confounding.

We analyzed data from 14,559 Health and Retirement Study participants over 12 biennial waves (1996-2018). The analytic sample consisted of participants aged 60 years or older at the end of follow-up. Baseline was defined as each participant's first wave with a valid cognitive assessment using the 10-word immediate- and delayed-recall tests. At each wave, HIP was defined as pain that limits every day activities (e.g., work or household chores) with the reference group of no pain/low impact pain. Memory was operationalized as the sum of immediate and delayed 10-word recall (range: 0-20). We fit linear mixed-effect models to estimate the association between lagged HIP and memory scores two years later, adjusted for baseline age, gender, race and ethnicity, and education. Stabilized inverse probability (IP) weights were estimated using logistic regression to account for baseline and time-varying confounding.

The average baseline age was 57.6 [SD=7.9] years (57.8 for those without HIP, and 57.2 with HIP). In unweighted models, HIP was associated with worse memory two years later (β= -0.24; 95% CI: -0.30,-0.18). After accounting for time-varying confounding, estimates for recent symptoms were attenuated (β= -0.05; 95% CI: -0.09, 0.05).

High-impact pain was associated with worse memory performance in unweighted models, but this association was substantially attenuated after accounting for time-varying confounding. These findings suggest that previously observed links between pain and memory loss may partly reflect dynamic health and social processes that co-evolve with pain over time. Future research should continue to model pain as a dynamic process and examine how cumulative exposure, severity, and specific pain progression types play a role in cognitive aging.

LATEBREAKER

Behavior

Examining Life Satisfaction as a Moderator of Housing Cost Burden Effects on Cigarette Smoking: A 2023 NHIS Analysis Bhumika Desai* Chia-Shuan Chang Bhumika Desai Ebbie Kalan Cheryl Knott

Background:
Housing cost burden is a well-established social determinant of health, but its influence on health behaviors is less
understood. This study examined the association between housing cost burden and cigarette smoking among U.S.
adults and assessed whether this relationship was moderated by life satisfaction.
Methods:
Data from adults aged ≥18 years (N = 27,715) in the 2023 National Health Interview Survey were analyzed. Housing
cost burden was defined as reporting an inability to pay mortgage, rent, or utility bills in the past 12 months. Current
cigarette smoking was coded as yes (smoked every day or some days) versus no. Life satisfaction was coded as
“satisfied” versus “dissatisfied” with life. A housing cost burden × life satisfaction interaction term with was included to
test moderation effects. Survey-weighted logistic regression models estimated odds ratios (ORs) and 95% confidence
intervals (CIs), adjusting for demographic and psychosocial covariates. Multicollinearity was assessed using variance
inflation factors (VIFs).
Results:
In unadjusted analyses, adults experiencing housing cost burden had significantly higher odds of current cigarette
smoking compared to those without housing cost burden (OR = 2.66; 95% CI: 2.33–3.04). After adjusting for
demographic and psychosocial covariates (age, sex, race, income, marital status, education, depressive symptoms,
and life satisfaction), the association remained significant but was attenuated (OR = 1.65; 95% CI: 1.42–1.91). A
significant interaction between housing cost burden and life satisfaction was observed (p = 0.036). Stratified analysis
revealed higher odds of current smoking among adults who reported being dissatisfied with life (OR= 2.40; 95% CI:
1.56–3.69) compared to those who reported being satisfied (OR= 1.55; 95% CI: 1.32–1.81), indicating effect
modification by life satisfaction. Although the magnitude of association differed by life satisfaction, the relationship
remained statistically significant.
Conclusion:
Housing cost burden is associated with a higher likelihood of current cigarette smoking. Life satisfaction moderates

this relationship, with a potential buffering effect against the impact of housing cost burden. Future longitudinal
research is needed to examine causal pathways. Integrating housing support with mental health and wellness
interventions may help reduce smoking risk among cost-burdened adults.

Behavior

Association of Stress on Ethanol Intake and Alcohol Use Disorder and the Role of Age at First Drink in this Relationship: An Epidemiological Study Tulshi Saha* Tulshi Saha

Purpose: The link between alcohol drinking, stress, and the development of alcohol use disorder (AUD) is a critical and fascinating area in epidemiologic research. The purpose of this study is to examine the association of different types of stress on ethanol intake and AUD and the role of age at the onset of drinking in this relationship using nationally representative data.

Data: Data were derived from the National Institute of Alcohol Abuse and Alcoholism's (NIAAA) 2012-2013 National Epidemiologic Survey on Alcohol and Related Conditions (NESARC)-III (n=36,309), 2001-2002 NESARC Wave 1 (n=43,093), and 2003-2004 NESARC Wave 2 (n=34,653).

Method: Bivariate and multivariate regression analyses were used to determine whether increased ethanol consumption volume and the risk of developing AUD increased with increasing exposure to multiple stressors, while controlling for socio-demographic variables. In addition, the age of onset of drinking was investigated as a modifying factor of the relationship between stress and alcohol use behavior.

Results: We **found** a positive association between stress and drinking behavior. Early-onset drinking increased the positive association of past-year stress level with the increased volume of ethanol intake or the probability of having AUD. The volume of ethanol intake increased proportionately at higher rates for a job or psycho-financial-related stress than for illness or death-related stress. Even after adjusting for background characteristics, increasing stress levels were associated with a more significant increase in alcohol consumption among individuals who started drinking at ages 14 and younger than among those who began drinking at older ages.

Conclusion: The results of this study have important implications for public health. They indicate that while experiencing stress predicts an increase in ethanol intake and the likelihood of developing AUD, this relationship differs by the nature of stress as well as the first drink. This understanding can guide the development of targeted interventions to address alcohol use disorder.

Cancer

Hispanic and Asian American/Pacific Islander ethnic enclave, neighborhood socioeconomic status, and renal cell carcinoma incidence in California Zhengyi Deng* Zhengyi Deng Annie Vu Hannah Begna Kevin L'Esperance Samuel L. Washington III David H. Rehkopf June M. Chan Benjamin I. Chung Shuchi Gulati Iona Cheng Marvin E. Langston Rebecca E. Graff

Objective: This study evaluated associations of neighborhood socioeconomic status (nSES) and ethnic enclave with renal cell carcinoma (RCC) incidence among Hispanic and Asian American/Pacific Islander (AAPI) populations in California.

Methods: We conducted a population-based study including 7476 Hispanic and 2266 AAPI individuals in the California Cancer Registry diagnosed with RCC during three peri-censal periods: 1988-1992, 1998-2002, and 2008-2012. Using race- and ethnicity-specific population counts from 1990, 2000, and 2010 Census data, we calculated incidence rates and incidence rate ratios (IRRs) across nSES and ethnic enclave quintiles and for cross-classified categories of binary nSES and binary ethnic enclave. Analyses were conducted overall and by sex, age at diagnosis, tumor histology, tumor stage, and time period.

Results: Higher nSES quintiles compared with the lowest quintile demonstrated positive IRRs for both Hispanic (IRRs ranged 1.04-1.13) and AAPI (IRRs ranged 1.14-1.40) individuals. Higher acculturation quintiles were also associated with positive IRRs in Hispanic (IRRs ranged 1.09-1.24) and AAPI individuals (IRRs ranged 1.01-1.21). Compared with low nSES/less acculturated neighborhoods, residing in high nSES and/or more acculturated neighborhoods showed increased RCC incidence in both populations. These associations were generally similar according to sex, age at diagnosis, and tumor histology and were mainly observed for localized stage RCC. Differences in incidence rates by nSES emerged in later time periods in both populations, whereas differences by acculturation level were consistent over time in the Hispanic population only.

Conclusion: We observed higher RCC incidence among Hispanic and AAPI individuals residing in higher nSES and more acculturated neighborhoods. These patterns may reflect differences in access to healthcare and RCC diagnosis, as well as potential etiologic influences of neighborhood factors.

Cancer

Body Mass Index- and Waist-Hip Ratio-defined Obesity and Risk of Hypertension in Female Cancer Survivors MAHFUJA LUNA* Mahfuja Luna Olabowale Olola Hazel B. Nichols Katie M. O'Brien Michael G. Fradley Daehyun Lee Mario Schootman Michael R. Thomsen Benjamin C. Amick III Clarice R. Weinberg Dale P. Sandler Yong-Moon Mark Park

Background: Cardiotoxic treatments and lifestyle changes after cancer diagnosis may alter the impact of risk factors for hypertension, such as central or overall obesity, in survivor populations.

Methods: We assessed obesity in relation to hypertension risk among 1,151 women ages 35-74 years who enrolled in the Sister Study in 2003-2009 with a history of prior cancer (excluding breast cancer). Blood pressure, weight, height, and waist and hip circumference were examiner-measured at enrollment. Eligible participants were hypertension-free (systolic/diastolic blood pressure <140/90 mmHg, no prior hypertension diagnosis or antihypertensive medication use) at enrollment. Incident hypertension was defined as self-reported physician diagnosis or antihypertensive medication use through Sept 2021. Obesity was defined by body mass index (BMI)≥30 kg/m2 or waist-hip ratio (WHR)≥0.85, in four phenotypes (none, WHR-only, BMI-only, and both WHR/BMI obesity). Multivariable Cox regression models were used to estimate hazard ratios (HR) and 95% confidence intervals (CI) for hypertension risk.

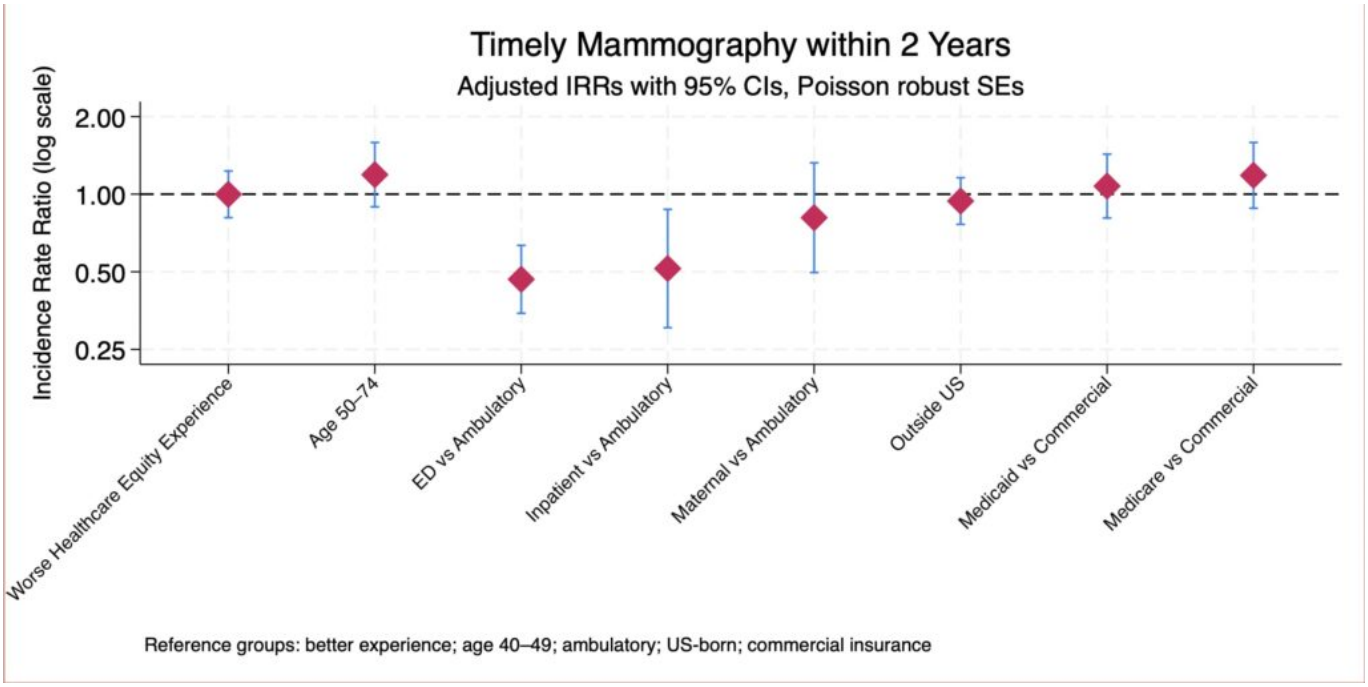
Results: Among 1,151 female survivors, 14.5% met thresholds for obesity by WHR only, 11.6% by BMI only, and 9.4% by both. Over follow-up (median=11.6 years), 400 women (34.8%) developed hypertension. Compared with no obesity, obesity by BMI (HR 1.66, 95% CI 1.20-2.29) and both WHR/BMI (HR 1.63, 95% CI 1.18-2.26) was associated with increased risk of hypertension; WHR-only associations were not statistically significant (HR 1.24, 95% CI 0.92-1.67). There was no evidence of multiplicative interaction. BMI-based "overweight" (≥25 kg/m^2) was also positively associated with hypertension risk (BMI-only: HR 1.29, 95% CI 1.01-1.63; WHR/BMI: HR 1.52, 95% CI 1.14-2.01). Associations did not depend on time since cancer diagnosis.

Conclusion: Obesity defined by BMI alone or combined with WHR (as a measure of central obesity) was positively associated with hypertension incidence in female cancer survivors.

Cancer

Patient-Reported Equity Experiences, Care Setting, and Timely Mammography in an Urban Hospital in Central Brooklyn Moyouri Bhattacharjee* Moyouri Bhattacharjee Gwendolyn Lewis Aimee Afable Victor Puac-Polanco

Despite improvements in guideline-based care, disparities in breast cancer screening rates persist. The objective of this study was to determine whether negative healthcare equity experiences are associated with delays in breast cancer screening rates in an urban hospital system. We conducted a longitudinal observational analysis linking health equity experience data from the Brooklyn Health Equity Index (BKHI) survey to EHR records of mammography completion over a two-year follow-up period. The final sample included 678 women aged 40–74, who completed the 10-item BKHI during an index hospital encounter at a central Brooklyn health system and were eligible for breast cancer screening. Patient health equity experience was summarized using latent class analysis (LCA) to identify 2 common experience profiles. The outcome was timely mammography, defined as receipt of screening within two years of the index encounter. We used multivariable Poisson regression with robust standard errors, and adjusted for age, care-setting, nativity, and insurance coverage type. Participants were predominantly Black (91.0%), aged 50–74 years (78.5%), and publicly insured (Medicaid 42.6%; Medicare 32.0%), and 34.2% completed a mammogram. Latent patient experience class was not associated with timely mammography after adjustment (IRR 1.00; 95% CI 0.81–1.23). However, care setting showed strong associations, with emergency department encounters (IRR 0.47; 95% CI 0.35–0.63) and inpatient encounters (IRR 0.51; 95% CI 0.30–0.87) associated with lower screening rates, compared to ambulatory encounters. Age group, nativity, and insurance type were not independently associated with screening in adjusted models. Our models showed no statistically significant difference by health equity experience class, and improvements in breast cancer screening rates may need to focus on care-setting specific processes that support preventive follow-up, in addition to patient health equity experience.



Cancer

Oral contraceptive use and the expression of stromal markers in benign breast tissue

Maisey Ratcliffe* Maisey Ratcliffe Yujing J. Heng Brian Sardella Bernard Rosner Rulla Tamimi Lusine Yaghjyan

Purpose:

Oral contraceptives (OC) have been shown to influence breast cancer (BCa) risk, particularly among current and recent users. Breast stroma, particularly fibroblasts, may play an important role in breast carcinogenesis. It is unclear whether OCs can influence stromal fibroblasts. We investigated, for the first time, the association of OCs with the expression of stromal fibroblast markers alpha-smooth muscle actin (αSMA), tenascin-C (TNC), fibroblast activation protein (FAP), calcyclin (s100A6), and matrix metallo-peptidase (MMP14).

Methods:

This study included cancer-free women with biopsy-confirmed benign breast disease (BBD) from an incident BBD study within the Nurses' Health Study II cohort. OC use and BCa risk factor data were obtained from biennial questionnaires. Immunofluorescence (IF) of stromal markers was performed on tissue microarrays. The % positivity for each core was quantified using inForm v2.6.0. Generalized linear regression was used to examine the associations of OCs (use status, total duration, age at 1st and last use, and time since last use) with log-transformed marker expression, adjusted for relevant BCa risk factors.

Results:

Among 693 cancer-free women, OC use status at biopsy was positively associated with FAP expression (current vs. never β=0.99, 95% Confidence Interval [CI] 0.08, 1.90; past vs. never β=0.59, 95% CI 0.06, 1.12; p-trend=0.01). Total duration of use was positively associated with TNC (β per 1-year=0.08, 95% CI 0.02, 0.15; β for ≥10 vs. ≤1-year=1.24, 95% CI 0.06, 2.41; p-trend=0.03). No associations were found for αSMA, s100A6, and MMP14. Age at 1st use, years since last use, age at last use, and use before 1st pregnancy were not associated with any of the markers.

Conclusion:

Our findings suggest increased breast stromal fibroblast activity (as captured by higher FAP and TNC expression) in current and past OC users, and those with longer total duration of OC use. Further studies are needed to confirm these findings.

Cancer

The Burden of Cancer Among Middle Eastern and North African (MENA) Populations in the US: A Systematic Review Madison Willard* Madison Willard Florence J Dallo Annabel Shaffou

Background

Cancer is the second leading cause of death in the United States (US), yet cancer burden is unknown for Middle Eastern and North African (MENA) populations. Until recently, individuals of MENA descent were aggregated into the “White” ethnic and racial classification, limiting the ability to identify cancer incidence patterns, stage at diagnosis, and disparities unique to this population.

Purpose

This systematic review synthesizes existing evidence on cancer incidence, risk factors, screening behaviors, and interventions among MENA populations.

Methods

PRISMA-ScR guidelines were followed to compile cancer research. PubMed, EMBASE, and CINAHL were searched through October 10, 2026. Of 2,300 records identified, 28 articles met inclusion criteria of primary or cross-sectional research on MENA populations in the US. Descriptive statistics were calculated.

Results

Among included studies 29.6% collected primary data and 70.4% were cross-sectional. Individuals were identified as MENA (37.0%), Somali (22.2%), and Iraqi (11.1%). Most studies took place in Michigan and California. Cancers studied included breast (29.6%), colorectal (18.5%), prostate (14.8%), and cervical (14.8%). Among studies examining incidence and stage at diagnosis, 71.4% reported higher cancer incidence and 85.7% reported higher late-stage diagnosis among foreign-born MENA individuals compared to US-born MENA individuals and Non-Hispanic Whites.

Discussion

This review emphasizes the health and disease status of MENA Americans, finding higher cancer burden and later-stage diagnosis among foreign-born MENA populations. Breast cancer was most frequently reported with the highest incidence rate, followed by prostate, colorectal, and cervical cancers. Additional quantitative and qualitative studies are needed to clarify these disparities and inform specific interventions for MENA populations.

Cancer

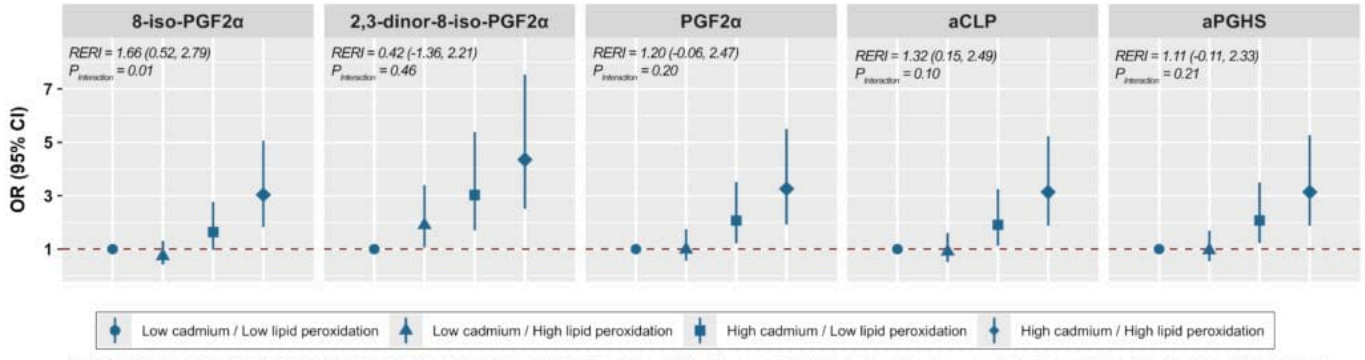
Associations of lipid peroxidation biomarkers with renal cell carcinoma and interactions with metals and micronutrients Wei-Jen Chen* Wei-Jen Chen Chih-Yin Wu Chao-Yuan Huang Yu-Mei Hsueh

Oxidative stress is a key biological mechanism linking environmental exposures to renal cell carcinoma (RCC). Experimental evidence suggests that increased lipid peroxidation in renal proximal tubules contributes to renal carcinogenesis. Given that 8-isoprostaglandin-F2α (8-iso-PGF2α), a reliable biomarker of lipid peroxidation, has been associated with kidney failure, we aimed to investigate the associations of lipid peroxidation biomarkers with RCC and their interactions with metal exposure and micronutrients.

We conducted a clinic-based case-control study of 204 incident RCC cases and 628 matched non-cancer controls in Taipei City, Taiwan. At enrollment, blood cadmium and lead and plasma selenium, folate, and vitamin B12 were quantified. Urinary lipid peroxidation biomarkers [8-iso-PGF2α, 2,3-dinor-8-iso-PGF2α, and prostaglandin-F2α (PGF2α)] were measured, and 8-iso-PGF2α fractions from chemical (aCLP) and enzymatic (aPGHS) pathways were characterized. Multivariable logistic regression examined associations of each metal, micronutrient, and lipid peroxidation biomarker with RCC. Combined effects of exposures (metals or micronutrients) and lipid peroxidation biomarkers on RCC were evaluated on additive and multiplicative scales.

All lipid peroxidation biomarkers were positively associated with RCC. Compared with participants with low cadmium/low 8-iso-PGF2α (or aCLP), the OR for RCC was elevated among those with high cadmium/high 8-iso-PGF2α (or aCLP), with positive interaction on both additive and multiplicative scales. For micronutrients, the OR for RCC was also elevated among participants with low plasma folate and high aCLP, with evidence of a positive interaction. No interactions were identified for lead, selenium, and vitamin B12 with lipid peroxidation biomarkers.

Our study provides evidence of the combined effects of selected metals/micronutrients and lipid peroxidation on RCC, providing insights into potential mechanisms underlying environmentally related RCC.



Combined effects of blood cadmium and lipid peroxidation biomarkers on RCC. Abbreviations: RERI, relative excess risk due to the interaction; $P_{interaction}$, *p*-value for the product term of the interaction; aCLP, absolute concentrations of chemical lipid peroxidation; aPGHS, absolute concentrations of prostaglandin-endoperoxide synthases. Low and high concentrations of blood cadmium were defined using the median values among controls (1.26 μg/L). Low and high concentrations of lipid peroxidation biomarkers were defined using the median values among controls (8-*iso*-$PGF_{2\alpha}$: 0.200; 2,3-dinor-8-iso-$PGF_{2\alpha}$: 0.393; $PGF_{2\alpha}$:0.597; aCLP: 0.084; aPGHS: 0.083 μg/g creatinine). The models were adjusted for age, sex, educational level, smoking status, consumption of alcohol, tea, coffee, and diabetes and hypertension status.

Cancer

A prospective investigation on DNA methylation-based inflammation risk scores and lung cancer among never smokers Mohammad Rahman* Mohammad Rahman Aishani Gargapati Wei Zheng Jason Y.Y. Wong Lauren Hurwitz Batel Blechter Wei Hu Qiuyin Cai Jirong Long Yu-Tang Gao Nathaniel Rothman Xiao-Ou Shu Qing Lan

Introduction: Inflammation plays a key role in carcinogenesis. We previously observed an inverse association between plasma C-reactive protein (CRP) and lung cancer risk among never-smokers. CRP fluctuates with acute inflammation, and a single measurement may not capture inflammation relevant for carcinogenesis. DNA methylation–based inflammation risk scores (DNAm-IRS) may better reflect longer-term inflammatory biology. Here, we evaluate DNAm-IRS with lung cancer among never-smokers.

Methods: This nested case-control study included 683 never-smoking women with incident lung cancer and 683 matched controls from the Shanghai Women's Health Study. Four DNAm-IRS were calculated as weighted sums of CRP-related CpG sites using established algorithms: IRSLigthart (52 CpGs), IRSElnet (1,334 CpGs), IRSWielscher (1,333 CpGs), and IRSHillary (32,196 CpGs). Conditional logistic regression, adjusting for age and body mass index, was used to evaluate associations with overall lung cancer and lung adenocarcinoma, the most common histologic subtype among never smokers.

Results: Among controls with plasma CRP data (n = 214), Spearman correlations between biochemical CRP and DNAm-IRS were 0.20 ($p= 3.4\times10^{-3}$) for IRSLigthart, 0.31 ($p= 4.6\times10^{-6}$) for IRSElnet, 0.13 ($p= 6.7\times10^{-2}$) for IRSWielscher, and -0.02 ($p= 7.4\times10^{-1}$) for IRSHillary. Higher DNAm-IRS was associated with lower lung cancer risk among never-smoking women. Per SD increase, IRSWielscher was associated with reduced risk of overall lung cancer (OR=0.87; 95% CI: 0.77–0.97; p=0.017) and lung adenocarcinoma (OR=0.83; 95% CI: 0.71–0.97; p=0.018). IRSLigthart was also inversely associated with overall lung cancer risk (OR=0.85; 95% CI: 0.78–0.97; p=0.003).

Conclusion: Our results suggest that, in the absence of a prevailing inflammatory trigger such as smoking, select CRP-related DNAm signatures are associated with lower lung cancer risk. Replication and mechanistic studies are needed.

Cancer

Evaluating the Effect of Continued FIT Screening: A Target Trial Emulation Using the Clone–Censor–Weight Method Buket Öztürk Esen* Buket Öztürk Esen Lars Pedersen

Background: The effectiveness of the fecal immunochemical test (FIT) in reducing colorectal cancer (CRC) mortality is well-known. However, studies evaluating the effect of attending a second FIT screening following a negative initial result remain limited.

Objective: To evaluate the effect of attending a second FIT screening on CRC-specific mortality and CRC diagnosis risk among individuals with an initial negative FIT.

Methods: We conducted a cohort study of 622,265 individuals with an initial negative FIT. We used an emulated trial design with clone–censor–weight (CCW) methodology to compare two screening strategies: 1) attending a second FIT screening, versus 2) not attending a second FIT screening.

Results: At 6-year follow-up, the risk of CRC-specific mortality was 0.07% (95% CI: 0.06%; 0.08%) for those attending a second FIT screening versus 0.17% (95% CI: 0.14%; 0.21%) for those not attending. This resulted in a relative risk (RR) of 0.39 (95% CI: 0.30; 0.52) and a risk difference (RD) of -0.10% (95% CI: -0.14%; -0.07%). For CRC diagnosis, the 6-year risk was 0.63% (95% CI: 0.61%; 0.66%) in the attendance group versus 0.66% (95% CI: 0.59%; 0.74%) in the non-attendance group, yielding an RR of 0.96 (95% CI: 0.85; 1.08) and an RD of -0.03% (95% CI: -0.11%; 0.05%).

Conclusion: Participation in a second FIT screening following an initial negative result reduces the relative risk of CRC-specific mortality. However, even though the RR is large, the RD is small. Furthermore, despite the use of the CCW method to mitigate bias, residual selection bias due to unmeasured factors cannot be ruled out. This indicates that while the intervention is effective in relative terms, the absolute benefit is small due to the low baseline risk in the years immediately following a negative FIT, which may inform discussions on optimal screening intervals.

Cancer

Population differences in the association between lactate dehydrogenase and survival outcomes in multiple myeloma Malaika Jade Mason* Malaika Jade Mason Brian C. Chiu

Elevated lactate dehydrogenase (LDH) is an established prognostic factor in multiple myeloma (MM). Studies of lymphoma and some solid tumors have reported racial differences in elevated LDH and survival, but whether this difference exists in MM is largely unknown. We evaluated the association between elevated LDH and overall survival (OS)/progression-free survival (PFS) among African American (AA) and European American (EA) patients with newly diagnosed MM in two prospective cohorts: the UChicago Multiple Myeloma Epidemiology study (UCMME) and the Multiple Myeloma Research Foundation (MMRF) CoMMpass study. Vital status for both studies was ascertained from the National Death Index. LDH was defined as normal (≤240 U/L) or elevated (>240 U/L). OS was defined as time from diagnosis to death from any cause. PFS was defined as time from diagnosis to a progression event or death. Multivariable Cox proportional hazards models adjusted for age and relevant clinical factors were used to calculate HRs and 95% CIs for survival outcomes. Among patients with available LDH measurements (UCMME: EA=325, AA=124; MMRF: EA=441, AA=88), 147 deaths (EA=94, AA=49) occurred in the UCMME cohort (median follow-up 69.2 months) and 134 deaths (EA=105, AA=29) occurred in the MMRF cohort (median follow-up 38.3 months). In both cohorts, elevated LDH was associated with worse OS [UCMME HR: 1.7 (1.2, 2.5); MMRF HR: 1.6 (1.0, 2.3)]. When stratified by race, elevated LDH was associated with worse OS among EA patients [UCMME HR: 2.0 (1.3, 3.3); MMRF HR: 1.6 (1.0, 2.5)], while elevated LDH was not significantly associated with OS for AA patients in either cohort [UCMME HR: 1.3 (0.7, 2.3); MMRF HR: 0.4 (0.1, 1.3)]. Similar patterns were observed for PFS. In both datasets, elevated LDH was associated with worse OS and PFS for EA patients, but not AA patients. Our findings suggest that whereas elevated LDH has been associated with poor MM outcomes, this needs to be separately considered for AA patients.

Cancer

Dimensions of Social and Environmental Vulnerability and Ovarian Cancer Risk and Mortality Rachel Pomazal* Rachel Pomazal Minh Tung Phung Amy Schultz Ronald Gangnon Shaneda Warren Andersen Amy Trentham-Dietz

Background: Ovarian cancer is the fifth leading cause of cancer-related death among women in the U.S. Some evidence suggests that environmental pollutants and social economic status are associated with ovarian cancer risk and mortality. Environmental and social factors are typically analyzed separately, though they often co-occur. This study evaluated the association between environmental and social factors, jointly and separately, with ovarian cancer risk and mortality.

Methods: We used data from an ovarian cancer case-control study (592 cases, 3489 controls) and publicly available data on social and environmental vulnerability indicators. We constructed a modified environmental justice index (EJI), which included dimensions of environmental and social vulnerability, based on 8 domains: air pollution, hazardous sites, the built environment, transportation, neighborhood SES, housing type, household characteristics, and racial/ethnic minority proportion. The EJI ranged from 0 to 8, with higher scores indicating more vulnerability. We used hierarchical logistic regression and Cox proportional hazards regression to assess associations between the EJI, its domains and its components with ovarian cancer risk and mortality.

Results: Domains of social and environmental vulnerability were similar between cases and controls, with limited racial diversity in the sample. Neither the EJI overall nor the domains were associated with ovarian cancer risk or mortality. A tertile increase in air pollution exposure was associated with 10% higher risk (95% CI: 0.99, 1.22) but not mortality (HR 0.99, 95% CI 0.84,1.15).

Conclusions: Air pollution may represent a modifiable risk factor for ovarian cancer risk. Further analyses will pursue mixtures analysis methods and more granular air pollution exposure assessment to further investigate factors associated with ovarian cancer risk and mortality. Future studies with more diverse populations are warranted.

Figure 1a. Adjusted OR (95% CI) of ovarian cancer risk according to the modified EJI and its domains

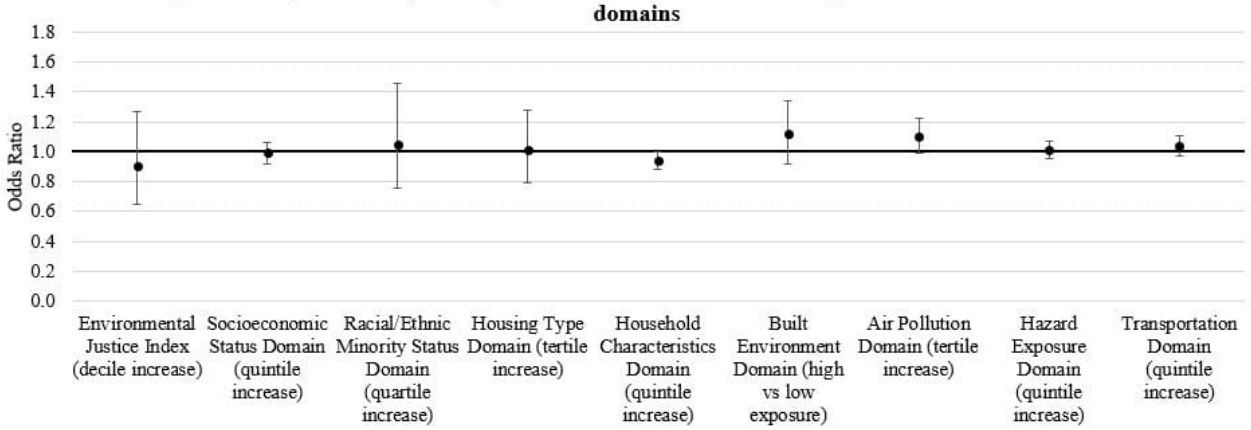
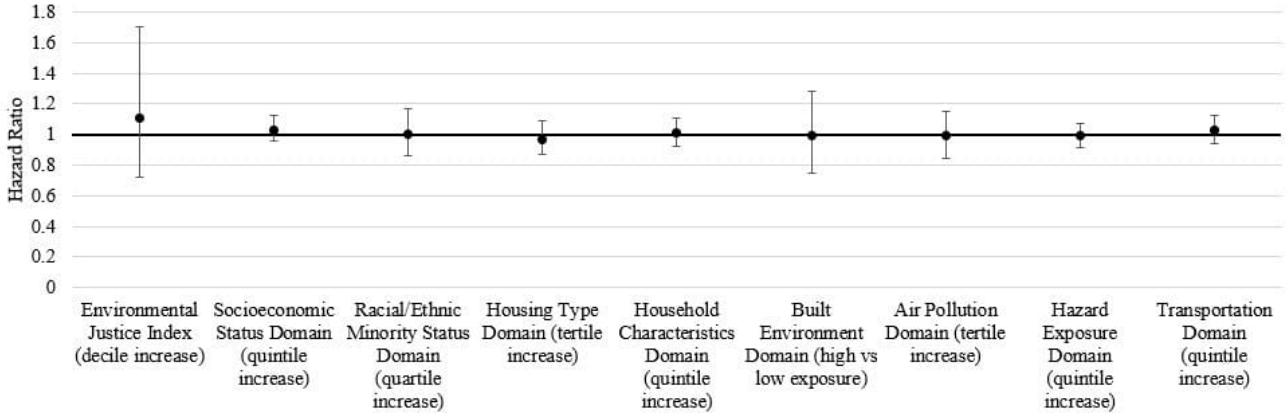


Figure 1b. Adjusted HR (95% CI) of ovarian cancer mortality according to the modified EJI and its domains



LATEBREAKER

Cancer

Geographic and Racial Variation in Prostate Cancer Incidence and Mortality: A Comparative Analysis of the U.S., New York State, and the Bronx Daleep Grewal* Daleep Grewal Ilir

Background: Prostate cancer (PCa) is the most commonly diagnosed cancer and the second leading cause of cancer-related death among men in the U.S. The Bronx has experienced higher PCa incidence and mortality rates than the national average. This study examined trends in PCa incidence and mortality across racial, ethnic, and geographic groups to identify patterns contributing to disparities.

Methods: PCa incidence data (2000–2018) were obtained from the Surveillance, Epidemiology, and End Results (SEER) Program and the New York State Cancer Registry. Population denominators were derived from the 2000 U.S. Census data. Age-adjusted incidence and mortality rates were compared across the U.S., New York State, New York City, and the Bronx, focusing on non-Hispanic Whites (NHWs), non-Hispanic Blacks (NHBs), and Hispanic men. SEER*Stat software was used to calculate average annual percentage changes (APCs) and 95% CIs to assess trends by race, ethnicity, and region.

Results: While PCa incidence and mortality declined nationally between 2000–2018, decreases were significantly slower in the Bronx. The APC in Bronx PCa incidence was smallest among NHBs and Hispanic men (−2.9; 95% CI: −3.8, −2.1) compared with NHWs (−3.4; 95% CI: −4.6, −2.2). PCa mortality declined more among NHBs (−3.7; 95% CI: −4.0, −3.4) than among NHWs (−2.7; 95% CI: −3.0, −2.4) or Hispanics (−2.6; 95% CI: −2.9, −2.2). A higher proportion of distant-stage PCa occurred in the Bronx during 2014–2018, particularly among NHB and NHW men.

Conclusions: Geographic and racial disparities in PCa persist, with the Bronx disproportionately affected. Elevated PCa rates may reflect the Bronx's larger male population of African ancestry and structural barriers to timely diagnosis and treatment. Higher mortality among Bronx NHWs may reflect inequities in access to care and underscores the need for improved early detection and post-PCa management. Updated analyses are underway to assess recent regional patterns.


”]

LATEBREAKER

Cancer

Associations between greenspaces and cancer outcomes in the U.S: the NIH-AARP Diet and Health study Jeonggyo Yoon* Jeonggyo Yoon Chris Lim

Greenspace exposure has been linked to various health outcomes, but evidence for cancer remains scarce and inconsistent. Few longitudinal studies have incorporated time-varying measures of greenness, cancer subtypes, and comprehensive adjustment for confounders. We investigated the long-term effects of greenspace exposure on cancer mortality, incidence, and survivorship in the U.S. NIH-AARP Diet and Health Study. We included 417,148 cancer-free participants enrolled in 1995–1996 and followed through 2011. Residential greenness was quantified using the Normalized Difference Vegetation Index (NDVI) from Landsat images with 30 m X 30 m spatial resolution and linked to participants at the census tract level. Cox proportional hazards models with time-varying exposures were used to capture changes in greenness over time, adjusting for demographic, socioeconomic, and behavioral factors (age, sex, race/ethnicity, education level, smoking history, physical activity level, and BMI). Survival time was calculated for each cancer outcome (mortality, incidence, and survivorship) for obesity-related cancers. Among cancer patients, individuals with higher exposure to green spaces had a lower mortality risk from all-types of cancer and lung cancer, with hazard ratios of 0.87 (95% CI: 0.79–0.95) and 0.92 (95% CI: 0.89–0.96), respectively. We provided large-scale longitudinal evidence on whether long-term residential greenspace exposure is associated with cancer mortality, incidence, and survivorship across multiple cancer sites. Our findings are expected to inform urban planning and public health policies that seek to leverage greenspace as a potential component of cancer prevention and survivorship support in aging populations.

LATEBREAKER

Cardiovascular

Serum Perfluoroalkyl Substances and Hypertension Risk in U.S. Adults Felix Opoku* Felix Opoku Asa Bradman Alec Chan-Golston

Background

Hypertension is a leading contributor to global cardiovascular disease burden. Per- and polyfluoroalkyl substances (PFAS) are persistent environmental contaminants widely detected in U.S. adults and have been implicated in cardiovascular dysfunction. However, epidemiologic evidence linking PFAS exposure to hypertension is limited and inconsistent. We therefore examined the association between serum PFAS concentrations and hypertension in a nationally representative sample of U.S. adults.

Methods

We conducted a cross-sectional analysis using data from the 2017–2020 National Health and Nutrition Examination Survey (NHANES), a nationally representative survey of the U.S. population conducted at the Centers for Disease Control and Prevention (CDC). The study included adults aged ≥20 years with complete data on serum PFAS concentrations, blood pressure measurements, and relevant demographic and laboratory covariates.

Results

The analytic sample included 2,551 U.S. adults aged ≥20 years. Perfluorooctane sulfonic acid (PFOS) and perfluorooctanoic acid (PFOA) were detected in 100% of participants, while perfluorohexane sulfonic acid (PFHxS) and perfluorononanoic acid (PFNA) were detected in 98.4% and 94.8% of participants, respectively. PFAS concentrations varied significantly by age, sex, race/ethnicity, smoking status, income, and body mass index, with higher levels observed among older adults and males (all $p < 0.001$). Participants with high blood pressure had slightly higher PFOS concentrations than those with normal blood pressure. In multivariable logistic regression models, serum PFOA concentrations were inversely associated with hypertension (OR = 0.71, 95% CI: 0.55, 0.92), whereas PFOS, PFHxS, and PFNA were not significantly associated with hypertension. Older age, non-Hispanic Black and Asian race/ethnicity, and overweight/obesity were independently associated with higher odds of hypertension.

Conclusion

Our findings suggest that PFAS exposure is nearly universal among U.S. adults. While serum PFOA concentrations were inversely associated with hypertension, no significant associations were observed for other PFAS compounds.

Cardiovascular

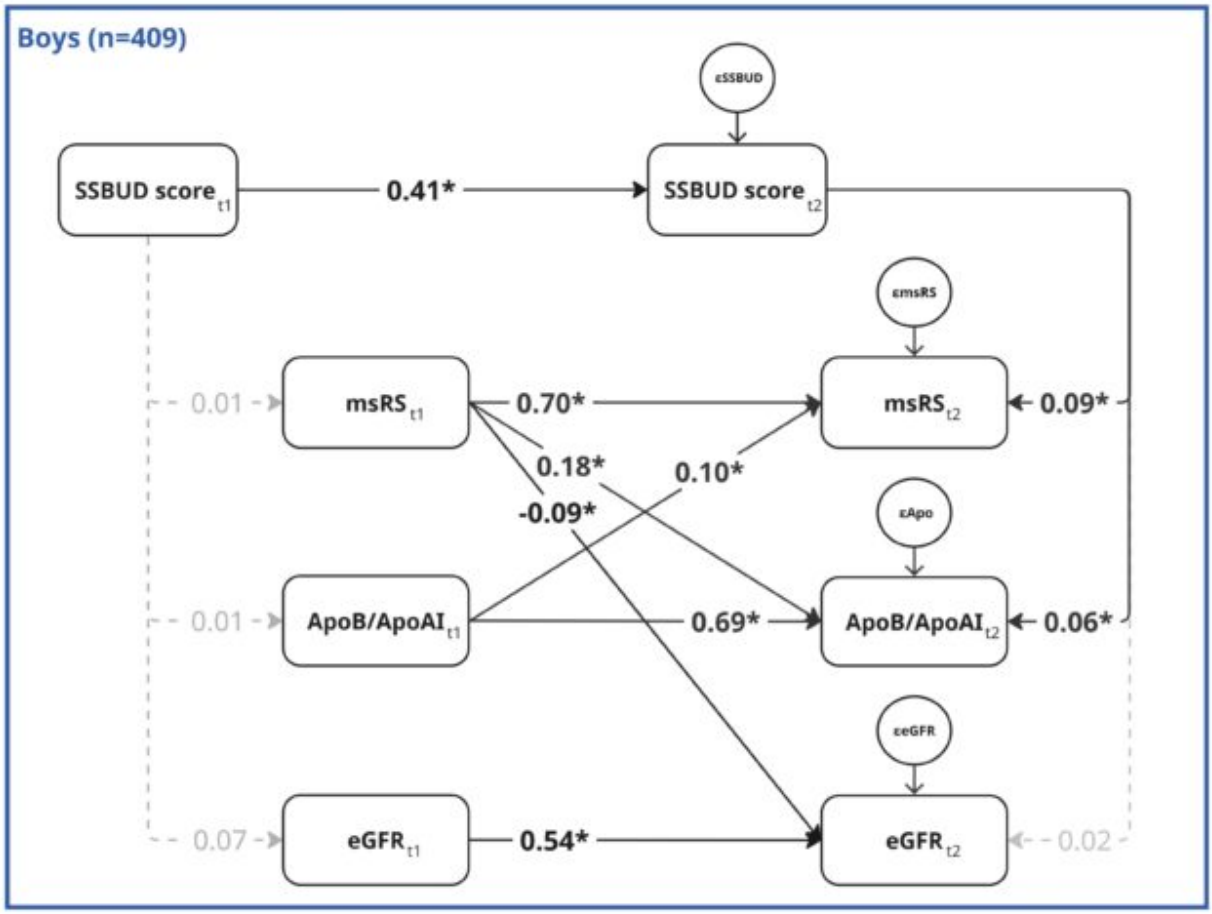
Sugar-Sweetened Beverage Use Disorder and Dynamic Interrelationships Among Cardio-Renal-Metabolic Risk Markers in Adolescents Sharon Tsai* Yu-Ting Chin Chien-Hung Lee Wei-Ting Lin Yun Chen Pei-Wen Wu

Background: Excessive sugar-sweetened beverage (SSB) intake is linked to cardio-renal-metabolic (CRM) risk markers, including metabolic syndrome risk score (msRS), apolipoprotein B to apolipoprotein A1 ratio (ApoB/A1), and estimated glomerular filtration rate, which may interact across metabolic pathways. Existing assessments primarily quantify intake volume and overlook addictive-like traits that may perpetuate CRM risk. This study aimed to develop and validate a SSB use disorder (SSBUD) construct, derive related risk score, and examine its longitudinal associations with CRM outcomes, while accounting for reciprocal interrelationships among CRM risk markers in adolescents.

Methods: A cross-sectional study of representative Taiwanese adolescents (n=3089) was conducted to develop the SSBUD construct, followed by a 2.5-year cohort study (n=1736) to validate the construct and assess its impact on CRM risk. We used confirmatory factor analysis and latent trait modeling to derive SSBUD risk scores, and cross-lagged panel models to assess reciprocal interrelationships among CRM risk markers. Temporal associations between the SSBUD score and CRM outcomes were estimated within a structural equation modeling framework, adjusting for covariates.

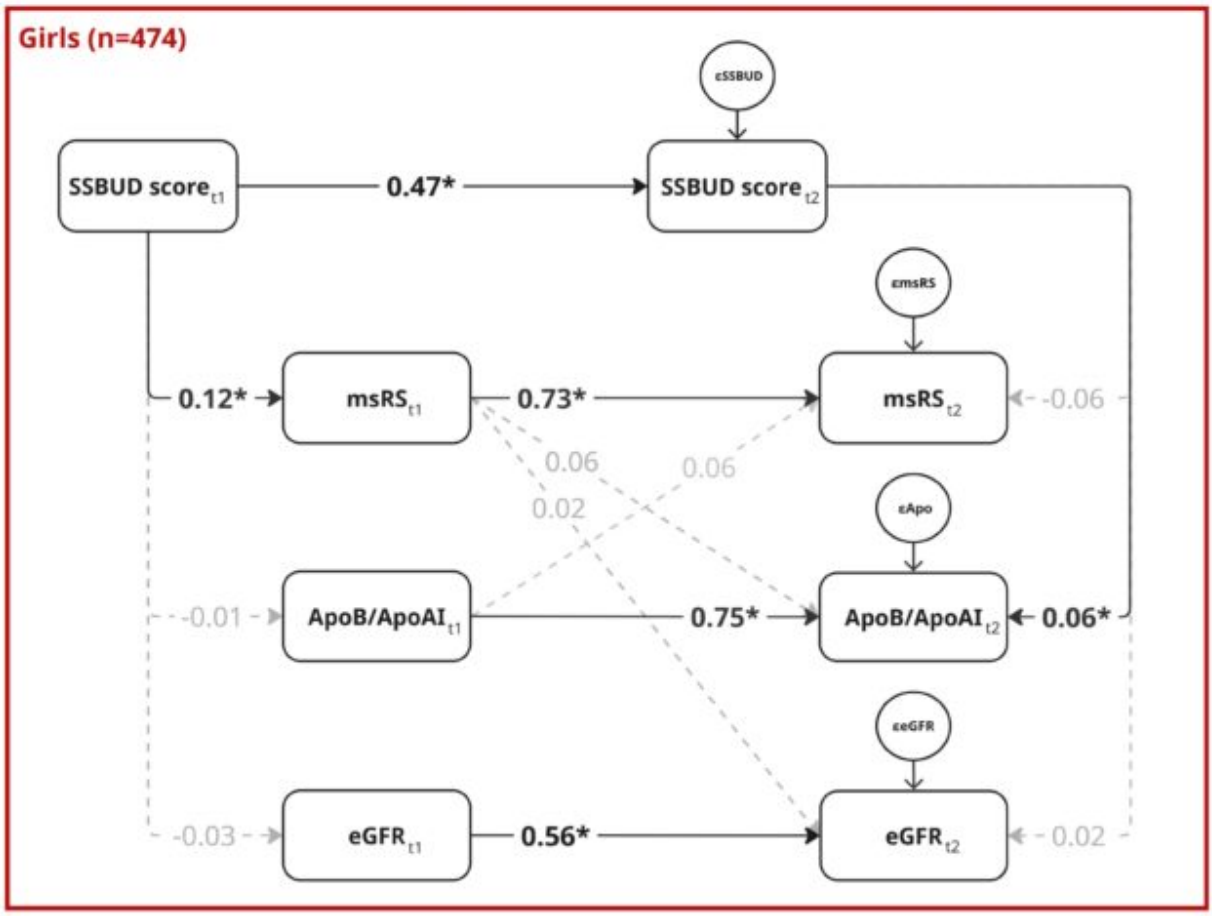
Results: The SSBUD exhibited a unidimensional structure with excellent model fit, strong item discrimination (a=0.89–2.63) and appropriate item difficulty (b=0.14–2.15). Cross-lagged models revealed reciprocal associations between baseline msRS and follow-up ApoB/A1 in both sexes (adjusted βs: boys, msRS→ApoB/A1=0.17, ApoB/A1→msRS=0.12; girls, 0.06 and 0.07). In boys, sustained high SSBUD scores predicted subsequent increases in both msRS and ApoB/A1, whereas in girls they were associated only with subsequent higher ApoB/A1.

Conclusion: Sustained high SSBUD scores predict subsequent elevations in CRM risk markers, highlighting problematic SSB intake as a modifiable behavioral target for early CRM risk prevention in adolescents.



Model Fit Index

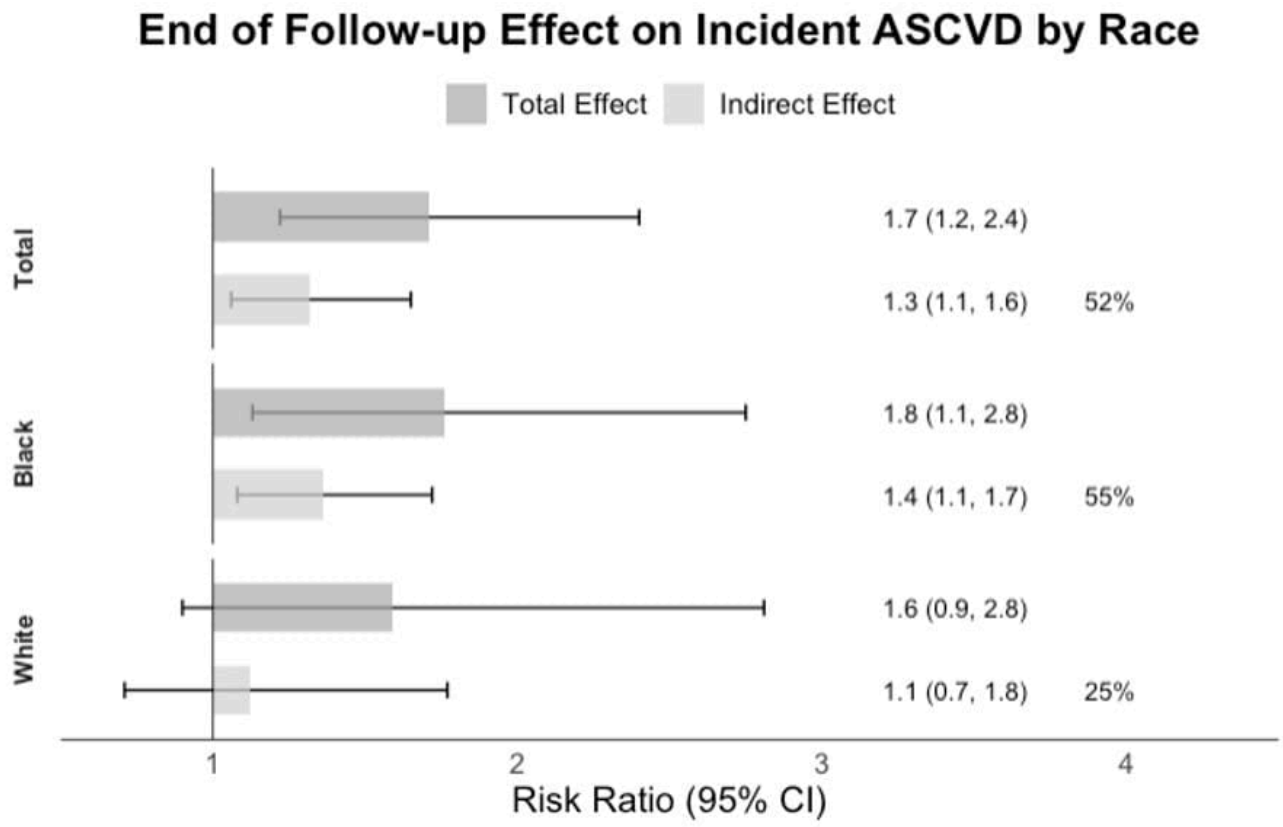
χ^2 (df): 105.790 (64); RMSEA: 0.038; CFI: 0.984; SRMR: 0.039



Cardiovascular

Racial Heterogeneity in the Mediated Effect of Young-Adulthood Insulin Resistance (IR) on Later-Life Atherosclerotic Cardiovascular Disease (ASCVD) Through Midlife Metabolic Syndrome (Mets) in CARDIA Cohort Chuyue Wu* Chuyue Wu Nathan D. Wong Liwei Chen Wenjun Fan Marissa J. Seamans Hua Zhou Roch A. Nianogo

Insulin resistance (IR) often emerges in young adulthood and contributes to the development of atherosclerotic cardiovascular disease (ASCVD), yet the life-course mechanisms and racial heterogeneity of this association remain unclear. **The objective was** to quantify the proportion of the association between young-adulthood IR and later-life ASCVD mediated by midlife metabolic syndrome (MetS) and to assess racial differences in these mediation pathways. We analyzed 3,622 Black and White participants from the CARDIA cohort (baseline ages 18–30 years) who had fasting insulin and glucose measured at baseline. Young-adulthood IR was defined based on body mass index (BMI) and the homeostatic model assessment of insulin resistance (HOMA-IR): BMI >28.9 kg/m^2, HOMA-IR >4.65, or BMI >27.5 kg/m^2 combined with HOMA-IR >3.60. Midlife MetS was assessed at Year 20 (ages 38-50 years) using harmonized criteria, defined by the presence of at least three of five components: central obesity, elevated triglycerides, reduced high-density lipoprotein cholesterol, elevated blood pressure or use of antihypertensive medication, and elevated fasting glucose or use of hypoglycemic medication. Incident fatal and nonfatal ASCVD events were ascertained from Year 20 to 35 (through 2021). Causal mediation analysis for time-to-event outcomes was conducted using parametric G-computation with pooled logistic regression, adjusting for baseline confounders and accounting for midlife lifestyle (diet quality and physical activity) as an exposure-induced mediator-outcome confounder. During a median of 14 years of follow-up, 143 events occurred. At the end of follow-up, young-adulthood IR was associated with 1.7-fold increased ASCVD risk (95% CI, 1.2-2.4). Midlife MetS mediated 52% of this effect. Among Black participants, 55% of the IR–ASCVD association was mediated by midlife MetS, compared with 25% among White participants (**Figure**). IR in young adulthood substantially increases later-life ASCVD risk primarily through progression to midlife metabolic syndrome, with stronger mediation among Black adults. Early IR identification and intervention may reduce ASCVD burden and racial disparities.


End of Follow-up Effect on Incident ASCVD by Race
Total Effect
Indirect Effect
Total
Black
White
1.7 (1.2, 2.4)
1.3 (1.1, 1.6)
52%
1.8 (1.1, 2.8)
1.4 (1.1, 1.7)
55%
1.6 (0.9, 2.8)
1.1 (0.7, 1.8)
25%
1
2
3
4
Risk Ratio (95% CI)

Cardiovascular

Estimating the Causal Effects of Adolescent Health Behaviors on Future Cardiovascular Risk Prince Addo* Prince Nii Ossah Addo Angela D. Liese Jiajia Zhang Glenn Weaver Anwar T. Merchant Monique J. Brown

Background: While research indicates that poor sleep health, depressive symptoms, and substance use are each linked to poor cardiovascular health independently, their combined effects during adolescence on future cardiovascular disease (CVD) risk remain unclear. We aimed to study how the occurrence of these factors during adolescence influences subsequent CVD risk.

Methods: We performed a secondary analysis using Waves I, II, and IV of the Add Health dataset. The main exposure variable (sleep health) was calculated from three sleep factors, sleep duration, bedtime, and insomnia, measured at Wave I. Depressive symptoms were evaluated at Wave II with the Center for Epidemiological Studies Depression Scale (CES-D). A combined substance use measure was created based on self-reported smoking, binge drinking, and marijuana use at Wave II. The primary outcome variable was the 30-year Framingham CVD risk score, measured at Wave IV. Using marginal structural models, we estimated the controlled direct effect of adolescent sleep health on future cardiovascular disease, mediated through depressive symptoms and substance use during adolescence, while adjusting for potential confounders. Essentially, this analysis addressed: “What is the impact of poor adolescent sleep health on adult CVD risk if all participants were depressed or used substances versus if they were not?”

Results: Approximately 61% of study participants (n=1,942) experienced poor sleep health. The prevalence of depressive symptoms and substance use was 7.8% and 25%, respectively. Adolescents with poor sleep health who also used substances had a significantly higher CVD risk in adulthood (OR: 1.83, 95% CI: 1.28, 2.64) compared to those with poor sleep health who did not use substances.

Conclusion: Adolescents with poor sleep health who use substances are more likely to develop CVD in adulthood. Future initiatives should target adolescents with sleep problems and substance use to effectively lower CVD risk.

Causal Inference

Novel g-computation algorithm for time-varying actions with recurrent and semi-competing events Alena Sorensen D'Alessio* Alena D'Alessio Lucas Neuroth Jessie K Edwards Chantel L Martin Paul N Zivich

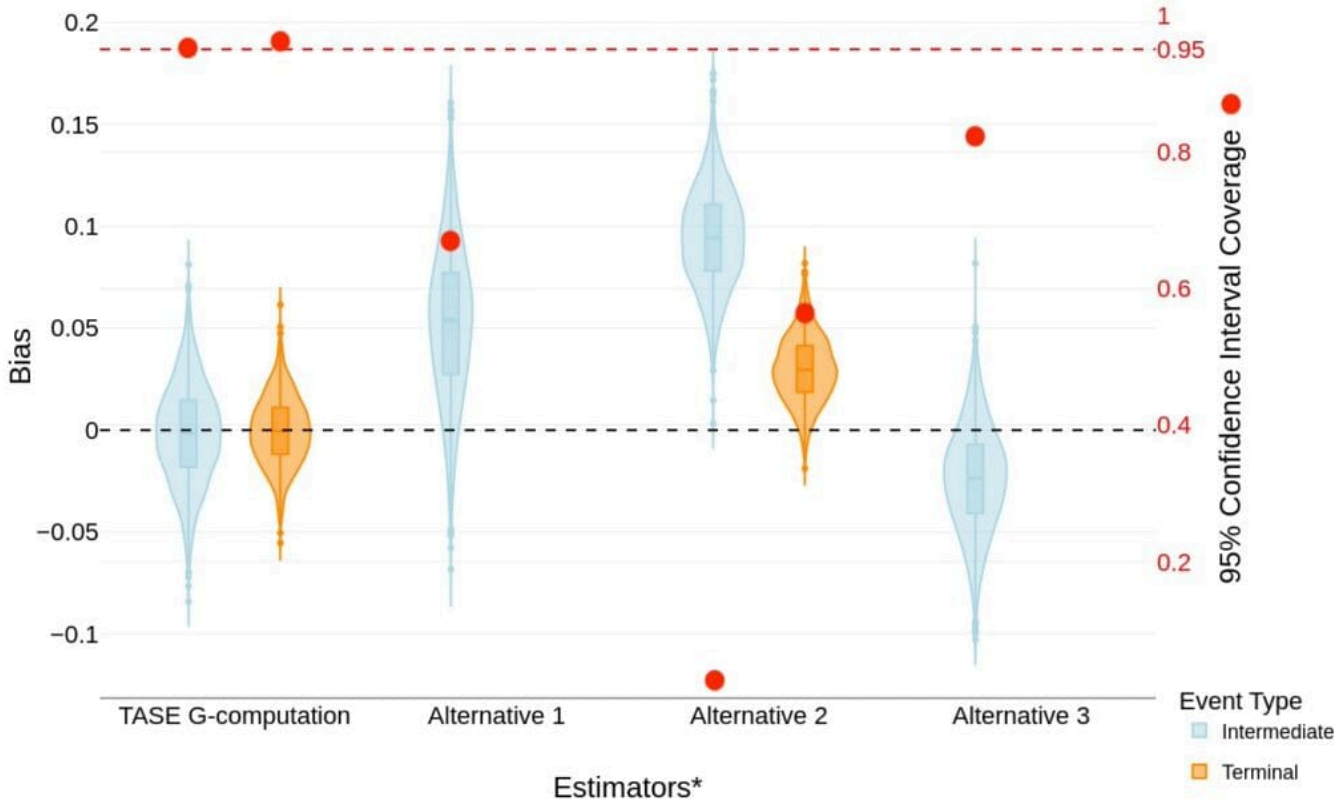
Background: A core aspect of epidemiology is determining the impacts of various interventions in public health. Suppose we were interested in how preventing cigarette smoking throughout young-adulthood and mid-adulthood might impact later-life hypertension. Because cigarette smoking is a time-varying action, we must address two challenges: 1) time-varying confounding; and 2) death before end of follow-up. Standard methods do not address both time-varying confounding and semi-competing events (where a terminal event (e.g., death) precludes an intermediate event (e.g., hypertension), but not the reverse).

Methods: We propose an iterated conditional expectation g-computation algorithm for causal effects with Time-varying Actions with Semi-competing Events (TASE). To explore the performance of our novel TASE g-computation estimator, we conducted a Monte Carlo simulation study. We also applied TASE g-computation in the context of cigarette smoking prevention and prevalent hypertension using data from Waves III (aged 18-26 years) – VI (aged 39-51 years) of the National Longitudinal Study of Adolescent to Adult Health.

Results: Our simulations show the TASE g-computation estimator has little bias and appropriate confidence interval coverage (Figure 1). It outperformed existing alternative estimators across sample sizes. In the illustrative application, TASE g-computation identified a small reduction in prevalence of hypertension and risk of death in mid-life had all cigarette smoking been prevented across follow-up compared to the natural course of smoking. The alternative estimators had reduced precision and diverging estimates.

Conclusion: As long-running cohorts progress in age, death within the study sample will become an increasing concern for studies of aging-related outcomes, life course analyses, and investigations into chronic disease development. TASE g-computation provides a solution for both time-varying confounding and semi-competing events.

Figure 1: Simulation Results (N=2,000)



* Alternative 1 ignores time-varying confounding; ignores semi-competing events; Alternative 2 ignores time-varying confounding; accounts for semi-competing events; Alternative 3 accounts for time-varying confounding; ignores semi-competing events.

Causal Inference

Effect of Nirmatrelvir-ritonavir During Acute COVID-19 on Long COVID Prevention: A Trial Emulation Ning Zhang* Ning Zhang Jessie K. Edwards Stephen R. Cole Justin Lessler Bonnie E. Shook-Sa Katie R. Mollan Jessica R. Keys William A. Fischer David A. Wohl

Background Evidence on Nirmatrelvir-ritonavir (NMV/r) use during acute COVID-19 on long COVID prevention is mixed, and NMV/r initiation timing and completion have not been accounted for.

Methods We evaluated the effect of NMV/r treatment during acute COVID-19 on long COVID onset by emulating six nested trials aligned with treatment initiation 0 to 5 days after symptom onset using data from the VISION study, a longitudinal prospective cohort of adults with acute COVID-19 in North Carolina. We compared two protocols: (1) initiation of NMV/r within 5 days of symptom onset with completion as prescribed, and (2) no initiation of NMV/r within 5 days of symptom onset. We estimated the per-protocol effect of NMV/r on long COVID from 8 to 72 weeks post treatment initiation using g-computation, adjusting for age, sex, race, ethnicity, vaccination recency, prior infection, comorbidity, and urbanicity. We also assessed whether earlier NMV/r initiation (within 3 days of symptom onset) was associated with greater long COVID risk reduction.

Results Among 2,274 participants, 1,061 initiated NMV/r within 5 days of symptom onset (median age 58 years (IQR: 43, 67), 69% female, 46% vaccinated ≤6 months), and 1,213 did not (median age 43 years (IQR: 34, 56), 75% female, 31% vaccinated ≤6 months). The estimated 72-week risks of long COVID were 35.7% (95% CI: 32.4%, 39.1%) of initiators treated within 5 days with completion as prescribed, and 39.8% (95% CI: 36.1%, 43.3%) who did not, corresponding to a risk difference of -4.0 percentage points (95% CI: -8.8, 1.3). Earlier initiation was associated with a 72-week risk difference of -4.6 percentage points (95% CI: -9.8, 0.5).

Conclusions Long COVID risk was substantial in this population. Timely initiation and completion of NMV/r was associated with a modest but imprecise reduction in long COVID risk. Our findings align with prior evidence of limited benefit of NMV/r use for acute COVID-19 in long COVID prevention.

Table. Per-protocol cumulative risk (%, 95% CI) of long COVID under NMV/r initiation strategies.

Initiation (≤5 days of symptom onset vs. not)			
Week since NMV/r initiation*	**Protocol 1: Initiated NMV/r ≤5 days of symptom onset and completed treatment as prescribed**	**Protocol 2: No initiation of NMV/r ≤5 days of symptom onset**	**RD (95% CI)**
8-week	22.4 (20.4, 25.2)	25.1 (22.3, 28.0)	-2.7 (-6.0, 0.9)
12-week	28.2 (25.4, 31.5)	31.6 (28.3, 34.5)	-3.3 (-7.4, 1.1)
26-week	31.2 (28.1, 34.4)	34.9 (31.5, 38.2)	-3.6 (-8.0, 1.2)
36-week	32.8 (29.5, 36.1)	36.6 (33.1, 40.0)	-3.8 (-8.3, 1.2)
52-week	34.4 (31.0, 37.8)	38.4 (34.9, 41.8)	-3.9 (-8.6, 1.3)
72-week	35.7 (32.4, 39.1)	39.8 (36.1, 43.3)	-4.0 (-8.8, 1.3)
Early initiation (≤3 days of symptom onset vs. not)			
Week since NMV/r initiation*	**Protocol 1: Initiated NMV/r ≤3 days of symptom onset and completed treatment as prescribed**	**Protocol 2: No initiation of NMV/r ≤3 days of symptom onset**	**RD (95% CI)**
8-week	22.4 (20.0, 25.3)	25.5 (22.8, 28.2)	-3.1 (-6.7, 0.4)
12-week	28.1 (25.1, 31.5)	31.9 (28.7, 34.9)	-3.9 (-8.1, 0.4)
26-week	31.0 (27.7, 34.5)	35.1 (31.9, 38.3)	-4.2 (-8.7, 0.5)
36-week	32.5 (29.0, 36.1)	36.8 (33.5, 40.0)	-4.3 (-9.1, 0.5)
52-week	34.1 (30.5, 37.7)	38.6 (35.2, 41.8)	-4.5 (-9.5, 0.5)
72-week	35.3 (31.6, 38.9)	39.9 (36.3, 43.1)	-4.6 (-9.8, 0.5)

*Follow-up time is aligned at NMV/r initiation for treated participants and at the corresponding pseudo-initiation time for untreated participants.

Causal Inference

A multi-state Causal Framework for Estimating the Effects of Treatment Regimes over the Course of Chronic Disease Ming Ding* Ming Ding

The development of chronic disease is a long-term process involving multiple endpoints, and limited methods can assess the health benefits of treatment regimes over the disease course. Existing multi-state Cox models are not easy to use for comparing the effectiveness of treatment regimes. To address this, a discrete-time split-state framework has been proposed [1], which divides disease states into substates by conditioning on past history. As this framework is both “memoryless” and “memorable”, the time-specific transition rates can be synthesized into summary measures, multimorbidity-adjusted life year (MALY) and substate-specific life year (SSLY) [2]. In this abstract, building on this framework, we propose to investigate the causal effects of static and dynamic treatment regimes over the disease course, under the assumptions of constant baseline confounders and instantaneous effects of interventions on transition rates. Our method identifies the optimal treatment regime that generates the most benefits using MALY, and elucidates the mechanisms through which treatment regimes affect disease progression using SSLY. In the application, we identified the optimal body mass index (BMI) intervention using data from the Atherosclerosis Risk in Communities (ARIC) study, where the disease course was modeled in healthy, at metabolic risk, coronary heart disease, heart failure, and mortality states. Compared to Regime 1, the MALY was 1.80 years higher under Regime 4 (**Figure**), and the estimated SSLY shows that the gain in MALY for Regime 4 is due to prolonged life expectancy in all substates except the healthy state. In summary, our method provides a framework to evaluate the health benefits of treatment regimes over the disease course and has the potential to improve the precision prevention of chronic diseases. This abstract has a preprint online.[3]

[1] Ding et al. BMC Med Res Methodol. 2025;25(1):54.

[2] Ding et al. BMC Med Res Methodol. In revision

[3] Ding. https://doi.org/10.1101/2025.07.25.25332203

Table 1. Difference in multimorbidity-adjusted life years (MALY) across body mass index (BMI) regimes in the Atherosclerosis Risk in Communities (ARIC) Study, 1987 – 2019 (n=15027).

	MALY, Life year (95% CI)	Difference in MALY, Life year (95% CI)
Regime 1	35.08 (22.63, 47.11)	Reference
Regime 2	35.52 (23.02, 47.39)	0.37 (0.10, 0.86)
Regime 3	35.54 (23.04, 47.40)	0.38 (0.07, 0.90)
Regime 4	36.95 (24.28, 48.56)	1.80 (0.62, 2.78)

95% CI: 95% Confidence interval

Regime 1: Normal weight (BMI<25 kg/m^2) in all disease states.
Regime 2: Normal weight (BMI<25 kg/m^2) in healthy, at-metabolic-risk, and CHD states, and overweight (BMI 25-30 kg/m^2) if the person develops heart failure.
Regime 3: Normal weight (BMI<25 kg/m^2) in healthy and at-metabolic-risk states, and overweight (BMI 25-30 kg/m^2) if the person develops CHD or heart failure.
Regime 4: Normal weight (BMI<25 kg/m^2) at the start of intervention, and change to overweight (BMI 25-30 kg/m^2) if age >65y.

Causal Inference

Application and description of Bayesian doubly robust conditional quantile treatment effect estimation: A use case with sensitivity analysis Hayden L. Smith* Hayden Smith Caitlin Sanderman Owen Millers Sarah Pandullo Carlos Pelaez Matthew Trump Jonathan Hurdelbrink

Background: Treatment effect heterogeneity is a central topic in precision medicine and policy evaluation. Common means-based causal effect estimators (e.g., conditional average treatment effects (CATE)) summarize outcomes at the population level and fail to capture distributional differences. Doubly robust conditional quantile treatment effects (CQTE) assist in overcoming this limitation.

Methods: A Bayesian CQTE approach was used to examine for effect modification (EM) in an analgesia-first sedation protocol implemented at a Midwestern Intensive Care Unit (ICU) in the United States. The study had a pre-/post-study design examining changes in hourly morphine milligram equivalents (MME) administered to patients with mechanical ventilation. The EM variable of interest was whether or not the patient had a primary complaint related to a respiratory condition. Stabilized inverse propensity scores were estimated via Bayesian additive regression trees and a conditional outcome model fit separately for the pre- and post- intervention groups using Bayesian quantile regression (i.e., tau: 0.1-0.9) with asymmetric Laplace likelihoods. Posterior predictions were combined with propensity scores to construct doubly robust estimates aggregated by the EM variable.

Results: Post-protocol MME changes in the ICU revealed heterogeneity in treatment effects across the outcome distributions (Figure). Specifically, effect modifier subgroups showed differences across quantiles, indicating different benefits based on the modifier. Sensitivity analyses will be presented at the conference and will include comparisons to QTE, CATE, and ATE, as well as varied propensity score and uncertainty methods.

Conclusion: CQTE provide a flexible framework for evaluating heterogeneity across outcome distributions in non-randomized settings. By combining propensity score weighting with conditional quantile modeling, the process mitigates confounding bias and allows for subgroup-specific inference.

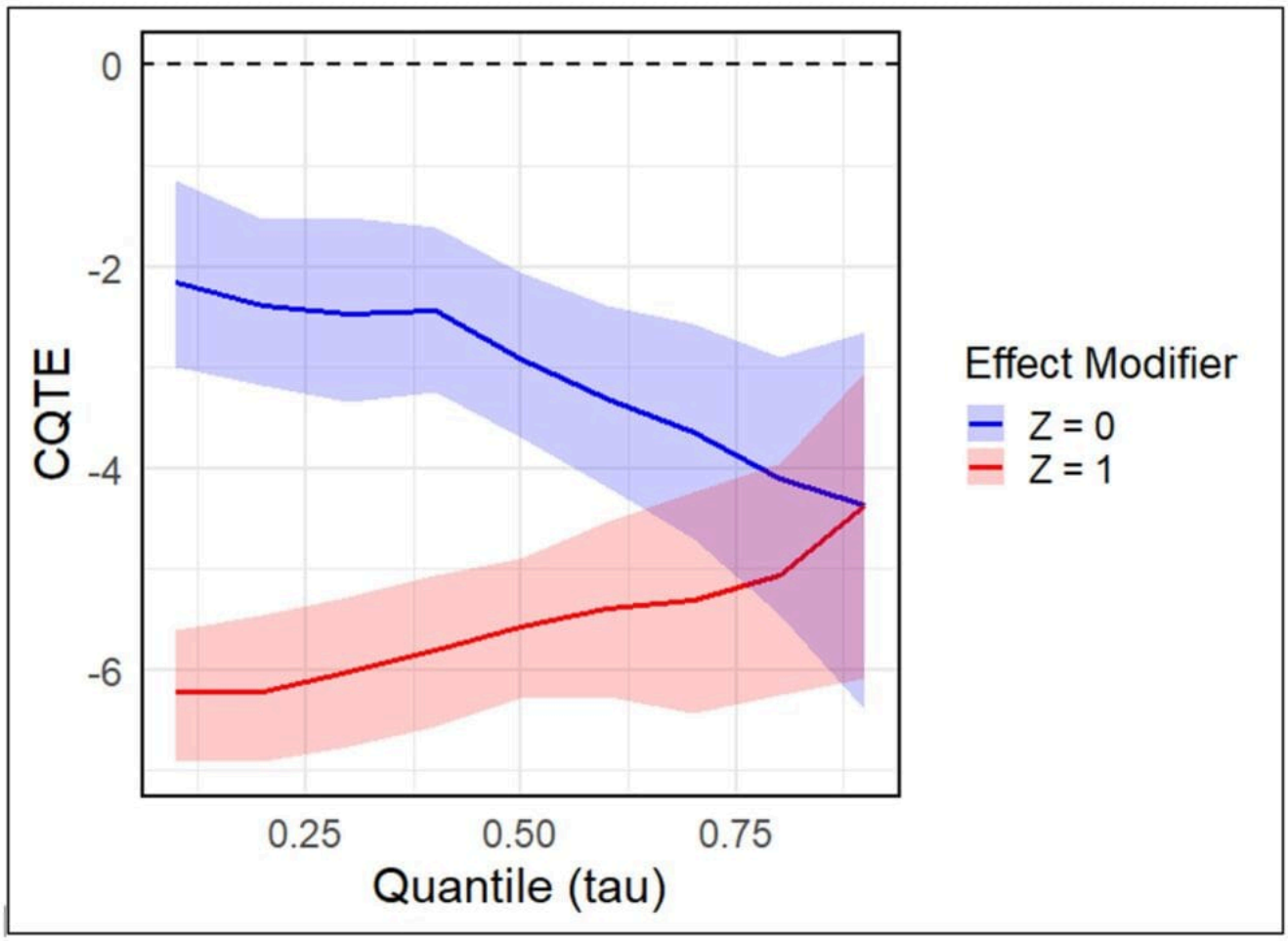


Figure: Plotted changes in morphine milligram equivalents administered by the presence of a primary respiratory complaint (Z) for patients after the implementation of an analgesia-first sedation protocol. Results calculated using Bayesian conditional quantile treatment effects (CQTE) and presented by quantile for 202 Intensive Care Unit patients receiving mechanical ventilation at a Midwestern center in the United States.

COVID-19 Pandemic

Social support and resilience among individuals with long COVID: Findings from a cross-sectional survey within the Arizona CoVHORT longitudinal cohort study Chidera Ejike* Chidera Ejike Kristen Pogreba-Brown

Objective: We examined whether feeling supported within a social support network is associated with resilience among individuals with Long COVID (LC+), and whether this relationship is modified by symptom burden or functional disability status.

Methods: We analyzed data from 589 LC+ participants in the Arizona CoVHORT with complete data on key variables. Linear regression models estimated unadjusted and adjusted associations between having social support for their LC symptoms (Y/N) and Brief Resilience Scale scores (5 questions, 1-5 Likert scale), controlling for age, gender, race, symptom burden, and disability status. Effect modification by symptom burden and disability was assessed using interaction terms. Multiple imputation using predictive mean matching (20 imputations, 50 iterations) evaluated the robustness of results to missing data.

Results: Among people with LC, having social support was significantly associated with greater resilience scores in unadjusted analyses (β = 0.24, 95% CI: 0.08–0.41, p = 0.005). After adjustment for covariates, the association attenuated but remained positive (β = 0.15, 95% CI: –0.01–0.31, p = 0.064). Neither symptom burden (interaction β = 0.002, 95% CI: -0.016–0.020, p = 0.82) nor disability status (interaction β = -0.20, 95% CI: -0.55–0.15, p = 0.26) significantly modified this relationship. Multiple imputation produced results nearly identical to the complete case analysis (β = 0.154 vs. β = 0.151), indicating strong robustness to missing data.

Conclusions: Social support shows a consistent positive association with resilience among individuals with Long COVID, independent of symptom burden and functional disability. These findings suggest that social support interventions may benefit individuals across the spectrum of Long COVID severity.

COVID-19 Pandemic

Sex differences in COVID-19 infection and mortality in Hong Kong Hoi Ting (Alexandra) Law*
Hoi Ting (Alexandra) LAW Benjamin John Cowling

Background: More men are dying from COVID-19 than women in Hong Kong. We aimed to characterize the sex difference in infection and mortality patterns across different pandemic waves, and investigate the reasons behind the males' COVID-19 disadvantages.

Methods: We estimated sex-specific case-fatality risks (CFRs), hospital-fatality risks, and the number of cases per 100,000 population, particularly among older adults, from waves 1 to 8 of the pandemic. Parametric bootstrapping was employed to account for statistical uncertainty in the risk assessments. The adjusted and unadjusted age-specific risks were estimated and compared to explore the relationships between death and health-related variables. We also estimated the cause-specific sex mortality ratio to compare that of COVID-19 and other major causes of death.

Results: Hong Kong recorded 2876110 confirmed cases and 12737 deaths from waves 1 to 8, with 1317368 cases (45.8%) and 7523 (59.1%) mortality being males. The infection rate is similar for both sexes across waves. The odds ratios for CFRs, hospital-fatality risks, and the number of cases per 100,000 population were higher in men across all waves. Males have a significantly higher mortality risk after adjusting for all factors, and the odds of death for males were the highest among 65-79 years old in wave 7 (2.44, 95% CI: 1.62, 3.69), and were at a similar level for the population aged 80 or above for all waves. The sex mortality ratio of COVID-19 from 2020 to 2023 is similar to respiratory diseases (excluding COVID-19), cardiovascular diseases, and diabetes.

Conclusions: Despite similar infection rates for males and females across 8 waves, males experienced higher mortality risks. COVID-19 shares a similar sex ratio of mortality with respiratory diseases excluding COVID-19, suggesting the causal pathway of respiratory and COVID-19 is the same. The common health statuses, for example, smoking, could explain the disparity in COVID-19 and respiratory mortality.

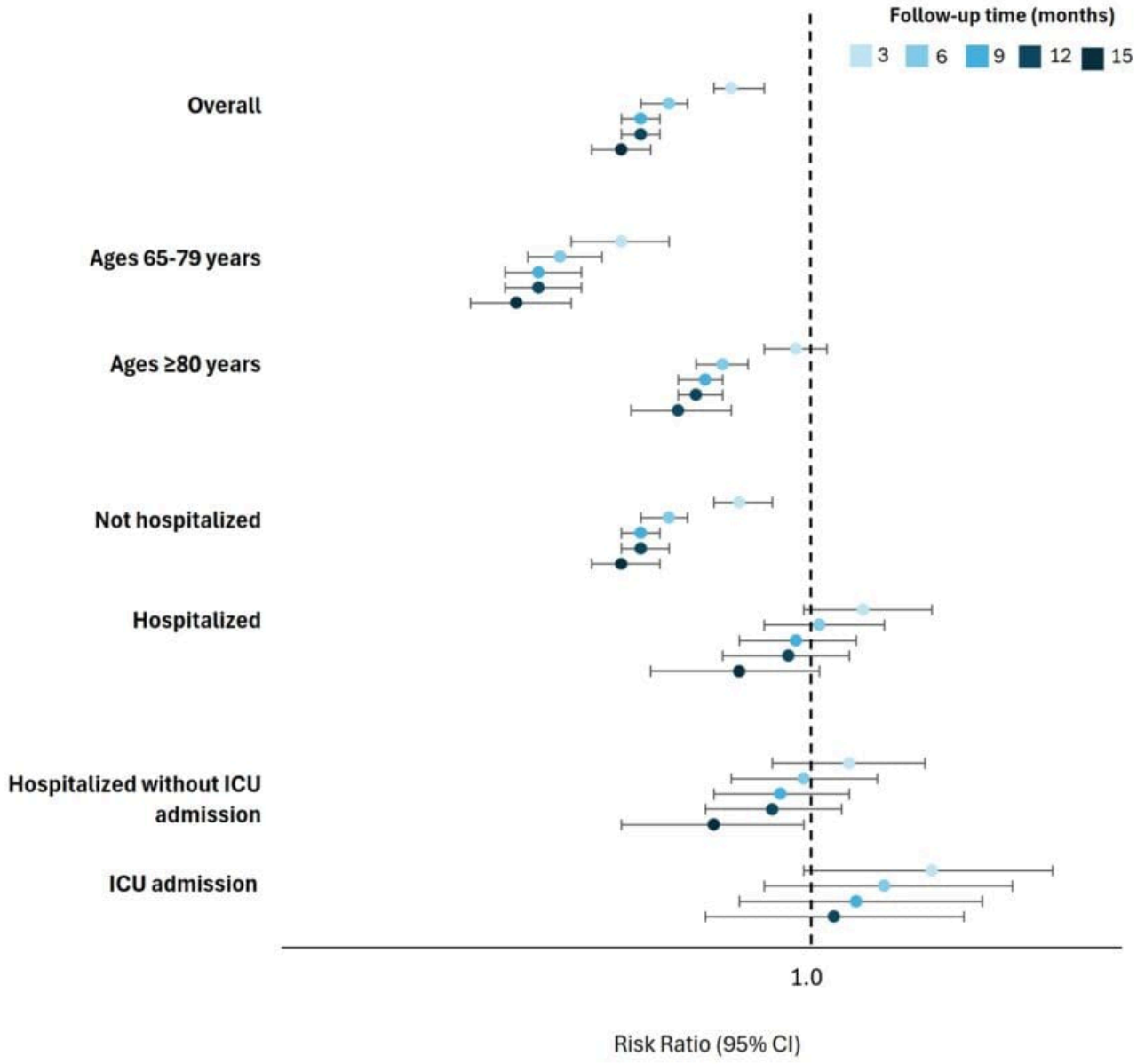
COVID-19 Pandemic

Long-term, All-Cause Mortality Following COVID-19 among Older U.S. Adults With and Without a Bivalent or 2023-2024 COVID-19 Vaccine Dose Nicole D. Ford* Nicole Ford Alexandra Dalton Ruth Link-Gelles Amanda Payne Sharon Saydah

Background: Little is known about COVID-19 vaccination and long-term, all-cause mortality risk following COVID-19. We assessed the effect of receiving a bivalent or 2023-24 COVID-19 vaccine dose on long-term mortality following COVID-19 diagnosis among older U.S. adults.

Methods: We developed a retrospective cohort of Medicare fee-for-service (FFS) beneficiaries aged ≥65 years from the Centers for Medicare and Medicaid Services Chronic Conditions Warehouse database. Eligible adults had evidence of any COVID-19 vaccination prior to September 2022 and a documented COVID-19 diagnosis September 2022–December 2023. The exposure was receipt of a bivalent or 2023-2024 COVID-19 vaccine dose prior to their COVID-19 diagnosis. We estimated hazard ratios for all-cause mortality following COVID-19 diagnosis using Cox Proportional Hazards models comparing beneficiaries with and without the COVID-19 vaccine dose. We used survival analysis to calculate risk difference and risk ratios comparing these groups at 3-, 6-, 9-, 12-, and 15-months post-COVID-19 diagnosis. All analyses used propensity score weighting to balance participant characteristics.

Conclusion: These findings highlight the ongoing benefit of COVID-19 vaccination in reducing long-term all-cause mortality.



Estimates are weighted risk ratios (95% CI) for all-cause mortality comparing Medicare Fee-For-Service beneficiaries, aged ≥65 years with and without evidence of bivalent or 2023-2024 COVID-19 vaccine dose prior to index COVID-19 diagnosis, overall, by age group, and severity of acute COVID-19 illness. (N=1,456,669). Overall estimates and estimates among non-hospitalized beneficiaries were weighted to account for race, region, rural-urban classification, SVI quartile, flu vaccination, cardiovascular disease, diabetes, and dementia. By age group, estimates for beneficiaries aged 65-79 years were weighted to account for race, region, rural-urban classification, SVI quartile, flu vaccination, diabetes, and dementia. Estimates for beneficiaries aged 80 years and older additionally account for cardiovascular disease and mental health conditions. Estimates for hospitalized beneficiaries and hospitalized beneficiaries who were not admitted to the ICU were weighted to account for race, region, SVI quartile, flu vaccination, and diabetes. Estimates for beneficiaries admitted to the ICU were weighted to account for age, sex, race, region, SVI quartile, flu vaccination, cancer, mental health conditions, and dementia.

COVID-19 Pandemic

Latent Class and K-modes Analyses of Comorbidities of COVID-19 Patients According to CO-RADS Classification Ayse Ulgen* Ayse Ulgen Sirin Cetin Ozge Pasin

Background: This pioneering study compares Latent Class and K-modes analyses for stratifying COVID-19 patients by risk, aiming to identify high-risk individuals based on COVID-19 Reporting and Data System (CO-RADS) categories and comorbidities. CO-RADS is a standardized chest CT scoring system that classifies the likelihood of COVID-19 lung involvement from 1 (very low) to 6 (confirmed). **Methods:** This retrospective study included 600 patients diagnosed with COVID-19, and the analysis utilized CO-RADS levels along with comorbidity variables such as hypertension, diabetes, COPD, etc. for each patient. The objective of the study is to compare the output from Latent class analysis and K-modes clustering. Model performance was measured using AIC/BIC values and the kappa statistic. **Results:** Both latent class and K-modes analyses consistently identified cardiometabolic disorders and chronic conditions, particularly diabetes mellitus, hypertension, hyperlipidemia, chronic heart and kidney diseases, and respiratory comorbidities such as COPD and asthma, as key characteristics distinguishing high-mortality risk groups among COVID-19 patients ($p < 0.001$). Mortality analyses revealed comparable class distinctions across methods, with Latent Class Analysis indicating a 39.4% mortality rate in the low-risk group and 23.4% in the high-risk group, while K-modes clustering identified similar patterns with mortality rates of 40.2% and 21.3%, respectively. Latent Class Analysis formed homogeneous subgroups using parametric distributions, while K-modes handled heterogeneous data by optimizing intra- and inter-cluster variability. Their 62% concordance underscores complementary strengths and combined utility in clinical datasets. **Conclusion:** This study integrates advanced statistical techniques to develop a scalable model for understanding and managing complex diseases like COVID-19, offering a robust framework for personalized risk stratification across diverse conditions.

Latent Class and K-modes Analyses of Comorbidities of COVID-19 Patients According to CO-RADS

Background

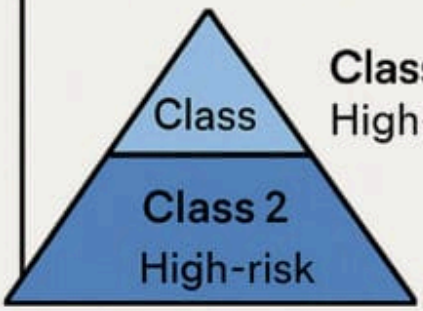
No research has used both Latent Class and K-modes analysis to comparatively classify COVID-19 patients by CO-RADS categorization and comorbidities

Methods

- Retrospective analysis of 500 COVID-19 patients
- Classified by CO-RADS level (1–5) and comorbidities
- Latent Class and K-modes analyses

Results

Latent Class analyses



Significantly higher mortality in Class 1 (62% agreement between methods)



Conclusion

Risk of death was effectively distinguished between patient classes using Latent Class and K-modes analyses

- Diabetes mellitus
- Hypertension
- Hyperlipidemia
- Chronic heart disease
- Asthma
- COPD
- Chronic kidney disease

COVID-19 Pandemic

Smoking and time to SARS-CoV-2 Reinfection: an analysis of reinfection-free time in a prospective cohort study Keith Gray* Keith Gray Dinelka Nanayakkara Becky Straub Marina Hendricks Jessica Keys Katie Mollan David A Wohl William A Fischer, II

Background:
Smoking is associated with immune system dysregulation and increased severity of acute COVID-19. However, the effect of smoking on susceptibility to repeat SARS-CoV-2 infection in the Omicron era is poorly understood. Understanding whether smoking influences reinfection risk in real-world conditions is important as COVID-19 is now endemic and reinfections are common.

Methods:
We used data from the VISION study, a prospective cohort of adults in North Carolina with acute COVID-19 to estimate the effect of baseline smoking history (ever vs never) on time to SARS-CoV-2 reinfection. The primary estimand was the difference in restricted mean survival time through 365 and 448 days, the maximum follow-up. Secondary analyses were conditioned on vaccination to assess robustness. We also fit a marginal structural Cox model over 448 days using inverse probability weights to adjust for baseline confounding, time-varying vaccination, and study dropout with robust variance estimation.

Results:
Among 3,190 participants analyzed (829 ever smoked), 583 reported a reinfection over a median of 448 days (interquartile range: 255, 448) follow-up. Ever smokers experienced 8.4 fewer reinfection-free days through 365 days (95% CI: −15.6 to −1.2) and 11.9 (-21.6, -2.2) fewer days through 448 days compared to never smokers in crude analyses. Conditioning on ever receiving a vaccine over at-risk follow-up, these differences increased to 9.7 (95% CI: -16.8, -2.7) and 13.7 (-23.2, -4.2) fewer days through 365 and 448 days, respectively. In our marginal structural model, ever smoking was associated with a higher hazard of reinfection (HR: 1.25, 95% CI: 1.00 to 1.57).

Conclusion:
Smoking was associated with shorter reinfection-free time and increased risk of SARS-CoV-2 reinfection. The widening difference with longer follow-up suggests a cumulative disadvantage for ever smokers. These findings emphasize the importance of SARS-CoV-2 prevention for people who have ever smoked.

LATEBREAKER

Data infrastructure

Introducing the Public Access Tabulated Health Statistics (PATHS) system: a modular data management system for curating, archiving, and disseminating public-use health datasets

Justin Amarin* Justin Amarin Shawn Savannah William Creea Jesse Peter

Epidemiologic research that addresses community and geographic influences in the United States increasingly depends on publicly available measures. When researchers lose access to historical data releases, they face workflow disruptions and compromised reproducibility. Recent analyses exposed two distinct vulnerabilities in centralized data infrastructure: the removal or alteration of long-standing federal data and the cessation of continual data releases. To address the former, systems that preserve existing datasets and ensure continued access independent of upstream changes are urgently needed. In response, we developed Public Access Tabulated Health Statistics (PATHS), a modular data management system for curating, archiving, and disseminating public-use health datasets (**Figure**). PATHS comprises four integrated components: (1) a Registry, built on Research Electronic Data Capture (REDCap), that catalogs dataset metadata (e.g., source URL, download date, and reference year); (2) a Repository that stores unmodified and digitally fingerprinted copies of original datasets with standardized documentation; (3) Modules, configured by resource-specific YAML files, that harmonize join fields across datasets; and, (4) a Data Builder, a REDCap-based interface through which researchers request compiled multisource data via an automated extract, transform, load pipeline. The modular architecture allows new data sources to be integrated into PATHS semiautomatically, with potential for full automation. The catalog currently includes 54 county-level files from sources such as the CDC/ATSDR Social Vulnerability Index and AHRQ Community-Level Health Database, with infrastructure designed to scale to additional sources and geographies (e.g., census tract, ZIP Code, or state). In conclusion, we have designed PATHS to be a minimalist, reproducible safeguard against disruptions to the public health evidence base, with all assets made fully available to our research community.

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Diabetes

Uptake of Diabetes Self-Management Education among Diabetic cancer Survivors Michelle Asiedu-Danso* Michelle Asiedu-Danso

Introduction: Recent advancement in cancer research has prolonged the life of survivors thus patients must be prepared for chronic conditions such as diabetes that may arise later in life or due to cancer therapy exposure. Diabetes Self-Management Education (DSME) has been shown to improve diabetes management and prevent complications, yet access remains limited. This study aims to investigate the uptake of DSME and explore how the sequence of diabetes diagnosis among cancer survivors impacts its uptake.

Methods: Three cycles of the Behavioral Risk factor Surveillance System (BRFSS) were analyzed to assess receipt of DSME by patients who had reported a diagnosis of cancer and diabetes (2022,2023,2024). Bivariate analysis and multivariable logistic regression analysis were conducted to investigate the relationship between socio-demographic and health factors and the receipt of DSME among diabetic cancer survivors. A Cochran-Armitage Tend test was also conducted to assess the annual trends in DSME receipt among survivors.

Results: There is a steady decline in the receipt of DSME among diabetic cancer survivors (50% to 45%, $p<0.0001$). People who received a diabetes diagnosis after or concurrently with a cancer diagnosis had 26% lower odds of receiving DSME compared to those who had a diabetes diagnosis before a cancer diagnosis (aOR:0.74, $p<0.0001$). College graduates had 22% lower odds of receiving DSME compared to those with high school or less (aOR: 0.74, $p<0.0001$). Females had 41% higher odds of receiving DSME. Similarly Non-Hispanic Blacks had 27% higher odds of receiving DSME compared to their white counterparts. Interestingly, obesity and insurance status did not play a role in receiving DSME ($p>0.05$).

Conclusion: The declining uptake of DSME is of concern to this vulnerable health group. This may highlight the need for interprofessional care of patients and interventions geared at improving access to DSME for diabetic cancer survivors.

Diabetes

Long-Term Renal Consequences of Fetal Exposure to Maternal Diabetes – Results from the TEAM Study Shelley Ehrlich* Shelley Ehrlich Jane Khoury Katherine Bowers

While in utero exposure to maternal diabetes mellitus is associated with increased adverse health outcomes in offspring, including obesity, insulin resistance and diabetes, human evidence regarding in utero exposure to maternal diabetes and long-term renal disease risk in offspring is limited. The goal of this study was to determine 1) if there is a transgenerational effect of in utero exposure to dysglycemia on renal health outcomes in adult offspring of women with insulin dependent diabetes mellitus (IDDM); 2) to identify the gestational periods where glycemic dysregulation is most predictive of adverse renal outcomes in adulthood. The Transgenerational Effects on Adult Morbidity (TEAM) Study followed-up offspring of mothers with pre-pregnancy IDDM, who participated in a Program Project Grant (PPG). These women were closely monitored with detailed characterization of glycemic measures across pregnancy in addition to having obstetric and delivery data. Offspring participated in a complete clinical exam, which included markers of renal function (estimated glomerular filtration rate (eGFR), and urine albumin creatinine ratio (UACR)). Linear and logistic regression were used to identify associations between trimester-specific maternal glycohemoglobinA1 standard deviation (HbA1SD) and maternal glucose profiles (functional PCA) with offspring eGFR and UACR, adjusting for covariates (maternal history of microvascular disease, hypertensive disorders of pregnancy, BMI at LMP). In 161 offspring (mean age 32.3 years) increased HbA1SD and increased fluctuations in blood glucose levels in the third trimester were associated with lower eGFR, Also, increased HbA1SD in all 3 trimesters and higher fluctuations in trimester 2 were associated with increased UACR. Our findings indicate an association between maternal glycemia, as early as the first trimester of pregnancy, and decreased renal function in adult offspring.

LATEBREAKER

Diabetes

Perceived Neighborhood Environment and HbA1c Levels in Older Adults: Changes Over Time by Self-reported Diabetes Status Hyungkyung Kim* Hyungkyung Kim Kelvin Choi Kosuke Tamura

Purpose: Neighborhood characteristics such as violence, crime, and poor social support are barriers to glycemic control; however, prior research has largely focused on individuals with diabetes at a single time point. Less is known about the role of perceived neighborhood factors in glycemic control among those without diabetes or whether these associations change as people age. We examined associations between perceived neighborhood environment (safety, disorder, and social cohesion) and HbA1c levels and whether these associations changed over time as participants aged and differed by self-reported diabetes status.

Methods: We analyzed data from the Health and Retirement Study, including 5,507 participants in 2006 and 2,553 in 2016 (mean ages 67.1 and 74.0 years). Perceived neighborhood safety, disorder, and social cohesion were self-reported. Continuous HbA1c levels were used as the outcome. Multiple linear regression models were conducted separately by survey year and stratified by self-reported diabetes status.

Results: Associations differed across years and by diabetes status. Higher perceived neighborhood unsafety and lower social cohesion were associated with higher HbA1c in both years (Table), whereas higher neighborhood disorder was associated with higher HbA1c only in 2006 (β: 0.04; 95% CI: 0.01, 0.07). Among participants without diabetes, higher unsafety (β: 0.02; 95% CI: 0.004, 0.04) and disorder (β: 0.03; 95% CI: 0.01, 0.05) were associated with higher HbA1c in 2006, but in 2016 only lower social cohesion was associated with higher HbA1c (β: 0.02; 95% CI: 0.001, 0.04). Among those with diabetes, only higher unsafety in 2006 was associated with higher HbA1c (β: 0.13; 95% CI: 0.05, 0.21).

Conclusion: Perceived neighborhood environment was associated with glycemic levels. The associations changed as participants aged and depended on diabetes status. Further research is needed to clarify mechanisms underlying these changes.


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LATEBREAKER

Diabetes

Hemoglobin A1c Trajectories from Young Adulthood to Midlife and Cognitive Performance: Evidence from the National Longitudinal Study of Adolescent to Adult Health Youngjoon Bae* Youngjoon Bae Jennifer Momkus Kamaryn Tanner Farizah I. Rob Aanya Bahl Allison E. Aiello

Poor glycemic control is a well-established risk factor for cognitive decline; however, the association between long-term changes in HbA1c and cognitive performance remains underexplored, particularly in midlife. Leveraging repeated HbA1c measurements from young adulthood (ages 24–32) to midlife (ages 40–49) and assessments across multiple cognitive domains, we evaluated whether cumulative HbA1c and its trajectories were associated with cognitive performance in midlife.
This study used data from the National Longitudinal Study of Adolescent to Adult Health (Add Health), including up to 7,109 U.S. adults; analytic sample sizes varied across models depending on the availability of HbA1c measurements and cognitive assessments. HbA1c was measured at Waves IV–VI. Cognitive performance was assessed at Wave VI using four TestMyBrain (TMB) cognitive assessments: Verbal Paired Associates, Digit Symbol Matching, the Gradual Onset Continuous Performance Test, and Backward Digit Span. We estimated (1) OLS models using mean HbA1c across Waves IV–VI to capture cumulative glycemic exposure and (2) OLS models incorporating individual HbA1c intercepts and slopes derived from linear mixed-effects models to characterize long-term glycemic trajectories as predictors of Wave 6 cognitive performance. All models were adjusted for age, sex, race, and education, and incorporated survey weights.
Models using mean HbA1c indicated that greater cumulative glycemic exposure was associated with poorer cognitive performance. Similarly, trajectory-based models demonstrated that steeper increases in HbA1c over time (slope) were associated with worse performance on these tests at Wave VI. These findings suggest that sustained glycemic exposure and long-term increases in HbA1c from young adulthood to midlife are associated with poorer cognitive performance in specific cognitive domains at midlife, including processing speed and executive function, underscoring the importance of early and sustained metabolic control for cognitive health.


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Diabetes

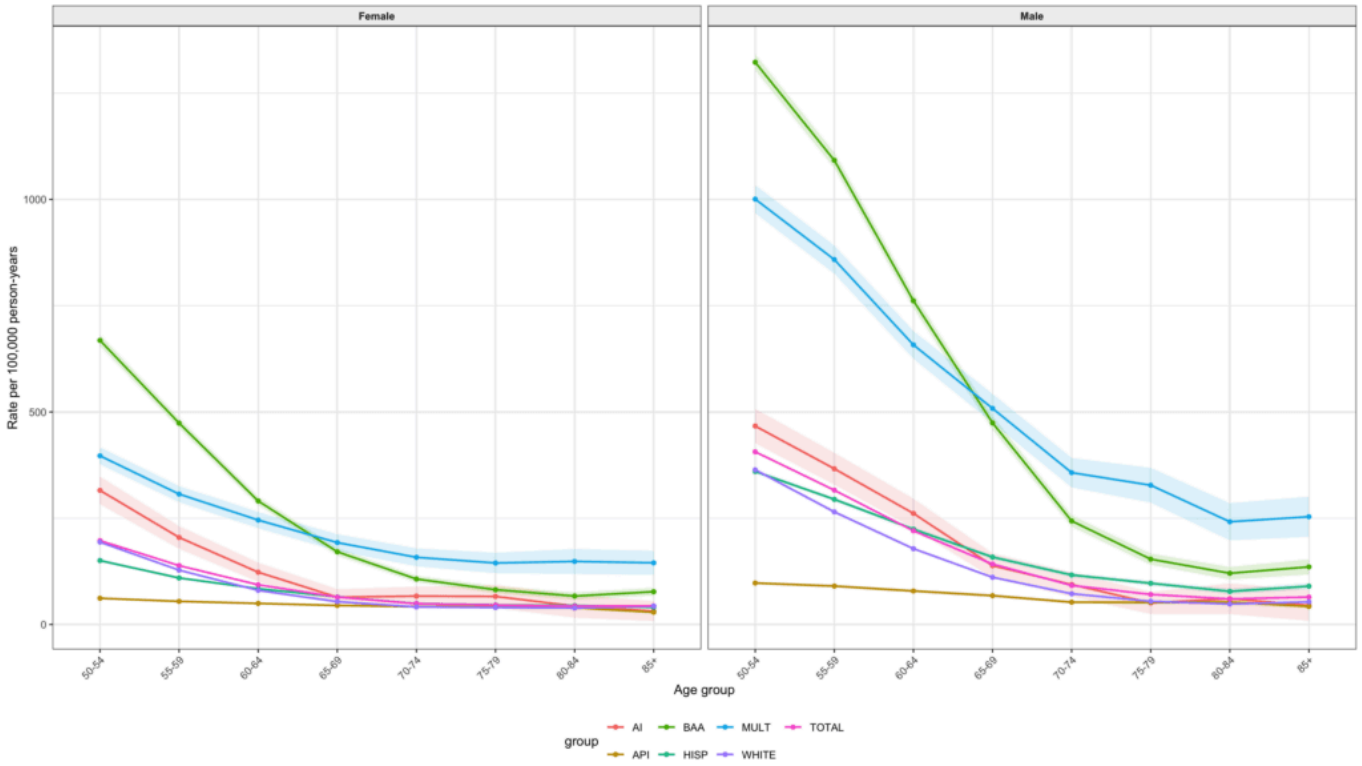
Violent victimization of older Multiracial adults in California, 2005-2022 Tracy Lam-Hine*
Tracy Lam-Hine Emily F. Liu Caitlin S. Chan Jennifer Ahern

Background: Violence against older adults is a growing public health concern. Prior studies have found elevated rates of violent victimization (hospitalization or death due to interpersonal violence) among Black older adults. Little is known about violence patterns among older Multiracial adults, who are often aggregated with other groups or excluded. Late-life violent victimization may occur in distinct social and relational contexts; thus, understanding these patterns is important for prevention in an aging population.

Methods: We obtained statewide hospital discharge data and death records for California residents from 2005–2022, defining violent victimization as a hospital visit (inpatient or ED) or death due to interpersonal violence. We restricted analyses to adults aged 50 years and older and stratified results by sex and race and ethnicity. We calculated age-specific victimization rates per 100,000 person-years and 95% confidence intervals using Census-based population estimates.

Results: Among 2,333,871 events, rates of violent victimization declined with age for females and males of all racial and ethnic groups. Across ages 50-64, Black adults had the highest violent victimizations rates, but at ages 65 and older Multiracial adults exhibited the highest and persistently elevated rates across groups; among those aged 85 years and older, victimization rates among Multiracial adults were 145.1 per 100,000 person-years among females and 253.6 among males, compared with 77.1 and 135.6 among Black females and males, and 42.9 and 53.2 among White females and males, respectively.

Discussion: Elevated violent victimization among older Multiracial adults contrasts with lower rates and more substantial decline observed in other racial and ethnic groups. As the older adult population grows and diversifies, further research on the life experiences of older Multiracial adults is needed to improve understanding of the conditions shaping late-life risk across groups.


Female
Male
Rate per 100,000 person-years
1000
500
0
50-54
55-59
60-64
65-69
70-74
75-79
80-84
85+
Age group
group
AI
BAA
MULT
TOTAL
API
HISP
WHITE

LATEBREAKER

Diabetes

Elevated blood lead levels and cardiovascular disease among Older Adults with Diabetes

May Baydoun* Sri Banerjee Jagdish Khubchandani

Lead exposure later in life has been associated with chronic disease and adverse overall health outcomes. Occupational hazards are the predominant cause of increased lead levels in adults. In this study, we assessed whether increased blood lead levels are associated with cardiovascular disease (CVD) among people with diabetes. The study was conducted on adults aged 55 years or older living in the United States from the National Health and Nutrition Examination Survey (NHANES) survey for the years 1999 to 2018. Diabetes and CVD were ascertained through self-reported data. Blood lead levels (BLL's) were considered to be elevated at ≥ 1.30 µg/dL. Cross-sectional analysis was performed using complex samples logistic regression with adjustment for known confounders to determine the relationship of elevated lead levels and CVD, as experienced by patients who have diabetes. For CVD, the overall unadjusted odds ratio (OR) of elevated BLL to normal BLL was 1.46 (95% confidence interval [CI], 1.23-1.73, $p < 0.01$). Adjusted OR was elevated, 1.32 (CI 1.07-3.30, $p < 0.01$), among patients with diabetes and elevated BLLs but closer to 1.0 (1.01 CI 0.88-1.15, $p = 0.92$) among patients without diabetes and normal BLLs, after controlling for medical (hypertension and obesity) and demographic risk factors (age, ethnicity, smoking status, education, marital status, and poverty-income-ratio). There was a complex interplay between elevated BLLs, diabetes, and CVD with a direct linkage between elevated BLLs and CVD. For people with diabetes, elevated BLLs may lead to more severe outcomes. Assessment for CVD should include biomonitoring of environmental health factors to identify and prevent poor potential outcomes.

EHR

Unique diagnosis days as a proxy for healthcare visits in electronic health record data
Maxwell Salvatore* Maxwell Salvatore

Electronic health record (EHR) data, which are not collected for research purposes, are subject to clinical informative observation processes that can introduce bias into their analysis. Therefore, EHR data analyses need to consider measures of healthcare utilization.

The total number of visits (TNV) is one conceptually simple metric that can present logistical challenges. For example, visit data are often stored separately from data of primary interest (e.g., diagnoses), and researchers may need to consider which visit types (e.g., outpatient, telehealth) are relevant. To limit data sharing, researchers may only have access to diagnosis code data. One alternative metric used in published research is the number of days with a diagnosis (NDD).

Using data from the 340,390 NIH All of Us Research Program participants, I explored (a) the partial correlation coefficients (adjusted for demographics) between TNV and each of 92 defined visit types, (b) the Pearson correlation coefficient between TNV and NDD overall and by sex and race/ethnicity, and (c) whether the choice between TNV or NDD substantially changes the regression coefficient for sex on bladder cancer.

Partial correlations between visit types and TNV varied substantially, ranging from less than 0.001 to 0.918 (outpatient visit).

The correlation between TNV and NDD was remarkably strong (0.877 [95% CI: 0.877, 0.878]). Some heterogeneity was observed across sex (0.885 among males and 0.873 among females) and race/ethnicity (Non-Hispanic (NH) Asian: 0.903; NH Black: 0.850; Hispanic/Latino: 0.854; NH White: 0.893).

The choice to adjust for TNV (male OR 2.63 [95% CI: 2.41, 2.86]) or NDD (2.69 [95% CI: 2.47, 2.93]) did not result in substantially different estimates of the association between sex and bladder cancer.

The use of NDD is straightforward to obtain and can serve as a proxy for TNV in analyses. Future work should validate NDD as a proxy across healthcare settings and patient subgroups.

Environment/Climate Change

Drinking water contaminants and risk of lymphohematopoietic malignancies in the Iowa Women's Health Study Rena R. Jones* Luz Villanueva Mary H. Ward Jared A. Fisher Maya Spaur Anna Prizment Laura E. Beane Freeman

Background: Some drinking water disinfection byproducts and nitrate/nitrite that endogenously form carcinogenic N-nitroso compounds are suspected lymphomagens and leukemogens, but studies are limited.

Methods: Among 15,577 postmenopausal women in the Iowa Women's Health Study, followed 1986-2016, using public water supplies (PWS) >10 years, we computed pre-enrollment, residential duration-based average concentrations of total trihalomethanes (TTHM), the sum of five haloacetic acids (HAA5), and nitrate-nitrogen (NO3-N) from PWS monitoring data. We estimated hazard ratios (HR) and 95% confidence intervals (CI) for continuous exposures (per log2) and quartiles (Q1 referent) with leukemia (N=127 cases) and non-Hodgkin lymphoma (NHL; N=344) and its major subtypes: chronic lymphocytic leukemia (CLL); multiple myeloma; follicular lymphoma; diffuse large b-cell lymphoma. Models adjusted for age, body mass index, and smoking; we also evaluated mutual adjustment of contaminants.

Results: We observed no clear associations for leukemia and NHL overall with TTHM (HRper-log2[CI]=1.01[0.96-1.06]; 1.01[0.96-1.05], respectively) and HAA5 (1.01[0.99-1.04]; 1.02[0.99-1.06]). Although we found no exposure-response in categorical analyses for follicular lymphoma (N=48) with TTHM (p-trend=0.53) or HAA5 (p-trend=0.49), risk was elevated for continuous exposures HRper-log2=1.10[1.00-1.20]; 1.12[0.99-1.26]). We observed non-significant positive associations with continuous HAA5 for other NHL subtypes. CLL risk (N=78) was elevated non-monotonically across HAA5 categories (p-trend=0.34), with the strongest association in Q3 (HRQ3vsQ1=2.18[1.11-4.29]), and weaker and imprecise associations in Q2 (HRQ2vsQ1=1.56[0.82,2.96]) and Q4 (HRQ4vsQ1=1.11[0.53,2.30]). Mutual adjustment did not change these associations. We found no associations with nitrate.

Conclusion: We report the first, albeit modest, evidence of relationships between HAA5 and risk of some NHL subtypes. Larger study replication is needed.

Environment/Climate Change

Determinants of total perfluoroalkyl substance (PFAS) body burden among postmenopausal women Maud Muosieyiri* Maud Muosieyiri Katherine Reeves

Background: Perfluoroalkyl substances (PFAS) are highly persistent synthetic chemicals that have long biological half-lives. Although exposure to individual PFAS compounds has been widely studied, most epidemiologic studies examine predictors of individual PFAS, despite evidence that humans are exposed to complex mixtures of PFAS. Thus, less is known about determinants of overall PFAS burden, especially in adults. We aimed to identify predictors of PFAS exposure in a population of postmenopausal women.

Methods: We measured serum concentrations of seven PFAS in 263 cancer-free postmenopausal women. Individual PFAS concentrations were converted to molar units and summed to derive a total PFAS molar sum. Multivariable linear regression estimated adjusted predicted geometric means, accounting for age, education, race, BMI, smoking, alcohol use, breastfeeding history, parity, and postmenopausal hormone therapy use. Effect modification was evaluated using interaction terms. Results are presented as predicted geometric mean PFAS concentrations with 95% confidence intervals.

Results: Age was the strongest predictor of total PFAS exposure, with PFAS molar sum increasing steadily across older age groups. Higher education was also associated with higher PFAS molar sum. A significant race-by-BMI interaction was also observed, with the most significant racial differences in exposure among underweight and normal-weight women where non-White women had a greater mean concentration than their White counterparts.

Conclusion: Total PFAS exposure varied by age, education, race, and BMI among postmenopausal women. A significant race–BMI interaction indicated that racial disparities in PFAS exposure were most pronounced among underweight and normal-weight women, emphasizing the importance of joint social and biological effects. Characterizing determinants of overall PFAS burden helps identify subgroups with high exposure and supports mixture-based approaches for PFAS exposure assessment.

Environment/Climate Change

Impact of extreme heat on mortality in a medically vulnerable population of kidney transplant recipients: a national cohort study Ting Lu, MS* Ting Lu Kyle R. Jackson, MD, PhD

Background
Extreme heat increases mortality risk in the general population, but data for vulnerable groups like kidney transplant (KT) recipients who are immunosuppressed with high comorbidity burdens are limited. We evaluated associations between weekly ambient heat index (HI) and post-transplant mortality and death-censored graft failure. We used Mundlak decomposition to separately examine the impact of short-term HI deviations from average norms versus longer-term place-based differences in typical heat exposure.
Methods
We studied 286,522 adult KT recipients (USRDS, 2000–2021) linking to recipients' time-varying residence. Daily ZCTA-level HI was computed from PRISM 800-m gridded climate inputs using spatially area-weighted and summarized as weekly mean HI. We fit negative binomial mixed models with ZCTA random effect, adjusting for calendar trends and seasonality. We compared: (i) single-term weekly HI models and (ii) Mundlak decomposition separating within-ZCTA weekly deviations from between-ZCTA season-specific mean HI differences. Effects are reported per 1°C HI increase.
Results
Analyses included 17,613,719 ZCTA-weeks (86,001 deaths; 58,828 graft failures) full-season and 7,383,358 ZCTA-weeks (32,914 deaths; 22,786 graft failures) warm-season across 23,379 ZCTAs. Single-term models showed higher weekly HI linked to mortality and graft failure, strongest in warm season (mortality IRR=1.009 [1.007–1.011], p<0.001). Mundlak models showed no association with short-term within-ZCTA deviations; however, between-ZCTA season-specific mean HI showed consistent positive associations, stronger in warm season (mortality IRR=1.015 [1.012–1.018], p<0.001).
Conclusions
Higher weekly heat exposure increases mortality and graft failure risk, particularly in warm seasons. Long-term place-based heat differences dominate associations, suggesting a need for local temperature context in risk assessment and targeted heat-preparedness for KT recipients during warmer months.

Table. Adjusted IRRs (95%CI) for weekly mean HI and KT outcomes: single exposure vs Mundlak decomposition

Outcome	Season window	Model A: Single HI term (HI)	Model B: Between-ZCTA mean HI	Model B: Within ZCTA deviation HI
Death	Full year	1.001 (1.000, 1.002)	1.003 (1.002, 1.005)	0.999 (0.997, 1.001)
Death	Warm (May-Sep)	1.009 (1.007, 1.011)	1.015 (1.012, 1.018)	0.997 (0.994, 1.001)
Graft loss	Full year	1.003 (1.002, 1.005)	1.005 (1.003, 1.007)	1.001 (0.999, 1.003)
Graft loss	Warm (May-Sep)	1.007 (1.004, 1.009)	1.011 (1.008, 1.015)	0.999 (0.995, 1.003)

Incidence Rate Ratios (IRRs) from negative binomial mixed models with log(person-weeks) offset and a ZCTA random intercept
Adjusted for calendar time (natural splines for year), seasonality(month), ZCTA-level recipient composition (median age and % female)
HI was summarized as weekly mean and modeled per 1°C increase.

LATEBREAKER

Environment/Climate Change

Associations of maternal urinary perchlorate, thiocyanate, and nitrate with maternal thyroid function during pregnancy: Modification by iodine status in the MARBLES study

Hyuna Jang* HyunA Jang Deborah H. Bennett Andrew N. Hoofnagle Elizabeth N. Pearce Rebecca J. Schmidt Hyeong-Moo Shin

Background: Perchlorate, thiocyanate, and nitrate are ubiquitous environmental contaminants known to disrupt thyroid homeostasis by inhibiting iodide uptake into the thyroid gland. However, evidence linking prenatal exposure to these chemicals with alterations in maternal thyroid function remains limited and inconsistent. This study investigated these associations and evaluated potential effect modification by maternal iodine status.

Methods: We included 192 pregnant women (2007–2020) from MARBLES (Markers of Autism Risk in Babies; Learning Early Signs), a prospective pregnancy study enriched for familial autism risk, who provided repeated urine and serum samples during pregnancy. Urinary perchlorate, thiocyanate, and nitrate concentrations were measured and adjusted for creatinine. Serum total triiodothyronine, total thyroxine (TT4), free thyroxine (FT4), and thyroid-stimulating hormone (TSH) levels were quantified. Single-pollutant associations were estimated using generalized estimating equation models and linear quantile mixed models. Mixture effects were evaluated using Bayesian kernel machine regression. Analyses were stratified by maternal iodine status (urinary iodine concentration [UIC] <150 vs. ≥150 µg/L).

Results: In the full sample, higher urinary thiocyanate concentrations were associated with lower FT4 levels (β = -0.17, 95% CI: -0.30, -0.04), and no overall mixture effects were observed. Among women with UIC <150 µg/L, associations were stronger: higher thiocyanate was associated with lower FT4, higher nitrate was linked to higher TT4 and lower TSH, and mixture exposure showed a decreasing trend in FT4. No statistically significant associations were observed among women with UIC ³150 µg/L.

Conclusions: These findings suggest that prenatal exposure to thiocyanate and nitrate may be associated with alterations in maternal thyroid function, particularly among women with insufficient iodine.

LATEBREAKER

Environment/Climate Change

The Associations between the Child Opportunity Index and Pediatric Asthma Exacerbations (2013-2021) Sneha Kannoth* Sneha Kannoth Itai Kloog Ryan Michael Leon Hsu Cecilia Alcala Maayan Yitshak-Sade Elena Colicino Kecia Carroll

Introduction

Studies suggest that neighborhood conditions influence pediatric respiratory health, but few accounted for residential greenness and atopic history. We studied the link between the Child Opportunity Index (COI), a quality measure of neighborhood resources, and asthma exacerbations, assessing interaction by atopic history and adjusting for residential greenness.

Methods

We studied children with asthma (ages 5-17) receiving primary care in the Mount Sinai Health System (2013-2021), using electronic health record data. We assessed associations between overall and domain-specific COI z-scores (SES: Social and Economic; ED: Education; HE: Health and Environment), and asthma exacerbation (any hospitalization, emergency department visit, or outpatient oral corticosteroid use) in the subsequent year. We used mixed-effects logistic regression, adjusting for age, sex, race/ethnicity, insurance, and interaction by atopic history. In extended models, we adjusted for residential greenness, using Normalized Difference Vegetation Index (NDVI) scores at 300-meter buffers with Landsat data (summer, 2012-2021).

Results

Among 4,579 children with asthma, 16.6% (n=761) experienced exacerbation. Higher overall COI was associated with lower exacerbation risk (RR:0.62; 95%CI:0.50-0.75), with similar findings for domain-specific COI scores. Findings suggest interaction by atopic history (p=0.04), with stronger protective associations among those without atopy (Non-atopy RR:0.25; 95%CI:0.13-0.48; Atopy RR:0.67; 95%CI:0.54-0.83). After adjusting for residential greenness, COI remained protective, but interaction by atopy was no longer significant (p>0.05).

Discussion

Greater neighborhood opportunity is linked with reduced pediatric asthma exacerbation risk. Interaction by atopy was observed before adjusting for residential greenness. Considering both patient atopy and environmental exposures can improve understanding of how neighborhood resources influence pediatric asthma burden.

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LATEBREAKER

Environment/Climate Change

Associations between plasma metal(loid) concentrations and early neurodegenerative findings estimated from MRI in cognitively normal adults Ruby Hickman* Ruby Hickman Haomin Li Terry Zhou Priya Esilda D'Souza Dana Boyd Barr Allan I. Levey Deqiang Qiu James Lah Thomas S. Wingo Donghai Liang Anke Hüls

Objective: Exposure to certain metal(loid)s (MM) has been linked with dementia-related neuropathology, but many remain understudied. Furthermore, research on associations between plasma levels of MM and neuroimaging outcomes is sparse.

Methods: We assessed associations between plasma MM concentrations and later neuroimaging outcomes in 300 participants (mean age 65 (standard deviation [SD]: 6.6), 39% with >1 imaging timepoint) from the Emory Healthy Brain Study. Concentrations of 15 MM (arsenic (As), barium (Ba), beryllium (Be), cadmium (Cd), chromium (Cr), cobalt (Co), cesium (Cs), manganese (Mn), mercury (Hg), nickel (Ni), antimony (Sb), tin (Sn), tellurium (Te), uranium (U), and vanadium (V)) were quantified in plasma using inductively coupled plasma-mass spectrometry and dichotomized (detect/non-detect) based upon the limit of detection (LOD). Total grey matter volume, left and right white matter and hippocampus volumes, and left and right cortical thickness and volumes were measured using magnetic resonance imaging (MRI). Associations between MM detection and neuroimaging measures were assessed in single-pollutant mixed effects models adjusted for age, sex, race/ethnicity, education, and estimated total intracranial volume.

Results: Hg, Cr, Cd, Mn, and Ba had <3% of samples above the LOD so were excluded. Remaining 10 MM had frequencies of detection ranging from 4.0% (Cs) to 96.3% (U). We found variable associations between MM detection and cortical thickness (Sn: 0.49 SD higher left cortical thickness (95% confidence interval [CI]: 0.09, 0.89), Sb: -0.28 SD left cortical thickness (95% CI: -0.55, -0.01)). Nominally positive associations between Ni and white matter volume outcomes were observed; no other significant associations were observed.

Conclusion: In single-pollutant models, we found mixed associations between plasma MM and cortical thickness, but generally non-significant associations with other neuroimaging outcomes.

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Environment/Climate Change

Dust Storms, Air Pollution, and Non-Communicable Disease Burden in Uzbekistan Sergey Soshnikov* Sergey Soshnikov Olga Tsvetkova

Background

Uzbekistan has experienced significant economic growth, implemented transformative health policy reforms, and faced alarming environmental challenges. This has resulted in a complex set of environmental health challenges, in particular climate change, dust and sand storms, air pollution, and heat/cold waves. There has been significant progress in the country in controlling infectious diseases, reducing child mortality, and increasing life expectancy.

Methodology

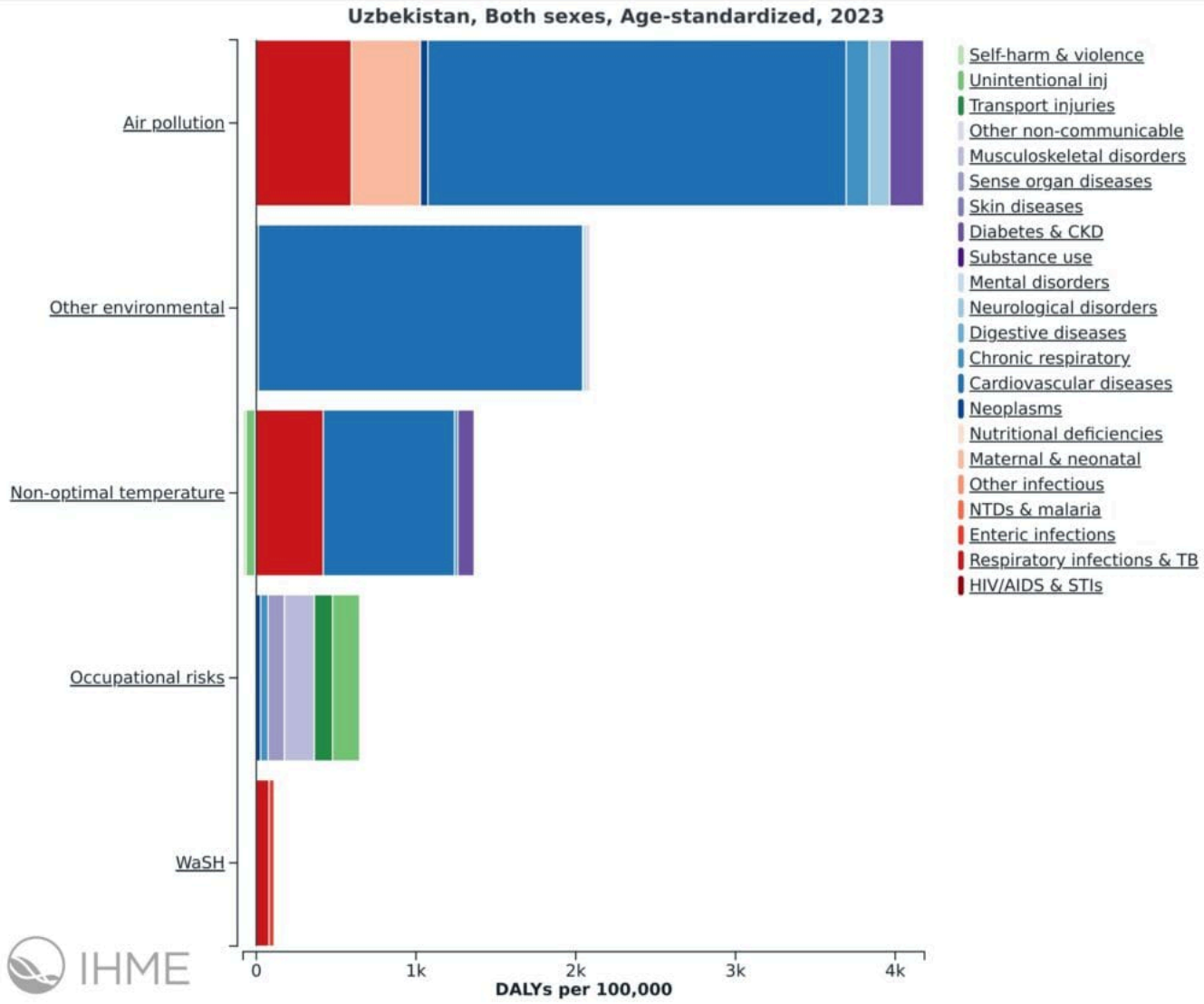
Estimates from the Global Burden of Disease from 1990 to 2023 have been used to discover trends in mortality, years of life lost (YLLs), and disability-adjusted life years (DALYs), including those related to climate and air pollution. The age-standardized rates for the significant risk factors (including ambient particulate matter, household air pollution, and temperature), as well as for death and YLLs, and DALYs due to metabolic, behavioral, and environmental risks. The YLD-to-YLL ratio was used to assess the epidemiological transition.

Results

Ischemic heart disease, stroke, and lower respiratory infections are the leading causes of age-standardized mortality in 2023. There was an alarming 170% increase in diabetes-related mortality. Leading NCDs were ischemic heart disease with 4,800 DALYs, lower respiratory infections 3000 DALYs, neonatal disorders 2847 DALYs, stroke 1929 DALYs, and depressive disorders 544 DALYs – all per 100,000 population. Ambient particulate matter and other pollutants were core drivers of DALYs lost from cardiovascular diseases (7.8% of all DALYs), respiratory infections (1.8% of DALYs), and 1.4 % of neonatal disorders DALYs.

Conclusions

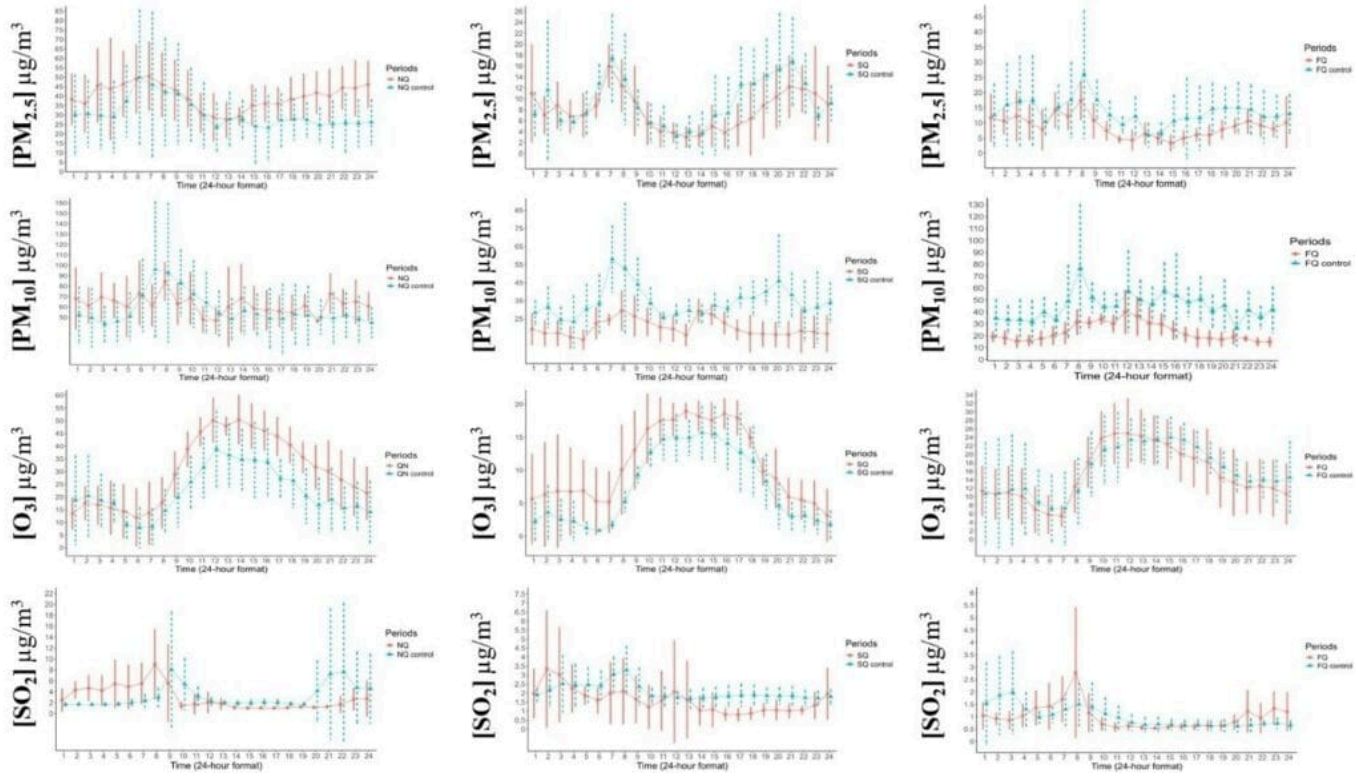
Surviving the rapidly growing burdens from the climate crisis and air pollution, especially from cardiometabolic and climate-sensitive diseases, remains the key to further advancements.


Uzbekistan, Both sexes, Age-standardized, 2023
Air pollution
Other environmental
Non-optimal temperature
Occupational risks
WaSH
Self-harm & violence
Unintentional inj
Transport injuries
Other non-communicable
Musculoskeletal disorders
Sense organ diseases
Skin diseases
Diabetes & CKD
Substance use
Mental disorders
Neurological disorders
Digestive diseases
Chronic respiratory
Cardiovascular diseases
Neoplasms
Nutritional deficiencies
Maternal & neonatal
Other infectious
NTDs & malaria
Enteric infections
Respiratory infections & TB
HIV/AIDS & STIs
IHME
0
1k
2k
3k
4k
DALYs per 100,000

Environment/Climate Change

Effect of social restriction intensity during the SARS-CoV-2 pandemic on air pollution: A natural experiment Karen P. Ayala* Aníbal A. Teherán Luis M. Pombo Gabriel Camero-Ramos Jaime A. Robayo William J. Rodríguez Karen P. Ayala

To improve air quality, regulatory actions targeting road traffic and industrial emissions must be implemented. This study determined the effect size (ES, Cohen's δ) and the significance of progressive quarantine restrictions (Levels NQ+, SQ++, FQ+++) on air pollution in Bogotá, Colombia, during the SARS-CoV-2 pandemic. A natural experiment showed that, during SQ and FQ phases, concentrations of [PM10, 20.2 µg/m3; PM2.5, 8.03 µg/m3; SO2, 1.61 µg/m3] and [PM10, 23.2 µg/m3, PM2.5, 8.84 µg/m3], respectively, were significantly lower than during equivalent pre-pandemic periods (year 2019; p <0.001). Effect sizes were larger during FQ (PM10: -1.220, PM2.5: -6.05) than during SQ (PM10: -1.180, PM2.5: -0.252, SO2: -0.388). Although pollutant concentrations remained below regulatory thresholds (environmentally significance), the ES for [PM10 µg/m3; PM2.5 µg/m3] were larger during SQ and FQ. These findings support public health strategies aimed at strengthening the control of emission sources that degrade air quality, particularly those increasing [PM10, PM2.5], Moreover, the introduction of the concept of "environmentally significant" effects may further improve decision-making and address environmental problems that affect human well-being.



Environment/Climate Change

Applications of Statistical Analysis Methods to Sparse Data at Low Fine Particulate Matter Concentrations Jacob Kremer* Jacob Kremer Tiffani Fordyce Ethan Roubenoff Megan Leonhard Jessica Lin

Fine particulate matter (PM2.5) has been demonstrated to adversely affect human health and mortality. However, considerable debate exists over estimation of the precise Concentration Response Function (CRF) describing the relationship between PM2.5 and all-cause mortality. To evaluate potential improvements to CRF modeling techniques when applied to sparse data at low exposures, Al-Kindi et al., 2019 was chosen as the basis for a replication analysis and method development. Techniques used for exposure data modeling included Inverse Distance Weighting and Kriging (Gaussian Process Modeling); CRF modeling included Poisson GAM and Pohar Perme estimation of net survival. Overall, the replication analysis showed agreement with Al-Kindi et al.'s estimated treatment effects but found a lower mortality hazard at lower levels of PM2.5 exposure, suggesting that mortality is driven by higher levels of exposure.

Environment/Climate Change

Housing Type Modifies the Association Between Ambient Temperature and Indoor Cardiac Arrest in a Large Japanese City Akihiko Narisada* Akihiko Narisada Tomohiro Umemura Nauta Yamanaka Kohta Suzuki

Background: Climate change is increasing the frequency and intensity of heat exposure, raising concerns about heat-related cardiovascular events. Indoor heat exposure, influenced by housing characteristics and cooling behaviors, may be particularly important for severe outcomes such as cardiac arrest. The World Health Organization's Housing and Health Guidelines emphasize maintaining safe indoor temperatures through adequate housing and appropriate air conditioner use. In Japan, however, housing conditions and air conditioner use differ between detached houses and apartment buildings. This study examined the association between ambient temperature and emergency ambulance transport for cardiac arrest occurring in living rooms, stratified by housing type, in a large Japanese city.

Methods: We analyzed ambulance transport records for out-of-hospital cardiac arrest occurring in living rooms of residential dwellings in Nagoya City, Japan (population ~2 million), between April 2016 and March 2022. A time-stratified case-crossover design was used to assess short-term associations between daily mean temperature and cardiac arrest risk. Temperature effects were modeled using distributed lag nonlinear models, with 15°C as the reference. Analyses were stratified by housing type: detached houses and apartment buildings.

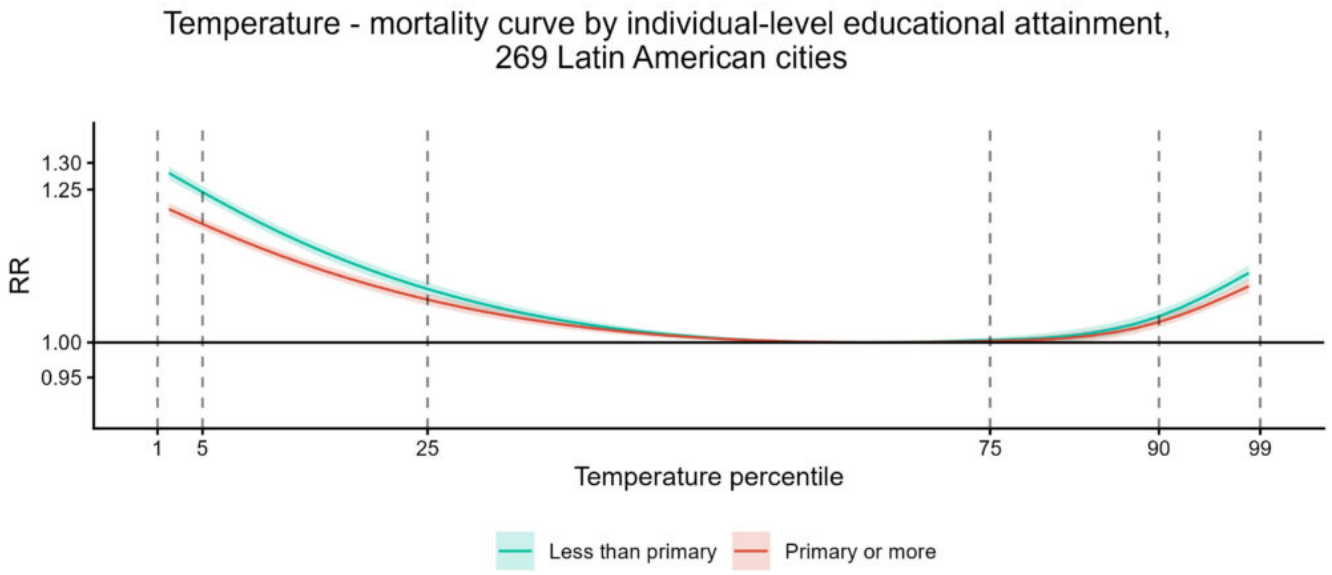
Results: A total of 5,489 cardiac arrest cases were included (3,147 in detached houses and 2,342 in apartment buildings). No increased risk was observed at low temperatures in either housing type. At high temperatures, risk differed by housing type. No increase was observed in detached houses at 30°C (RR 1.01, 95% CI 0.73–1.41), whereas a significant increase was observed in apartment buildings (RR 1.45, 95% CI 1.01–2.08).

Conclusions: In the context of climate change and increasing indoor heat exposure, residents of apartment buildings showed elevated risk of heat-related cardiac arrest occurring indoors, while no such increase was observed in detached houses. Promoting appropriate air conditioner use in apartment buildings during hot periods may be critical for preventing heat-related cardiac arrest.

Environment/Climate Change

Modification of extreme temperature effects in mortality by individual-level education in Latin American cities Diana Higuera-Mendieta* Diana Higuera-Mendieta Josiah Kephart Brisa Sanchez Usama Bilal Andres Totta Karla Yohannessen Maria Pia Muñoz Giovanna Valentino Celia Jimenez Ortiz Laura Rodriguez Villamizar Penelope Brou-Gonzalez Ana V Diez-Roux

Background
Extreme temperatures are known to increase population mortality. However, few studies have examined whether these effects differ across social groups in highly unequal, highly urbanized contexts. Latin America has high levels of urbanization and urban inequalities, which may magnify the health effects of extreme temperatures due to differential exposure, susceptibility, or adaptive capacity.
Objective
To examine whether individual-level educational attainment modifies the effects of extreme ambient temperatures on all-cause mortality across 269 Latin American cities between 2000 and 2022.
Methods
We linked individual-level death records with population-weighted daily temperature for each city. We conducted a case-time series analysis and fitted a nonlinear, 21-day distributed-lag Poisson model pooling all cities. We controlled for age, included an interaction term of temperature with educational attainment, and examined temperature percentiles to facilitate cross-city comparisons. A total of 17,588,842 all-cause deaths across 1,567,628 city-days were analyzed.
Results
The median daily temperature was 20.8 °C (range: −11 to 41.3 °C). The relative risk (RR) of mortality per 1 °C decrease in extreme cold temperatures (<5th percentile) among individuals with less than primary education was 2.55 (95% CI: 2.34–2.77), compared with 2.07 (95% CI: 1.92–2.24) among those with primary education or more. Under extreme heat (>95th percentile), the RR per 1 °C increase was greater in lower education (2.47 [95% CI: 2.06–2.96]) versus higher education (2.11 [95% CI: 1.80–2.48]) individuals.
Conclusion
There are inequalities in temperature-related mortality by individual educational attainment. These differential effects are observed predominantly in extreme cold. These results underscore the need for targeted heat- and cold-adaptation strategies that address individual social vulnerability in Latin American cities.


Temperature - mortality curve by individual-level educational attainment,
269 Latin American cities
RR
1.30
1.25
1.00
0.95
1
5
25
75
90
99
Temperature percentile
Less than primary
Primary or more

Genetics

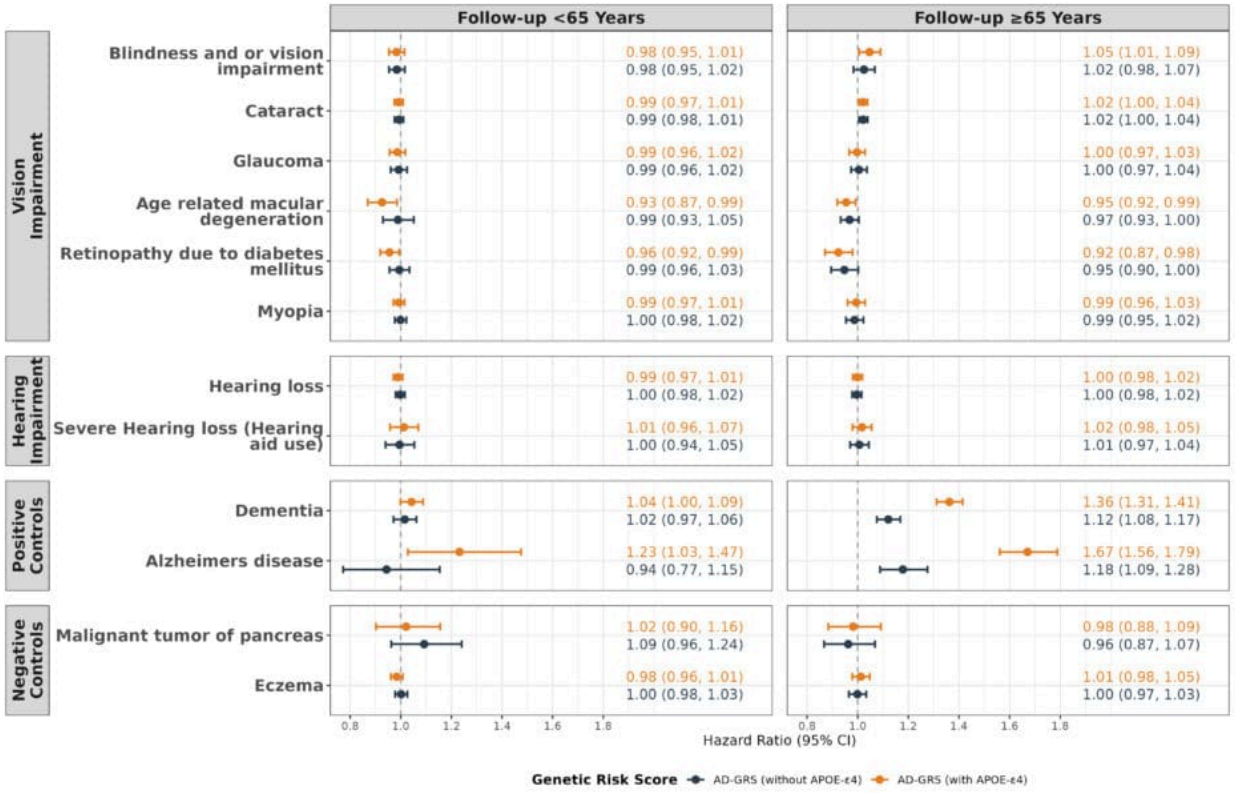
Reverse Mendelian Randomization of Alzheimer's Disease Genetic Risk Score and Sensory impairments Peter T. Buto* Minhyuk Choi Scott C. Zimmerman, MPH Peter T. Buto, MPH Jingxuan Wang, PhD Thomas J. Hoffmann, PhD Paige D. Wartko, PhD Hélène Choquet, PhD Dima L. Chaar, PhD Yulin Hswen, PhD M. Maria Glymour, ScD Willa D. Brenowitz, PhD

Background: Identifying prodromal changes associated with incipient Alzheimer's Disease (AD) is essential to guide prevention efforts. Sensory impairments have been hypothesized as early manifestations of AD pathophysiology. Using a reverse Mendelian Randomization (MR) design, we aimed to establish causal and temporal associations between AD genetic risk and time to sensory impairment diagnosis.

Methods: We used electronic health record data from the NIH All of Us Research Program (N=258,585). For each sensory impairment (vision impairment, cataract, glaucoma, age related macular degeneration (AMD), diabetic retinopathy, myopia, hearing loss, and severe hearing loss), outcome-free individuals were followed from 2014, until the earliest date of: sensory impairment diagnosis, death, or the data cut-off (Sep. 2023). We calculated a z-scored AD genetic risk score (AD-GRS) using 85 genetic instruments (with and without *APOE*-ε4). Cox models estimated the association between AD-GRS and time-to-first sensory impairment diagnosis. Positive controls (dementia, AD) and negative controls (pancreatic cancer, eczema) were included. Analyses were stratified by follow-up period: early-to-mid life (follow-up restricted to <65 years) and late-life (follow-up ≥65 years). Models adjusted for sex, race, baseline age, and genetic ancestry.

Results: In early-to-mid life, AMD (HR: 0.95 [0.91, 0.98]) and diabetic retinopathy (HR: 0.95 [0.92, 0.98]) were inversely associated with the AD-GRS with *APOE*-ε4 but not when excluding *APOE*-ε4 . In late-life, small positive associations were observed between AD-GRS (with *APOE*-ε4) and cataracts (HR: 1.02 [1.00, 1.04]) and blindness/vision impairment (HR: 1.05 [1.01, 1.09]). Associations with sensory impairments were minimal compared to the association with dementia (Figure 1).

Conclusion: Late-life analyses demonstrated small positive associations of AD genetic risk with cataracts and blindness, but overall null or inverse across other outcomes.


Follow-up <65 Years
Follow-up ≥65 Years
Vision Impairment
Blindness and or vision impairment
0.98 (0.95, 1.01)
0.98 (0.95, 1.02)
1.05 (1.01, 1.09)
1.02 (0.98, 1.07)
Cataract
0.99 (0.97, 1.01)
0.99 (0.98, 1.01)
1.02 (1.00, 1.04)
1.02 (1.00, 1.04)
Glaucoma
0.99 (0.96, 1.02)
0.99 (0.96, 1.02)
1.00 (0.97, 1.03)
1.00 (0.97, 1.04)
Age related macular degeneration
0.93 (0.87, 0.99)
0.99 (0.93, 1.05)
0.95 (0.92, 0.99)
0.97 (0.93, 1.00)
Retinopathy due to diabetes mellitus
0.96 (0.92, 0.99)
0.99 (0.96, 1.03)
0.92 (0.87, 0.98)
0.95 (0.90, 1.00)
Myopia
0.99 (0.97, 1.01)
1.00 (0.98, 1.02)
0.99 (0.96, 1.03)
0.99 (0.95, 1.02)
Hearing Impairment
Hearing loss
0.99 (0.97, 1.01)
1.00 (0.98, 1.02)
1.00 (0.98, 1.02)
1.00 (0.98, 1.02)
Severe Hearing loss (Hearing aid use)
1.01 (0.96, 1.07)
1.00 (0.94, 1.05)
1.02 (0.98, 1.05)
1.01 (0.97, 1.04)
Positive Controls
Dementia
1.04 (1.00, 1.09)
1.02 (0.97, 1.06)
1.36 (1.31, 1.41)
1.12 (1.08, 1.17)
Alzheimers disease
1.23 (1.03, 1.47)
0.94 (0.77, 1.15)
1.67 (1.56, 1.79)
1.18 (1.09, 1.28)
Negative Controls
Malignant tumor of pancreas
1.02 (0.90, 1.16)
1.09 (0.96, 1.24)
0.98 (0.88, 1.09)
0.96 (0.87, 1.07)
Eczema
0.98 (0.96, 1.01)
1.00 (0.98, 1.03)
1.01 (0.98, 1.05)
1.00 (0.97, 1.03)
0.8
1.0
1.2
1.4
1.6
1.8
Hazard Ratio (95% CI)
Genetic Risk Score
AD-GRS (without APOE-ε4)
AD-GRS (with APOE-ε4)

Global Health

Algorithmic Transportability of Pediatric Tuberculosis Treatment Models: The Impact of Measurement Heterogeneity and Missing Data Ieza Arshad* Ieza Arshad Meredith Brooks Amyn Malik

Background: Pediatric tuberculosis (TB) remains a diagnostic challenge due to nonspecific clinical presentations and limited bacteriologic testing. Clinical prediction models offer pragmatic tools for treatment decision-making, yet their transportability across diverse contexts remains uncharacterized. We assessed whether performance degradation in external settings is driven by patient characteristics and structural discrepancies such as predictor measurement heterogeneity and missing data mechanisms.

Methods: We validated two logistic regression pediatric TB models (derived in Pakistan and Bangladesh) using the INSPIRE dataset (a harmonized cohort of 4,718 children from 13 studies across 12 countries). We quantified the drop in discriminative performance (Youden's J index) across settings. We evaluated the influence of inconsistent predictor definitions (e.g., "TB contact") and conducted sensitivity analyses to identify the structural impact of missing data assumptions.

Results: Transportability was poor; Youden's J declined by a mean of 0.42 in same-setting comparisons and averaged 0.27 in same-country cohorts. This was linked to data inconsistencies. For the Bangladesh model, specificity decreased by up to 67.5 percentage points (from 75.4% to 7.9%) in populations with different predictor distributions. Similarly, "pragmatic" missing data assumptions proved unstable: altering imputation from "missing=0" to "missing=1" reduced specificity by 17.4% in the Bangladesh model and 23.4% in the Pakistan model. Inconsistent definitions of "TB contact" and variable missingness (2.7% to 90%) introduced structural biases distorting risk scores.

Conclusion: Limited transportability stems from epidemiologic, measurement, and data-quality mismatches. Harmonized definitions, improved data completeness, and setting-specific recalibration are essential for equitable, reliable pediatric TB diagnostics. Future work should prioritize prospective validation and adaptive modeling.

Global Health

Investigating the relationship between long-term, stable partnership and pregnancy outcomes among women in the Mombasa Reproductive and Perinatal Health Study Hanna Shephard* Hanna Shephard Kishor Mandaliya Walter Jaoko Marianne Mureithi R. Scott McClelland

Background: Women engaged in sex work face intersecting social and health vulnerabilities that may shape their perinatal outcomes. While marriage and long-term partnership have been associated with lower risks of stillbirth and child mortality in general populations, their relationship to pregnancy outcomes among women engaged in sex work is poorly understood. The Mombasa Reproductive & Perinatal Health (MRPH) Study was designed to generate longitudinal evidence on reproductive and perinatal health in this population.

Objective: We tested the hypothesis that being in a stable, long-term partnership during pregnancy would lead to an increased probability of live birth among women in the MRPH Study.

Methods: We collected information on participants' (up to ten most recent) prior pregnancies, including the outcome of each pregnancy and their partnership status during each pregnancy. The exposure of this study was stable, long-term partnership or marriage during pregnancy (yes/no). The outcome was live birth versus other all other pregnancy outcomes (miscarriage, termination, stillbirth, and ectopic pregnancy). Relative risks (RR) and 95% confidence intervals (CI) were estimated using modified Poisson regression with cluster-robust standard errors to account for multiple pregnancies per participant and adjusting for maternal age and education.

Results: Among 641 gravid participants contributing 2,124 pregnancies (≈3 per participant), 81.2% of pregnancies resulted in live birth, 10.9% miscarriage, 5.6% termination, and 2.3% stillbirth. The proportion of pregnancies resulting in live birth was higher among pregnancies with a stable partnership (88.3%) compared to those without (74.5%). In unadjusted analyses, stable partnership was associated with an 18% higher probability of live birth (RR 1.18, 95% CI 1.13–1.25), and was only slightly attenuated after adjusting for age and education (RR 1.15, 95% CI 1.10–1.21).

Conclusions: Among MRPH study participants, stable, long-term partnership during pregnancy was associated with a modest but meaningful increase in the probability of live birth. Findings underscore the potential importance of relationship stability and support as protective factors in perinatal health within this group.

LATEBREAKER

Global Health

Modal Age at Death and Lifespan Variation at Shared Life Expectancy Levels in the East Asian Countries: A Decomposition Analysis Using Global Burden of Disease 2023 data Ikhan Kim* Ikhan Kim Jongjin Park

Background: We compared modal age at death and lifespan variation at shared life expectancy level across East Asian countries and between East Asian and selected non–East Asian countries. In addition, age- and cause-specific contributions to differences in the modal age at death and lifespan variation to global average values were analyzed.

Methods: Data from the Global Burden of Disease 2023 were used to obtain sex-specific population and cause-specific death numbers in 5-year age groups (0, 1–4, …, 95+) for six East Asian countries and 37 non-East Asian countries from 1980 to 2023. Sex- and year-specific life tables were constructed by country. Abridged probabilities of dying were interpolated into single-year probabilities of dying. The CoDe 2.1 model was fitted, and the estimated parameters were used to estimate the modal age at death, lifespan variation indicators, and life expectancy at birth.

Results: During the entire study period, the modal age at death generally increased, and lifespan variation decreased across the East Asian countries, although the specific patterns varied by country. Japan, the Republic of Korea, and China exhibited similar modal age at death and lifespan variation at shared levels of life expectancy for both sexes. However, Taiwanese males showed relatively higher values for both the modal age at death and lifespan variation than in other countries. Although both Mongolia and the Democratic Republic of Korea experienced fluctuations in life expectancy during the 1990s, their patterns differed. In Mongolia, declines in life expectancy were accompanied by decreases in both the modal age at death and lifespan variation. In the Democratic Republic of Korea, however, the modal age at death showed little change, while lifespan variation increased. Comparisons of the modal age at death and lifespan variation in East Asian countries at shared levels of life expectancy with 37 non–East Asian countries, as well as decomposition analyses, are currently underway.

Conclusion: Across the study period, East Asian countries showed an upward trend in the modal age at death and a downward trend in lifespan variation, although detailed patterns differed by country. Examining the modal age at death and lifespan variation at shared levels of life expectancy not only provides a more nuanced understanding of historical trends in mortality patterns but also helps inform projections of future trends.

Health Disparities

The Price of Delay: Interactions Between Addiction, Depression, and Inequality Youngseo Cheon* Youngseo Cheon Krishna Vaddiparti

Objectives: To examine whether delayed therapy due to treatment cost is associated with the co-occurrence of substance use and depression in U.S. adults and whether these conditions interact synergistically on the additive scale, consistent with a syndemic framework.

Methods: We analyzed data from the 2024 National Health Interview Survey Sample Adult (n=19,054). Weighted group comparisons and logistic regression models were used to examine associations between delayed therapy due to cost and co-occurrence of conditions. Additive interaction was evaluated using the relative excess risk due to interaction (RERI), attributable proportion (AP), and synergy index (SI), with odds ratios used as approximations of risk ratios.

Results: Overall, 4.2% of adults reported co-occurring substance use and depression. Delayed therapy due to cost was strongly associated with co-occurrence (AOR = 2.35; 95% CI: 1.90, 2.90). Women had more than twice the odds of co-occurrence compared to men (AOR= 2.09; 95% CI: 1.73, 2.53). Additive interaction analyses showed significant evidence of positive interaction between delayed therapy and female sex (RERI = 1.30; AP = 0.27; SI = 1.51), indicating a more-than-additive joint effect. In contrast, delayed therapy and low educational attainment demonstrated a sub-additive interaction (RERI = –1.19), despite each factor being independently associated with higher risk; however, the interaction was not statistically significant.

Conclusion: Delayed therapy due to cost is a robust correlate of the co-occurrence of substance use and depression. Additionally, the effect of delayed therapy increases synergistically among women, reflecting stronger joint effects in female populations. These findings suggest that social barriers to care intersect with gendered vulnerabilities and underscore the importance of a syndemic-informed approach that recognizes clustered social and behavioral risks.

Health Disparities

Guideline-Concordance Along the Cancer Care Continuum and Breast Cancer Mortality by Race and Ethnicity: a SEER-Medicare Study Emma L Herbach* Emma Herbach Ryan M Carnahan Lauren E McCullough Bradley D McDowell Michaela Curran Kai Wang Ingrid M Lizarraga Mary E Charlton Sarah H Nash

Purpose. To examine the relationship between guideline-concordant breast cancer care and hazard of cancer death by patient race and ethnicity.

Methods. We used SEER-Medicare data to identify 212,555 older women diagnosed with invasive breast cancer between 2000-2017. Guideline-concordant diagnostic workup, locoregional treatment, and initiation of systemic therapy were defined using NCCN guidelines. Hazards of breast cancer death 2- and 5-years from diagnosis by each guideline-concordance outcome overall and stratified by race and ethnicity were estimated using Cox proportional hazards models.

Results. Non-concordant diagnostic workup, locoregional treatment, and systemic therapy initiation were each associated with increased hazards of 2- and 5-year breast cancer mortality (diagnostics HR2-year (95% CI) 1.33 (1.25-1.41), HR5-year 1.29 (1.23-1.35); locoregional HR2-year 2.10 (1.98-2.23), HR5-year 1.83 (1.76-1.90); systemics HR2-year 1.67 (1.51-1.84), HR5-year 1.56 (1.45-1.68)). Non-concordant diagnostic workup and systemic therapy initiation were associated with greater hazard of 2- and 5-year breast cancer death among Black, Asian/Pacific Islander, Hispanic White, and non-Hispanic White patients; there was no consistent association among American Indian/Alaska Native patients for either outcome. Locoregional treatment was strongly associated with hazards of cancer death for all groups.

Conclusions. Equitable delivery of guideline-recommended breast cancer care from diagnosis through treatment across racial and ethnic groups may mitigate survival disparities. Efforts to improve access to high-quality care must be informed by and responsive to the social and structural root causes of health inequities.

Health Disparities

Assessing mediation of sexual orientation disparities in miscarriage by age at pregnancy

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

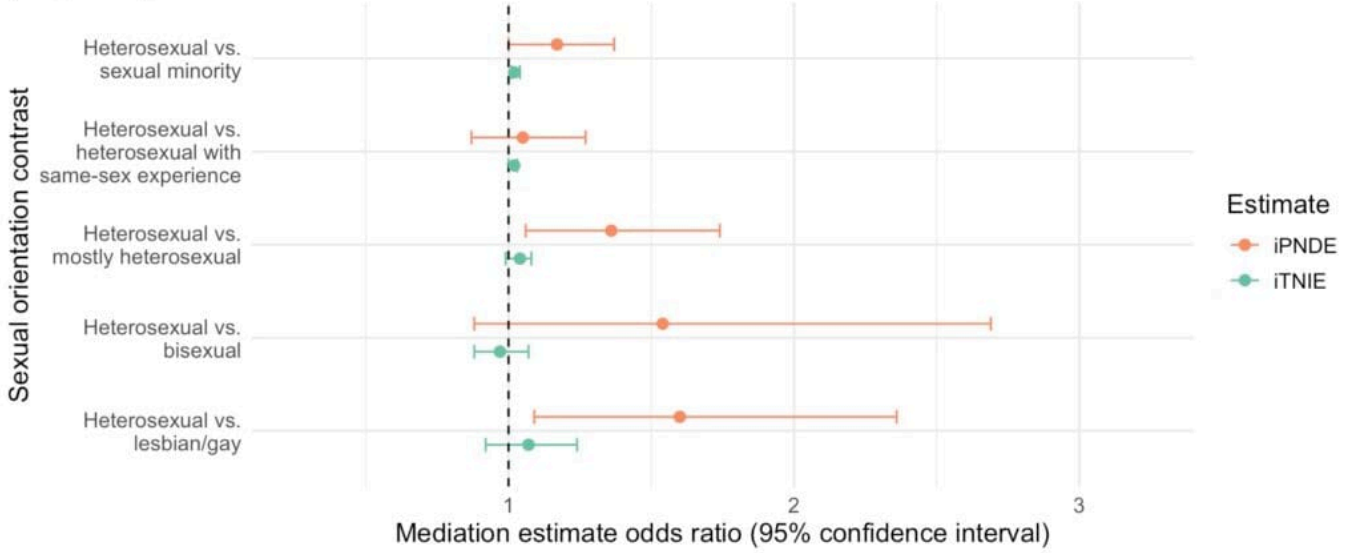
Background: Existing studies show sexual orientation-related disparities in miscarriage. Because age is strongly associated with miscarriage and may lie on the causal pathway (e.g., higher rates of both teen and later-life pregnancies among sexual minority people), conventional age adjustment fails to produce direct effect estimates. To address this, we used formal mediation methods to evaluate the role of age at pregnancy in sexual orientation disparities in miscarriage.

Methods: We used pregnancy data from the Nurses' Health Study 2, randomly selecting one pregnancy per person as pregnancy outcomes within a person are correlated. Because exposure induced mediator-outcome confounding was likely present, we estimated interventional mediated effects (interventional pure natural direct effect [iPNDE] and total natural indirect effect [iTNIE]). Our outcome was miscarriage (yes vs. no). We treated age as multinomial (pregnancies at age <20 or ≥35 vs. 20–34 years). We examined sexual orientation dichotomously (sexual minority vs. heterosexual) and with sexual minority groups disaggregated (heterosexual with same-sex experience, mostly heterosexual, bisexual, and lesbian/gay). Baseline covariates included measures of social origin and mediator-outcome confounders included a variety of demographic and health factors.

Results: Among 64,713 participants, 12% had a miscarriage. About 3% of pregnancies occurred at age <20 and 16% at age ≥35 years. We found some evidence of mediation by age comparing sexual minority groups combined to heterosexual participants (iPNDE: 1.17; 95% CI: 1.00–1.37; iTNIE: 1.02; 95% CI: 1.01–1.04; proportion mediated: 12%). Results varied for sexual orientation subgroups (Figure).

Conclusions: Age at pregnancy may contribute to a small portion of sexual orientation disparities in miscarriage. Analyses of other clinically relevant pregnancy characteristics, such as use of medically assisted reproduction, are ongoing.

Figure. Assessing mediation of sexual orientation disparities in miscarriage by age at pregnancy*



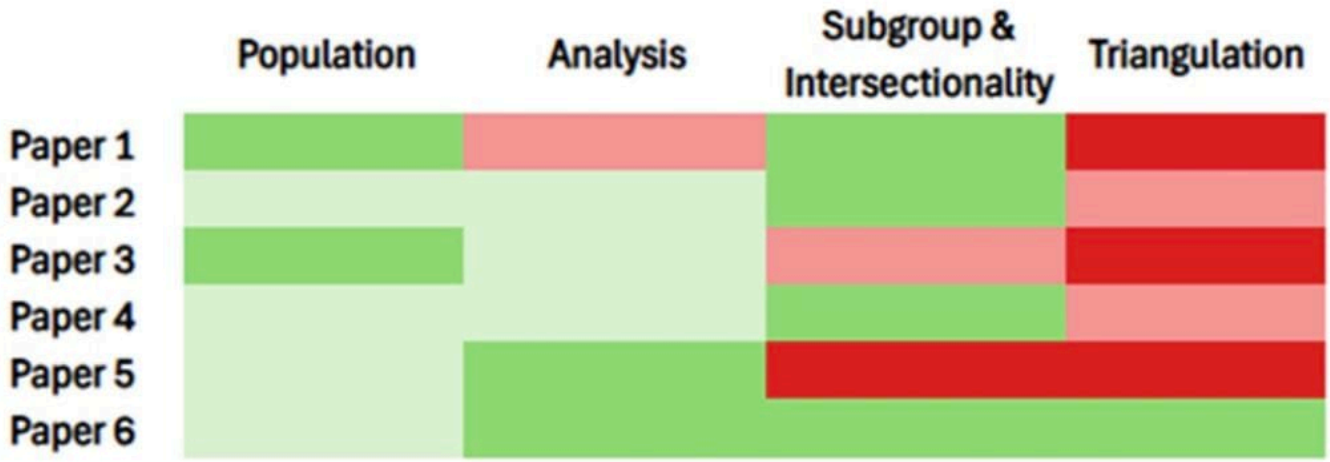
*We examined interventional mediated effects (interventional pure natural direct effect [iPNDE] and total natural indirect effect [iTNIE]) via marginal structural models. Sexual orientation (exposure) was modeled using logistic regression (binary) and multinomial logistic regression (disaggregated), miscarriage (outcome) was modeled using logistic regression, and age (mediator) was modeled using multinomial logistic regression. We allowed for exposure-mediator interaction. Our outcome was whether the pregnancy ended in miscarriage (yes vs. no). We treated age as multinomial (pregnancies at age <20 or ≥35 vs. 20–34). Baseline confounders included year of birth and race/ethnicity. Post-exposure confounders included PCOS, endometriosis, prior miscarriage, gravidity, partner status, SES, healthcare use, hormonal condition, autoimmune condition, cancer, and depression/anxiety. We used multiple imputation to account for missing data on confounders.

Health Disparities

DARE: A Health Disparities Assessment Rubric for Epidemiologic Data Analysis Yulin Hswen* Maggie Hurley Yulin Hswen Paola Gilsanz Shelli Vodovozov Tanisha G. Hill-Jarrett Maggie Hurley Jacqueline Torres Roch Nianogo M. Maria Glymour Yvette Cozier

Addressing disparities is often essential to maximize the population health impact of epidemiologic research results. However, manuscript planning rarely systematically considers disparities. We developed the **DARE (**Health **D**isparities **A**ssessment **R**ubric for **E**pidemiologic Data Analysis), a structured tool designed to integrate such considerations throughout paper development. The rubric covers 4 domains, scored from 1 (weakest) to 5 (strongest integration of items): *Populations* (e.g., does the sample include populations disproportionately affected by the outcome?), *Analysis* (e.g., are systemic drivers considered? Are covariates appropriately selected considering plausible mechanisms?), *Subgroups & Intersectionality*, and *Triangulation* (e.g., efforts to ensure robustness of results such as multiple data sources and/or methods and transparency in limitations). To pilot DARE in our research project, 2 reviewers independently applied the rubric to 6 paper proposals across the domains. Reviewer scores were collapsed into low (1 to 2), moderate (3), and high (4 to 5). Observed agreement between reviewers was highest for the Populations domain (100 %), followed by Analysis (83.3%), Subgroup & Intersectionality (66.7 %), and Triangulation (33.3 %) (Figure 1). Dark green cells indicate exact agreement on the original 5-point score, while light green cells reflect agreement within collapsed integration categories. Light red cells denote scores falling into adjacent collapsed categories +/- 1-point difference on the original scale, and dark red cells indicate disagreement across non-adjacent categories with a difference > 1 point. DARE may assist research teams that are committed to maximizing population health impact identify weak areas in their approach, integrate health disparities considerations effectively into their methodology, and strengthen the relevance and interpretability of epidemiologic findings for population health.

Figure 1. **DARE** (Health Disparities Assessment Rubric for Epidemiologic Data Analysis) Heatmap of reviewer agreement in scoring



Health Disparities

The Timing of Financial Instability Matters: Midlife Income Variability and Hypertension Risk in a National Cohort Mehrnaz Siavoshi* Mehrnaz Siavoshi

Background

While socioeconomic status is a well-established determinant of cardiovascular health, less is known about how changes in income at different life stages independently affect chronic disease risk. Guided by the Life Course Theory, this study examines whether the timing of income variability, specifically early adulthood versus midlife, is associated with hypertension risk.

Methods

Using longitudinal data from 4,844 participants in the Panel Study of Income Dynamics with at least 30 years of follow-up, income variability was measured as the coefficient of variation of inflation-adjusted annual income. Participants were classified into four groups based on high or low variability during early adulthood (ages 20–35) and midlife (ages 36–50). Cox proportional hazards models adjusted for age, race, sex, marital status, employment, and birth decade estimated the hazard of self-reported hypertension diagnosis.

Results

Hypertension prevalence differed significantly across timing groups. Individuals whose income variability decreased from early adulthood to midlife had the lowest hypertension risk (HR 0.75, 95% CI 0.66-0.85) while those with newly emergent variability in midlife had the highest risk (HR 1.19, 95% CI 1.07-1.32). Persistent high variability was not significant after covariate adjustment. These associations remained directionally consistent after controlling for demographic and cohort effects.

Conclusion

These findings suggest that the timing of income instability matters for cardiovascular health. Resolving financial instability by midlife is protective, whereas new midlife volatility elevates hypertension risk. Economic interventions promoting stability during midlife may help mitigate cumulative cardiovascular risk across the life course.

Health Disparities

Macroeconomic Context Shapes Individual-Level Income Volatility Effects on Hypertension: A Cohort Comparison Mehrnaz Siavoshi* Mehrnaz Siavoshi

Background
Individual economic experiences unfold within historical contexts of varying macroeconomic stability. We tested whether birth cohort modifies the association between personal income variability and hypertension risk, reflecting the time and place principle of life course theory.

Methods
Among 8,021 PSID participants born 1940s-1980s with 30+ years follow-up, we examined timing-specific income variability during early adulthood (ages 20-35) versus midlife (ages 36-50). Participants were categorized into four timing groups based on high/low variability in each period. Cox models stratified by birth decade tested whether cohort moderated variability-hypertension associations.

Results
Timing patterns varied dramatically by cohort. The 1940s cohort experienced predominantly low early variability with emerging midlife instability (42.8% Low+High), while 1960s/1970s cohorts showed opposite patterns (36.6% and 34.0% High+High) (χ^2=20.03, p<0.01). Among 1960s/1970s cohorts exposed to Reaganomics and dot-com volatility, high early-life variability was protective against hypertension (HR 0.84, 95% CI 0.78-0.91), whereas high midlife variability increased risk (HR 1.29, 95% CI 1.19-1.40). The 1940s cohort, who experienced post-WWII expansion, showed attenuated effects.

Conclusion
The health consequences of individual income instability depend on macroeconomic context. Cohorts entering adulthood during eras of structural volatility may develop different adaptive responses than those experiencing predictable economic expansion. These findings highlight that individual-level risk factors cannot be fully understood without considering the historical moment, with implications for targeting interventions to cohorts differentially exposed to economic upheaval.

Health Disparities

Nativity-Based Disparities in Postpartum Mental Health Diagnoses in a Hospital-Based Birth Cohort Shashi Sarnaik* Shashi Sarnaik Farah Qureshi Celia Karp

Background: Postpartum mental health conditions are a leading cause of maternal morbidity, and their identification varies across populations. Immigrant mothers face unique challenges that influence whether these conditions are diagnosed, yet disparities in clinically documented postpartum mental health conditions remain poorly characterized. This study examined nativity-based differences among a hospital-based birth cohort in Boston.

Methods: Participants were 2,442 mothers in the Boston Birth Cohort. Nativity was defined as U.S.-born versus foreign-born. Postpartum mental health conditions were assessed via health records and defined as new diagnoses of stress or adjustment disorders, depression, anxiety, or other related disorders within one year postpartum. Differences in prevalence by nativity were assessed descriptively, while associations between nativity and postpartum mental health diagnoses were evaluated using logistic regression adjusted for sociodemographic, obstetric, and pregnancy-related clinical covariates.

Results: 20.9% of participants received a mental health diagnosis. Foreign-born mothers had a lower prevalence of diagnosis than U.S.-born mothers (13.0% vs. 33.8%). Foreign-born status was associated with lower odds of postpartum mental health diagnosis relative to U.S.-born status (aOR = 0.37, 95% CI: 0.29–0.47), with differences consistent across categories of mental health disorder.

Conclusions: Foreign-born mothers were less likely than U.S.-born mothers to receive a clinically documented postpartum mental health diagnosis. While this pattern may reflect lower mental health risk, existing evidence of disparities in screening, diagnosis, and mental health stigma suggests that structural and health-system factors may play a role in shaping nativity-based inequities in postpartum mental health. Findings underscore the need to distinguish true mental health risk from inequities in care access and utilization among postpartum immigrant populations.

Health Disparities

Early-Life Trauma, Minority Stress, and Hypertensive Disorders of Pregnancy: Evidence from a Large Prospective Cohort Michelle Tam* Michelle Tam Isa Berzansky Colleen Reynolds Payal Chakraborty Sarah McKetta Cindy Veldhuis Brittany Charlton

Background: Early-life trauma, such as childhood physical and sexual abuse, is linked to hypertensive disorders of pregnancy (HDP) in adulthood. Sexual minority (SM) individuals experience higher rates of childhood abuse and HDP. It is unclear whether sexual orientation modifies the association between early-life trauma and HDP.

Methods: The Nurses' Health Study 3 is a longitudinal cohort of nurses born on or after January 1, 1965, living in the US or Canada (N=36,834 pregnancies from 13,854 participants). We assessed type (i.e., physical and sexual abuse) and severity of early-life trauma and prevalence of HDP (i.e., gestational hypertension, preeclampsia) across sexual orientation groups (completely heterosexual, heterosexual with same-sex experiences/mostly heterosexual, and bisexual/lesbian). We used modified Poisson models to estimate risk ratios (RRs).

Results: Compared to completely heterosexual individuals, all SM groups had higher prevalence of childhood physical abuse (ranging from 49.2% to 51.9% vs. 39.8%) and childhood sexual abuse (ranging from 37.1% to 49.4% vs. 27.5%). Pregnancies in all SM groups had higher prevalence of HDP—heterosexual with same-sex experience (9.3%), mostly heterosexual (8.5%), bisexual (9.9%), and lesbian (11%)—compared to the completely heterosexual group (7.3%). Severe physical abuse (risk ratio [RR] 1.19, 95% confidence interval [CI], 1.01–1.41) and sexual abuse (RR 1.12, 95% CI, 1.02–1.24) were associated with increased risk of HDP among all participants compared to no abuse, respectively. Within strata of childhood physical abuse or sexual abuse, no significant differences in HDP were observed across sexual orientation groups.

Conclusion: Both childhood abuse and sexual minority status increase HDP risk, largely through parallel rather than interacting pathways, underscoring the impact of socially patterned trauma on pregnancy health.

Health Disparities

Disparities in mean years of potential life lost from all-cause mortality by health insurance, mental health, and health behaviors in the US, 1997—2019 David Adzrago* David Adzrago Faustine Williams

Introduction: Years of Potential Life Lost (YPLL) is a population health metric that quantifies premature mortality and its associated socioeconomic impact. While health insurance coverage is strongly linked to mortality risk, differences in mean YPLL by insurance status across mental health and health-related behaviors remain understudied. We assessed differences in mean YPLL between insured and uninsured adults across psychological distress (PD), BMI, smoking status, alcohol consumption, and physical activity (PA).

Methods: This population-based cohort study included adults aged > 18 years (N= 54,433) from the 1997–2018 National Health Interview Surveys linked to 1997–2019 National Death Index data. YPLL was calculated by deducting age at death (18–74) from a standard age of 75 years and then summing each YPLL across individual deaths. Analyses accounted for the complex survey design.

Results: The overall mean YPLL was 10.3 years (95% CI= 10.2, 10.5). Compared with insured adults, uninsured adults at baseline who died had an excess mean YPLL of 10.5 (95% CI=10.0–11.0). Uninsured adults consistently experienced significantly higher mean YPLL across all PD levels, BMI categories, smoking status, alcohol consumption, and PA. Excess YPLL among uninsured adults ranged from 6.5 to 11.7 years across PD levels, 9.0 to 11.0 years across BMI, 8.1 to 11.1 years by smoking status, 8.3 to 11.3 years by alcohol use, and 9.4 to 14.8 years across PA levels. Differences were largest among adults meeting both aerobic and strength PA guidelines and smallest among those with severe PD.

Conclusions: Uninsured adults experienced higher premature mortality than insured adults irrespective of mental health status and health-compromising or health-promoting behaviors. These findings suggest that expanding access to health insurance and integrating primary and behavioral health interventions may contribute to reducing premature mortality disparities between uninsured and insured individuals.

Health Disparities

Differences in Health Outcomes and Health Factor Domains of the 2020 County Health Rankings Across Urban-Rural-Frontier Counties in the United States Brody Gibson, BS*
Brody Gibson Laurie Grieshober, MS, PhD Chen Chen, MSPH, PhD Britton Trabert, MS, MSPH, PhD Tracy Onega, MA, MPAS, MS, PhD Jennifer Anne Doherty, MS, PhD

Urban-rural health disparities are well documented, yet variation by degree of rurality and remoteness remains poorly understood. This study examines county-level population health using the 2020 County Health Rankings, which summarize standardized domains of health outcomes (Length of Life and Quality of Life) and health factors (Health Behaviors, Clinical Care, Social and Economic Factors, and Physical Environment). We assessed these domains across one urban (metropolitan) and four rural groups—micropolitan, frontier-micropolitan, noncore, and frontier-noncore—using Integrated Metropolitan-to-Frontier Area Codes (IMFAC). We summarized the proportion of counties by domain quartiles and IMFAC category, and estimated odds ratios of being in the most disadvantaged (Q4) for each rural group relative to urban using logistic regression with state fixed effects. Proportions of counties in Q4 increased with rurality and remoteness for Length of Life, Quality of Life, Clinical Care, and Social and Economic Factors, while Health Behaviors showed greater disadvantage in micropolitan and frontier-micropolitan counties. The odds of Q4 ranking for Length of Life increased from micropolitan (OR=2.16; 95%CI:1.64–2.84) to frontier-noncore (OR=4.05; 95%CI:3.06–5.37) relative to urban counties. Clinical Care showed the largest rural disadvantage, with noncore (OR=4.40; 95%CI:3.47–5.58) and frontier-noncore counties (OR=7.40; 95%CI:5.55–9.88) at increased odds of greater disadvantage. For Quality of Life, all rural subgroups had higher odds of being in Q4, greatest in frontier-micropolitan (OR=3.03; 95% CI:2.07–4.41) and frontier-noncore counties (OR=3.53; 95%CI:2.67–4.66). Physical Environment showed an inverse pattern, with rural counties at lower odds of disadvantage than urban, particularly frontier-noncore counties (OR=0.09; 95%CI:0.06–0.13). These findings show that rural health disadvantage is not uniform and that broad urban-rural comparisons may mask important differences.

Health Disparities

Is Early Childhood Education Quality Associated with Risk of Diabetes Mortality in a Racially Diverse Cohort of Autoworkers? Jess Arbuckle* Jess Arbuckle Sadie Costello Sepideh Modrek Ellen A. Eisen

Diabetes is the 7th leading cause of death in the United States, and Black adults experience disproportionately higher rates of Type 2 Diabetes Mellitus (T2DM) mortality compared to White adults. While educational attainment is known to influence chronic disease risk, few studies have examined educational quality, and none have focused on educational quality in relation to T2DM in a population that includes Black adults. We assessed the association between the quality of early childhood education and T2DM mortality in an occupational cohort of Black and White unionized Michigan autoworkers who have similar midlife blue-collar jobs with similar access to healthcare. We also examined effect modification by race. The United Autoworkers-General Motors (UAW-GM) cohort includes workers employed for at least three years at three plants in Michigan and followed from 1941 to 2015. The analytic sub-cohort consists of 3,216 male autoworkers born 1920 to 1940, who died before 2007 and could be linked to the 1940 U.S. Census. Using the Census, we examined three county-level measures of early childhood educational quality: student–teacher ratio, % children aged 6-14 enrolled, and % teachers with college education. Cox proportional hazards models were fit to estimate hazard ratios (HR) and 95% confidence intervals (CI), adjusting for race, urban/rural, farm living, North/South, and parental education. Results suggest that of the three education quality measures, only % enrolled provided any protection against T2DM mortality; compared to the lowest category in pooled analysis, the HR was 0.79 (95%CI:0.51-1.21) and 0.53 (95%CI: 0.30-0.95) in the middle and high categories, respectively. There was little evidence of effect modification, although average educational quality of all three measures was higher among White autoworkers. Future studies will examine how work characteristics may mask benefits associated with structural advantages, such as better childhood educational quality.

Health Disparities

Scaling the health system inequity metric to identify and address healthcare inequities
Joanna Dos Santos* Joanna Dos Santos

Background:

Systematic measurement of health inequities is critical for equitable healthcare delivery, yet few standardized approaches exist that are feasible for routine health system use. The Health System Inequity Metric (HSIM), developed at Trillium Health Partners, is a validated approach that quantifies inequities in healthcare utilization and outcomes across socioeconomic gradients using routinely collected administrative data. HSIM is designed to support organizational accountability by embedding equity measurement within standard performance reporting.

Methods:

HSIM applies regression-based modelling to estimate inequities across ordered population groups, generating a single, interpretable metric that reflects the magnitude and direction of disparity. The approach allows comparison across services and over time, while accommodating local population characteristics and data availability. HSIM was applied across health services using linked administrative and area-level sociodemographic data. As an example of applied use, HSIM informed a breast cancer screening initiative, complemented by focus groups with historically underrepresented communities to contextualize identified inequities and inform intervention development.

Results:

HSIM enabled systematic identification of inequities and prioritization of services for equity-focused action. Its standardized yet flexible structure supports meaningful interpretation across diverse service contexts without requiring new primary data collection.

Conclusions:

HSIM provides a scalable, methodologically rigorous approach for translating equity measurement into action. Building on demonstrated success at Trillium Health Partners, HSIM is now being implemented in additional organizations, highlighting its potential to support system-level equity monitoring, intervention planning, and performance improvement across healthcare settings.

LATEBREAKER

Health Disparities

Demographic Correlates of Secondhand Cigarette, Cigar, Electronic Vapor Product, and Cannabis Smoke Exposure among US Adults Joyce Lokanga Milandu* Joyce Lokanga Milandu Dennis Buckman Marianne Hyer Folly Folivi Kristen Hamilton-Moseley Bambi Jewett Kelvin Choi

Secondhand exposure to cigarette/cigar smoke, electronic vapor products (EVP) aerosol, and cannabis smoke has been associated with detrimental health effects. There is limited research examining demographic correlates of exposure to other forms of tobacco products and cannabis. This study investigates demographic correlates of secondhand exposure to EVP aerosol, cigarette, cigar, and cannabis smoke.

A nationally representative sample of 3200 US adults (≥21 years) reported demographic information, current cigarette, cigar, EVP and cannabis use, and hours of secondhand exposure to their smoke/aerosol in the past 7 days. Weighted cragg's double hurdle regressions were used to examine the relationship between demographics and hours exposed.

Among individuals not using these products, 21% reported cigarette smoke exposure hours>0 (n=469, weighted mean [M]=8.9, SD=24.8), 13% reported cigar smoke exposure (n=358, M=3.1, SD=4.5), 18% reported EVP aerosol exposure (n=465, M=6.9 hours, SD=18.3), and 14% reported cannabis smoke exposure (n=356, M=4.1 hours, SD=1.4). Comparison of the predictive margins from the hurdle regression models show the following: Older individuals had lower hours of exposure to smoke from cigarettes, cigars, EVP, and cannabis in comparison to 21-30-year-olds ($p<.05$). Compared to White individuals, American Indian/Alaska Native and Black individuals had higher exposure, while Asian individuals had lower exposure to cigar and cannabis smoke ($p<.05$). Individuals with annual incomes greater than $25,000 had lower hours of cannabis smoke exposure, compared to those making below $25,000 ($p<.05$).

Our findings indicate demographic disparities in secondhand exposure to cigarette smoke, cigar smoke, EVP aerosol, and cannabis smoke, varying somewhat by product. Further research examining whether secondhand exposure is associated with statewide smokefree air laws, cannabis legalization, and excise tax rates can inform policy actions.

Health Services/Policy

The Impact of the Universal Child Care Benefit on Acute Mental Health Service Use Among Parents: A Controlled Interrupted Time Series Study Jasleen Arneja* Jasleen Arneja Arijit Nandi Brice Batomen

The Universal Child Care Benefit (UCCB), implemented in Canada in July 2006, was a universal income transfer that gave all families with children <age 6 an annual $1,200. Prior research has found that the UCCB was linked to reductions in BMI and the prevalence of obesity among mothers of younger children and improved maternal mental health and life satisfaction. It also reduced food insecurity, with stronger impacts in lower income households and single parent families.

Resource constraints (e.g., poverty and food insecurity) lead parents make trade-offs between food and other basic necessities, leading to stress, anxiety, and depression. Additional income received through the UCCB may increase parents' disposable income and reduce financial stress. We aim to examine the population level impact of the UCCB on acute mental health service use among parents.

We used a controlled interrupted time series design to compare parents of children aged 0-6 to parents of children aged 6-17 who were not eligible for UCCB. Data came from health administrative databases and tax files, and an open cohort of health system users in Canada was developed—individuals who visited the hospital or ED and filed taxes at least once between 2004–2008. Our study included 26 months of pre-policy data (04/2004-06/2006) and 42 months of post-policy data (07/2006-12/2009).

Parallel pre-policy trends were confirmed. Count regression models accounting for overdispersion and autocorrelation were used to calculate rate differences in monthly mental health-related hospital and ED visits, including those for anxiety, mood disorders, substance use, and intentional self-harm. Newey-West standard errors were used to calculate 95% confidence intervals. We examined effect measure modification through stratified analyses by parent sex, marital status, and low-income status.

This study adopts a health-in-all-policies approach to inform evidence-based income support policies targeting families with children.

HIV / STI

Hazardous Alcohol Use, Sexual Behavior, and HIV Incidence across 11 Eastern and Southern African Countries Domonique M. Reed* Domonique M. Reed Jeffrey W. Imai-Eaton

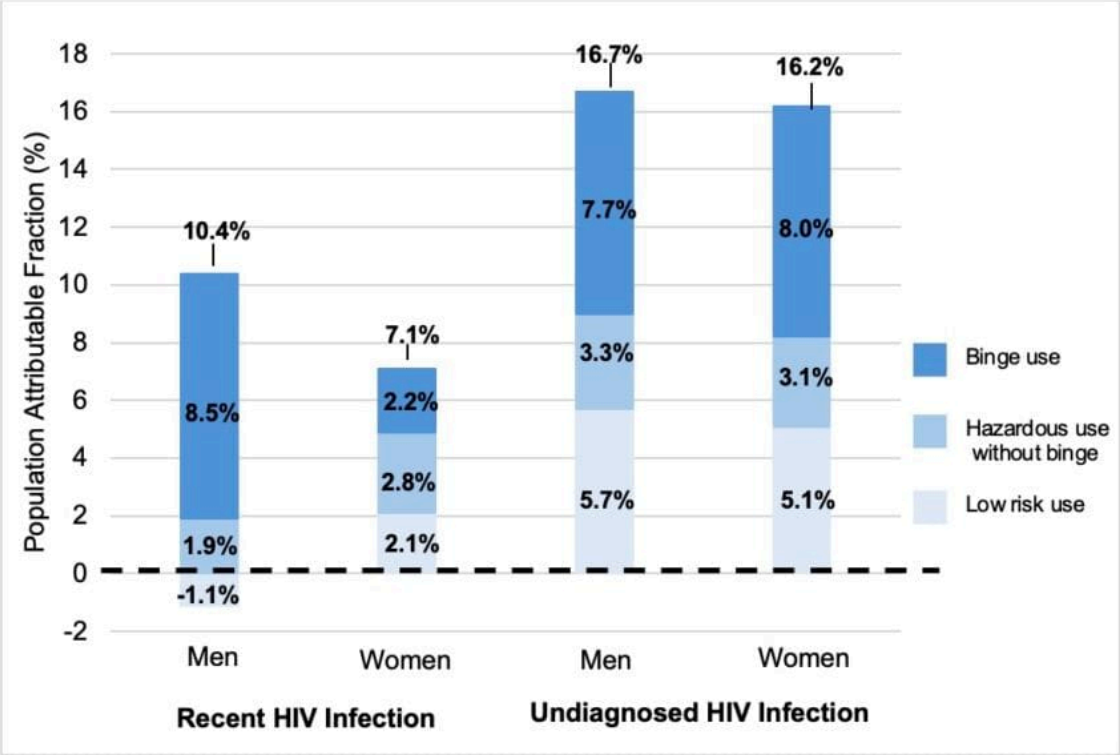
Alcohol use has broadly been associated with HIV acquisition through its influence on sexual risk behaviors, but evidence distinguishing different use patterns across Africa remains limited. We estimated the prevalence of hazardous and binge alcohol consumption and their association with high-risk sexual behaviors and HIV incidence proxies.

We analyzed data on sexually active adults aged ≥15 years from 16 nationally representative household surveys in 11 Eastern and Southern African countries (2015-2023). Alcohol use patterns were classified using the AUDIT-C (non-drinkers/low risk users/hazardous drinkers without binge/binge use). Outcomes included sexual risk behaviors, lab-determined recent HIV infection, and undiagnosed HIV infection. We estimated survey-weighted alcohol use prevalence, logistic regression models, and population attributable fractions by gender, adjusting for sociodemographic covariates.

Analyses included 251,931 adults (HIV-negative, n=245,253; recent or undiagnosed HIV infection, n=6,678). Between 5.75%-21.12% reported binge alcohol use, and 3.70%-15.7% reported hazardous use across countries, with large gender differences. Sexual risk increased progressively with drinking severity among both men and women. Compared to non-drinkers, alcohol use was associated with higher odds of undiagnosed HIV infection; adjusted ORs ranged from 1.32 (1.16-1.50) for low-risk users to 1.52 (1.34-1.72) for binge users among men and 1.28 (1.13-1.46) to 1.55 (1.31-1.82) among women. Alcohol use accounted for 16.7% of infections among men and 16.2% among women (Figure), with contributions across drinking categories. Estimates for associations with recent HIV infection followed a similar pattern, with wider uncertainty.

Both hazardous and binge alcohol use are associated with sexual risk and HIV incidence in Eastern and Southern Africa. Integrating HIV prevention into alcohol-reduction strategies may address around 16% of HIV acquisition risk across the region.

Figure. Population Attributable Fraction (%) of Recent and Undiagnosed HIV Infection by Alcohol Use Pattern and Gender across 11 Eastern and Southern African countries (2015-2023), N=251,931



HIV / STI

Increasing PrEP Access: Potential Pharmacy Integration in the Southeastern US Siena Senn* Siena Senn Johnathan Edwards Kristin Harrington Natalie Crawford

Background

Although pre-exposure prophylaxis (PrEP) can prevent up to 99% of HIV transmissions with proper adherence, uptake remains low and disparities persist, especially in the Southeastern United States (US). Pharmacies represent a practical avenue to expand access to PrEP, but little is known about their proximity compared to PrEP-prescribing locations.

Methods

Data was compiled from the 2024 National Council for Prescription Drug Programs for active retail and community pharmacies, PrEP Locator for public and private PrEP-prescribing locations, and census block population-weighted centroids for 3 states in the Southeastern US with the highest HIV burden (Florida, Georgia, and Louisiana). ArcGIS Pro was leveraged to determine the straight-line distance in miles to the closest pharmacy and PrEP-prescribing location from each centroid.

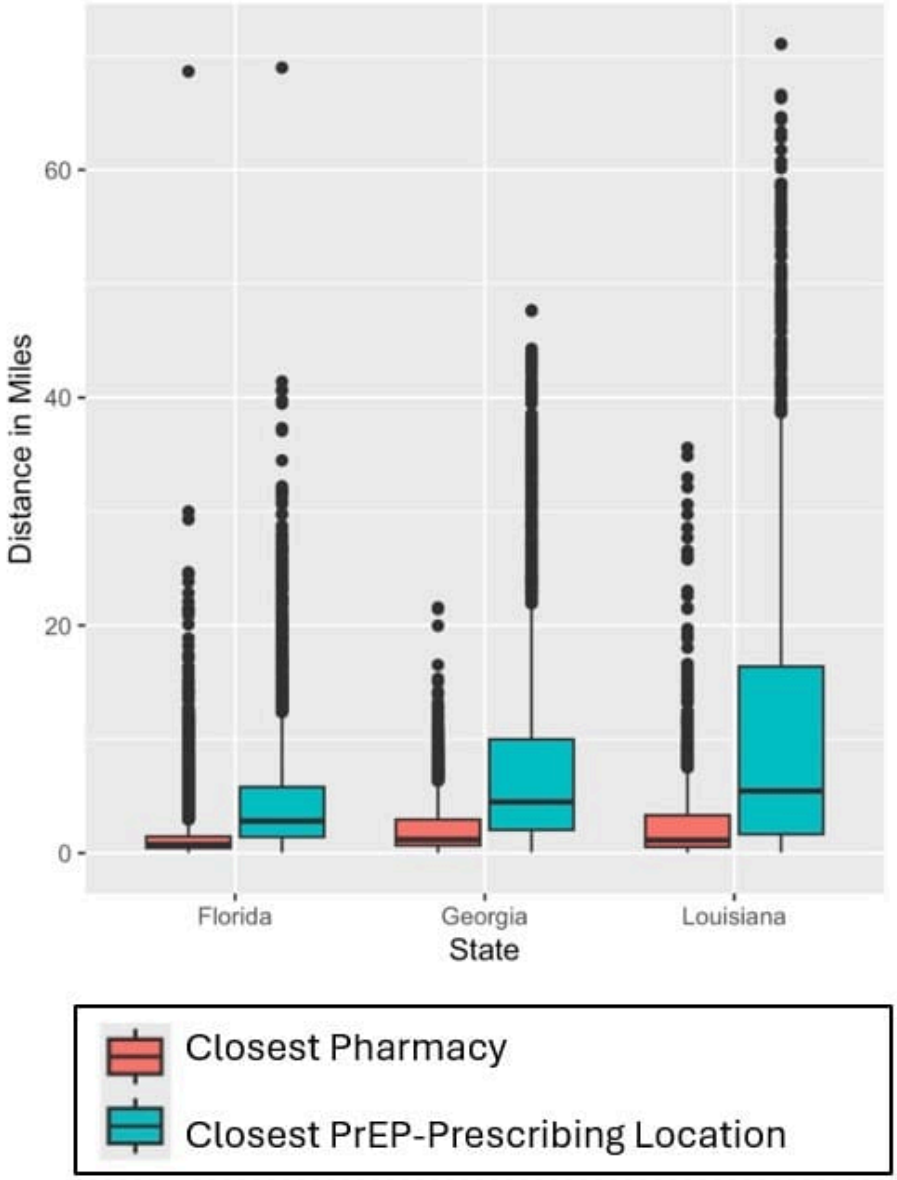
Results

Across all 3 states, the median distance to the nearest pharmacy was 0.89 miles vs. 3.46 miles for PrEP-prescribing locations. Separately, the median distance to the closest pharmacy vs. PrEP-prescribing location as well as the respective minimums and maximums were 0.74 miles [0.01, 68.6] vs. 2.81 miles [0.03, 69.0] for Florida (n = 5,160 census blocks), 1.18 miles [0.01, 21.6] vs. 4.48 miles [0.06, 47.7] for Georgia (n = 2,796 census blocks), and 1.12 miles [0.02, 35.60] vs. 5.45 miles [0.04, 71.1] for Louisiana (n = 1,388 census blocks). Notably, a wide range of values was observed but PrEP-prescribing locations were consistently farther from people than pharmacies. (Figure 1).

Conclusion

These findings suggest a substantial potential decrease in distance to pharmacies versus PrEP-prescribing locations. Legislation providing pharmacists with the authority to dispense PrEP is thus needed to improve HIV prevention efforts from a convenience and access perspective.

Figure 1. Distance to Pharmacies and PrEP-Prescribing Locations by State



HIV / STI

Mental health disorders and all-cause hospitalizations among people with HIV before and during the COVID-19 pandemic in the US Xianming Zhu* Xianming Zhu Brenna Hogan Yue Zhang N. Sarita Shah Michael A. Horberg Kathleen Akgun Jennifer O. Lam Thibaut Davy-Mendez Joseph A. C. Delaney Sonia Napravnik Milton L. Wainberg Angela Parcesepe Keri N. Althoff

Background: Over half of people with HIV (PWH) have a mental health disorder (MHD), which may elevate their hospitalization risk. Limited studies of the impact of the COVID-19 pandemic on PWH with MHD have produced mixed results. We examined disparities in hospitalization rate among PWH by MHD before and during the pandemic.

Methods: We included PWH (>18 years) enrolled in 9 US cohorts in the North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD) with available MHD and hospitalization data from 01/01/2018-12/31/2021, who had ≥1 CD4 or HIV viral load measurement or hospitalization two years before or during study period. Diagnoses of schizophrenia/schizoaffective disorder (SZ/SZA), bipolar, depression, and anxiety were time-varying and based on ICD-10 codes. Negative binomial models with generalized estimating equation were used to estimate the all-cause hospitalization rate ratio comparing those with vs without each MHD, with an interaction term between MHD and the COVID-19 pandemic (before vs after 03/01/2020), and were adjusted for cohort, age, sex, race/ethnicity, HIV acquisition group, and HIV viral suppression at this study entry.

Results: A total of 62,408 PWH were included (88% male, 44% Black, median age 54 [IQR: 41-62] years, 52% had any MHD). Across all MHD examined, PWH with (vs without) each MHD had a higher hospitalization rate both before and during the pandemic, with the rate declined in all groups. Disparities in hospitalization rate among PWH with (vs without) SZ/SZA and bipolar disorder marginally narrowed during vs before the pandemic, while disparities among PWH with (vs without) other MHD remained similar across the two time periods.

Conclusions: PWH with MHD may be a target group for preventing hospitalizations. Future research is needed to explore factors contributing to the decline in hospitalization rate among PWH with MHD during the pandemic, such as the impact of telehealth, limited elective surgeries, and social demands.

Figure. Incidence rate and adjusted incidence rate ratios (aIRR) for all-cause hospitalization among people with HIV with mental health disorders (MHD) before and during the COVID-19 pandemic

Abbreviations: MHD: mental health disorder; SMI: Severe mental illness; SZ/SZA; schizophrenia/schizoaffective disorder; IR: incidence rate; aIRR: adjusted incidence rate ratio.
Note:
SMI include SZ/SZA and bipolar.
Any MHD represents one or more diagnosis of SZ/SZA, bipolar, depression, or anxiety.
‡In SZ/SZA analysis, the comparison was made between those with SZ/SZA (including those who had both SZ/SZA and bipolar) vs. no SZ/SZA or bipolar.
§In bipolar analysis, the comparison was made between those with bipolar (excluding those who had both SZ/SZA and bipolar) vs. no bipolar or SZ/SZA.
†In depression and anxiety analysis, individuals with SMI prior to study entry were excluded, and individuals who developed SMI during follow-up were censored at the time of diagnosis.

All-cause hospitalization	IR MHD	IR control	aIRR (95%CI)	aIRR (95%CI)	P-interaction
Any MHD, N = 62,408					
(Ref. no MHD)					0.35
Before pandemic	7.3 (7.0, 7.5)	3.4 (3.3, 3.6)	2.04 (1.92, 2.15)		
During pandemic	5.9 (5.7, 6.1)	2.9 (2.7, 3.0)	1.97 (1.86, 2.10)		
SZ/SZA, N = 58,330					
(Ref. no SZ/SZA‡)					0.039
Before pandemic	17.2 (15.6, 18.7)	4.8 (4.7, 5.0)	2.87 (2.61, 3.16)		
During pandemic	13.2 (11.8, 14.6)	4.2 (4.0, 4.3)	2.60 (2.33, 2.90)		
Bipolar, N = 59,557					
(Ref. no bipolar§)					0.002
Before pandemic	9.5 (8.8, 10.3)	4.8 (4.7, 5.0)	1.99 (1.83, 2.16)		
During pandemic	7.1 (6.5, 7.7)	4.2 (4.0, 4.3)	1.72 (1.57, 1.89)		
Among those without SMI					
Depression, N = 55,384					
(Ref. no depression†)					0.49
Before pandemic	6.3 (6.1, 6.6)	3.4 (3.2, 3.5)	1.76 (1.66, 1.86)		
During pandemic	5.3 (5.0, 5.5)	2.9 (2.8, 3.0)	1.71 (1.61, 1.83)		
Anxiety, N = 55,384					
(Ref. no anxiety†)					0.41
Before pandemic	5.7 (5.4, 6.0)	4.3 (4.2, 4.5)	1.51 (1.42, 1.61)		
During pandemic	4.8 (4.5, 5.0)	3.7 (3.5, 3.8)	1.47 (1.37, 1.57)		



HIV / STI

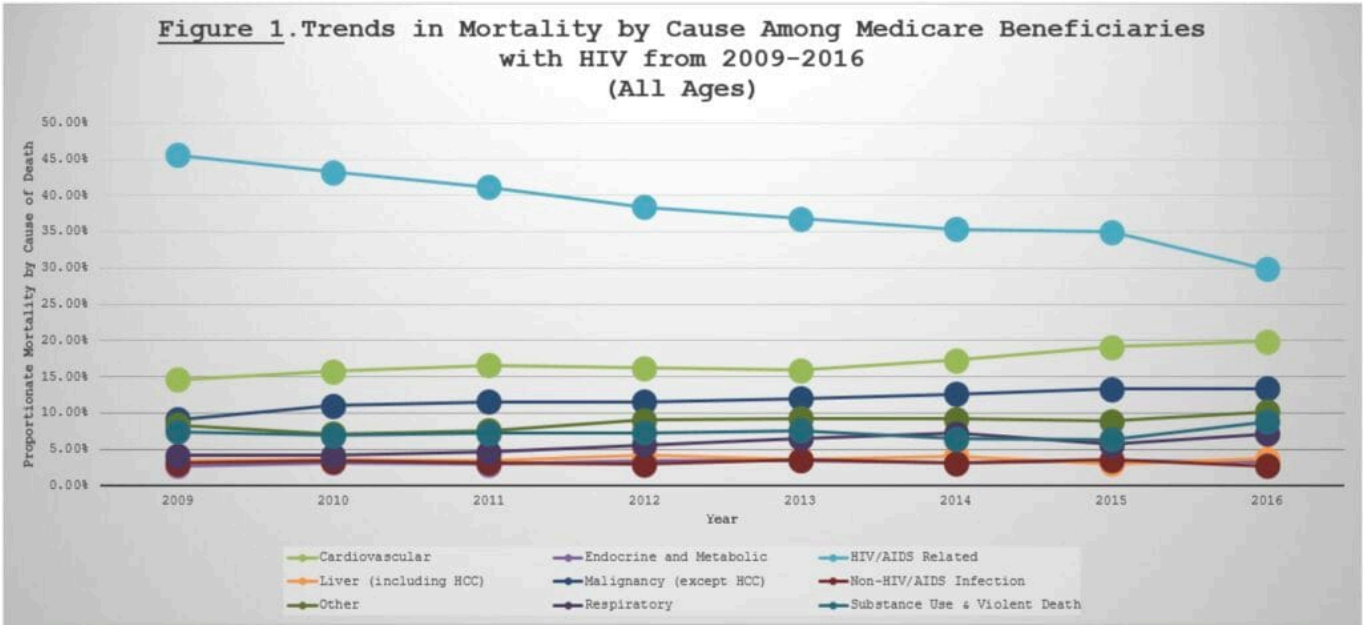
Patterns of Mortality by Cause among People with HIV in the United States from 2009-2016 Onumaraekwu Opara* Onumaraekwu Opara Fabrizio Drago Carolyn W. Kinkade Kylie Getz Perry N. Halkitis Tobias Gerhard Jason A. Roy Silvia S. Martins Michael T. Yin Mackey R. Friedman Stephen Crystal Stephanie Shiau

As mortality patterns among people with HIV (PWH) evolve, analysis of these trends is needed to develop focused prevention measures. We characterized patterns of mortality by cause and differences by age, sex, and race/ethnicity among PWH decedents.

We constructed annual cross-sectional cohorts of Medicare beneficiaries with HIV who died between 2009-2016 and were linked to the National Death Index to determine cause of death. Descriptive statistics summarized trends of proportionate mortality by cause over time, stratified by age group (<50, 50-64, and 65+ years). Logistic regression models were fit to assess associations between sex and race/ethnicity and cause of death across all years, adjusted for age, Rural-Urban Commuting Area, dual eligibility with Medicaid, and Medicare enrollment reason.

The final sample included 20,290 PWH that died between 2009-2016. The number of deaths remained stable from 2009 (2586 deaths) to 2016 (2595 deaths). HIV/AIDS was the leading cause of death across all years and age groups (Figure 1), though its contribution declined by one-third from 45.6% in 2009 to 29.9% in 2016 (p<0.0001). Among those <50 years, HIV/AIDS, substance use/violent death, and cardiovascular causes were the top causes of death. For those 50-64 and 65+ years, HIV/AIDS, cardiovascular causes, and malignancy were the top causes of death. Female PWH were less likely to die from HIV/AIDS (aOR 0.84, CI:0.76-0.93) and substance use/violent deaths (aOR 0.65, CI:0.54-0.80) than males. Racial and ethnic minorities were more likely to die from cardiovascular causes (Black aOR 1.22, CI:1.09-1.37) and HIV/AIDS (Black aOR 1.24, CI:1.13-1.36), but less likely to die from malignancy (Hispanic aOR 0.67, CI:0.48-0.95) and substance use/violent deaths (Black aOR 0.53, CI:0.45-0.63; Hispanic aOR 0.60, CI:0.41-0.89) than Whites.

Among PWH, disparities in mortality by cause persist along sociodemographic lines, underscoring the need for targeted prevention and treatment efforts.


Figure 1.Trends in Mortality by Cause Among Medicare Beneficiaries with HIV from 2009-2016 (All Ages)
Proportionate Mortality by Cause of Death
50.00%
45.00%
40.00%
35.00%
30.00%
25.00%
20.00%
15.00%
10.00%
5.00%
0.00%
2009
2010
2011
2012
2013
2014
2015
2016
Year
Cardiovascular
Endocrine and Metabolic
HIV/AIDS Related
Liver (including HCC)
Malignancy (except HCC)
Non-HIV/AIDS Infection
Other
Respiratory
Substance Use & Violent Death

HIV / STI

Assessing Causal Effects of HIV Testing on HIV Incidence in Rural KwaZulu-Natal, South Africa Ke Zhang* Ke Zhang Ashley Buchanan Natallia Katenka Laura Forastiere Donna Spiegelman Collins lwuji

Although there are effective strategies to control the HIV epidemic, it remains a significant individual and public health challenge in South Africa. HIV testing is the gateway to HIV treatment in those who have acquired HIV and HIV prevention in those who tested HIV negative. Existing studies have suggested that HIV testing has a significant effect in reducing HIV incidence. However, these studies have not fully assessed spillover effects, the effects of one's HIV testing on HIV incidence among unexposed others. Assessing spillover can provide a more complete understanding of the impact of HIV testing. The data we used is from ANRS 12249 treatment as prevention (TasP) trial, conducted in a rural region of South Africa from March 2012 to July 2016. We grouped participants by homesteads and assumed partial interference limited to the homestead, estimated both the direct (i.e., the intervention effect under exposure versus no exposure while holding other factors constant) and spillover effects of altering the proportion of HIV testing in the homestead on subsequent HIV incidence. Estimation was carried out with a marginal structured model fit with inverse probability weights. The results suggested that, on average, (1) Risk of HIV infection decreased by 42.3% (95% confidence interval: [19.4%, 58.8%]) under HIV testing versus no testing, with HIV testing for others in the homestead remained constant (i.e., direct effect); (2) No statistically significant spillover effect detected comparing two different proportions of exposed homestead members. Further research is needed to understand the underlying mechanisms.

LATEBREAKER

HIV / STI

Impacts of the COVID-19 pandemic on HIV care among Medicaid beneficiaries, 2016-2021

Jacqueline Rudolph* Jacqueline Rudolph Yiyi Zhou Maylin Palatino Karine Yenokyan Xiaoqiang Xu Eryka Wentz Keri Calkins Corinne Joshu Bryan Lau

The COVID-19 pandemic posed challenges to chronic condition management, including HIV. However, innovations were implemented in the US to minimize care disruptions for people with HIV (PWH), including telehealth and longer antiretroviral therapy (ART) prescriptions. Further data are needed on the impact of the pandemic on HIV care in diverse nationwide samples. We analyzed Medicaid claims data from 24 US states and DC. We included 87,015 PWH who were enrolled for the 18 months prior to March 2020. We followed beneficiaries through September 2021, death, age 65, or loss of Medicaid eligibility. We examined whether the monthly prevalence of ART adherence and rates of routine care visits (overall, in-person, telehealth) and of HIV laboratory tests (i.e., CD4 cell count, HIV viral load) differed before vs. during COVID using Bayesian structural time series models. To inform the prediction of the counterfactual where the pandemic did not occur, we accounted for a control sample of PWH who were followed September 2016-September 2019; we used odds weights to standardize the distribution of age, sex, race, state, and number of Charlson comorbidities to that seen in the main sample in March 2020. In both samples, we used inverse probability of censoring weights to account for informative censoring. In the initial months following March 2020 (Figure), we saw a modest bump in prevalence of ART adherence, a large decrease in rates of in-person visits and lab tests, and a large increase in rates of telehealth visits. Rates of lab tests returned to pre-COVID rates 12 months after the pandemic. While in-person office visits did not return to the pre-COVID rates by 18 months, the decrease was offset by the increase in telehealth visits, in all months except March-May 2020. Frequency of engaging in care among PWH in Medicaid was not severely negatively impacted by COVID, in part due to the uptake of telehealth; however, lingering questions remain on the impact on quality of care.

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LATEBREAKER

HIV / STI

A mixed methods study of antiretroviral therapy engagement in long-term care Brianne Olivieri-Mui* Brianne Olivieri-Mui Mark Brennan-Ing Laura Senier Dae Hyun Kim Aneeka Ratnayake-Sargent

Antiretroviral therapy (ART) use in long-term care (LTC) is lower than expected making it critical that facilitators/barriers are identified. A convergent mixed-methods design, sought convergent, complementary, and contradicting factors related to ART adherence in LTC. Two identical quantitative analyses assessed the change in the proportion of days covered (PDC) by ART before and after transitioning to LTC in Medicare (LTC stays for people with HIV (PWH) in [1] 2017-2019 Medicare Advantage [MA]; [2] a 5% random 2014-2019 Traditional Medicare [TM] sample). Linear regression predicting change controlled for person-level and facility-level characteristics. Qualitative interviews from residents (n=11) and providers (n=6) of a HIV-specialized LTC facility focused on barriers/facilitators to ART adherence in LTC. Demographics of PWH were similar across qualitative and quantitative studies with mean age 60-61 years old, >50% were non-White. **Convergent:** Dual eligibility and Black race were associated with ART use. For-profit status was associated with not being on ART. The facility was not-for-profit, most participants were non-white, on Medicaid, all were ART adherent. **Complementary:** The facility ensured frequent patient-provider interactions, routine screening at admission, viral load monitoring, and a collaborative approach to care. **Contradictory:** Polypharmacy was associated with lower PDC. Interviews identified specific strategies to mitigate polypharmacy and optimize ART adherence, through team-oriented medication reconciliation. Quantitatively, PWH in MA and TM using LTC were similar and found more person-level facilitators of ART adherence, while qualitative findings showed environmental factors not found in claims data make a difference in ART adherence.

Infectious Disease

Early-season influenza forecasting for the 2025-2026 influenza season and importance of evaluating accuracy Sarabeth M. Mathis* Sarabeth Mathis Rebecca K. Borchering Annabella G. Hines Matthew Biggerstaff

Influenza-related hospitalizations are a major contributor to disease burden in the United States with CDC estimating 100,000 to 710,000 hospitalizations annually. Accurate predictions of influenza hospitalizations support public health planning and interventions.

CDC coordinated the FluSight forecasting challenge for the 2025-2026 influenza season beginning November 2025, and forecasting teams provided national and jurisdiction-specific probabilistic forecasts for weekly lab-confirmed influenza hospitalizations up to 3 weeks ahead of the current week. Each week, FluSight ensembled forecasts by calculating the unweighted median of each quantile among eligible forecasts and monitored the accuracy of the ensemble by evaluating coverage, a metric that summarizes how often the forecast prediction interval contains the observed value.

In the first four weeks of the FluSight challenge, the ensemble forecast included 34-36 models from 30 teams. National weekly influenza hospital admissions stayed below or around 5,000 admissions prior to December, and admissions then rapidly increased to exceed 30,000 by the end of December. Coverage values ranged from 92-96% for current week forecasts during the period of lower admissions but dropped substantially during the period of rapid influenza increases with weekly coverage values dropping to 60% for current week forecasts and 36% for 3-week ahead.

This decrease in coverage during periods of rapid increases has been observed previously. In 2024-2025, a high-severity season with multiple periods of increases in hospitalization, coverage values for the FluSight ensemble did not exceed 75% until early March 2025. Further efforts to identify the causes for the declines in forecast performance during these periods are needed to improve the utility of influenza forecasts. Continuous assessment of forecast performance is also critical to ensure performance remains in expected ranges and to inform transparent forecast communication.

Infectious Disease

Incorporating Behavior Change into Estimates of Transmission Parameters and Intervention Impact in Acute Infections Kayoko Shioda* Dehao Chen Judy L Donald Mark A Schimidt Samuel M Jenness Benjamin A Lopman Kayoko Shioda

Although behavioral changes in infectious individuals drive transmission, empirical contact data for acute infections remain scarce. Most transmission models for acute infections assume that contact rates remain constant or decrease to perfect isolation over the course of infection, introducing biases in key model-derived quantities—transmissibility per contact [β] and intervention impact. We aimed to characterize these biases. We conducted a longitudinal survey of social contacts in a cohort with acute respiratory or enteric infection from 2024-2025. We followed up with cases to measure their contact rates on the index date (when feeling most sick), 1 week, and 2 weeks after. We developed two versions of the mechanistic model for rotavirus: a behavior-dynamic model, incorporating our empirical data on behavioral feedback, and a behavior-naive model, assuming constant social contact patterns. We fitted both models to rotavirus gastroenteritis hospitalization rates in the US prior to vaccine introduction. We estimated β from both models. We simulated a non-pharmaceutical intervention of daycare closure by reducing contact among < 5-year-old cases. We found that contact rates among cases increased steadily from the index day through the 2-week follow-up. The dynamic model yielded β that was 1.3 times greater than that of the naïve model. Compared with the dynamic model, the naïve model overestimated the intervention impact (% reduction in cases with daycare closure vs. no closure) in the <5 age group by 3.1% when all infections (symptomatic and asymptomatic) were included, and by 14.3% when only symptomatically infected individuals stayed home. Overestimating contact rates leads to underestimating transmissibility per contact. In turn, the projected intervention impact for the target population—based on the underestimated β—is biasedly inflated.

Infectious Disease

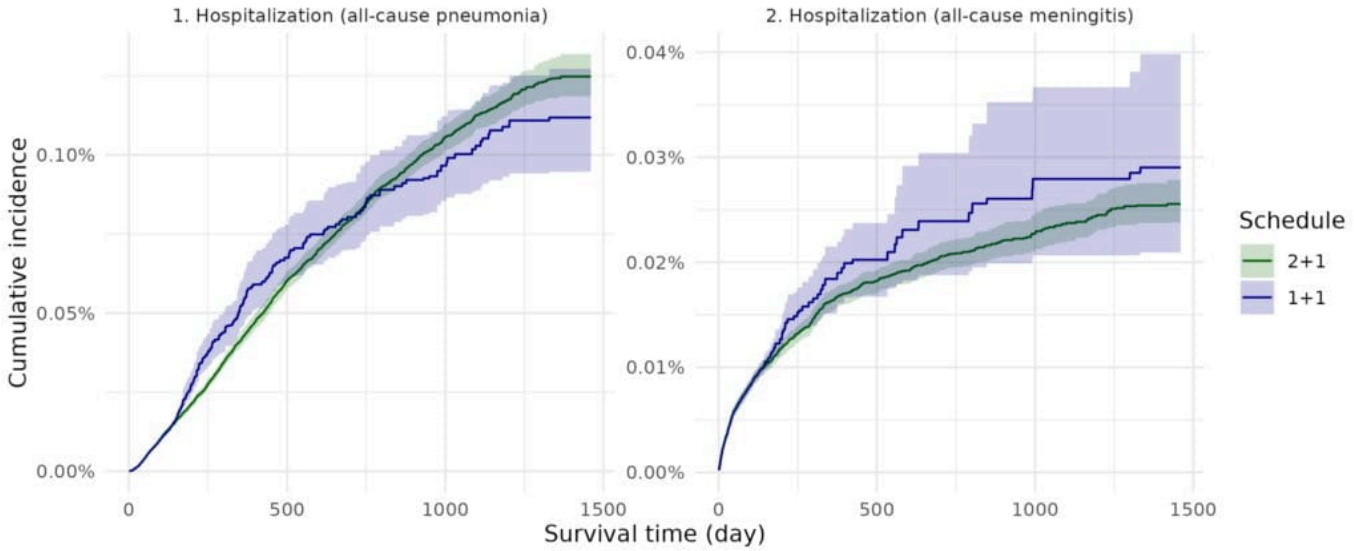
Comparative Effectiveness of Different Dosing Schedules of Pneumococcal Conjugate Vaccines among Children in Brazil: A Target Trial Emulation Study Using National Registries Katherine Jia* Katherine Jia Fan Bu Shae Gantt Caroline Gava João Carlos Lemos Sousa Ana Catarina de Melo Araujo Cristiana M Toscano Kayoko Shioda

Background: Pneumococcal conjugate vaccines (PCVs) prevent pneumococcal diseases in children but are among the most expensive vaccines in routine immunization programs, prompting interest in evaluating real world effectiveness of reduced dosing schedules. Brazil currently follows the WHO-recommended 3 dose schedule (a 2+1 schedule with two primary doses plus a booster). Considering recent evidence that a reduced 1+1 schedule (one primary dose plus a booster) achieved equivalent disease control in selected settings, we aimed at evaluating comparative effectiveness of different dosing schedules in a large developing country with a robust and high coverage PCV program. Target trial emulation (TTE) can leverage nationwide registry data to generate generalizable real-world evidence.

Methods: We emulated a target trial comparing 2+1 and 1+1 schedules among children born in Brazil, 2021-2024. Nationwide live birth, vaccination, hospitalization, and notifiable disease registries were individually linked by the Ministry of Health, covering all municipalities in Brazil. The study included children under four, who were followed up until end of 2024. We applied clone-censor-weight analysis to adjust for immortal time bias and baseline confounding.

Results: By age four, the cumulative incidence of hospitalization for all-cause pneumonia had children followed the 1+1 schedule was similar to that had they followed 2+1 (relative risk [RR]: 0.90; 95% CI: 0.76, 1.03). Likewise, the cumulative incidence of all-cause meningitis was similar (RR: 1.12; 95% CI: 0.82, 1.64) (**Figure**). Further analyses will include mortality outcome and use negative control exposures and outcomes to assess residual confounding.

Conclusions: In this nationwide TTE, a 1+1 PCV schedule appeared non-inferior to 2+1 for preventing all-cause pneumonia and meningitis hospitalization by age four. TTE offers a powerful and practical approach for generating real-world vaccine effectiveness evidence to inform policy.



Infectious Disease

Norovirus Outbreak Associated with a Restaurant Exposure and Secondary Transmission at Atlantic Coast Conference (ACC) Field Hockey Louisville Kentucky 2025 Jordan Adams* Molly Parsch Venetia Aranha Ryli Hockensmith Emily Covey Jennifer Khoury Terrel Young Wendii Brooks Harold Barrantes Debra Brown Sheri Streeter

Background: Norovirus is a leading cause of acute gastroenteritis in the United States and is highly transmissible through contaminated food, surfaces, and person-to-person contact. The virus causes an estimated $10.6 billion in annual U.S. economic losses.

Objective: To identify norovirus cases and characterize illness associated with restaurant exposure and secondary transmission among attendees of an Atlantic Coast Conference field hockey event.

Methods: We conducted a retrospective outbreak investigation using standardized case definitions to classify confirmed, probable, and secondary cases. Case identification occurred through chief complaints, interviews, and coordination with local and state health departments. Exposure histories were collected from individuals who dined at the restaurant between November 1–5 and from attendees of the field hockey event on November 4. Stool specimens from symptomatic individuals were tested for norovirus. Environmental health staff conducted on-site assessments of the restaurant, including evaluation of sanitation practices and employee illness reports.

Results: A total of 76 cases were identified. Illness onset occurred within six days of restaurant exposure. Common symptoms included vomiting (100%), diarrhea (92%), and fever (42%). Stool specimens tested positive for norovirus. Secondary cases became ill between November 4–6 after attending the field hockey event and were epidemiologically linked to restaurant-exposed cases. Ill food service employees were identified during environmental inspections. The primary mode of transmission at the restaurant remained undetermined.

Conclusion: Strengthening employee illness exclusion policies and enhancing regional specimen collection capacity may improve future norovirus outbreak detection and control.

Infectious Disease

Evaluating Wastewater Surveillance for COVID-19, RSV, and Influenza in Arizona: Correlation with Reported and Syndromic Cases, 2020–2025 Patrick Montine* Patrick Montine Sarah Avalle Reshma Neupane Joli Weiss

Background:
Wastewater-based surveillance has become an increasingly important component of respiratory disease monitoring, offering a population-level signal that is less dependent on healthcare utilization and testing practices. This project evaluates how well wastewater viral concentrations for the effectiveness of COVID-19, RSV (respiratory syncytial virus), and Flu (Influenza A and B) track reported case and syndromic surveillance trends across Arizona during 2020-2025, and assesses the performance of legacy versus automated laboratory methods.

Methods:
We conducted an ecological study using wastewater viral concentration data and reported COVID-19, RSV, or Flu case/syndromic data. Sewersheds were aggregated at the state level and the population weighted. Rolling 7-day and weekly averages of normalized wastewater concentrations were calculated. Pearson and Spearman correlation analyses were performed to evaluate associations between wastewater viral activity and reported case trends, and to compare an older laboratory method with a newer automated method.

Results:
Across all pathogens, the automated wastewater method demonstrated consistently stronger correlations with reported cases and weekly averages than the old method. For COVID-19, correlations improved from moderate (old rolling $\rho = 0.60$, $r = 0.66$; weekly $\rho = 0.71$, $r = 0.80$) to stronger with the new method (rolling $\rho = 0.70$, $r = 0.70$; weekly $\rho = 0.80$, $r = 0.83$). Similar improvements were observed for influenza A and B, where correlations increased substantially with the automated method, and for RSV, where weak or negative correlations using the old method shifted to strong positive correlations for rolling averages using the new method ($\rho = 0.87$; $r = 0.88$).

Conclusions:

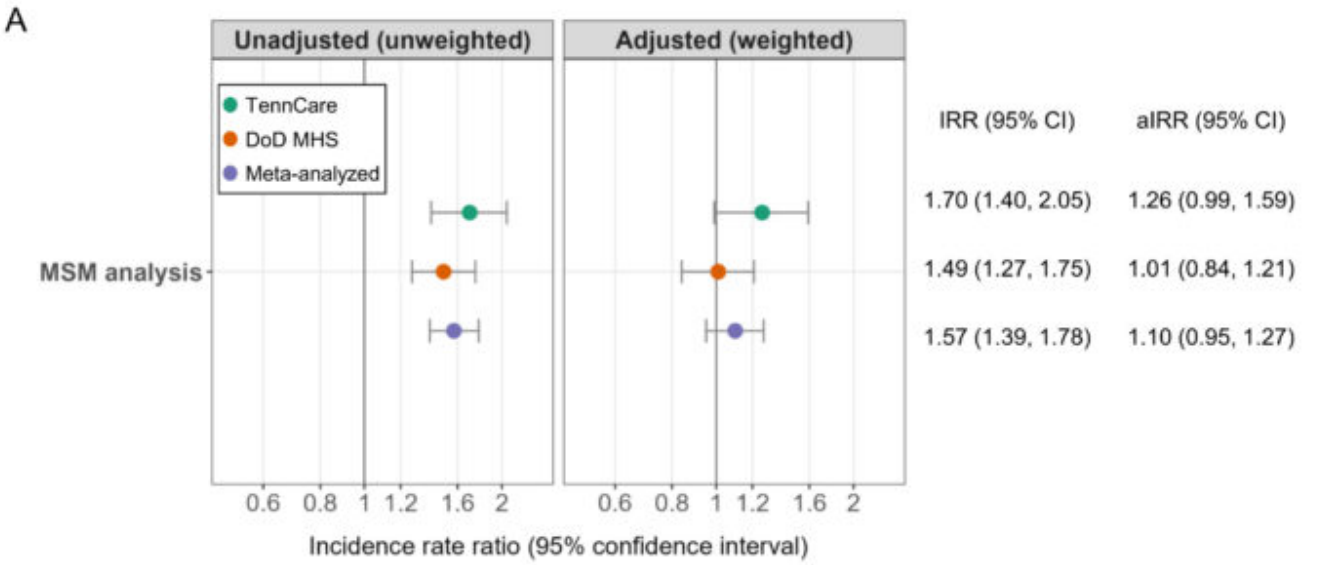
Wastewater surveillance reflects population-level respiratory disease trends, with improved methods enhancing performance and supporting its use as a scalable, resilient tool for routine monitoring and lead–lag analyses for early warning.

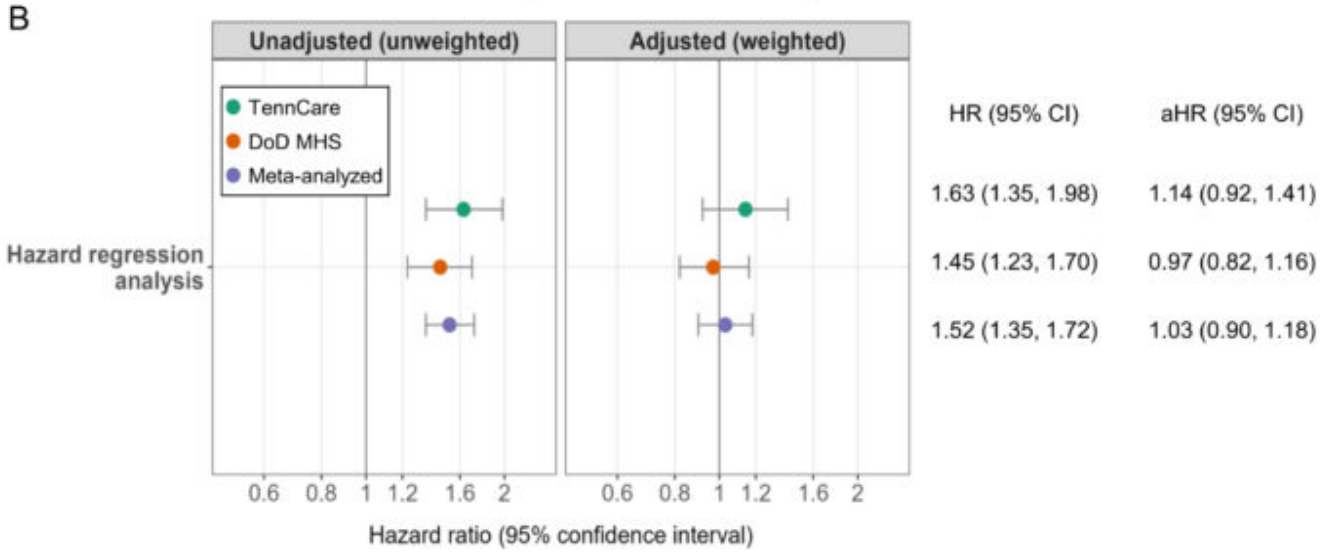
Infectious Disease

Effect of leukotriene-modifying agents on severe influenza illness: Comparative analysis of three analytical approaches Brittney M. Snyder* Brittney Snyder Corinne A. Riddell Tebeb Gebretsadik Tan Ding Rees L. Lee William D. Dupont Justin R. Ortiz Veronika Pav Thomas J. Braciale Pingsheng Wu Tina V. Hartert

Animal and in vitro studies suggest that leukotriene modifying agents (LMAs) may decrease susceptibility to influenza illness. We estimated the effect of LMAs on severe human influenza illness in a retrospective cohort using three analytic designs and corresponding methods to mitigate potential biases: 1) a marginal structural model, 2) a proportional hazards model, and 3) a case-time-control design. Study populations included individuals with asthma and/or allergic rhinitis for whom LMAs are FDA approved and who were enrolled in Tennessee Medicaid (TennCare) or Department of Defense Military Health System (DoD MHS) from 1995–2019. Exposed periods were defined by LMA prescription start dates plus days' supply. Severe influenza illness was defined using previously validated International Classification of Diseases criteria. Montelukast accounted for 99% of LMA prescription fills. Adjusted incidence rate ratios from the marginal structural model and adjusted hazard ratios from the proportional hazards model were 1.26 (95% CI 0.99, 1.59) and 1.14 (95% CI 0.92, 1.41) for TennCare and 1.01 (95% CI 0.84, 1.21) and 0.97 (95% CI 0.82, 1.16) for DoD MHS, respectively. Adjusted odds ratios from the case-time-control were 1.11 (95% CI 0.74, 1.65) for TennCare and 1.91 (95% CI 1.29, 2.84) for DoD MHS. Findings in different populations and designs do not support the use of LMAs for chemoprophylaxis of severe influenza illness. Conclusions regarding LMAs other than montelukast were not possible.

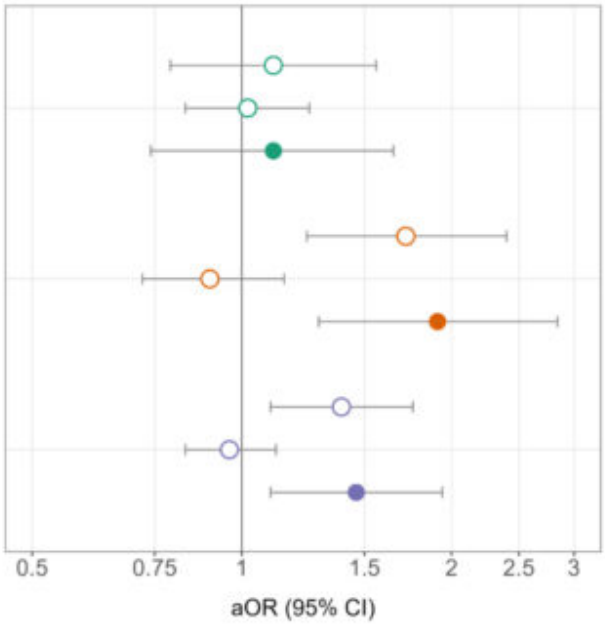
Figure. Association between leukotriene modifying agent use and severe influenza illness in the A) marginal structural model (MSM) analysis, B) proportional hazards model analysis, and C) case-time-control design.





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	aOR (95% CI)
TennCare	
Case-crossover cases	1.11 (0.79, 1.56)
Case-crossover controls	1.02 (0.83, 1.25)
Case-time-control ratio	1.11 (0.74, 1.65)
DoD MHS	
Case-crossover cases	1.72 (1.24, 2.40)
Case-crossover controls	0.90 (0.72, 1.15)
Case-time-control ratio	1.91 (1.29, 2.84)
Meta-analyzed	
Case-crossover cases	1.39 (1.10, 1.76)
Case-crossover controls	0.96 (0.83, 1.12)
Case-time-control ratio	1.46 (1.10, 1.94)



Infectious Disease

Effectiveness of maternal influenza vaccination against influenza-associated emergency department and urgent care encounters among infants aged >6 months – VISION Network, 2023–2024 and 2024–2025 seasons Emily Reeves* Emily Reeves Zachary Weber Duck-Hye Yang Shaun J. Grannis Toan C. Ong Sarah W. Ball Malini B. DeSilva Kristin Dascomb Stephanie A. Irving Karthik Natarajan Nicola P. Klein Caitlin Ray Amanda B. Payne Shikha Garg Samantha M. Olson Jennifer DeCuir Sara Tartof

Studies have shown that maternal influenza vaccination during pregnancy provides protection for infants aged <6 months, a population at increased risk of severe influenza and without a licensed influenza vaccine. We evaluated maternal influenza vaccine effectiveness (VE) against influenza-associated emergency department or urgent care (ED/UC) encounters among infants during two U.S. influenza seasons (2023-2025).

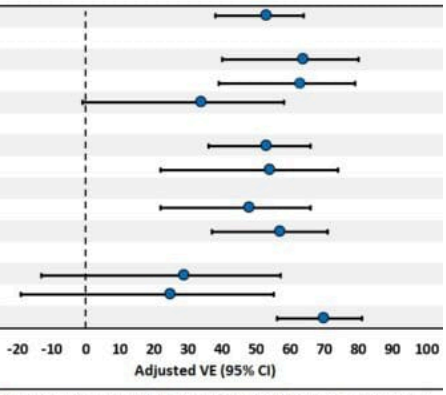
A test-negative, case-control study was conducted among infants <6 months with linkage to maternal vaccination records. Infants with acute respiratory illness (ARI)-associated ED/UC encounters who tested positive or negative for influenza and negative for SARS-CoV-2 and RSV via molecular testing at seven VISION Network health systems were included. VE was estimated using logistic regression comparing the odds of maternal influenza vaccination (≥14 days before delivery) in influenza positive cases vs influenza negative controls, adjusting for site, infant age, race/ethnicity, calendar time, and season.

Among 3,815 ARI encounters in infants, 455 (12%) tested positive and 3,360 (88%) tested negative for influenza; 69 (15%) cases vs 1,018 (30%) controls were born to mothers who received an influenza vaccine in pregnancy. Overall VE was 53 (95% CI: 38–64). VE was statistically significant among infants 0–1 month (64%, 95% CI: 40–80), 2-3 months (63%, 95% CI: 39–79), and third trimester maternal vaccination (70%, 95% CI: 56–81). VE was not statistically significant among infants 4-5 months (34%, 95% CI: -1–58), first (29%, 95% CI: -13–57), and second trimester vaccination (25%, 95% CI: -19–55).

Maternal influenza vaccination was effective against influenza-associated ED/UC encounters in infants <6 months. VE point estimates were highest in those 0–3 months and when vaccinated in the third trimester. These findings provide evidence of infant protection from maternal influenza vaccination and may help inform clinical decisions about timing of influenza vaccination during pregnancy.

Figure 1. Maternal influenza vaccine effectiveness against influenza-associated emergency department or urgent care encounters among infants aged <6 months–VISION, October 2023-April 2025

Subgroup	Cases Number vaccinated/total (%)	Controls Number vaccinated/total (%)	Medians days from maternal vaccination to infant encounter (IQR)	Adjusted vaccine effectiveness (95% CI)[a]
Overall	69/455 (15%)	1018/3360 (30%)	163 (110-253)	53 (38-64)
Infant age				
0-1 month	15/76 (20%)	409/1121 (36%)	107 (76-156)	64 (40-80)
2-3 months	25/144 (17%)	334/1128 (30%)	158 (128-206)	63 (39-79)
4-5 months	29/235 (12%)	275/1111 (25%)	322 (201-362)	34 (-1-58)
Influenza type				
Influenza A	53/356 (15%)	1018/3360 (30%)	163 (110-253)	53 (36-66)
Influenza B	16/99 (16%)	1018/3360 (30%)	162 (110-232)	54 (22-74)
Influenza season				
2023-2024	28/175 (16%)	521/1670 (31%)	164 (117-238)	48 (22-66)
2024-2025	41/280 (15%)	497/1690 (29%)	160 (109-261)	57 (37-71)
Trimester of vaccination				
First trimester	22/408 (5%)	233/2575 (9%)	341 (292-372)	29 (-13-57)
Second trimester	20/406 (5%)	277/2619 (11%)	172 (144-206)	25 (-19-55)
Third trimester	27/413 (7%)	508/2850 (18%)	115 (81-158)	70 (56-81)



[a] Influenza vaccine effectiveness (VE) was estimated using multivariable logistic regression models comparing the odds of maternal influenza vaccination between influenza-positive cases and influenza-negative controls. Models were adjusted for site, infant age in months, infant race/ethnicity, calendar time, and season.

Infectious Disease

Trust in health system for COVID-19 vaccine information among unvaccinated US adults: Association between trust in other entities and trust in healthcare providers Victor Puac-Polanco* Victor Puac-Polanco Sharifa Nasreen

Rising hesitancy toward vaccinations, especially COVID-19 vaccines, is influenced by trust. However, understanding how trust in other entities affects people's health decisions remains limited. To address this gap, we assessed whether trust in other health entities and sex and racial concordance were associated with trust in a personal doctor or healthcare provider to provide COVID-19 vaccine information among unvaccinated individuals. We conducted a cross-sectional analysis using public data from the Urban Institute's 2021 Health Reform Monitoring Survey. The outcome was trust in a personal doctor or health care provider as the source of information for the COVID-19 vaccine. The independent factors included trust in pharmacists, religious leaders, local elected officials, social services, and family and friends, and sex and racial concordance. Associations were examined using multinomial logistic regression models to estimate relative risk ratios (RRR) with 95% CIs, adjusting for sociodemographic factors. Analyses used post-stratification weights. Unvaccinated individuals were younger (mean age 38.6 vs. 44.1 years, $p<0.0001$), with the highest non-vaccination rates among those aged 18–24 (17.9%) and 25–34 (26.0%). Hispanic and Black non-Hispanic adults were more likely to be unvaccinated than white non-Hispanic individuals ($p=0.0001$). Adjusted models showed that distrust in elected officials significantly increased the likelihood of neither trust nor distrust (RRR 2.56, 95% CI 1.67-3.94) and of distrust (RRR 4.71, 95% CI 1.92-11.43) in a personal doctor or health care provider. Distrust in social services, family/friends, also increased the likelihood of neither trust nor distrust and of distrust in a personal doctor or health care provider. Gender and racial concordance showed no consistent associations. Partnering with local officials, social services, and family/friends may help address distrust in personal doctors and healthcare providers among the unvaccinated.

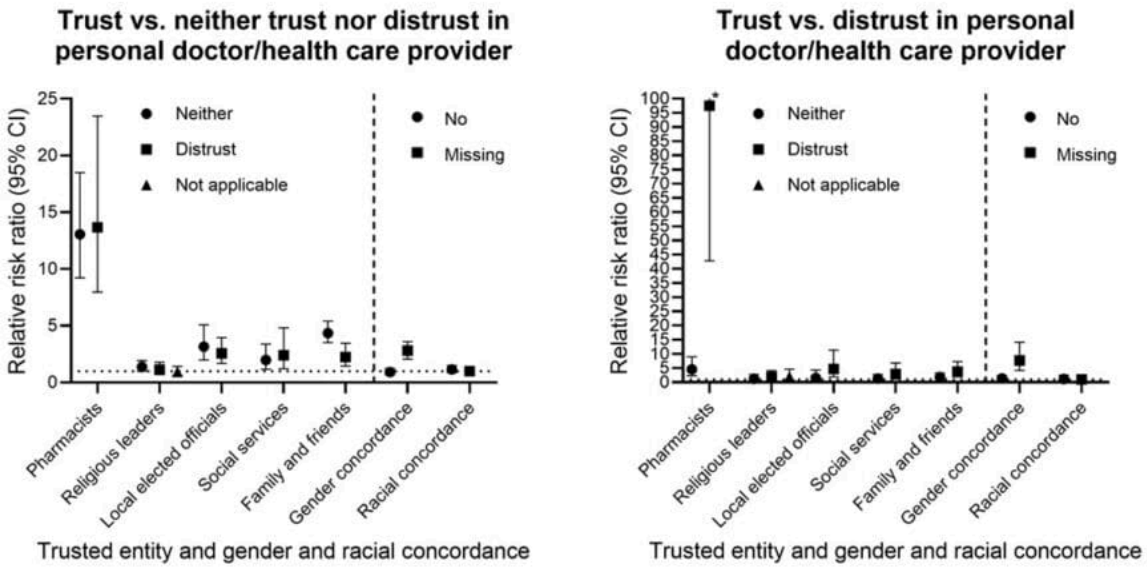


Figure: Association between trust in personal doctor/personal health care provider/a doctor or health care provider in the community and other entities in the community and gender and racial concordance among unvaccinated individuals. *95% CI of related risk ratio truncated at 100.

Infectious Disease

What distinguishes those who get lyme disease? a case-control study of knowledge, attitudes, and practices in canada Danny Szaroz* Danny Szaroz Manisha A. Kulkarni Jamie Mader Molly Praest Tanya Gilpin Nicole Giourdis Robert Brison Elizabeth Stringer Kate Zinszer

The rapid rise in the incidence of Lyme disease (LD) in Canada, indicates that more public health action is needed to target high-risk populations. In regions with increasing endemic risk, it is important to understand how the independent contributions of knowledge, attitudes and practices affect health behaviour and disease status.

The study's aim is to identify characteristics associated with higher levels of LD knowledge and protective behaviours.

We conducted a matched case-control study in Kingston, Ontario and Lunenburg, Nova Scotia, using LD data from geographically stratified paper surveys administered in emergency rooms and primary care clinics from 2019 to 2024. Frequency matching was used based on age group, biological sex, and site. Cases were defined as individuals who have been diagnosed with early-stage LD while controls were defined as individuals who did not have a previous diagnosis of LD. Questionnaire aimed to collect information on sociodemographic, KAP, and other risk factors for LD like income and education. We compared domain-specific Principal Component Analysis (PCA) for KAP domains to preserve within domain structure, to the profiling of KAP scores as a global composite score, treating KAP as a unified construct. Disease outcome is regressed on KAP via logistic modelling adjusted for confounding.

Domain-specific dimensionality reduction revealed targeted associations generalized by composite scoring approach, primarily revealing confounding by socio-economic factors. Crude analyses with domain-specific comparisons revealed that knowledge showed no association while the attitudes revealed protective effects. After adjusting for confounding, this association reversed with knowledge showing strong protective effects and attitudes showing no significant association. Among socio-economic factors, 'postgraduate education' conferred 97% lower odds of disease while low income (<$50,000) was associated with 93% higher odds.

This study will offer insights into how variations in socioeconomic status exerts confounding influence, masking the underlying association between heath knowledge and LD status. The findings can be used to inform and guide the development of targeted LD prevention strategies including education campaigns in vulnerable areas, to help reduce the risk of infections within the Canadian population.

LATEBREAKER

Infectious Disease

VaxImpact: An interactive RShiny App Quantifying the Health and Economic Consequences of Declining Childhood Vaccination Across U.S. States Mahmud Sheku* Mahmud Sheku Connor Van Meter Benjamin A. Lopman Robert A. Bednarczyk

Background: Recent declines in childhood vaccination coverage in the United States are likely to continue or accelerate. Vaccine hesitancy is increasing while federal guidelines are changing to remove universal recommendations for several childhood vaccines. To provide state-specific projections of health and economic impacts, we developed an interactive tool to estimate the additional burden from declining infant vaccination.

Methods: We used calibrated, state-level equilibrium transmission models for rotavirus, pertussis, and invasive pneumococcal disease (IPD). Rotavirus was modeled using a Susceptible-Infection-Recovered model; pertussis and IPD used a Susceptible-Infection-Recovered-Susceptible model with waning immunity. Vaccine coverage declines of 0-20 percentage points were applied to infant cohorts. We calculated the impacts after one and five years of reductions accumulated across birth cohorts. Outcomes included additional annual cases, hospitalizations, deaths, and total costs.

Results: After a 20% decline in coverage over one year, we estimated annual impacts of 230,358 additional rotavirus cases (3,294 hospitalizations), 13,559 pertussis cases (644 hospitalizations), and 1,426 IPD cases (1,183 hospitalizations), with additional costs of $259M, $44M, and $25M, respectively. When coverage declined by 20% for five years, the annual impacts were 809,819 rotavirus cases (11,580 hospitalizations), 56,502 pertussis cases (2,768 hospitalizations), and 4,631 IPD cases (3,844 hospitalizations), with costs exceeding $911M, $183M, and $81M, respectively.

Conclusions: Sustained vaccination declines are projected to generate substantial and escalating health and economic losses. VaxImpact provides an interactive, state-specific platform enabling policymakers and public health practitioners to quantify projected disease and economic burden under varying decline scenarios, supporting immunization policy decisions and outbreak prevention efforts.

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LATEBREAKER

Infectious Disease

Leveraging wastewater-based epidemiology to assess the prevalence, antibiogram and infection risks of Listeria monocytogenes in wastewater effluents in South Africa: A critical tool for public health surveillance Chidozie Declan* Chidozie Declan Iwu

Introduction: Wastewater-based epidemiology (WBE) is a valuable tool for monitoring public health risks, offering insights into the prevalence and antimicrobial resistance (AMR) of pathogens like Listeria monocytogenes in community settings. This study investigates the prevalence, AMR profiles and infection risks of L. monocytogenes in final effluents of three wastewater treatment plants (WWTPs) in the Eastern Cape Province, South Africa.

Methods: Presumptive L. monocytogenes in wastewater effluents were detected using standard plate count methods, followed by the confirmation and screening for nine virulence markers using polymerase chain reaction (PCR) assays. Antibiotic susceptibility of confirmed isolates against 18 antibiotics was done using the disk diffusion method, and relevant resistance genes were screened via PCR. The potential risk of infection attributed to L. monocytogenes was assessed using the Quantitative Microbial Risk Assessment (QMRA) modelling. Monte Carlo simulation with 10,000 iterations was used to characterise the risk.

Results: The prevalence of L. monocytogenes in wastewater effluents was statistically significant ($P < 0.05$), ranging from log10 1.00 CFU/100 ml to log10 3.75 CFU/100 ml. Of 280 presumptive isolates, 20 (7.1%) were confirmed, with virulence genes detected at varying frequencies: inlA (95%), inlB (90%), actA (85%), hlyA (80%), and iap (75%). High phenotypic resistance was observed to tetracycline (80%), doxycycline (65%), cefotaxime (50%), penicillin (30%), and chloramphenicol (60%), with resistance genes detected as follows: tetA (60%), tetB (55%), tetC (50%), sulI (40%), sulII (35%), aadA (30%), aac(3)-IIa (25%), blaTEM (20%), blaCTX-M group 9 (15%), blaVEB (10%), and AmpC (10%). The average annual infection risk of 6.70×10^{-2} (range: 9.10×10^{-3} to 1.00) exceeded the World Health Organization standards.

Conclusion: This study highlights the utility of WBE in detecting the prevalence, AMR, and infection risks of L. monocytogenes, emphasizing its value as a critical tool for public health surveillance and risk mitigation.

LATEBREAKER

Infectious Disease

The effect of wildfire smoke exposure on tuberculosis diagnoses in Brazil: a case-crossover analysis Lauren Linde* Lauren Linde Moreno M Rodrigues Artur T L Queiroz Leandro Macedo Beatriz Barreto-Duarte Rodrigo C. Menezes Weeberb Requia Mary Willis Bruno B. Andrade Leonardo Martinez

Background

Wildfires are increasing in size, frequency, and severity around the world. Wildfire smoke exposure has been linked to numerous adverse health outcomes, but few studies have investigated potential effects on infectious respiratory diseases. We assessed the effect of wildfire smoke exposure on tuberculosis (TB) diagnoses in Brazil, a high-TB-burden country heavily impacted by wildfires.

Methods

We conducted a time-stratified, bidirectional case-crossover analysis using the national TB case registry in Brazil (SINAN) from 2015-2022, anchored on the diagnosis date. Daily concentrations of wildfire-attributable fine particulate matter (PM2.5) were estimated for the municipality of residence using the 3D chemical transport model GEOS-Chem. Primary analyses assessed the count of days of exposure to wildfire-attributable PM2.5 with concentration >35µg/m3 (the EPA 24-hour exposure standard) using a one-year hazard window immediately preceding the date of TB diagnosis and two commensurate-length bidirectional control periods. Secondary analyses assessed 180-day hazard/control windows.

Results

We identified 743,563 individuals with TB from 2015-2022 (Figure). On average, participants experienced 0.54 days with wildfire-attributable PM2.5 >35µg/m3 in the year preceding diagnosis with TB (range:0-95). Using one-year hazard and control periods, each additional day of exposure in the hazard period was associated with a 0.6% increase in the odds of TB diagnosis (OR: 1.006, 95% CI: 1.004, 1.007). Using 180-day windows, each additional day of exposure in the hazard period was associated with a 4% increase in the odds of TB diagnosis (OR: 1.037, 95% CI: 1.035, 1.040).

Conclusion

Among individuals with TB in Brazil, residential exposure to high concentrations of wildfire-attributable PM2.5 was more frequent during risk periods immediately preceding diagnoses compared to more distal referent periods.


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Injuries/Violence

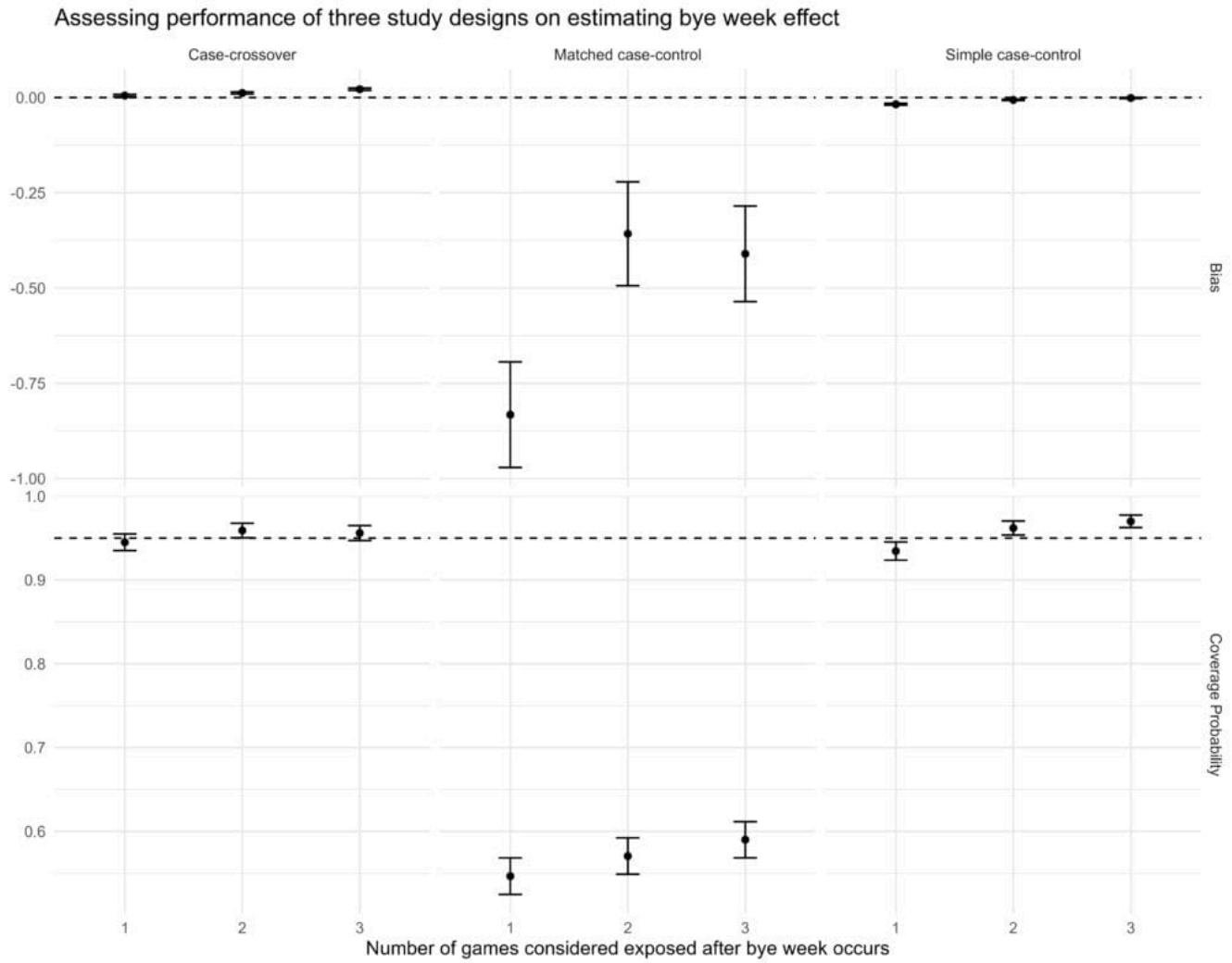
Causal inference for repeated events, case-crossover or case-control: application to sport injuries George Stefan* George Stefan Brice Batomen Aya Mitani Ian Shrier Dhiren Naidu Robert McCormack

Recurrent events such as injuries are commonly encountered in health research but often not properly evaluated. We were interested in evaluating the ability to correctly estimate the causal effect of bye (rest) weeks in professional football using two commonly used designs—case-crossover and case-control.

Using simulations, we generated data that mimic real data from the Canadian Football League. We simulated eight teams with approximately 45 players each, competing over 14 weeks across 10 seasons. Based on current theory, we set the intervention—whether the week preceding the game week was a bye week—as well as season, players' age, team, game order, and opposing team to be associated with individual player injury risk. We accounted for within-team correlation of players and within-player temporal correlation by using a nested random effects structure.

In the case-crossover setting, we matched (1) each individual to themselves and (2) the injury game with the most recent previous injury-free game. In the matched case-control setting, we matched players with an injury to players without an injury playing in the same game on the opposing team. As a secondary analysis, every case was randomly assigned to controls from any games. We estimated the effect of bye week on the presence of injury from conditional logistic regression models.

We found that the case-crossover and simple case-control designs recovered the true effect with minimal bias and coverage close to the nominal level, while the matched case-control design was heavily biased. When consecutive injury games occurred, case-crossover exhibited less bias when only using the first injury game in the series as opposed to all injuries, whereas the opposite was observed for the simple case-control design.



Number of simulations is 2000, with error bars representing Monte Carlo error. Dashed lines indicate zero bias and 95% coverage probability, respectively.
Bias is defined as the estimate minus the true parameter. Coverage probability is defined as the proportion of 95% confidence intervals containing the true parameter.

Injuries/Violence

Model-based data dashboard for estimating mild traumatic brain injury and musculoskeletal injury risk in United States service members Alexander Ivan B. Posis* Alexander Ivan Posis Meg Robinson Juan Diego Vera Amy Silder James M. Zouris Andrew J. MacGregor John J. Fraser Daniel J. Crouch Pinata H. Sessoms

Background: Mild traumatic brain injury (mTBI) and musculoskeletal injury (MSKI) have negative impacts on service member (SM) readiness. There is a need for effective tools to understand injury risk, and interaction of risk between mTBI and MSKI. We developed a data dashboard for model-based estimation of mTBI and MSKI in US SMs.

Methods: This data dashboard used data from the Military Health System Data Repository to create a career archival cohort of 777,811 US SMs who joined between 2016 and 2020, with follow-up data to 2023. Mild TBI and MSKI events were identified using ICD-10 codes. We fit logistic regression models to estimate bidirectional risk of MSKI or mTBI based on prior injury, and demographic and military-relevant covariates. MSKI predictions were conditional estimates in a propensity score-matched sample of 26,784. We then estimated marginal population-level probabilities from bidirectional models. We used the Python tkinter package to develop a data dashboard of model-based estimates of mTBI or MSKI risk, conditional on user-defined parameters such as age and branch of service.

Results: The average age of the cohort was 20.6±3.4 years, 19% were female, 2.4% had an mTBI, and 69.9% had an MSKI. Median and interquartile ranges (IQRs) were used as cut points for “low,” “medium,” and “high” risk of injury in the data dashboard. For the MSKI-to-mTBI model, median probabilities were 0.023 (IQR = 0.016-0.032). For the mTBI-to-MSKI model, median probabilities were 0.500 (IQR= 0.402-0.598). Figure 1 provides a data dashboard example of high risk of mTBI, after providing covariate values.

Conclusions: We developed a data dashboard for model-based estimation of mTBI and MSKI risk in US SMs. Our methods may be adapted for other injury surveillance and medical planning purposes. Data dashboards for injury risk can be flexible and scalable tools for supporting injury prevention strategies and informing patient counseling.

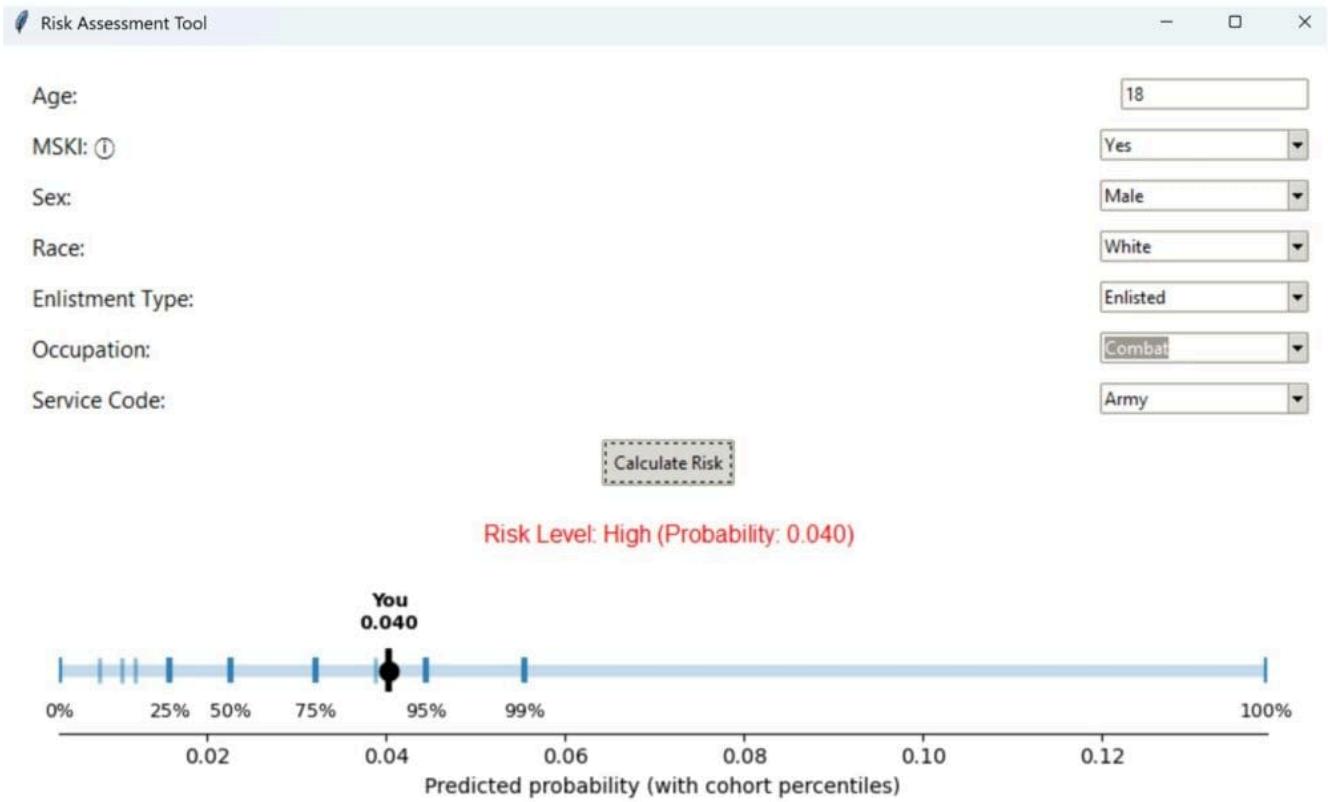


Figure 1. Data dashboard example of a male service member in the Army, aged 18 years, with prior musculoskeletal injury (MSKI), who identifies as White, resulting in a mild traumatic brain injury probability of 4.0%, which is considered to be high risk.

Injuries/Violence

Demographic Differences in Suicide Mortality, Attempts, and Ideation Among Publicly Insured, Privately Insured, and Health System Patients in North Carolina, 2006-2020 Grace Yeboah-Kodie* Grace Yeboah-Kodie Brian W. Pence Vanessa Miller Hillary Mortensen Naoko O. Fulcher Matthew M. Turnure Shabbar I. Ranapurwala

Background: Assessing differences in suicide-related outcomes based on demographics and healthcare access can inform suicide prevention strategies. We analyzed suicide mortality, attempts, and ideation in North Carolina (NC) by age, sex, and race and ethnicity in three subpopulations based on insurance coverage and patient status in a healthcare delivery system.

Methods: We examined suicide-related outcome rates in three NC subpopulations: individuals enrolled in Medicaid, individuals enrolled in a statewide private health insurance plan, and patients of a large integrated healthcare delivery system. We estimated standardized mortality ratios (SMRs) stratified separately by sex, age, and race and ethnicity, comparing suicide mortality in each subpopulation with the NC population. We additionally estimated similarly stratified rates of suicide mortality, attempts, and ideation in each subpopulation.

Results: Private insurance enrollees consistently had less suicide mortality, and Medicaid enrollees and health system patients had excess suicide mortality, compared to the NC population across demographic strata. However, Medicaid enrollees aged 12-24 years had an SMR of 0.78 (95% CI: 0.76, 0.81). The most elevated suicide mortality was observed among Medicaid enrollees aged 25-34 years (SMR: 1.69 (95% CI: 1.63, 1.74)), 35-44 years (SMR: 1.83 (95% CI: 1.77, 1.89)), and 45-54 years (SMR: 1.85 (95% CI: 1.79, 1.91)). For all subpopulations, males had age-adjusted suicide mortality rates more than three times those of females, while White non-Hispanic individuals had the highest SMRs relative to other race and ethnicity groups.

Conclusions: These findings highlight differences in suicide-related outcomes across demographic strata in NC, emphasizing the need for suicide prevention strategies that serve publicly insured populations. There is a clear need for interventions accounting for the intersecting influences of insurance coverage, access to healthcare, and demographics.

Mental Health

The Association Between Body Shape Index and Depression among Young Adults Aged 18-30 Years in the USA Tinsae Abeya Geleta* Tinsae Abeya Geleta

Background: Globally, an estimated 280 million people are affected by depression. In the United States, approximately 21 million adults are currently experiencing depression. Depression is 50% more prevalent among women than men. The recently published articles have indicated that body shape is associated with mental health, with younger populations appearing to be more vulnerable than other age groups. This study aimed to examine the association between body shape index and depression among young adults in the United States and to examine the effect of gender on the association between body shape index and depression.

Methods: This study was conducted in the United States and utilized data from the 2021–2023 National Health and Nutrition Examination Survey. It included young adults aged 18 to 30 years. Depression was assessed using the Patient Health Questionnaire-9, and the Body Shape Index (ABSI) was calculated. The data was analyzed using Stata version 17, with complete case analysis. Descriptive statistics, logistic regression, sensitivity, and subgroup analyses were performed.

Results: The weighted prevalence of depression among young adults was 19.63%. The multivariable logistic regression analysis revealed no significant association between ABSI and depression [AOR = 1.39, 95% CI: 0.75, 2.57]. The sensitivity analysis results were consistent with the main finding [AOR = 1.18, 95% CI 0.93-1.49]. The subgroup analysis results indicated that gender did not significantly modify the association between ABSI and depression.

Conclusion: This study found no statistically significant association between ABSI and depression among young adults in the United States. Future research, longitudinal designs with a larger sample size, is recommended to confirm these results.

Table 1 Association between Body Shape Index and Depression, Adjusted for Sociodemographic, Behavioral, and Medical Factors, NHANES 2021-2023 Weighted Data

Variable	n (weighted%)	Model 1 COR (95%CI)	Model 2 AOR (95%CI)	Model 3 AOR (95%CI)
ABSI categorical				
Q1	217(24.81%)	1	1	1
Q2	214(23.9%)	0.71(0.39, 1.25)	0.81(0.44, 1.47)	0.73(0.39, 1.36)
Q3	215 (25.25%)	0.93(0.54, 1.58)	1.13(0.65, 1.94)	1.05(0.59, 1.88)
Q4	215(26.05%)	1.40(0.74, 2.67)	1.72(0.93, 3.20)	1.39(0.75, 2.57)
ABSI continuous	863	1.19(0.93,1.52)	1.29 (1.02, 1.63) *	1.18 (0.93, 1.49)

Model 1: Unadjusted
Model 2: Adjusted for age, ethnicity, and sex
Model 3: Adjusted for age, ethnicity, sex, alcohol, smoking, physical activity, hypertension, and cholesterol. **ABSI continuous**: For sensitivity analysis, ABSI was treated as a continuous variable. -**COR**: Cured Odds Ratio -**AOR**: Adjusted Odds Ratio -*Indicated p-value less than 0.05.

Table 2: Subgroup Analysis of the Gender Effect on Association Between Body Shape Index and Depression, NHANES 2021-2023 Weighted Data

Gender	ABSI	n (%)	AOR (95%CI) *	*P* for interaction**
Male	Q1	79(18.81)	1	0.114
	Q2	114(27.14)	1.16 (0.35 - 3.81)	
	Q3	115(27.38)	1.63 (0.08 - 3.23)	
	Q4	112(26.67)	1.44 (0.59 - 3.51)	
Female	Q1	138(31.29)	1	
	Q2	100(22.68)	0.54 (0.26 - 1.12)	
	Q3	100(22.68)	0.78 (0.33 - 1.87)	
	Q4	103(23.36)	1.53(0.65 - 3.58)	

Footnote: *Lincom command interaction test result. **Global test of interaction P-value.

Mental Health

Estimating causal effects of screen time and social media use on adolescent wellbeing: an instrumental variable analysis across 54 countries Yi Yang* Yi Yang Jane Maddock Aaron Kandola Praveetha Patalay

Background: The relationship between adolescent screen time, social media use, and wellbeing is debated, partly because most studies use observational data and methods prone to reverse causation and confounding. Yet, policy reforms and public health interventions targeting adolescents' digital media use are being implemented often ahead of definitive causal evidence, underscoring the urgent need for robust, causally informed research.

Methods: We apply an instrumental variable approach to estimate causal effects of digital use on wellbeing, using data from 615,133 15-year-olds in 54 countries. To address endogeneity, country- and year-linked instrumental variables were used: International Telecommunication Union (ITU) internet usage for screen time and DataReportal social media penetration for social media use. Causal effects were estimated with two separate instrumental variable models (Two-Stage Least Squares), controlling for individual demographic and socioeconomic covariates plus country-level GDP per capita and urbanization. A Three-Stage Least Squares framework including both exposures and their interaction was also applied. Extensive robustness checks assessed instrument validity and quantified uncertainty.

Results: Higher screen time and more frequent social media use were causally linked to lower life satisfaction, with consistent effects across subgroups defined by usage levels and gender. Among adolescents whose digital use was influenced by the instruments, screen time and social media use were associated with approximately 1- and 0.8-point reductions in wellbeing, respectively. Robustness tests indicated strong instrument relevance and offered supporting evidence for the plausibility of IV assumptions.

Conclusion: Leveraging cross-national variation in digital infrastructure, this study provides timely and robust causal evidence to inform public health and policy responses to adolescents' digital media use.

Mental Health

Risk factors of Trajectories of Depression in Adults over 65 years old Sujeong Han* Sujeong Han Jiyeon Jung

[Background]

With advancements in science and medical technology, human life expectancy has increased, making aging societies a global phenomenon. Aging is accompanied by various physical and psychological changes, including declines in cognitive and slower emotional responses, and personality changes. Among these, emotional changes particularly depression are of significant concern in older adults. Late life depression is known to be associated with several factors such as gender, age, chronic diseases, lifestyle habits, and subjective health status. Rather than examining these associations at a single point in time, a longitudinal approach that captures the trajectories of depressive symptoms over time provides a more appropriate framework for understanding the evolution of depression in older populations.

[Purpose]

This study aims to identify distinct trajectories of depressive symptoms in adults aged 65 and older, and to examine how previously established risk factors influence differences between these trajectory groups.

[Methods]

Data from the Korean Longitudinal Study of Aging from 2006 to 2022 were analyzed. A total of 10,254 participants aged 65 years and above were included in the final analysis. Group-Based Trajectory Modeling was applied to identify heterogeneous patterns of depression over time. Subsequently, risk factors identified in previous literature were included as independent variables in a multinomial logistic regression model to explore their associations with trajectory group membership.

[Results]

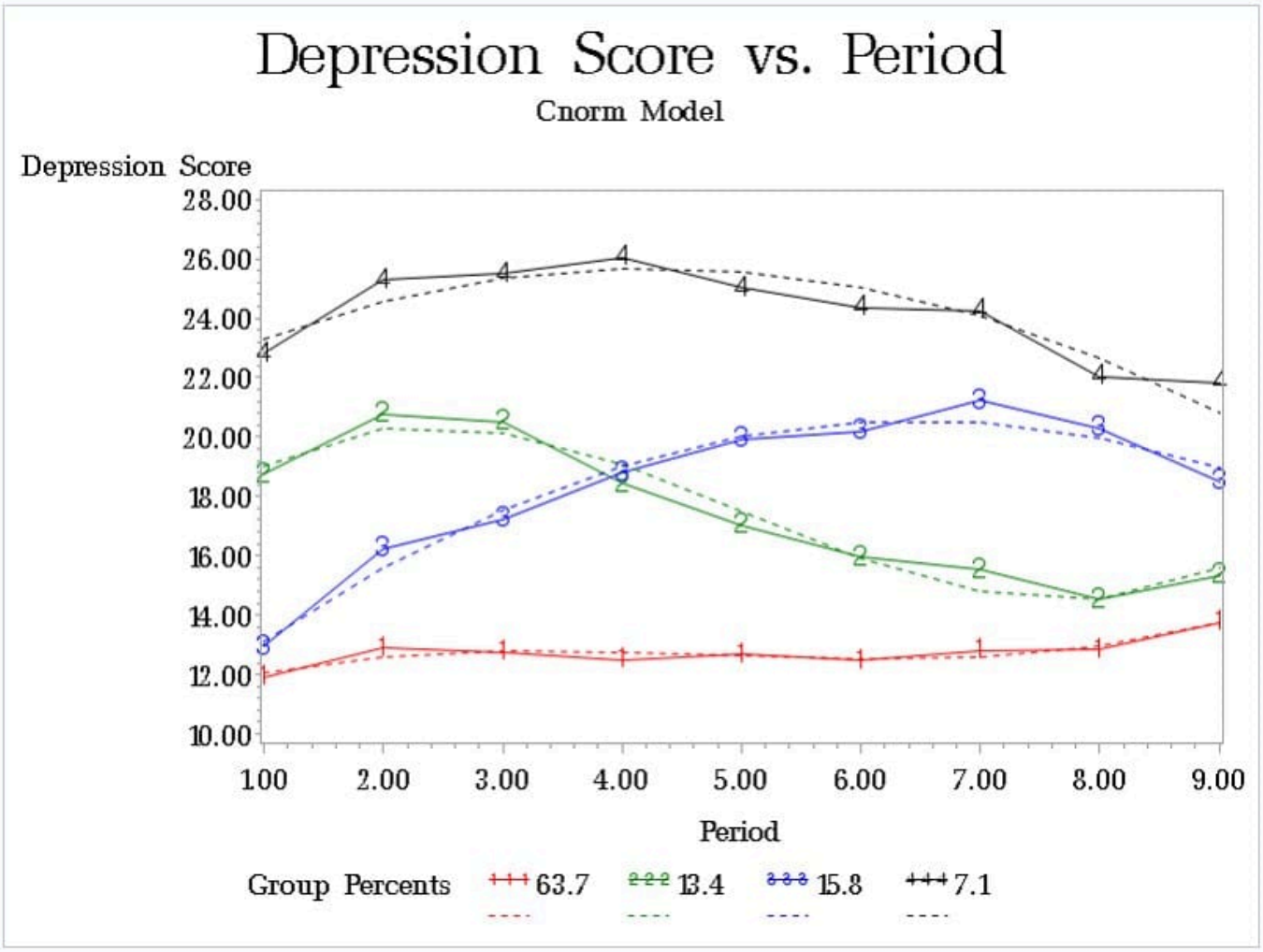
This study identified four distinct trajectories of depressive symptoms among older adults: a group with consistently low levels of depression, a group with initially high symptoms that decreased over time, a group whose symptoms increased over the study period, and a group with persistently high levels of depression.

Individuals with poor lifestyle behaviors such as smoking, alcohol consumption, and physical inactivity were more likely to belong to the persistently high depression group compared to those with stable low depressive symptoms. In addition, lower household income, lower levels of education, and a lack of engagement in social activities were significantly associated with increased odds of being in the high depression trajectory group. The presence of chronic conditions was also linked to a greater likelihood of maintaining high levels of depression over time.

[Conclusion]

These findings highlight the need for targeted interventions, including improvements in health behaviors, economic support, and facilitation of social and economic engagement for older adults.

Such strategies may help prevent or alleviate chronic depressive symptoms in the aging population.

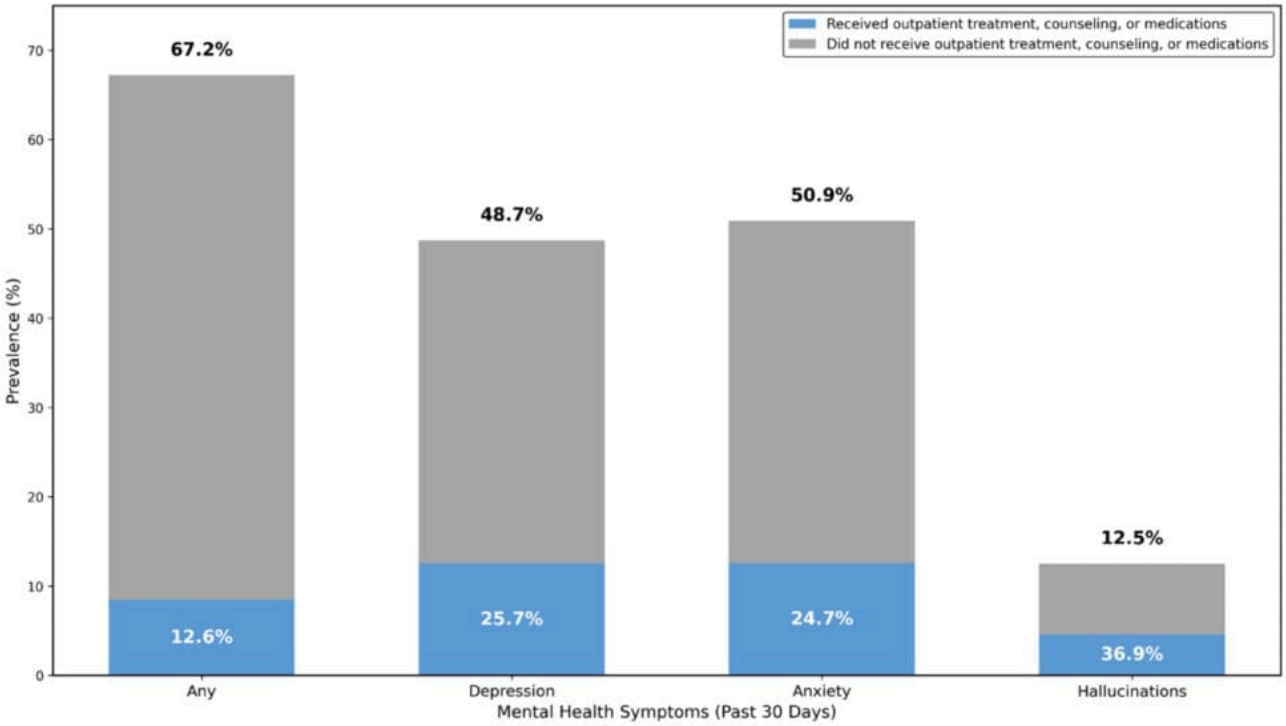


Mental Health

Mental health and treatment utilization among adults experiencing homelessness in California Anna Krasnova* Anna Krasnova Natrina L. Johnson J. Margo Pottebaum Ryan D. Assaf Margot Kushel

In 2024, over 187,000 people experienced homelessness (PEH) on one night in California, representing 24% of PEH in U.S. There is a bidirectional relationship between homelessness and mental health; people with mental health problems are at higher risk of experiencing homelessness and homelessness worsens mental health problems and impedes treatment. In the largest representative study of homelessness in 30 years, we describe the prevalence of mental health symptoms and treatment utilization. The California Statewide Study of People Experiencing Homelessness used a multi-stage, venue-based sampling frame enhanced by respondent driven sampling to create a representative sample (2021-2022). We calculated weighted population prevalence estimates to describe self-reported symptoms of depression, anxiety, and hallucinations; post-traumatic stress disorder (PTSD) diagnoses, and lifetime suicide attempt. We described past 30 days outpatient mental health treatment or medication and past 6 months psychiatric hospitalization. Among 3,200 adults, the mean age was 46.1 years, 67.2% were cisgender male, 26.3% Black, 26.4% Latine, and 27.9% white. In the past 30 days, 67.2% of participants reported any mental health symptoms, 48.7% symptoms of depression, 50.9% anxiety and 12.5% hallucinations. A quarter (25.4%) reported a PTSD diagnosis and 31.3% a lifetime suicide attempt. Among those with any mental health symptoms, 12.6% had received recent outpatient treatment or medication; among those with symptoms of depression, anxiety and hallucinations 25.7%, 24.7% and 36.9% had, respectively. In the past 6 months, 5.3% reported a psychiatric hospitalization; among those with hallucinations, 22.2% had. Mental health symptoms were more prevalent, while treatment utilization, including psychiatric hospitalizations, was less prevalent than previously reported estimates from the last nationally representative study in 1996. There is an unmet need for mental health services for PEH in CA.

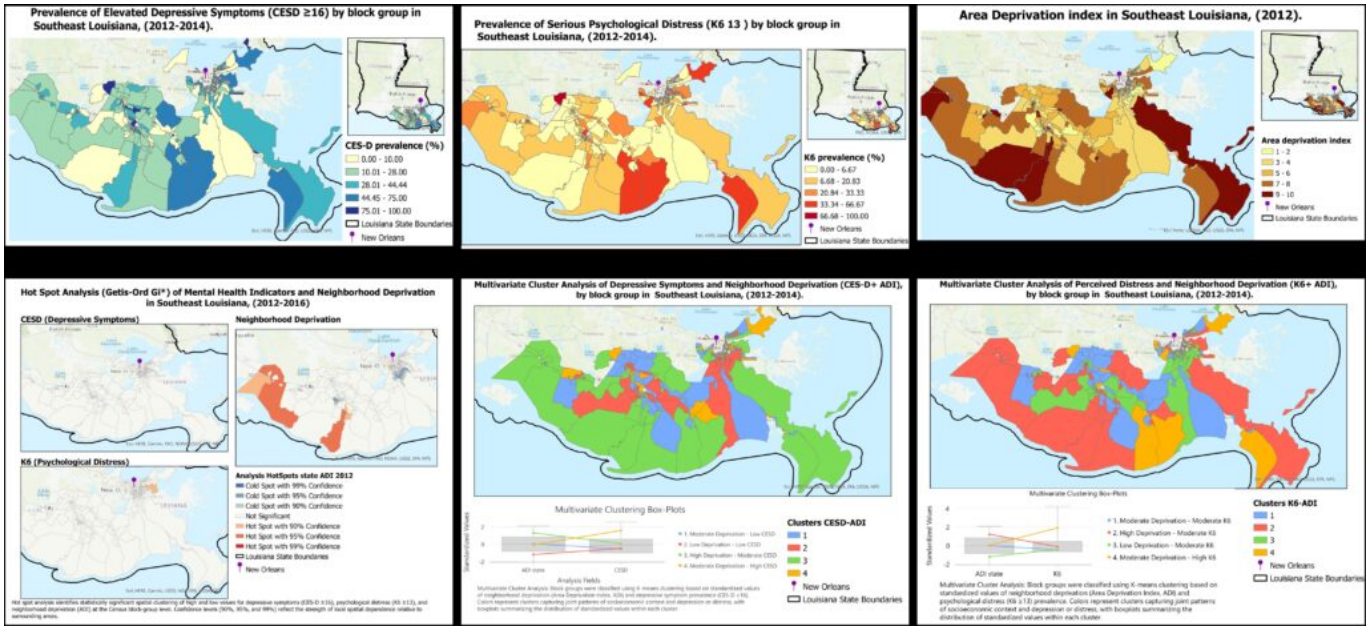
Figure 1: Prevalence of mental health symptoms and treatment utilization in the last 30 days among people experiencing homelessness in California, 2021-2022.



Mental Health

Mental Health And Neighborhood Deprivation, Results From A Spatial Distribution Analysis (2012-2014) In Southeast Louisiana Kristyne D Mansilla Dubon* Kristyne Mansilla Dubon Edward S. Peters Ariane Lisann Rung

Neighborhood disadvantage is linked to poorer mental health, yet few studies have explored the spatial distribution patterns of mental health and neighborhood deprivation. Literature on spatial analysis at the block-group level remains limited. We examined the spatial distribution of depression, distress, and neighborhood deprivation in Southeast Louisiana using data from a prospective cohort of women in the WaTCH Study recruited 2012-2014. Residential locations were geocoded and linked to block-group–level state Area Deprivation Index (ADI) from 2012. Mental health outcomes included depressive symptoms (CES-D ≥16) and psychological distress (K6 ≥13). Spatial analyses employed choropleth mapping, Getis–Ord Gi* hot spot analysis, and K-means clustering. Maps showed that depressive symptoms were spread across Southeast Louisiana, with higher-prevalence block groups concentrated in localized areas. Most block groups had low psychological distress prevalence, with only a few showing elevated distress. ADI choropleths demonstrated variation in neighborhood disadvantage, with both highly (ADI≥7) and less deprived (ADI≤4) block groups scattered across the region. The hotspot analysis revealed no statistically significant clustering for depression. We observed a single block group classified as a hot spot for psychological distress. ADI showed substantial spatial clustering with several block groups identified as hot spots (n=18) and cold spots (n=16). Cluster analysis identified distinct patterns. Related to depression, we observed: 1) moderate deprivation with low depression, 2) low deprivation with low depression, 3) high deprivation with moderate depression, and 4) moderate deprivation with high depressive symptoms. Related to psychological distress, we observed moderate deprivation with both higher and lower distress, while high deprivation clustered mainly with moderate distress. Neighborhood-scale spatial analyses are important to identify spatial variation of both mental health outcomes and neighborhood deprivation, which can be masked by individual-level analyses or state-wide averages. Block-group–level analyses identified localized clusters of psychological outcomes and provided insight on how specific neighborhood contexts may be related to mental health.



LATEBREAKER

Mental Health

Protecting Under the Hard Hat: An anonymous web-based screening tool for the construction workforce Roni Barak Ventura* Roni Barak Ventura Diana Silver

Construction workers comprise a high-risk population that experiences disproportionately high rates of mental health issues, including substance use and suicide. Stigma and low job security often limit disclosure and help-seeking. We developed Protecting Under the Hard Hat, an anonymous, mobile-accessible web tool designed to enable private self-screening and immediate connection to resources. The tool screens for depression, alcohol and drug use, and gambling, and provides tailored feedback including crisis lines, assistance program links, and self-management tools. To begin quantifying the prevalence of these issues, an anonymous back-end data collector is enabled, recording user responses, timestamps, geolocation, and repeat device access. In collaboration with the Associated Construction Contractors of New Jersey and health and safety managers, we plan statewide deployment during May’s Mental Health Awareness Month using banners and stickers with QR codes.

To prepare for deployment and optimize workers’ engagement with the tool, we conducted formative focus groups with construction workers, including individuals with lived experience of recovery, to assess the usability of the interface, perceived privacy, cultural relevance, and outreach materials. Participants reported strong acceptability of anonymous, on-site access and emphasized the importance of clear privacy assurances, non-clinical language, and rapid completion time. They also recommended peer-oriented framing and visible placement of materials in break areas and restrooms. Iterative refinements were implemented following this feedback. A pilot deployment across fifteen active construction sites is planned for April 2026. Here, we describe prototype development, formative user-testing results, and plans for the upcoming deployment.

LATEBREAKER

Mental Health

Cannabis use and anxiety among youth: a rapid review Hayden Adair* Hayden Adair Denise Walker Derek Manis

Many jurisdictions in high-income countries have created markets for retail cannabis use over the last decade. Initial cannabis use is prevalent among youth (i.e., 10-19 years of age) but characterizing the directionality of cannabis use among youth and the development of anxiety is a notable gap that requires further study. A rapid review was registered on the Open Science Framework and was conducted in accordance with best practices for rapid reviews to address this knowledge gap. PubMed, Medline (via Ovid), Embase (via Ovid), and PsycINFO (via Ovid) were searched on December 29, 2025 for peer-reviewed observational studies in high-income countries that were published in English between 2000 to 2025. Articles were exported to Covidence for screening; one reviewer conducted screening, and a second reviewer reviewed a five percent random sample for agreement. Period of observation, sample size, country, exposures and outcomes, results, and limitations were extracted and narratively synthesized. Risk of bias assessments were conducted using the Newcastle-Ottawa Scale for non-randomized studies. There were 3,463 articles that were exported from database searches and screened; 21 articles were included and synthesized in the review (N = 52,299 youth). The period of analysis ranged from 1987 to 2021 across the U.S., Canada, Australia, U.K., Switzerland, and Norway. Cannabis use among youth was strongly associated with emergency room visits for generalized anxiety and the development of anxiety and panic attacks in adulthood. Nine studies were of good quality; 10 studies were of fair quality; and two studies were of poor quality. These findings affirm the importance of public health messaging to youth and parents about the risks of cannabis use, and they also underscore the importance of regulatory actions (e.g., restriction, packaging labels, etc.) on all cannabis products.

LATEBREAKER

Mental Health

Spatial clustering of ninth-grade female depression in California: structural determinants and rural context Daekiara Smith-Ireland* Daekiara Smith-Ireland Hirut Gebrekristos

Background

Adolescent depression is increasing nationally, yet geographic patterning and structural determinants remain underexamined at the county level.

Methods

We conducted a county-level ecological analysis of 58 California counties in 2019. Ninth-grade female depression prevalencewas the outcome. Predictors included low school connectedness, poverty rate, uninsured rate, and rural–urban classification. Multiple imputation was used to handle missing data (10–14%). Global Moran's I assessed spatial autocorrelation, and local indicators of spatial association identified clustering. Multivariable linear regression models were estimated.

Results

County-level female ninth-grade depression demonstrated significant positive spatial autocorrelation (Moran's I = 0.148, p = 0.047), whereas no spatial clustering was observed for county-level ninth-grade male depression. Local indicators identified three high–high clusters in rural Northern and Sierra counties and two low–low clusters along the Central Coast. Four low–high counties were observed, representing spatial outliers with lower depression prevalence adjacent to higher-burden regions. Rural counties had a higher mean prevalence of female depression than urban counties (44.9% vs 41.6%). In adjusted models, low school connectedness (β = 0.52, p = 0.028) and rural context (urban vs rural: β = −5.12, p = 0.003) were independently associated with county-level prevalence of depression among ninth-grade females. Uninsured rate was inversely associated (β = −1.58, p < 0.001).

Conclusions

County-level female adolescent depression exhibits modest but statistically significant geographic clustering across California. Associations were sex-specific and concentrated in rural regions. Spatial epidemiologic approaches identify disparities in adolescent mental health that may help inform county-level public health efforts.

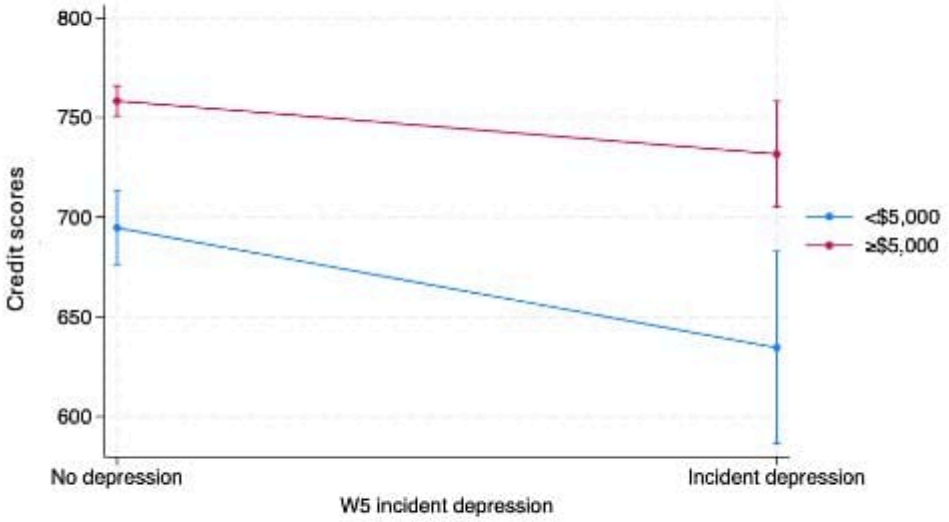
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Mental Health

Incident depression and credit scores in U.S. adults, 2023-2025 Catherine K Ettman*
Catherine Ettman Raj Satpathy Horton Elizabeth A. Stuart Sandro Galea

Little to no work has explored the relation between onset of depression and changes in consumer credit scores. Using linked credit score data from TransUnion and longitudinal panel survey data from 2023-2025, we aimed to 1) assess the relationship between incident depression and next-year consumer credit scores and 2) identify whether household savings modified the relationship, if any, between incident depression and credit scores. We used data from the Cumulative Life Stressors Impact on Mental Health and Well-Being (CLIMB) Study, a nationally representative survey of US adults collected annually in Spring of 2023, 2024, and 2025 and linked continuous, longitudinal credit scores for consenting adults (n=720). Incident depression was defined as screening positive for depression (PHQ-9≥10) in 2024 after screening negative in 2023. We used linear regression to model next-year credit scores for adults experiencing incident depression, adjusting for sex, race and ethnicity, age, education, household income, household savings, home ownership, Census region, and household size. We then estimated the predicted levels of next-year credit scores within incident depression and household savings groups using a second adjusted linear regression model with an interaction term between incident depression and household savings. In 2024, 64 (8.9%) adults with incident depression. Reporting incident depression was associated with an unadjusted estimated decrease of 63.9 points (95% CI: -92.7, -35.1) in next-year credit score; adjusted models estimated a decrease of 37.2 points (95% CI: -62.2, -12.2) in credit scores. Among adults with incident depression, individuals with savings below $5,000 had a 97.3 point (95% CI: -152.2, -42.3) lower credit score compared to individuals with savings higher than $5,000. In conclusion, incident depression was associated with meaningful drops in next-year credit scores; this association was more pronounced among persons with lower savings.

Figure 1. Predicted probability of credit scores by incident depression and household savings



Note: CLIMB 2023, 2024, 2025 longitudinal panel data used. N=720 . Model adjusted for sex, race and ethnicity, age, education, household income, household savings, home ownership, Census region, and household size.

Mental Health

Comorbid Depression and Anxiety in U.S. Adults: A Data-Driven Exploration of Predictive Correlates Debbie Huang* Debbie Huang Daniel Hagen Rasmika Kumar Margaret L. Lind Emily Goldmann

Depressive and anxiety disorders are highly comorbid and are linked with worse prognosis and greater disease burden. Identification of unique characteristics associated with comorbid depression-anxiety vs. either condition alone may aid clinical screening. Yet, efforts to examine an extensive range of factors for comorbid depression-anxiety are limited. We used the 2022 IPUMS-National Health Interview Survey dataset to identify factors most strongly associated with screening positive for both depression (Patient Health Questionnaire-8 score≥10) and anxiety (Generalized Anxiety Disorder-7 score≥10) vs. a single condition only among adult respondents (18+) using Lasso binary logistic regression. Model selection of the sociodemographic, behavioral, and clinical features was informed by previous literature. Among the 921 respondents who screened positive for either depression or anxiety (9%), 44% screened positive for both. Of the 38 examined predictors, 16 were retained. Residing outside of the Eastern region of the U.S., current marital status, family income below the poverty line, military experience, receipt of food stamps/SNAP, history of chronic obstructive pulmonary disease, history of chronic fatigue syndrome, greater functional disability, and lower life satisfaction were associated with higher odds of comorbidity. Older age, non-Hispanic Asian, having a usual place for medical care, and engaging in volunteer work were associated with lower odds. Some categories– household size, educational attainment, and general health status – were associated with lower odds and some with greater odds vs. the reference group. This data driven variable selection approach identified a unique set of factors, a few less described in the literature (e.g., volunteer work), that specifically characterize comorbid depression-anxiety. These findings may aid efficient screening for these conditions and inform research to further understand risk factors for comorbidity.

Mental Health

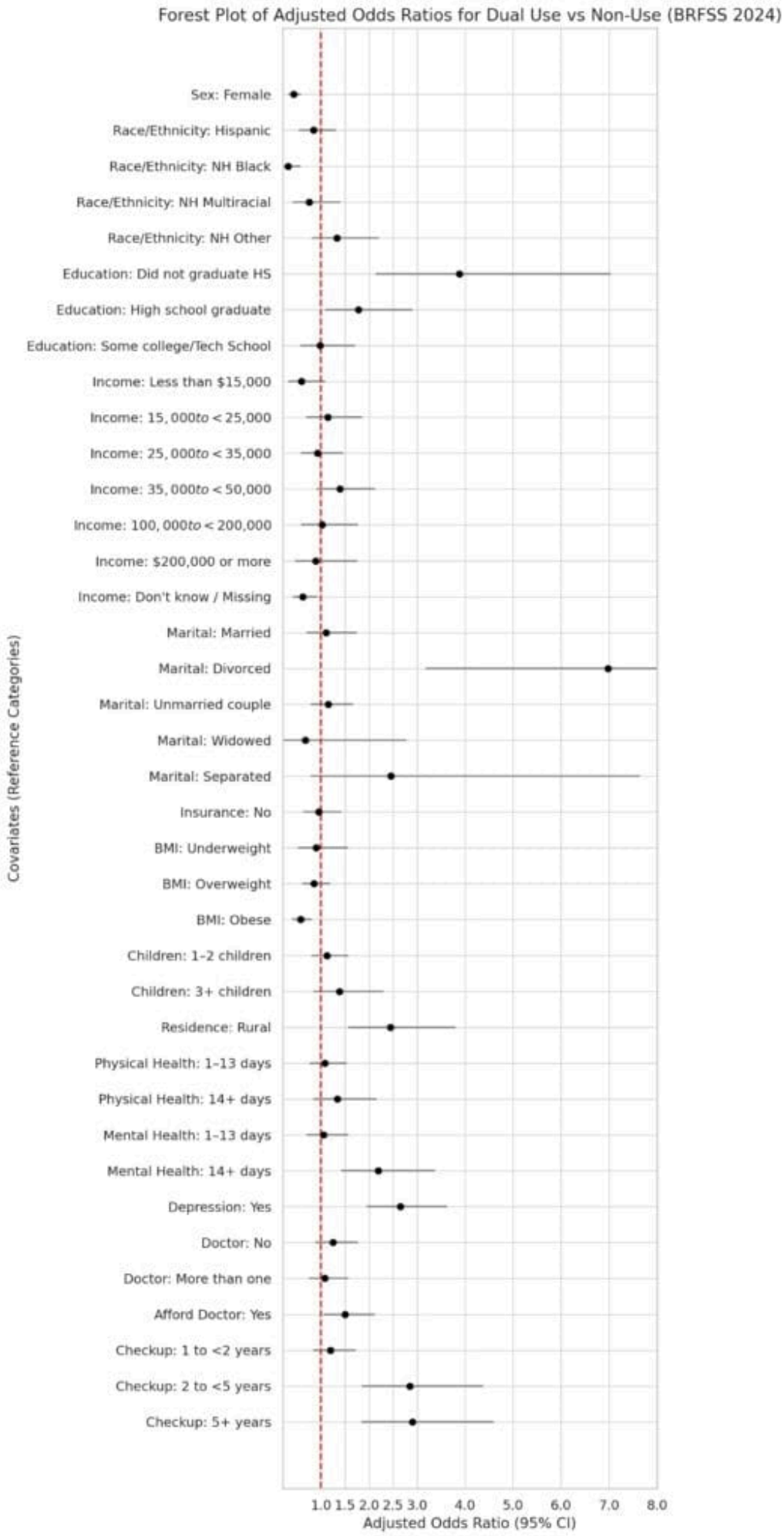
Dual use of cigarettes and e-cigarettes among young adults in the United States: associations with mental distress, race and ethnicity, and healthcare access Fahima Nasrin Eva* Fahima Nasrin Eva Gladys E. Ibanez

Objective
This study investigates the relationship between mental distress and dual use of cigarettes and e-cigarettes among U.S. young adults aged 18–24, with particular attention to racial/ethnic differences and indicators of healthcare access.

Method
A cross-sectional analysis of 2024 Behavioral Risk Factor Surveillance System (BRFSS) data was conducted among 19,245 young adults aged 18–24 (weighted N=20.49 million). Survey-weighted logistic regression estimated adjusted odds ratios (aORs) for dual use (vs non-use) in relation to mental distress, depressive disorder, race/ethnicity, and sociodemographic and healthcare-access factors. Analyses accounted for complex survey design, used two-sided $p<0.05$ to define statistical significance, and were conducted in SAS 9.4.

Result
Among 19,245 adults aged 18–24 in BRFSS 2024, 3.2% were dual users of cigarettes and e-cigarettes. In adjusted models, females had lower odds of dual use than males (AOR 0.43, 95% CI 0.32–0.58, $p<0.001$), as did non-Hispanic Black versus non-Hispanic White adults (AOR 0.31, 95% CI 0.17–0.57, $p<0.001$). In contrast, not completing high school (AOR 3.88, 95% CI 2.14–7.03, $p<0.001$), divorced status (AOR 6.98, 95% CI 3.18–15.34, $p<0.001$), and rural residence (AOR 2.44, 95% CI 1.56–3.80, $p<0.001$) were associated with higher odds of dual use. Frequent mental distress (14+ mentally unhealthy days; AOR 2.19, 95% CI 1.42–3.37, $p<0.001$), depressive disorder (AOR 2.65, 95% CI 1.95–3.62, $p<0.001$), inability to afford a doctor (AOR 1.50, 95% CI 1.05–2.12, $p=0.024$), and long intervals since routine checkup (≥2 years; AOR 2.85–2.90, all $p<0.001$) were associated with dual use.

Conclusion
Dual cigarette and e-cigarette use was relatively uncommon but highly concentrated among men, those with lower educational attainment, divorced and rural residents, and young adults experiencing frequent mental distress, depressive disorder, and healthcare barriers. Mental distress remained a strong correlate of dual use across racial/ethnic groups.


Forest Plot of Adjusted Odds Ratios for Dual Use vs Non-Use (BRFSS 2024)
Sex: Female
Race/Ethnicity: Hispanic
Race/Ethnicity: NH Black
Race/Ethnicity: NH Multiracial
Race/Ethnicity: NH Other
Education: Did not graduate HS
Education: High school graduate
Education: Some college/Tech School
Income: Less than $15,000
Income: 15,000to < 25,000
Income: 25,000to < 35,000
Income: 35,000to < 50,000
Income: 100,000to < 200,000
Income: $200,000 or more
Income: Don't know / Missing
Marital: Married
Marital: Divorced
Marital: Unmarried couple
Marital: Widowed
Marital: Separated
Insurance: No
BMI: Underweight
BMI: Overweight
BMI: Obese
Children: 1–2 children
Children: 3+ children
Residence: Rural
Physical Health: 1–13 days
Physical Health: 14+ days
Mental Health: 1–13 days
Mental Health: 14+ days
Depression: Yes
Doctor: No
Doctor: More than one
Afford Doctor: Yes
Checkup: 1 to <2 years
Checkup: 2 to <5 years
Checkup: 5+ years
Covariates (Reference Categories)
1.0 1.5 2.0 2.5 3.0 4.0 5.0 6.0 7.0 8.0
Adjusted Odds Ratio (95% CI)

Mental Health

Sleep Quality and Psychological Resilience Across Borders: Evidence from the WELL US and China Cohorts Eunhye Lee* Eunhye Lee Chi Chang Yi-Hsuan Wu Emily A. Hu April Myers Elizabeth Delzell Clete Kushida Catherine Heaney Yuwei Shi Shanjun Huang Ping Wang Ying Lu Shankuan Zhu Ann Hsing

Objective: Sleep is increasingly recognized as a modifiable determinant of psychological resilience, yet cross-cultural evidence remains limited. We examined whether the association between sleep quality and psychological resilience is consistent across the United States (US) and China.

Methods: We analyzed cross-sectional baseline data from the WELL cohorts in the US and China. Sleep quality was assessed using the Pittsburgh Sleep Quality Index (PSQI) among US (n=467) and Chinese (n=9,780) participants, with poor sleep defined as a score >5. We also examined the full US cohort (n=6,457) using a single-item sleep measure. Psychological resilience was measured using a 9-item scale adapted from the Brief and Connor-Davidson Resilience Scales (low resilience: below-median score). Multivariable logistic regressions estimated ORs and 95% CIs for the association between sleep quality and psychological resilience, adjusting for demographic and socioeconomic factors and mental health indicators including loneliness and history of depression.

Results: Poor sleep quality was significantly associated with increased odds of low psychological resilience in both countries, with findings replicated across two sleep measures in the US. The association did not differ by gender, age, or history of depression in either country (interaction P>0.05). Loneliness modified the association in China only (interaction P<0.05), with a larger magnitude of association among lonely participants (OR=2.1; 95% CI:1.6-2.7) than among non-lonely participants (OR=1.5; 95% CI:1.4-1.7).

Conclusions: Poor sleep quality was consistently associated with lower psychological resilience across both US and China cohorts. These findings provide cross-cultural evidence supporting sleep quality as a modifiable target for resilience-building interventions. The moderating role of loneliness suggests that promoting wider and more meaningful social connections may strengthen sleep interventions in China.

Mental Health

Predictors of hair cortisol concentrations in a North American preconception cohort study

Lauren Wise* Lauren Wise Eliza Pentz Kestutis Bendinskas Amelia Wesselink

Background: Hair cortisol concentrations (HCC) may reflect chronic stress, a determinant of adverse reproductive outcomes. Little is known about predictors of HCC during the preconception period.

Methods: We performed a cross-sectional analysis of baseline data from Pregnancy Study Online (PRESTO), a preconception cohort study of pregnancy planners enrolled during 2024-2025. Within 2-3 weeks of enrollment, 216 participants (199 females and 17 males) collected their hair samples via a mail-based kit. Participants were instructed by video and pamphlet to collect 10-20 mg of hair closest to the scalp from the posterior vertex region. We used ELISA to measure cortisol in hair samples, with 3 cm of hair reflecting average cortisol levels in the 3 months before enrollment. We fit mixed models to estimate the percent difference (β) in mean log-transformed HCC and 95% confidence intervals (CI) for associations with selected predictors including self-reported preconception measures of stress (Perceived Stress Scale-10), depressive symptoms (Major Depression Inventory), sleep duration, age, education, race, ethnicity, parenting history, body mass index, height, cigarette smoking, and cannabis use.

Results: Median HCC was 5.81 pg/mg (interquartile range: 4.18-11.66). The strongest predictors of higher HCC were sleep duration (<6 vs. 7-8 hours: β=141.0, 95% CI: -28.6, 713.5), age (5-year increase: β=21.5, 95% CI: 1.5, 39.2), depressive symptoms (10-unit increase in MDI score: β=12.5, 95% CI: -14.9, 48.6), and race and ethnicity (non-Hispanic Black: β=769.9, 95% CI: 257, 2020.1; Hispanic: β=37.3, 95% CI: -8.6, 106.2; and Non-Hispanic other race: β=37.5, 95% CI: -25.7, 154.4, vs. non-Hispanic White). Female participants had slightly lower HCC than male participants (β=-29.1, 95% CI: -60.8, 28.2). No appreciable associations were observed with other variables.

Conclusion: Selected socio-demographic and psychosocial variables were associated with HCC during the preconception period.

Methods/Statistics

Covariate selection and justification in studies of multidimensional indices of structural racism and health: A systematic review Annika Gompers* Annika Gompers Victoria Monge Lindsay J. Collin Lauren E. Barber Lauren E. McCullough Kaitlyn K. Stanhope

Background: There has been a substantial increase in research measuring structural racism, often using multidimensional indices, and its association with health. To date, there is no consensus on best practices for covariate selection for such studies. We aimed to identify and quantify commonly selected covariates and justifications for their use.

Methods: We conducted a MEDLINE search to identify studies meeting inclusion criteria: US-based, empirical studies measuring structural racism using an index comprised of at least three indicators of contemporary racial inequities in resources or opportunities (e.g., education, poverty) or contemporary policies (e.g., voter ID laws) and including a health outcome. Studies of interpersonal or self-reported experiences of racism were excluded. We extracted each study's exposure, outcome, selected covariates and stated justification, which we graded based on inclusion of references, stated relationship to exposure and outcome—including potential mediation—or mention of a causal diagram. The study protocol is published on PROSPERO.

Results: Fifty-four studies, published in 2020–2025, met inclusion criteria. Six studies (11%) did not adjust for any covariates, 15 (28%) adjusted for area-level variables, 13 (24%) for individual-level variables, and 20 (37%) for both. Seventeen studies (31%) used multiple adjustment sets. Seventeen (31%) did not state any justification for selected covariates, and an additional 16 (30%) did not cite any references in support of their approach. Selected covariates and justification paradigms are shown in **Table 1**.

Conclusions: Among studies of multidimensional structural racism indices, substantial heterogeneity exists in the covariates selected and the justifications employed, if at all. Given that these indices capture a diffuse construct with unclear etiologic timing, thoughtful approaches to model adjustment are necessary to strengthen inference from this rapidly growing literature.

Table 1: Selected covariates and justifications used in studies of multidimensional structural racism indices and health outcomes

Covariate*	Paradigm of covariate justification			*Total number of studies with this covariate*
	Potential mediator	Other justification†	No justification	
Variables INCLUDED in at least one model				
Individual-level variables				
Age	1 (2%)	7 (13%)	24 (44%)	**32 (59%)**
Sex or gender	0 (0%)	5 (9%)	13 (24%)	**18 (33%)**
Race	1 (2%)	0 (0%)	7 (13%)	**8 (15%)**
Socioeconomic variables	4 (7%)	5 (9%)	11 (20%)	**20 (37%)**
Health conditions	1 (2%)	6 (11%)	5 (9%)	**12 (22%)**
Area-level variables				
Socioeconomic variables/deprivation	2 (4%)	12 (22%)	7 (13%)	**21 (39%)**
Demographics	1 (2%)	6 (11%)	5 (9%)	**12 (22%)**
Region	0 (0%)	6 (11%)	4 (7%)	**10 (19%)**
Population density or rurality	0 (0%)	7 (13%)	9 (17%)	**16 (30%)**
Political climate	1 (2%)	2 (4%)	3 (6%)	**6 (11%)**
Historical structural racism	0 (0%)	2 (4%)	0 (0%)	**2 (4%)**
Total number of studies using this paradigm	**7 (13%)**	**25 (46%)**	**35 (65%)**	--
Variables explicitly EXCLUDED from all models				
Individual-level variables				
Age	0 (0%)	1 (2%)	0 (0%)	**1 (2%)**
Sex or gender	0 (0%)	2 (4%)	0 (0%)	**2 (4%)**
Race	0 (0%)	1 (2%)	0 (0%)	**1 (2%)**
Socioeconomic variables	4 (7%)	0 (0%)	0 (0%)	**4 (7%)**
Health conditions	5 (9%)	0 (0%)	0 (0%)	**5 (9%)**
Area-level variables				
Socioeconomic variables/deprivation	2 (4%)	0 (0%)	0 (0%)	**2 (4%)**
Demographics	1 (2%)	0 (0%)	0 (0%)	**1 (2%)**
Other variables	3 (6%)	0 (0%)	0 (0%)	**3 (6%)**
Total number of studies using this paradigm	**12 (22%)**	**2 (4%)**	**0 (0%)**	--

* Note that each covariate (or type of covariate, e.g., socioeconomic variables) is represented in this table, rather than each study being represented once. For example, if a study selected age, sex, and region as covariates, the study would be represented three times in this table.

† This includes referencing prior studies, noting the association of the variable with the exposure and/or outcome, and using a causal diagram.

Methods/Statistics

Describing Community-level Healthcare Gaps from Incomplete Claims Data by Emulating the Ideal Observational Study Taylor McCready* Taylor McCready Audrey Renson Ethan Cohen

Background

Policymakers and interventionists often seek to characterize healthcare gaps and disparities within geographically defined communities. However, healthcare data sources in the US are fragmented, limiting the completeness of population-based assessments. We address this by emulating an ideal observational study and treating real-world sources as incomplete or mismeasured realizations of that ideal, using colorectal cancer (CRC) screening adherence in Brooklyn, NY as an example.

Methods

We aimed to estimate the proportion of adults aged 45-75 on January 1, 2022, who ever had an open CRC screening gap during 2022 using claims dataset for a value-based care network at NYU. Roughly, the ideal cohort is a random sample of Brooklyn residents with linked all-payer claims. Relative to this, our data contains right censoring (due to switching insurance) and missing data (due to non-representativeness). We handled right-censoring with inverse probability-of-censoring weights (IPCW) including age group, sex, language group, payer type, and tract income quintile. We handled non-representativeness with inverse-probability of selection weights (IPSW) using the 2022 American Community Survey.

Results

The analysis included 15,034 adults. The claims dataset clearly overrepresented Medicaid (OR 1.98) and Medicare (OR 1.30) vs. commercial insurance, and underrepresented Spanish preferred language (OR 0.78). Using IPCW and IPSW, the estimated probability of ever having an open CRC screening care gap during 2022 was 45.9%, vs. 41.1% unweighted, an increase corresponding to 480 additional people per 10,000.

Conclusion

Our approach guides descriptive, population-based healthcare utilization research with fragmented data sources and may generalize to other administrative data sources. By treating real-world datasets as incomplete or mismeasured versions of an ideal community cohort, it links analytic decisions to explicit assumptions making estimates easier to interpret and critique.

Methods/Statistics

OptimalCutoff: an interactive web-based platform for ROC-based cutoff selection in epidemiological research Janos Tibor Fekete* Janos Tibor Fekete Balazs Gyorffy

Background: Receiver operating characteristic (ROC) curve analysis is widely used to evaluate the discriminatory performance of biomarkers and predictive models and to define decision-relevant cutoff thresholds. However, accessible platforms supporting advanced ROC frameworks beyond standard binary analysis are limited. We introduce OptimalCutoff, a web-platform for interactive binary, multiclass, and time-dependent ROC analysis with flexible cutoff selection strategies.

Methods: OptimalCutoff enables web-based ROC analysis of user-uploaded data, without the need for local statistical software or programming. The platform supports binary, multiclass, and time-dependent ROC frameworks and offers multiple cutoff selection strategies, including Youden optimization and sensitivity- or specificity-constrained thresholds. Interactive visualizations facilitate real-time exploration of ROC curves, operating points, and decision tradeoffs. As a methodological demonstration, data from the National Health and Nutrition Examination Survey (NHANES) were used to construct illustrative glycemic risk scores based on logistic regression models incorporating age, body mass index, and glycohemoglobin.

Results: In the NHANES demonstration dataset, an age- and BMI-based screening score showed good discrimination for prevalent diabetes (AUC = 0.80). Multiclass ROC analysis of glycemic status demonstrated strong overall discrimination (global multiclass AUC = 0.84), with distinct class-specific performance profiles. OptimalCutoff facilitated assessment of ROC behavior and cutoff sensitivity under alternative decision criteria. OptimalCutoff delivers figures and summary outputs to enhance reproducibility and reporting.

Conclusions: OptimalCutoff (https://optimalcutoff.com/) provides a web-based solution for ROC-based cutoff selection across binary, multiclass, and time-dependent frameworks, supporting transparent and context-aware decision making in epidemiologic research.

Methods/Statistics

Analyzing Irregularly Age-Binned Data Using Catalytic Models of Seroprevalence Robert Dettmann* Robert Dettmann Robertus van Aalst Aleksandra Stamper Rachel Baker Sarah Ackley

Seroprevalence data are often reported in aggregated age bins that differ across studies, limiting comparability and complicating pooled analyses. This heterogeneity often forces meta-analyses to collapse age categories, reducing resolution, or exclude informative studies with incompatible binning. Accurate age-specific seroprevalence estimates are critical for characterizing infection risk, identifying windows of susceptibility, and informing vaccination policy. We present a flexible framework for analyzing heterogeneously binned seroprevalence data

We develop a likelihood-based modeling approach in which expected seroprevalence within each age bin is obtained by integrating a parametric age-specific seroprevalence function, enabling binomial likelihoods to be specified directly from aggregated counts. Study-specific likelihoods are combined into a joint likelihood, allowing estimation of pooled and study-level parameters without harmonizing age bins or excluding studies. Applying this framework to varicella seroprevalence data from 18 countries (N = 35,898 participants in 16 studies), we compare competing models that vary assumptions about age specific hazards of infection (HOI). Models incorporating maternal antibody protection improved fits to the data. Under constant HOI assumptions, we estimated the pooled HOI across all studies to be 0.215, (95% CI: 0.210-0.220) per year. For the piecewise model, we estimated HOI of 0.247 (CI: 0.241-0.253) for ages <9.5y and 0.09 (CI: 0.06-0.13) for ages ≥9.5y, with optimal change-point at 9.5y (CI: 8.7-10.5). Likelihood-based comparisons favored the piecewise HOI model (AIC: 2860.4) over the constant HOI model (AIC: 3016.4).

This framework enables synthesis of seroprevalence data across studies with inconsistent age binning and supports formal comparison of competing HOI models. The approach generalizes to other pathogens and provides a strategy for meta-analytic inference using heterogeneously aggregated serological data.

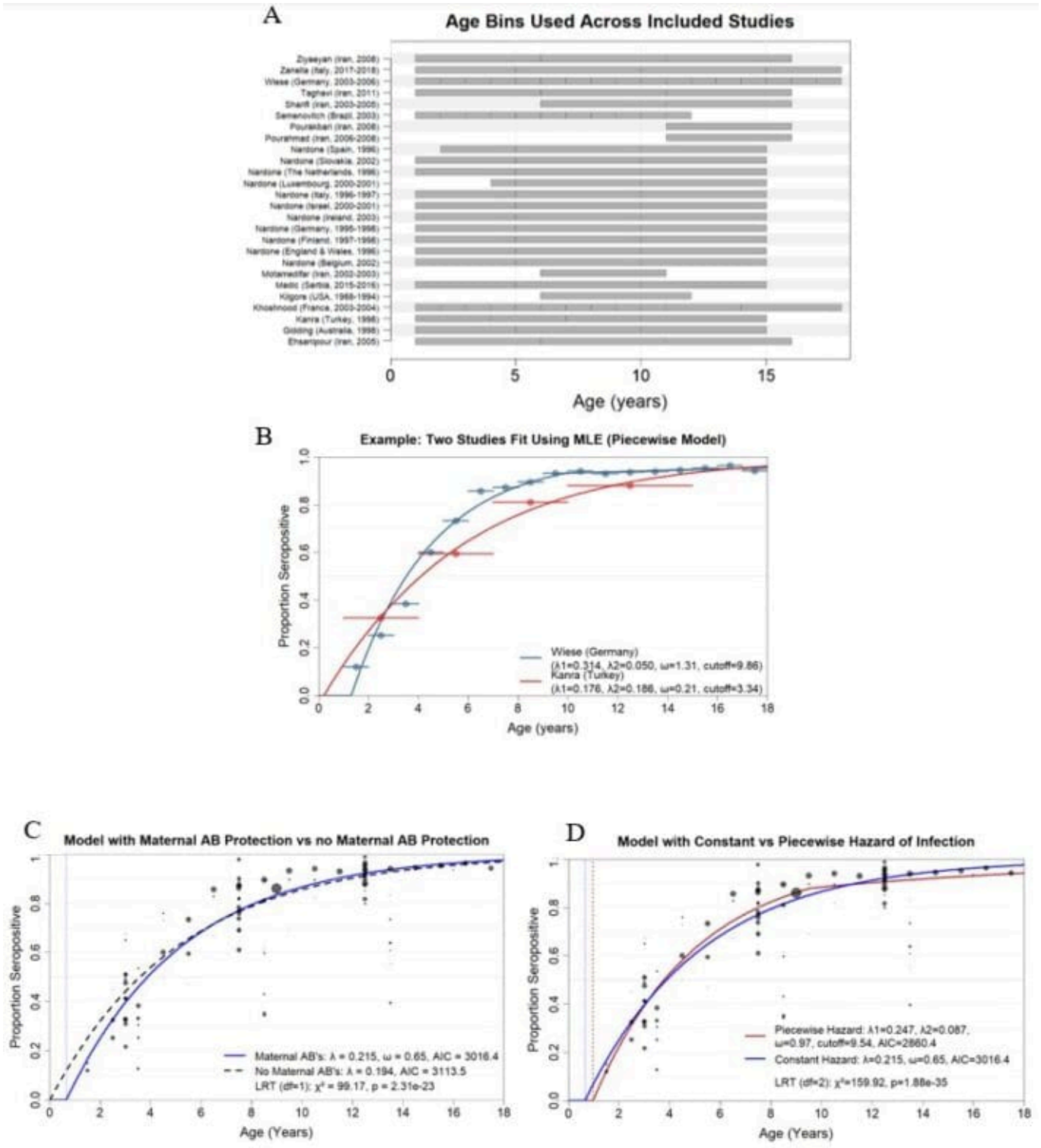


Figure 1: (A) Distribution of age bins by country/study: each grey bar represents the width of the seroprevalence age bin included in the country/study; (B) MLE-optimized seroprevalence curves of two example studies. Each horizontal line represents the width of the age bin utilized within the study. Individual points represent the midpoint of each age bin within each study; (C) Comparison of a model incorporating the age at which maternal antibodies cease to provide immunity (blue line) and a model that does not consider maternal antibodies (black line). Both models assume a constant hazard of infection. Each point represents the midpoint of each age bin present within the data; (D) Comparison of the model assuming a constant hazard of infection (blue line) versus an alternate hazard model, the piecewise model, which assumes two unique hazard of infection values which occur before and after the optimized age cut-off (red line). Vertical dotted lines represent the age at which maternal antibodies cease to provide immunity.

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LATEBREAKER

Methods/Statistics

Comparison of Last Observation Carried Forward and Multiple Imputation for Handling Missing Data in Longitudinal Studies Julia R. Bacci* Julia Bacci Lachlan Cribb Joanne Ryan Anne Murray Robyn L. Woods Michael Berk Michael Webster-Clark Michelle M. Mielke

Missing data are common in longitudinal epidemiological studies. Single imputation methods, such as last observation carried forward (LOCF), are easy to implement but underestimate uncertainty in imputed values. Multiple imputation (MI) better reflects uncertainty but is more computationally intensive and may encounter challenges in longitudinal studies in the presence of mortality, resulting in partially imputed datasets. In this study, we compared LOCF and MI for imputing depressive symptoms, body mass index (BMI), and smoking status in a community-based cohort of older adults three years after baseline. Bootstrapping (200 samples) was used for confidence intervals. For MI, two imputed datasets were generated within each bootstrap sample.

Participants included 11,942 adults aged ≥65 from the ASPREE trial. Depressive symptoms (CESD-10), BMI, and smoking status were assessed annually. For each variable, mean differences under LOCF and MI were examined in the total sample, among all participants with imputed data, and among participants with imputed data in both LOCF and MI datasets, using t-tests and chi-squared tests.

Prior to imputation, 1,009 participants (8.5%) were missing depressive symptom data, 1,445 participants (12.1%) were missing BMI, and 957 participants (8.0%) were missing smoking status. In the total sample, the LOCF dataset, compared to MI, had higher mean depressive symptoms and a lower proportion of current smokers. Among all participants with imputed data, the LOCF dataset had higher mean depressive symptoms, lower mean BMI, and a higher proportion of current smokers. Restricting analyses to participants with imputed data in both datasets, the LOCF dataset had higher mean depressive symptoms and BMI.

Meaningful differences were observed between the LOCF and MI datasets, with LOCF resulting in higher mean depressive symptoms. It is important to consider the differential impact of imputation methods when interpreting results from longitudinal studies.


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LATEBREAKER

Methods/Statistics

Quantifying the impact of temporal variability in contact patterns on RSV transmissibility and intervention effectiveness: A SickMix modeling study Kayoko Shioda* Anne Shapiro Dehao Chen Jessica Ibiebele Judy Donald Mark Schmidt Samuel Jenness Benjamin Lopman Kayoko Shioda

Background: Transmission models for acute infections often assume stable contact patterns or perfect isolation during acute infection. The SickMix study collected longitudinal social contact data throughout the course of infection to better understand temporal variability among people experiencing acute respiratory infection and acute gastroenteritis. We developed mechanistic models to quantify how this variability impacts the estimation of key model parameters and intervention impacts for respiratory syncytial virus (RSV).

Methods: We developed age-stratified deterministic compartmental models with early and late infectious phases to capture changing contact patterns over the course of acute infection. We developed two versions of the model: a behavior naïve model assuming stable contact patterns over time, and a behavior dynamic model incorporating temporal changes in contact patterns among symptomatic cases. We fit these models to nationwide RSV hospitalization data from the 2018-19 and 2019-20 seasons to estimate transmissibility per contact. We simulated multiple interventions reducing disease infectiousness (e.g., masking) and individuals' daily contacts (e.g., school closure) and compared the estimated impact between the two models.

Results: Estimated hospitalization rates for both seasons aligned well with reported data. The estimated transmissibility per contact in the behavior-dynamic model was 21% and 15% greater than the naïve model for the 2018-19 and 2019-20 seasons, respectively. Estimated impact of interventions varied between the behavior-naïve and behavior-dynamic models (Figure)

Conclusions: A lack of adjustment for reduced contacts during illness can result in underestimates of infectiousness and biases in case reductions from interventions. SickMix's data allow for more accurate estimation of intervention impacts in infectious disease modeling.

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Methods/Statistics

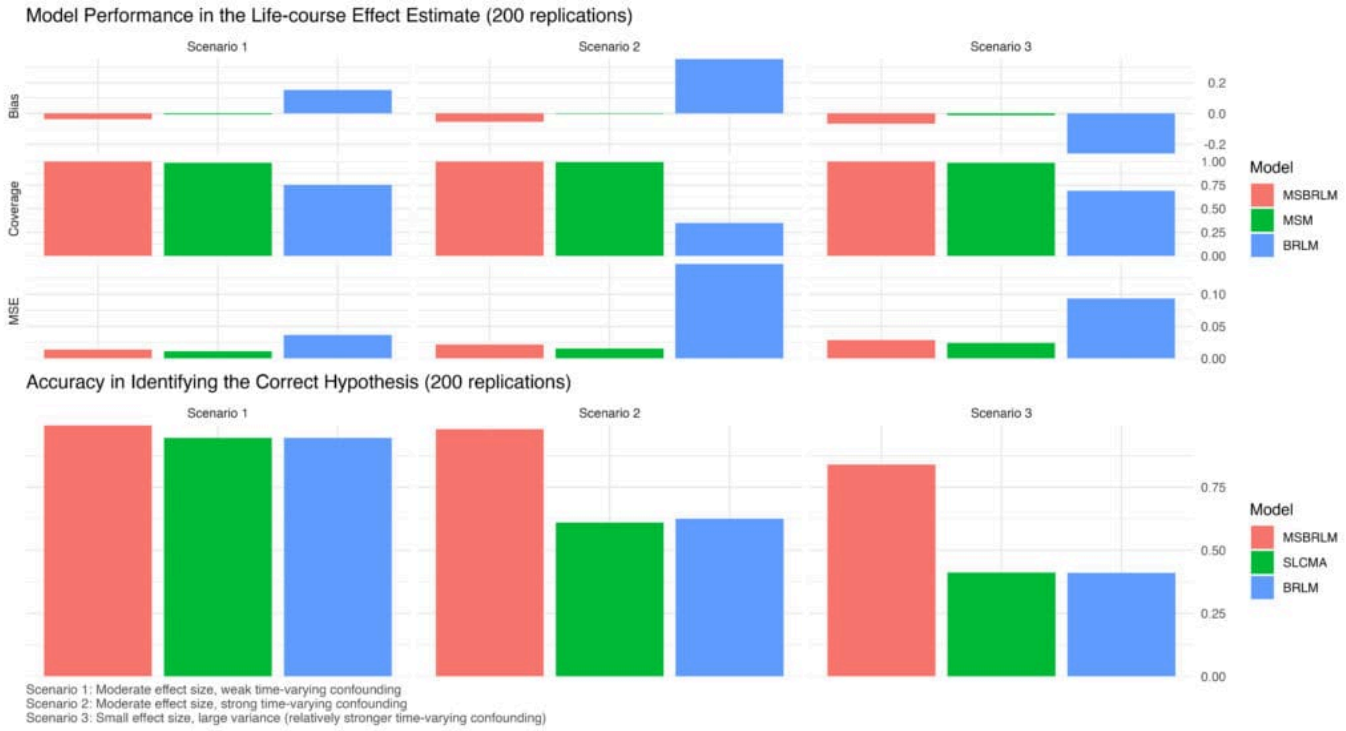
Quasi-U-shaped Generalized Additive Model Wenhui Zhu* Wenhui Zhu Wei Wang

Incorporating shape constraints into models is widely recognized to enhance both accuracy and interpretability of results by leveraging epidemiologically shape priors. However, existing shape-constraint methods cannot effectively account for the prior following a quasi-U shape—a composite pattern encompassing monotonic increase, monotonic decrease, and U-shaped curves, as exemplified by the exposure-response relationship between temperature and mortality. In this work, we developed a new method called quasi-U-shaped generalized additive model (qUGAM) and theoretically demonstrate its advantages in integrating the quasi-U-shaped priors. Simulation studies showed that qUGAM considerably outperformed conventional generalized additive model (GAM) in estimating quasi-U-shaped exposure-response associations. Specifically, qUGAM achieved comparable or superior performance in root mean squared error (RMSE), relative RMSE, mean absolute error (MAE), relative MAE, coverage percentage of 95% confidence interval, and interpretability. These improvements were particularly pronounced at both ends of the exposure range with threshold effects and under a small sample size. A case study examining temperature-mortality associations further supported these findings. Given the wide existence of quasi-U-shaped priors, qUGAM holds substantial potential for broad application across diverse scientific and public health practice.

Methods/Statistics

Marginal Structural Bayesian Relevant Life-course Model: A Novel Approach to Evaluate Life-course Hypotheses in the Presence of Time-varying Confounding Yinxian Chen* Yinxian Chen

Current life-course models, such as the structural life-course modeling approach (SLCMA) and the Bayesian Relevant Life-course Model (BRLM), are developed to assess life-course hypotheses that best explain the data, thereby informing optimal intervention strategies over the lifespan. Yet, they rely on baseline adjustment and cannot address time-varying confounding, risking biased identification of the best life-course hypothesis. The marginal structural model (MSM) can address time-varying confounding but cannot assess the compatibility of the data with given life-course hypotheses. Thus, we developed a marginal structural BRLM (MSBRLM). Like BRLM, MSBRLM estimates the effect of a life-course exposure and the importance of each period, while controlling for confounding via inverse probability weighting and computing valid 95% credible intervals (CrIs) via weighted finite population Bayesian bootstrapping. We generated simulated data with a time-varying exposure and covariate at three time points under the accumulation hypothesis (i.e., equal importance across periods). Under all scenarios, MSBRLM yielded slightly higher bias in life-course effect estimates than MSM, but substantially lower than BRLM. Under strong time-varying confounding, MSBRLM achieved 98% accuracy in identifying the correct hypothesis, whereas BRLM and SLCMA achieved 63% and 61%, respectively. Using data from the Future of Families and Child Well-being study, we estimated the life-course effect of neglect from ages 3 to 9 on the externalizing behavior (age 15). By accounting for time-varying confounding by prior externalizing behavior, the estimated effect from MSBRLM (θ=2.56, 95% CrI: 0.80, 4.32) was similar to MSM (θ=2.60, 95% CI: 1.22, 3.98). MSBRLM identified accumulation as the best hypothesis, while BRLM and SLCMA suggested recency (i.e., recent exposure matters more). MSBRLM could be a promising tool for assessing life-course hypotheses when time-varying confounding is present.



Methods/Statistics

Bias-Variance Implications of Outcome Missingness and Misclassification in EHR-Based Studies: A Simulation Study Elaona Lemoto* Elaona Lemoto Lexie Zidanyue Yang Jerome Reiter Sarah Peskoe Nrupen Bhavsar

Real-world data (RWD) are increasingly used to generate real-world evidence (RWE) for clinical and policy decision-making, yet such data are often affected by outcome missingness and misclassification, particularly for binary disease outcomes. Missing data are commonly categorized as missing completely at random (MCAR), missing at random (MAR), or missing not at random (MNAR), but less is known about how these mechanisms compare when missing outcomes are inadvertently misclassified as non-events. We conducted a simulation study motivated using data from the electronic health record (EHR) for the association between diabetes and cardiovascular disease (CVD). Data were generated with one exposure, one observed confounder, and one unobserved confounder, with correlation among covariates ranging from 0.1 to 0.8. Outcomes were generated as binary (CVD diagnosis) or continuous (CVD severity). Outcome missingness, with potentially subsequent misclassification, was imposed under MCAR, MAR (dependent on the observed confounder), and MNAR (dependent on the unobserved confounder), with proportion of missingness from 5% to 75% and sample sizes from 1,000 to 50,000. Logistic or linear regression models excluding the unobserved confounder were fit, and bias and 95% confidence interval coverage were evaluated using the full model with no missingness nor misclassification as the reference. For continuous outcomes, coverage was around 95% under MCAR and remained above 85% under MAR but dropped below 80% under MNAR at 75% missingness and below 30% with high correlation ($\rho=0.8$), ≥25% missingness, and N≥50,000. Binary outcomes with missingness maintained >90% coverage except under MNAR with high correlation or high proportion of missingness. Binary misclassification produced extreme bias (up to 120%) and near-zero coverage across all mechanisms as sample size increased. These findings indicate that outcome misclassification may be substantially more harmful than outcome missingness in EHR-based studies and underscore the importance of explicitly addressing misclassification when diagnoses are incompletely captured.

Methods/Statistics

Selection bias due to selective survival before study enrollment on the association between relative age and suicide Yoshikazu Komura* Yoshikazu Komura Kosuke Inoue Rory C. O'Connor Naoki Kondo Yuri Ito

Relative age, the age difference between individuals within a school grade, is an early-life determinant of long-term mental health, including suicidality. Although research on early-life factors often suffers from selection bias due to selective survival before study enrollment, it remains unclear how this bias affects estimates. We quantified this selection bias on the association between relative age and suicide, using vital statistics in Japan. This cohort study included individuals born in 1974–1983. Relative age was defined by birth date (younger [born Oct 1–Apr 1] or older [Apr 2–Sep 30]). Death by suicide was identified from death records. Characteristics at birth, such as birth year and household occupation, were collected from birth records. Using the Aalen–Johansen estimator, we estimated the risk of suicide at age 40 among those with younger and older relative ages, and calculated the risk difference (RD) and risk ratio (RR). To quantify the selection bias, we estimated these effects by restricting analytical samples to survivors at four different enrollment points (age 0 [target estimate], 10, 20, and 30), and calculated % bias, defined as the deviation of each estimate from the target estimate. In a cohort of over 17 million individuals with 85 372 deaths by suicide, we found no difference in characteristics at birth by relative age. Individuals with younger relative age had a higher suicide risk at age 40 (RD per 10 000: 2.08 [95% CI, 1.47–2.68]; RR: 1.05 [95% CI, 1.04–1.07]. The RD was underestimated among survivors at study enrollment points (% bias: 1.2%, −16.8%, and −54.3% at ages 10, 20, and 30). The RR was also underestimated but the degree of the bias was much smaller (% bias: 0.0%, −0.6%, and −0.4% at ages 10, 20, and 30). Future research on suicide related to relative age should account for selection bias due to selective survival before study enrollment to avoid overlooking the impact of relative age, particularly when relying on difference scale.

LATEBREAKER

Methods/Statistics

Proximal causal inference with binary proxies for continuous unmeasured confounders: robustness under violated completeness assumptions Zoey Song* Zoey Song Paul N. Zivich Til Stürmer Michele Jonsson Funk

Unmeasured confounding is a concern in studies relying on real-world data. Proximal causal inference (PCI) is a novel method that leverages proxy variables to validly estimate causal treatment effects with unmeasured confounding. However, when the unmeasured confounder is continuous, binary proxies will likely violate the PCI assumption of completeness.

To assess the robustness of PCI to completeness assumption violations with binary proxies for a continuous unmeasured confounder, we simulated 4000 cohorts of 1000 observations following a PCI structure with a binary exposure (A), a continuous outcome (Y), a continuous measured confounder (X), a continuous unmeasured confounder (U), and two proxy pairs (Z, W)—one continuous, one binary. The U-A and U-Y effects were both positive to create a confounding bias by U that overestimates a true positive effect of A on Y. Three U-Y confounding structures were specified: monotonic linear, restricted cubic splines, and step-wise (4 levels). We further varied U-A and proxy-confounder (U-Z, U-W) correlations. Both standard and PCI g-computation were applied to estimate the average causal effect using binary and continuous proxies separately. Performance metrics for the estimators included bias and 95% confidence interval coverage. Correctly specified bridge functions of observed proxy variables that reproduce the effect of an unmeasured confounder on the outcome were used for both proxy types.

Standard g-computation showed consistent residual confounding bias due to U in the expected positive direction (range: 0.072-0.244). When completeness was satisfied, PCI had biases near zero across all scenarios (range: -0.000 to 0.003) with nominal 95%CI coverage. When completeness was violated by use of binary proxies, PCI slightly over-corrected, producing bias opposite to the true confounding direction (range: -0.038 to -0.016) but with close to nominal 95%CI coverage (range: 93.7-95.7%). As U-A effect strengthened (OR: 1.22 to 3) and proxy-confounder correlations increased, PCI bias stabilized near zero while bias for standard g-computation persisted for both binary and continuous proxies.

These findings are based on an analysis of a causal effect on a continuous outcome, and results from this limited parameter space may not generalize to other scenarios. Further work on PCI robustness for binary outcomes and other mechanisms is underway.

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LATEBREAKER

Molecular

Proteomic Mediation of Systemic Autoimmune Rheumatic Diseases-Associated Interstitial Lung Disease George Lee* George Lee Choa Yun May Baydoun Minkyo Song

Systemic autoimmune rheumatic diseases (SARDs), including rheumatoid arthritis, systemic lupus erythematosus, and other autoimmune diseases, are associated with increased risk of interstitial lung diseases (ILD), but the underlying biological mechanisms remain poorly understood. We evaluated whether circulating proteins may mediate the association between SARDs and incident ILD in a prospective cohort.

Among the 52,996 participants with Olink plasma proteomic data, 49,338 were analyzed after excluding 3,658 people with prevalent non-SARDs autoimmune diseases or ILD. SARDs and ILD were defined using International Classification of Diseases and self-reported data. Cox proportional hazards models estimated hazard ratios adjusted for age, sex, ethnicity, assessment center, education, smoking, alcohol use, and body mass index. Mediation effects were assessed using generalized structural equation models (GSEM) with Weibull survival functions across 2,922 z-scored proteins. Significant proteins were further analyzed using Ingenuity Pathway Analysis (IPA) to identify biological pathways.

Of 49,338 participants, 1,095 individuals (female 76%) had SARDs at baseline. During a median follow-up of 12.7 years, 533 incident ILD occurred. SARDs were associated with a higher ILD incidence compared to participants without autoimmune diseases at baseline (HR: 4.60, 95% CI: 3.44-6.16). After Bonferroni correction in GSEM, 392 proteins were significant, with percentage mediated ranging from 1.5% to 29.6%. IPA of the proteins showed enrichment of cytokine-mediated inflammatory signaling, leukocyte adhesion and diapedesis, and extracellular matrix/fibrotic remodeling pathways. Predicted upstream regulators included TNF, TGFB1, IFNG, IL1B, and IL6.

These findings suggest that the association between SARDs and incident ILD may be partly explained by broad alterations in inflammatory, leukocyte trafficking, and tissue remodeling proteins, highlighting pathways for future mechanistic studies.

Neurology

Associations between plasma metal and metalloid levels and Alzheimer's disease and related dementias among a cognitively healthy population-based cohort Terry Zhou* Terry Zhou Ruby Hickman Priya Esilda D'Souza Dana Boyd Barr Allan I. Levey James J. Lah Thomas S. Wingo Donghai Liang Anke Hüls

Introduction

Exposure to metals and metalloids has been linked to Alzheimer's disease and related dementias (ADRD) pathology. However, research has been limited on the joint effects of multiple metal(loid) exposures on ADRD in human populations.

Methods

We estimated associations in 232 participants from the Emory Healthy Brain Study (EHBS) cohort. Concentrations of 13 metal(loid)s including beryllium (Be), vanadium (V), manganese (Mn), cobalt (Co), nickel (Ni), arsenic (As), cadmium (Cd), tin (Sn), antimony (Sb), tellurium (Te), cesium (Cs), barium (Ba), and uranium (U) were measured in plasma using inductively coupled plasma-mass spectrometry. ADRD was evaluated using the Mini Mental State Examination (MMSE). Associations between individual metal(loid) levels and MMSE were estimated using linear regression models, adjusting for potential confounding variables. Metal levels were dichotomized as detected/ not detected based on their limits of detection (LOD) due to high proportions of samples below the LOD. We applied quantile g-computation (qgcomp), using continuous exposure variables and adjusting for potential confounders, to estimate the joint effect of the total plasma metal mixture concentrations.

Results

Although detectable levels of Co, Cd, V, and Sb were associated with decreased MMSE scores (e.g., for Cd β=-0.26 (95% CI: -0.89, 0.38)), none of the associations was statistically significant. A statistically significant negative association was observed between the overall metal mixture concentration and MMSE (increasing all metal(loid) levels by one quantile β=-0.14 [-0.27, -0.01] (qgcomp)).

Discussion

While we found no significant associations between individual plasma metal(loid) levels and ADRD, the overall metal(loid) mixture concentration was significantly negatively associated with ADRD. Future research should further investigate the potential neurotoxic effects of these metal exposures to better target ADRD prevention measures.

Neurology

Estimating early-onset dementia population attributable fractions in the U.S. population using a counterfactual approach Katherine Giorgio* Katherine Giorgio Pamela Lutsey Etsuji Suzuki Sanaz Sedaghat Richard MacLehose

Introduction

Early-onset dementia (EOD; onset before age 65) affects 3.9 million people globally. While genetic predisposition contributes to EOD risk, there is growing evidence that modifiable risk factors also play an important role. We estimated the proportion of EOD cases in the U.S. which can be attributed to modifiable risk factors.

Methods

Depression, obesity, high cholesterol, diabetes, hypertension, low education, physical inactivity, smoking, alcohol over-consumption, and mild to severe head injury were examined as risk factors. Individual-level data was used to estimate population attributable fractions (PAFs). Data for effect estimates on EOD came from the UK Biobank study. Risk factor prevalence data for the U.S. population aged 45-65 years came from the National Health and Nutrition Examination Survey (NHANES). A Cox regression model for EOD, with age as the timescale and all risk factors, sex, and race as independent variables, was fit in the UK Biobank data. Model estimates were used to estimate PAFs comparing EOD incidence under observed NHANES risk factor distributions to the counterfactual outcome if no one was exposed. CIs were calculated by bootstrapping. A sensitivity analysis calculated PAFs using summary-level data.

Results

Risk factor prevalence is high, with 97% of the population having at least one. Large individual PAFs include head injury (34%), diabetes (20%), and physical inactivity (20%), and results were similar in sensitivity analysis. 74% (95% CI: 65 – 82) of EOD cases are attributable to these ten risk factors combined (43% in sensitivity analysis).

Discussion

Several risk factors may have a larger impact on the proportion of EOD cases than they do on dementia at any age, including head injury, diabetes, and physical inactivity. The combined estimates are similar, however, when using the same methods. These estimates are sensitive to the combination method. EOD incidence may be reduced by interventions for common health issues.

Neurology

Sleep Disturbance and Dementia Onset: A Cohort Study in Elderly Hispanics in the Sacramento area Miguel Cuevas* Miguel Cuevas Yu Yu Kimberly C. Paul Cynthia Kusters Beate Ritz

Introduction
Sleep disturbances are common in dementia but less is known about their contributions to dementia onset.
Methods
A cohort of 1,247 older Hispanics from Sacramento Area Latino Study on Aging were followed from 1998 to 2007. Sleep scores were calculated based on questions at baseline and follow-up visits. We categorized these scores into stable healthy, improving, worsening, and stable disturbed sleep patterns and performed Cox proportional hazard regression on dementia/cognitive impairment without dementia (CIND) adjusting for age, gender, education, smoking, physical activity, rural/urban setting, comorbidities, ambient noise, and APOE status.
Results
We estimated an increased hazard (HR=2.14, 95%CI: 1.30–3.55) of developing dementia/CIND among those with worsening compared to stable healthy sleep patterns. An increased hazard (HR=1.93, 95%CI: 0.94–3.95) was also observed among those reporting stable disturbed sleep.
Conclusion
This study indicates that worsening and consistently disturbed sleep patterns adversely affect the cognitive health of older Hispanics.

Nutrition/Obesity

Does weight stigma contribute to the relationship between body weight and health?: A systematic review protocol Ellen McGarity-Shipley* Ellen McGarity-Shipley Brooke Hebert Laura Colford Jordyn Cox Chelsea Dumasal Taniya Nagpal

Objective: This is a protocol for a systematic review which will synthesize studies that have explored the contribution of weight stigma in the relationship between body weight and health.

Introduction: High body weight is significantly stigmatized in North American society. Some studies suggest that weight stigma contributes to the relationship between body weight and health. However, there are currently no systematic reviews summarizing this literature.

Inclusion criteria: Quantitative peer-reviewed studies that have investigated weight stigma as either a mediator or a moderator of the relationship between body weight and health in adults (18 years of age or older) will be considered for inclusion. Health variables can include both physical and mental health measures. Weight stigma includes any weight stigma-related measure including weight bias internalization or weight self-stigma.

Methods: PubMed, Scopus, ScienceDirect, Embase, and PsycINFO will be searched (see sample search strategy for PubMed in **Figure 1**). Reference lists of relevant systematic reviews will be screened. Two researchers will independently screen studies at both the title and abstract screening stage and the full-text review stage. If there is disagreement, a third researcher from the team will be consulted. Standardized critical appraisal (Mixed Methods Appraisal Tool) and data extraction forms will be used. If two or more studies report on the same predictor, outcome, mediator/moderator variable and used the same statistical analysis, a meta-analysis will be performed with Jamovi (Sydney, Australia) to calculate pooled standardized beta coefficients and confidence intervals using a random-effects model. For studies that cannot be included in a meta-analysis due to heterogeneity of reported variables, a narrative synthesis will be completed.

Review registration: PROSPERO CRD42024623518

Search number	Query	Results
1	weight bias internalization	329
2	WBIS	115
3	weight bias internalization scale	118
4	weight self-stigma questionnaire	71
5	WSSQ	37
6	WBIS-M	21
7	modified weight bias internalization scale	39
8	shame	9,914
9	self-stigma	1,572
10	self concept[MeSH:NoExp]	62,641
11	body image[MeSH Terms]	20,915
12	social stigma[MeSH Terms]	14,931
13	shame[MeSH Terms]	3,274
14	weight prejudice[MeSH Terms]	295
15	perceived discrimination[MeSH Terms]	163
16	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15	101,308
17	weight	1,989,893
18	size	1,414,746
19	BMI	221,730
20	body mass index	335,831
21	body mass index[MeSH Terms]	157,526
22	body size[MeSH Terms]	397,655
23	#17 OR #18 OR #19 OR #20 OR #21 OR #22	3,446,672
24	mediat*	1,754,612
25	moderat*	816,569
26	#24 OR #25	2,525,402
27	#16 AND #23 AND #26	1,904

Nutrition/Obesity

Self-reported flossing frequency and odds of untreated interproximal coronal caries in US adults: evidence from NHANES 2015–2018 Edmond Appiah* Edmond Appiah Joseph Nimako-Boateng

Background: Interproximal dental caries remain prevalent among US adults despite overall declines in caries experience, and mechanical plaque removal via flossing is recommended for prevention. However, evidence on the specific efficacy of flossing frequency for reducing interproximal caries risk is mixed and limited, particularly regarding dose-response patterns.

Methods: We analyzed cross-sectional data from 6,959 US adults aged 30 years and older in the National Health and Nutrition Examination Survey (NHANES) 2015–2018 cycles. Untreated interproximal coronal caries were identified via clinical oral examinations. Self-reported flossing frequency was categorized as 0 days/week (reference), 1–3 days/week, or 4–7 days/week. Weighted multivariable logistic regression models estimated adjusted odds ratios (OR) and 95% confidence intervals (CI), controlling for age, sex, race/ethnicity, poverty-income ratio, education, insurance status, time since last dental visit, gum treatment history, smoking, diabetes, sugar intake tertile, and self-rated oral health. Rao-Scott chi-square tests assessed bivariate associations, and survey weights accounted for complex sampling design.

Results: Overall weighted prevalence of any untreated interproximal caries was 9.18% (95% CI: 7.55–10.81). Compared with flossing 4–7 days/week, never flossing showed higher unadjusted prevalence (11.11% vs 8.96%) and, after full adjustment, significantly lower odds of caries (OR 0.67, 95% CI: 0.48–0.94, p=0.022). Flossing 1–3 days/week showed a non-significant protective association (OR 0.72, 95% CI: 0.45–1.16, p=0.170). Bivariate differences were evident by socioeconomic factors, with higher caries prevalence among those with lower income, less education, and no recent dental visit.

Conclusions: Near-daily flossing is associated with reduced odds of untreated interproximal caries in a nationally representative sample, while occasional or no flossing confers less or no benefit after confounder adjustment. These findings support emphasizing consistent interdental cleaning in preventive oral health guidance and highlight opportunities to address disparities through targeted education and access to care.

Nutrition/Obesity

Association between Environmental Noise Exposure and Childhood Body Weight in Taiwan
Xin-Chun Peng* Peng Xin-Chun Yi-Di Wang Hsin-Yi Huang Siang-chen Chen Tsung-Chieh Yao Wen-Chi Pan

Association between Environmental Noise Exposure and Childhood Body Weight in Taiwan

Xin-Chun Peng, Yi-Di Wang, Siang-Chen Chen, Hsin-Yi Huang, Tsung-Chieh Yao, Wen-Chi Pan

Institute of Environmental and Occupational Health Sciences,
National Yang Ming Chiao Tung University, Taiwan

Background:

Childhood obesity is an emerging public health concern globally. Environmental noise may increase obesity risk through stress and sleep disturbance, yet findings remain inconsistent. As most research focuses on European and North American populations, evidence from Asian countries is limited, warranting further investigation.

Objective:

To evaluate the association between exposure to environmental noise and children’s obesity in a Taiwanese birth cohort study.

Methods:

We recruited participants based on the Longitudinal Investigation of Global Health in Taiwanese Schoolchildren (LIGHTS), a birth cohort that recruited 1513 newborns in 2010-2011 (baseline) in the northern Taiwan. We perform a follow-up contact in 2024-2025 and successfully re-contacted 241 children. Overweight and obesity was defined using International Obesity Task Force (IOTF) criteria. Noise exposure was assessed using low-cost noise sensors (i.e., EcoDecibel) followed by machine-learning algorithms to construct participants’ residential exposure to environmental noise. Logistic regression models were utilized to evaluate the association of noise exposure and risk of children’s obesity/overweight, adjusting for the potential confounders.

Results:

Overall, 54 participants (22.4%) were overweight or obese. After adjusting for the potential confounders, environmental noise was positively associated with overweight/obesity. An 1dBA increment on noise was significantly associated with 13% higher odds of overweight/obesity (OR = 1.13; CI: 1.004–1.270; p-value = 0.044). Stratified analyses indicated stronger effects among boys (OR = 1.11; CI: 0.96–1.30; p-value = 0.2) compared with those among girls (OR = 1.05; CI: 0.73–1.45; p-value = 0.8).

Conclusion:

Environmental noise was associated with increased overweight/obesity risk in Asian children, highlighting environmental noise as a metabolic determinant. Policies targeting this modifiable factor may help reduce childhood obesity.

Association between Environmental Noise Exposure and Childhood Body Weight in Taiwan

Xin-Chun Peng, Yi-Di Wang, Siang-Chen Chen, Hsin-Yi Huang, Tsung-Chieh Yao, Wen-Chi Pan

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Conclusion:

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LATEBREAKER

Nutrition/Obesity

Household Income and Early Adiposity Rebound: Evidence from a Propensity Score–Matched Longitudinal Cohort Jessie Ko* Jessie Ko Denise Payan Luohua Jiang Andrew Odegaard

Background: Early adiposity rebound (AR), defined as the age at which body mass index (BMI) reaches its nadir before increasing, is a strong predictor of later obesity and cardiometabolic risk. Socioeconomic status is inversely associated with childhood obesity; however, evidence linking resource-based socioeconomic indicators, such as household income, to AR timing is inconsistent. Prior studies have largely relied on conventional regression approaches that may inadequately address confounding.

Methods: We analyzed data from 927 participants in a U.S. longitudinal birth cohort with repeated BMI measures from birth to age 15 years. AR age was estimated using sex-specific mixed-effects cubic models of log-transformed BMI, with AR defined as the minimum predicted BMI between ages 2 and 9 years. Early AR was defined as <5 years. The exposure was early childhood household income, operationalized as an income-to-need ratio <1.85 versus ≥1.85 averaged across ages 1–24 months. Propensity scores were estimated using early-life sociodemographic and parental factors measured before age 2 years. After trimming and 1:2 nearest-neighbor matching within multiply imputed datasets, modified Poisson regression estimated risk ratios (RR) for early AR.

Results: Among 818 children with valid AR estimates, 49.5% experienced early AR. Propensity score matching achieved acceptable covariate balance (all standardized mean differences <0.2). Low household income was not associated with early AR (RR=0.91; 95% CI: 0.71–1.17). Findings were consistent in regression-adjusted and complete-case analyses.

Conclusions: **Conclusions**: In high-income countries such as the United States, children from low socioeconomic households are disproportionately affected by obesity and related risk factors, and early adiposity rebound is often presumed to follow this gradient. In this quasi-causal analysis, early childhood household income was not associated with AR timing. These findings suggest that extrapolating broader socioeconomic disparities to all developmental markers may obscure distinct etiologic pathways and underscore the need to identify specific mechanisms driving early adiposity rebound.

Nutrition/Obesity

Using signal detection analysis to identify subgroups of midlife women in Mexico City with differing prevalence of metabolic syndrome Yanxin Zhu* Yanxin Zhu Astrid N. Zamora Erica C. Jansen Abeer Aljahdali Alejandra Cantoral Libni A. Torres-Olascoaga Martha Maria Téllez-Rojo Karen E. Peterson

Objective: To identify heterogeneous subgroups of midlife women in Mexico City with varying prevalence of metabolic syndrome (MetS) using signal detection analysis (SDA).

Methods: This cross-sectional study included 443 women from the 2019-2023 visit of the Early Life Exposure in Mexico to ENvironmental Toxicants (ELEMENT) cohort. MetS was defined according to the National Cholesterol Education Program Adult Treatment Panel III criteria. Factors potentially associated with MetS were selected based on the socioecological model and included demographic characteristics, socioeconomic position, health behaviors, body mass index (BMI), and menopause-related measures. Data processing was conducted in R 4.4.2, and SDA was performed using ROC5 software.

Results: MetS prevalence was 49.0% in this population of midlife women (mean age: 48.4±6.3 years). SDA identified 8 mutually exclusive subgroups, with MetS prevalence ranging from 10.9% to 78.8%. BMI was the primary splitting variable, with additional differentiation by the number of children, age, sedentary time, moderate-to-vigorous physical activity, years of education, ultra-processed food (UPF), and total energy intake. The highest prevalence group (78.8%) was characterized by BMI≥30 kg/m2, <11 years of education, less than 17.6% grams/day from UPF intake, and sedentary time <11.5 hr/day. The lowest prevalence group (10.9%) was defined as BMI<25 kg/m2 and having fewer than 3 children.

Conclusion: Distinct combinations of BMI, age, socioeconomic status, diet, physical activity, and sedentary behavior distinguished subgroups with markedly different MetS prevalence among midlife women from Mexico City. These findings highlight the importance of considering intersecting risk profiles rather than single factors when identifying populations at elevated metabolic risk. Longitudinal research is needed to determine whether these subgroup patterns predict the progression of metabolic risk.

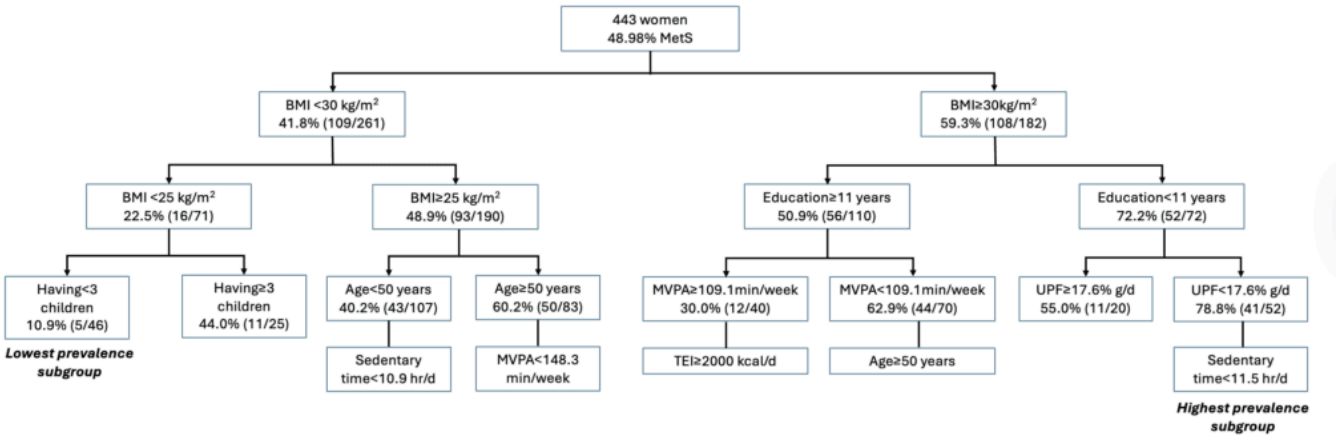


Figure 1. Subgroups of women with differing metabolic syndrome prevalence identified by signal detection analysis.
MetS: metabolic syndrome; BMI: body mass index; MVPA: moderate-to-vigorous physical activity; UPF: ultra-processed foods; TEI: total energy intake

Nutrition/Obesity

Maternal Dietary Intakes and Gastroschisis in Offspring Julie M. Petersen* Julie Petersen Yiqun Jiang Rashida Smith-Webb Kathleen Angell Deepanjali Bhale Muskan Ahuja Corrine Hanson Martha Werler

Gastroschisis is a serious congenital abdominal wall defect in which the intestines herniate outside the body. While young maternal age is a strong risk factor, few modifiable factors are known. We examined associations between maternal dietary intake and gastroschisis using the Slone Birth Defects Study, a North American case–control design (1998–2015). Cases included 273 pregnancies affected by isolated gastroschisis. Controls were 2,591 live borns without major anomalies, frequency-matched by center. Mothers completed standardized interviews within 6 months postpartum. Diet for the 6 months before pregnancy (proxy for early prenatal intake) was assessed with a modified Willett food frequency questionnaire. Quartiles for 28 macro- and micronutrients were derived based on the control distribution and energy-adjusted using the residual method. Gastroschisis associations with each nutrient were estimated using LASSO logistic regression, adjusting for age, race, education, income, parental relationship status, BMI, pregnancy intention, smoking, alcohol consumption, oral contraceptive use, nonsteroidal anti-inflammatory drug use, folic acid supplementation, parity, and the other nutrients. Nutrients were identified as relevant based on adjusted odds ratios (aORs), permutation-based changes in AUC, and Shapley values. Compared with the lowest quartile, moderate glutamic acid (aOR 0.57, 95% CI 0.34–0.97), vitamin E (0.72, 0.49–1.0), and polyunsaturated fat (0.80, 0.53–1.0), and high magnesium (0.60, 0.33–1.0) and calcium (0.76, 0.47–1.0), were associated with reduced odds of gastroschisis. Higher cryptoxanthin intake was associated with increased odds (1.29, 1.0–1.9). These results suggest a potential nutritional mechanism. While most nutrients showed protective benefits, finding high cryptoxanthin (in yellow/orange fruits/vegetables) was associated with increased odds was surprising. Replication and clarification of clinically relevant intake thresholds are needed.

Nutrition/Obesity

Associations of Childhood BMI and Waist Circumference Trajectories with MASLD Risk in Early Adulthood: Evidence from the Ewha Birth and Growth Cohort Hyelim Lee* Hyelim Lee Hyesook Park Seunghee Jun Hyeseung Jang Hye Ah Lee

Background: Metabolic dysfunction-associated steatotic liver disease (MASLD), formerly NAFLD, is defined by hepatic steatosis with at least one cardiometabolic risk. While body mass index (BMI) and waist circumference (WC) are established risk factors for MASLD, evidence has largely relied on measurements at a single time point. Therefore, this study examined whether BMI and WC trajectories from ages 3 to 13–15 years were associated with MASLD at age 19.

Methods: This study included 215 participants from the Ewha Birth and Growth Cohort who had been followed up to age 19. After excluding 27 participants with an AST/ALT ratio >2 or missing MASLD-related biomarkers, 188 participants were included in the final analysis. MASLD at age 19 was defined as FLI >30 or HSI >36. BMI and WC were assessed longitudinally from ages 3 to 13–15 years using sex- and age-specific z-scores. Trajectories were identified using group-based trajectory modeling; three BMI and three WC trajectories were selected based on BIC and interpretability. Logistic regression was used to assess associations with MASLD, adjusting for sex, mother's education, parental history of cardiometabolic disease, and physical activity, smoking, and alcohol drinking at age 19.

Results: Among 188 participants, 25% were classified as having MASLD at age 19. BMI and WC trajectories were each classified into three groups (BMI: low stable, moderate stable, high stable; WC: low U-shaped, moderate U-shaped, high increasing). Compared with the moderate BMI trajectory, the high stable BMI trajectory was associated with a higher risk of MASLD (adjusted OR 6.67, 95% CI 2.66–16.75). A similarly increased risk was observed for the high increasing WC trajectory compared with the moderate WC trajectory (adjusted OR 7.81, 95% CI 2.94–20.77). Of 46 participants classified as high in at least one trajectory-based group, 33 (72%) were classified as high in both. Notably, adolescents with concurrent high BMI and high WC trajectories had a higher risk of MASLD (adjusted OR 7.04, 95% CI 2.48–19.96).

Conclusions: Childhood BMI and WC trajectories were associated with MASLD risk at age 19, particularly among individuals with concurrent high trajectories. This suggests the relevance of monitoring both overall and central adiposity from early life to adolescence.

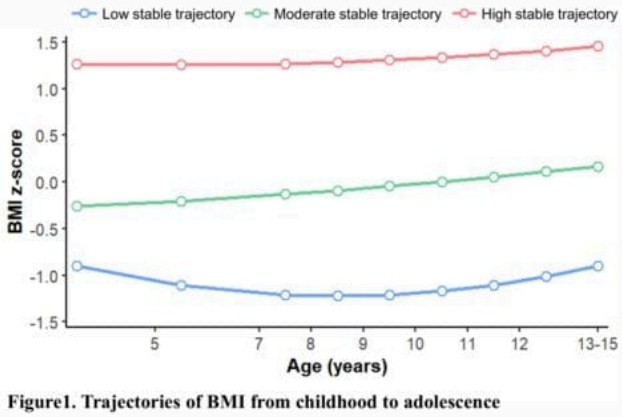


Figure1. Trajectories of BMI from childhood to adolescence

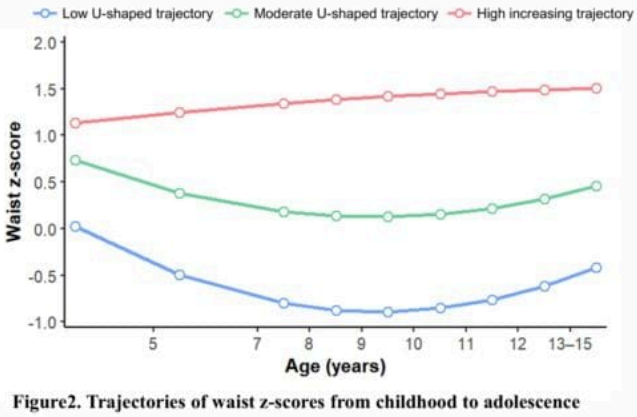


Figure2. Trajectories of waist z-scores from childhood to adolescence

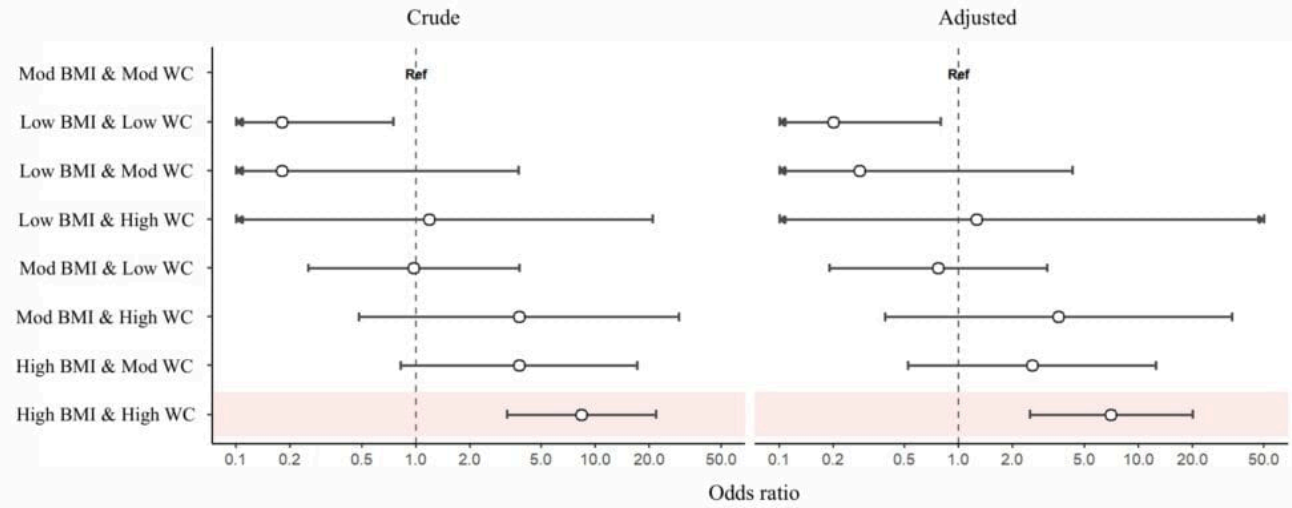


Figure3. Joint association of BMI and WC trajectory patterns with the risk of MASLD

Occupational

Beyond the crops: exploring precarious employment among California, Washington, and Oregon farmworkers and its association with chronic disease Miriam Flores Moreno* Miriam Flores Moreno Barbara Baquero Edward Kasner Mienah Sharif

Background: Farmworkers endure long hours, low wages, minimal employment benefits, and are exploited and mistreated because of their race and immigration status. These factors encompass precarious employment (PE) and increase farmworkers' risk of experiencing greater health disparities, and high rates of workplace injuries and fatalities compared to workers in other industries. We aim to understand PE and its association with chronic disease (diabetes, hypertension, and heart disease) among farmworker populations in California (CA), Washington (WA), and Oregon (OR), regions with high concentrations of farmworkers. Preliminary analysis explores one domain of PE, material rewards, with the indicator of average hourly wage.

Methods: We analyzed cross-sectional data from the National Agricultural Workers Survey, pooling data from 2011-2018 cycles and applying regional survey weights. The association between PE and diabetes, hypertension, and heart disease was analyzed using log-binomial regression, adjusting for confounders (age, gender, immigration status), and including health insurance status as an interaction term.

Preliminary Results: Among farmworkers in CA, WA, and OR, higher hourly pay was associated with increased odds of diabetes (POR = 1.13, 95% CI 1.02, 1.26) and high blood pressure (POR = 1.14, 95% CI 1.04, 1.24); these associations did not differ by insurance status for diabetes (POR= 0.98, 95% CI: 0.83, 1.16) and high bloop pressure (POR = 0.90, 95% CI 0.80,1.02). Conversely, pay was not associated with heart disease (POR = 1.13, 95% CI 0.94, 1.36), and insurance status did not modify this association (POR = 0.70, 1.06). Future analysis will encompass the multidimensional construct of PE.

Conclusion: Understanding PE in the context of farmworker health is significant, as it is modifiable through institutional and structural policy changes and may enhance farmworkers' health and well-being.

Occupational

Associations of per- and polyfluoroalkyl substances (PFAS) exposures and firefighting experience with microRNA signatures of Amyotrophic Lateral Sclerosis (ALS): a cross-sectional analysis of active-duty municipal and airport firefighters Brooke A Hawkes* Brooke A Hawkes Jaclyn M Goodrich Shawn C Beitel Cynthia Porter Jefferey L Burgess Melissa A Furlong

Background: Amyotrophic lateral sclerosis (ALS) is a fatal neurodegenerative disorder with unclear etiology in sporadic cases. Blood microRNA (miRNA) expression varies between individuals with and without ALS. Firefighters may face elevated ALS risks due to occupational exposures, including elevated serum per- and polyfluoroalkyl substances (PFAS) concentrations.

Methods: This study investigates the association between occupational firefighter characteristics (serum PFAS, years of experience, incumbent versus recruit status) and ALS-relevant miRNA expression in U.S. firefighters. MiRNA expression was quantified from blood collected from 833 firefighters across 15 U.S. sites. 302 of these same firefighters had nine PFAS analytes quantified in serum. We identified 19 ALS-related miRNAs using miRWalk's Disease Ontology. Adjusted linear regression models estimated associations between exposures and miRNA expression, controlling for demographic and occupational factors.

Results: Thirteen significant negative associations ($p<0.05$) were observed for PFAS and miRNA expression, including Sm-PFOS and hsa-let-7i-5p (β = -0.169, 95% CI: -0.287, -0.052), hsa-let-7c-5p (β = -0.128, 95% CI: -0.218, -0.037), and hsa-let-7e-5p (β = -0.113, 95% CI: -0.210, -0.017); PFNA and hsa-let-7c-5p (β = -0.126, 95% CI: -0.214, -0.037); and PFHxS and hsa-let-7i-5p (β = -0.126, 95% CI: -0.223, -0.029). Six remained significant after relaxed FDR adjustment for multiple testing ($q<0.20$). Of these, five were inversely associated with ALS in previous studies, suggesting that increased serum PFAS may be a risk factor for ALS. Twelve miRNAs were associated with incumbency, including miR-195-5p (β = 8.612, 95% CI: 5.028, 12.196) and miR-106b-5p (β = 168.742, 95% CI: 70.176, 267.308); all remained significant after FDR correction. Nine miRNA had a known direction of association with ALS, and in eight of these the directionality with incumbent status was consistent with a higher risk of ALS. MiR-23a-3p was associated with years of firefighting (β = -7.301, 95% CI: -13.246, -1.357), but not after FDR correction. Let-7e-5p was inversely associated with Sm-PFOS, n-PFOS, and incumbency, suggesting a potential combined risk of ALS from increased serum PFAS and firefighting status.

Conclusions: Significant associations between PFAS exposure, firefighting status, and ALS-related miRNAs suggest potential molecular links between occupational exposures and ALS risk, warranting further pathway-focused research.

Occupational

Occupational low-dose medical radiation exposure and risk of Parkinson's disease mortality in the U.S. Radiologic Technologists Study Isabelle van der Velpen* Isabelle van der Velpen Jim Elizabeth Dale Mark Martha Tae-Eun Haegin Choonsik Bruce Cari

Objective: Parkinson's disease (PD) is a neurological disorder that is increasing in incidence globally. Recent studies suggest that exposure to low-dose ionizing radiation may be associated with PD risk. We studied the association between occupational radiation exposure and PD mortality in a large U.S. medical worker cohort

Methods: U.S. Radiologic Technologists (USRT) Study participants (mean baseline age 41.0 years, 76.0% female) were followed from response date of the 1st (1983-1989) or 2nd survey (1994-1998) to December 31, 2021 (n=109,113). Estimated radiation absorbed dose to the brain was calculated for the exposure period 1916-2020. PD mortality included PD as any cause of death. Multivariable Poisson regression models were used to calculate excess relative rates (ERR) of PD mortality per 100 mGy, using 10-year lagged cumulative brain-absorbed dose. Multivariable Cox proportional hazards models were used to calculate hazard ratios for PD mortality associated with self-reported work history (decade first worked, total years worked per decade, procedures performed [fluoroscopically-guided interventional (FGI), nuclear medicine], number of times held patients, and ever exceeding exposure limit).

Results: During follow-up of 3,389,435 person-years, 433 PD deaths occurred. A linear dose-response relationship was observed for PD mortality (ERR/100mGy=1.53;95%CI:0.51-3.25), especially in male workers. Ever assisting with FGI procedures was associated with a higher PD mortality risk (HR=1.45;95%CI:1.06-2.00). Participants who assisted with FGI procedures daily post-1980s had a higher PD mortality risk than those who never/rarely assisted post-1980s (HR=2.58;95%CI:1.54-4.32).

Conclusion: Cumulative low-dose radiation exposure and daily assisting with FGI procedures were associated with higher PD mortality. These findings support continued efforts to limit occupational radiation exposure and provide additional support for a role of ionizing radiation in PD etiology.

LATEBREAKER

Occupational

The association between Shift Work and Mental Health Outcomes Among Korean Nurses
Soojeong shim* soojeong Shim Jin young

The association between Shift Work and Mental Health Outcomes Among Korean Nurses

Abstract

Objectives Shift work is a common occupational factor among nurses and has been associated with adverse health outcomes. However, evidence regarding its impact on mental health outcomes such as anxiety, depression, and fatigue remains limited in Korea. Therefore, the aim of this study was to investigate the association between shift work and mental health outcomes, including generalized anxiety disorder (GAD), depressive symptoms, and fatigue, among nurses.

Methods This study used the Korean Nurses' Health Study (KNHS) Cohort from 2013 to 2015, totaling 20,613 nurses. The measured outcomes included generalized anxiety disorder (GAD), depressive symptoms, and fatigue in relation to shift work. We used chi-square tests and multiple logistic regression analyses adjusting for sociodemographic and occupational covariates, with subgroup analyses stratified by sleep problems.

Results Shift workers showed a higher prevalence of [GAD: 62.7%], [depressive symptoms: 32.2%], and [fatigue: 76.7%] compared with non-shift workers. In multivariable logistic regression models, shift work was significantly associated with increased odds of GAD (OR: 1.18, 95% CI: 1.10-1.27), depressive symptoms (OR: 1.45, 95% CI: 1.32-1.59), and fatigue (OR: 1.41, 95% CI :1.30-1.53). Stratified analyses revealed that, even without sleep problems, shift work was associated with a 1.54-fold higher risk of depressive symptoms. These findings underscore the association between shift work and mental health, particularly depressive symptoms.

Conclusion Shift work was significantly associated with higher risks of anxiety, depression, and fatigue among Korean nurses, even in the absence of sleep problems. These findings highlight the need for workplace interventions and policies to mitigate the adverse effects of shift work on mental health.

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LATEBREAKER

Perinatal & Pediatric

Socioeconomic and prenatal care disparities in severe maternal morbidity by transfusion status Jin Young Nam* Jin Young Nam

Background: Severe maternal morbidity (SMM) encompasses a spectrum of life-threatening conditions, with blood transfusion being the most frequent indicator. However, transfusion-related SMM may reflect hospital practice patterns rather than intrinsic maternal risk. This study examined the differential associations of prenatal care adequacy and socioeconomic status (SES) with SMM with and without blood transfusion to better identify high-risk maternal populations.

Methods: Using the Korean National Health Insurance Service database (2003–2021), we analyzed 7,171,578 deliveries. SMM was defined per the Centers for Disease Control and Prevention (CDC) algorithm, and further categorized into (1) SMM including transfusion and (2) SMM excluding transfusion. Adequate prenatal care (PNC) was classified using the Kessner Index; SES was based on income quartiles. Modified Poisson regression with robust error estimation estimated adjusted relative risks (aRRs) for each SMM type.

Results: Overall, 2.1% of deliveries involved SMM. Inadequate prenatal care was associated with significantly higher risk of SMM both with and without blood transfusion (with blood transfusion: aRR = 1.16, 95% CI: 1.14–1.19; without blood transfusion: aRR = 1.20, 95% CI: 1.16-1.24). Women in the lowest income level receiving inadequate care had more than 30% higher risk for both SMM with transfusion (aRR = 1.35; 95% CI: 1.26–1.44) and without transfusion (aRR = 1.32, 95% CI: 1.28-1.38) compared to the highest-income level women with adequate PNC.

Conclusion: While both SMM types were associated with inadequate prenatal care and low income, the relative difference was smaller for non-transfusion SMM, likely reflecting its inherently severe nature and high baseline risk. Distinguishing transfusion-based from non-transfusion SMM can improve risk stratification and better guide targeted prenatal and perinatal interventions to reduce preventable maternal complications.

Perinatal & Pediatric

Prenatal Lead Exposure and Intelligence Across Developmental Stages: A Systematic Review and Meta-analysis Victor Florez-Garcia* Victor Florez-Garcia Edwin Guevara-Romero Esmeralda Santacruz-Salas Natalia Yumi Noronha María Talayero-Schettino Tania Acosta-Vergara Rafael Tuesca-Molina Jorge Acosta-Reyes Edgar Navarro-Lechuga Julia A Bauer

Background: Lead is a well-recognized neurotoxic metal with demonstrated consistent detrimental effects on children's intelligence quotient (IQ) in the postnatal period. However, there is no such consensus about the effects of prenatal exposures. **Aim**: We aimed to examine the effect of prenatal lead exposure on children's intellectual quotient. **Methodology**: We conducted a systematic review with meta-analysis based on three databases: PubMed (MEDLINE), Web of Science, and Lilacs (Latin American and Caribbean Health Sciences Literature). We included studies where exposure involved biomarkers of lead exposure (e.g., blood, urine, etc.) during the prenatal period, and global IQ assessments were conducted in children aged 5 years or older. We standardized the estimates to linear point estimates. The Risk of Bias (RoB) in Non-randomized Studies of Exposures (ROBINS-E) tool was used to evaluate potential systematic errors. We analyzed the pooled estimates using random effects models, also considering fixed effects models. Pooled effects were examined separately by sex. To assess heterogeneity across studies, we employed the I2 statistic and Cochran's Q test. **Results**: Only 7 studies were included in analyses. We found a modest negative association between prenatal Pb and standardized IQ scores (β: -0.06; 95%CI: -0.25, 0.13). This association was stronger in boys (β: -1.08; 95%CI: -3.08, 0.92), yet positive in girls (β: 0.64; 95%CI: -0.31, 1.60), with both results showing high heterogeneity. **Conclusion**: Results from our study suggest that prenatal lead exposure increases the risk of lower intelligence quotient scores in children 5 years and older. However, research is sparse and more studies are needed to investigate confounding factors and whether the effect varies by sex.

Perinatal & Pediatric

Association of maternal physical activity domains, intensities and duration with neonatal anthropometry in the NICHD Fetal Growth Studies – Singletons Kathryn Wagner* Kathryn Wagner Zhen Chen Jessica L. Gleason Madison Ouellette Dian He Susanna Mitro Roger B. Newman William A. Grobman Daniel W. Skupski Stefanie Hinkle Cuilin Zhang Jagteshwar Grewal Katherine L. Grantz

Prior studies have focused on total or exercise physical activity (PA) and birthweight (BW), potentially missing nuanced relationships between PA domains, intensities and duration with neonatal size, including fat measures.

In a prospective cohort (n=2441), self-reported first trimester PA (type, intensity and duration) were categorized as tertiles and whether they met ACOG guidelines. Neonatal anthropometrics (BW, g; birth length (BL, cm); circumferences (cm) – head (HC), mid-upper arm (MUAC), chest (CC), abdominal (AC), and mid-upper thigh (MUTC); and skinfold thicknesses (mm) –tricep (TSF), subscapular (SSF), abdominal (ASF), and anterior thigh (ATSF)) were measured after delivery or abstracted from medical records. Generalized linear regressions evaluated the associations, adjusted for covariates.

Home, work, light, moderate, and duration of PA and meeting ACOG guidelines were associated with smaller neonatal anthropometrics. Specifically, 3rd tertile home PA was associated with smaller MUAC (β=-0.15;SE=0.08), TSF (β=-0.19;SE=0.09), CC (β=-0.24;SE=0.12), ASF (β=-0.18;SE=0.09) and ATSF (β=-0.24;SE=0.12), compared to the 1st tertile. 2nd tertile work PA, but not 3rd, was associated with smaller BW (β=-89.6;SE=29.7). 2nd and/or 3rd tertile light PA was associated with smaller TSF (2nd: β=-0.17, SE=0.08; 3rd: β=-0.19;SE=0.08) and CC (3rd: β=-0.24;SE=0.11). 2nd tertile moderate PA was associated with several smaller measures (BW: β=-71.4,SE=26.8; HC: β=-0.19,SE=0.08; MUAC: β=-0.15,SE=0.07; CC: β=-0.22,SE=0.11; AC: β=-0.30,SE=0.011; ASF: β=-0.19,SE=0.08). 3rd tertile PA duration was associated with a smaller SSF (β=-0.16,SE=0.08). Meeting ACOG guidelines was associated with smaller BL (β=-0.21;SE=0.11), compared to not. Transportation, exercise, sedentary and vigorous PA were not associated with neonatal measures.

These findings highlight non-monotonic relationships of PA and neonatal anthropometry, as well as the importance of assessing PA domains beyond exercise.

Perinatal & Pediatric

Racial disparities in cesarean delivery at a rural-serving hospital in a state with limited access to obstetric services Andrew Williams* Andrew Williams

Background: Cesarean delivery increases risk of complications for mothers and infants. Understanding disparities in cesarean delivery rates in a state with limited access to obstetric services is necessary to improve equity in perinatal care. Using electronic medical records (EMR), trends in cesarean delivery rates, overall and by race, were described.

Methods: EMR for 21,168 pregnancies from January 2012-December 2024 from a birthing hospital in North Dakota (ND) were analyzed. Race/ethnicity (White, American Indian/Alaska Native (AIAN), Other race) was self-reported by patients and recorded on EMR. Cesarean delivery (yes/no), and birth year (2012-2024) were indicated in EMR. Cesarean delivery rate (%) was calculated overall, by race/ethnicity, and by year. Trends were assessed using SAS proc reg. North Dakota Vital Records statewide cesarean delivery rates from the study period were used as a population-based comparison.

Results: Overall, the cesarean delivery rate was 24%. By race/ethnicity, AIAN women had the highest rate of cesarean delivery (36%), followed by Other race women (25%) and White women (23%; $p<0.05$). Each year, AIAN had the highest rate of cesarean delivery compared to White and Other race women ($p<0.05$) The rate of cesarean delivery among AIAN women was higher than the overall hospital for each year, and was higher than the ND cesarean rate for each year except 2023 (AIAN 25.9%, ND 26.5%). Trend analysis suggests the cesarean delivery rate is trending downward for all racial/ethnic groups at the birthing hospital, yet AIAN women continue to experience higher cesarean rates compared to White women and other race/ethnicity women. Cesarean rates in ND were stable across the study period (about 27%).

Discussion: Racial disparities in cesarean delivery rates were persistent across the study period, with decreasing trends for all racial/ethnic groups. Data-informed strategies to reduce cesarean deliveries among AIAN women are warranted.

Perinatal & Pediatric

Linking Intervention Effectiveness in Reducing Exposure to Household Air Pollution and Adverse Health Outcomes: An Instrumental Variable Analysis in the Household Air Pollution Intervention Network (HAPIN) Trial Mohamed Alhassan* Mohamed Alhassan Maggie L Clark Kayleigh P Keller Jennifer L Peel

Rationale: Prenatal exposure to household air pollution is associated with adverse birth outcomes. Randomized trials of clean cooking interventions often yield null intention-to-treat estimates, possibly due to heterogeneity in achieving exposure reduction. Estimating causal effects among individuals whose exposure would be lowered by the intervention may provide insight regarding whether reduced prenatal exposure to fine particulate matter ($PM_{2.5}$) improves birth outcomes.

Methods: We evaluated the causal effect of achieving sustained prenatal $PM_{2.5}$ exposure below 35 $\mu g/m^3$, the World Health Organization (WHO) interim target, on birthweight and gestational age using data from 3,200 individuals in the Household Air Pollution Intervention Network (HAPIN) trial. Random assignment to a liquefied petroleum gas cooking intervention was used as an instrumental variable to estimate the average causal effect. Two-stage least squares models were fit for birthweight and gestational age, adjusting for maternal, household, and study-site covariates. Instrument strength was assessed using first-stage F-statistics.

Results: The adjusted estimated average causal effect of achieving $PM_{2.5}$ exposure below 35 $\mu g/m^3$ was a 65.5 g increase in birthweight (95% CI: -35.8, 166.7). No meaningful effect was observed for gestational age (adjusted mean difference: 0.13 weeks; 95% CI: -0.27, 0.52). Instruments were strong (first-stage F-statistics > 10).

Conclusions: In HAPIN, achieving prenatal $PM_{2.5}$ exposure below the WHO interim target resulted in higher birthweight and gestational age, though confidence intervals included the null. Effect estimates were larger than prior intention-to-treat estimates, reflecting a different target population defined by achieved exposure reduction. Although confidence intervals were wider, the estimated effect exceeded the original HAPIN minimum detectable effect, suggesting limited statistical power in this analysis.

Perinatal & Pediatric

Demographic and Clinic Characteristics Associated with Patient's Declining Universal Suicide Risk Screening in Pediatric Subspecialty Ambulatory Care Imme Kobayashi* Imme Kobayashi Sara Fernandes Cheryl Stein Becky Lois

Objective: Suicide is a leading cause of death for children in the US. The American Academy of Pediatrics recommends universal suicide risk screening for youth ages 12 years and older. There is limited knowledge regarding factors impacting patient decisions to accept or decline universal suicide risk screening in clinic settings.

Methods: We analyzed data from electronic health records for 19,053 patients ages 9 years and older attending 26,707 visits from October 2018 to March 2024 at pediatric ambulatory subspecialty care sites at an urban academic medical center. We examined demographic and clinic characteristics related to patient decisions to decline annual universal suicide risk screening.

Results: Patients declining universal suicide risk screening were more likely to be younger, male, and non-Hispanic White compared to patients accepting screening. Declining screening was more common at initial screening compared to screening at subsequent annual visits. There was variation in the prevalence of screen declines by clinic location within the institution. In adjusted models, patients aged 9–11 years were four times more likely (RR 4.2, 95% CI 3.7 – 4.7) to decline screening as compared to patients aged 18–26 years, adjusted for sex, need for interpreter, visit year, maximum number of screen-eligible visits, and clinic location.

Conclusion: Demographic and clinic characteristics appear related to patient decisions to decline universal suicide risk screening in pediatric ambulatory care subspecialty clinics. Understanding factors contributing to patient participation in universal suicide risk screening may inform institutional policies and procedures to maximize screening participation and ultimately ensure patient safety.

Perinatal & Pediatric

Individualized Growth Assessment Compared to Conventional Growth Charts for Detecting Growth-Related Morbidity Sarah Thornburgh* Sarah Thornburgh Madeline St. Ville Elizabeth Williams Zhen Chen Jessica Gleason Dian He Roger Newman Edward Chien William Grobman Daniel Skupski Angela Ranzini Anthony Sciscione Wesley Lee Jagteshwar Grewal Cuilin Zhang Fasil Tekola-Ayele Katherine Grantz

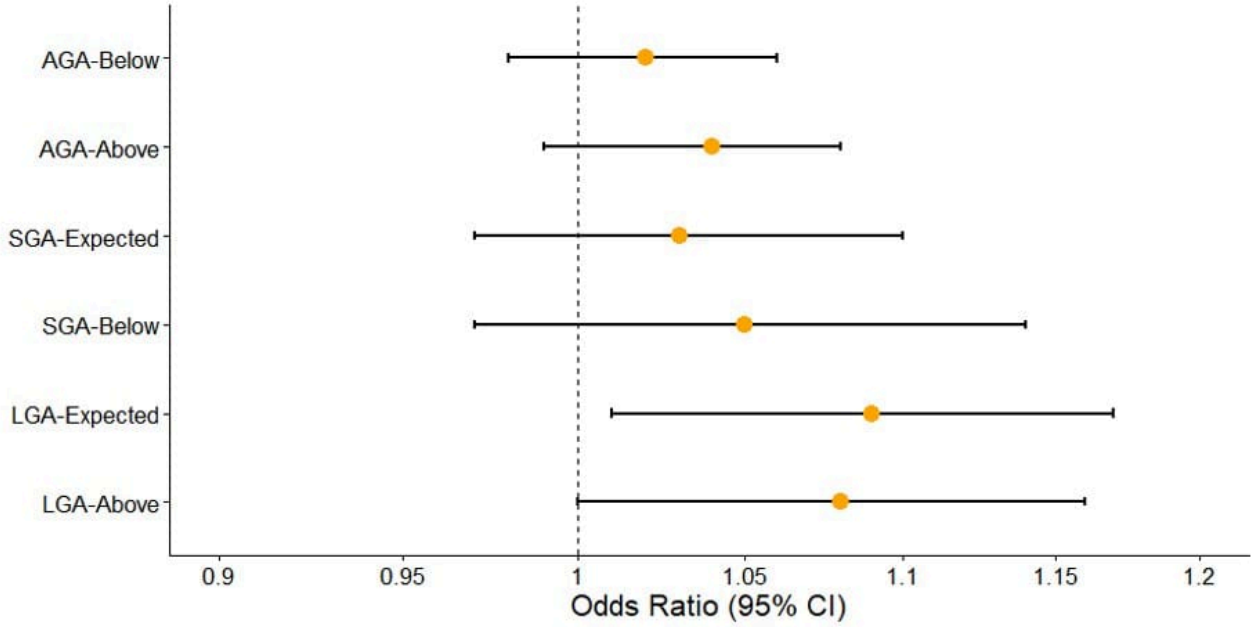
Individualized growth assessment (IGA) evaluates growth adequacy using each fetus as its own control. It is unclear whether IGA improves the ability to distinguish pathological fetal growth from constitutional small or large-for-gestational-age (SGA or LGA).

In a prospective cohort of 2,310 women with fetal measurements at up to 5 visits, we calculated estimated fetal weight (EFW) from 5,915 third trimester (3T) sonograms. EFW was categorized at each 3T scan by 2 methods: 1st as SGA, <10th; AGA, 10th-90th; or LGA, >90th percentile using NICHD unified growth charts; and 2nd by IGA which uses two second trimester scans and the Rossavik Growth Model to predict 3T growth potential and categorized each 3T scan as at, below, or above, expected growth potential. We compared categorization concordance, and predictive accuracy for composite neonatal morbidity/mortality (Fig legend). Logistic regression via GEE calculated odds of neonatal morbidity by discordant group (reference AGA-expected concordant group).

4,761 scans (80.5%) were categorized as AGA, 9.3% SGA, and 10.2% LGA using NICHD growth charts and 81.4%, 7.4%, and 11.2% at, below, or above expected using IGA. Among AGA, neonatal morbidity was 9.6% vs. 5.6% (p= 0.005) for above vs. expected by IGA, and 6.4% vs. 5.6% (p= 0.62) for below vs. expected. Among SGA, 9.2% vs. 6.6% (p= 0.26) for below vs. expected by IGA. Among LGA 8.8% vs. 10.3% (p= 0.54) for above vs. expected by IGA. Risk of composite neonatal morbidity/mortality was increased only for LGA-Expected, although LGA-Above had similar magnitude, but was statistically insignificant (Fig).

Evidence suggests IGA may improve detection of growth-related morbidity among smaller fetuses, but there was no improvement in our low-risk sample. Among larger fetuses, IGA may be less effective, as large size is an independent morbidity risk factor, e.g. birth injuries. Future comparisons should focus on high-risk pregnancies that may benefit most from improved detection.

Figure. Odds Ratios[a] of Composite[b] Neonatal Morbidity and Mortality by Discordant Group



[a]AGA-Expected used as referent group.

[b]A medical record indicating any of the following neonate outcomes was classified as a case of neonatal morbidity or mortality: neonatal intensive care unit (NICU) stay longer than 3 days, metabolic acidosis, pneumonia, respiratory distress syndrome, persistent pulmonary hypertension, seizures, hyperbilirubinemia, intrapartum aspiration, miscarriage/stillbirth, neonatal death, mechanical ventilation, hypoglycemia, sepsis, or birth injury.

Perinatal & Pediatric

Racial and Rural Disparities in Hybrid Prenatal and Postpartum Care Use During the COVID-19 Pandemic Taylor Lange* Andrew Williams Taylor Lange Rylie Fode Jaksen Perrin

Background: Disparities in access to prenatal and postpartum care in the US are persistent. COVID-19 accelerated telehealth adoption for perinatal care, but uptake varied, with racially minoritized and rural populations facing barriers like limited provider access and poor broadband. This study examines how telehealth prenatal and postpartum care use during COVID-19 in the US varied across race/ethnicity and rurality.

Methods: Analysis included 2020-2021 PRAMS participants completing the COVID-19 Supplement (weighted n=465,983). Participants reported care modality (in-person, hybrid telehealth/in-person, no care). Urban counties were Metropolitan Statistical Areas; rural counties were non-Metropolitan. Race/ethnicity was self-reported as AI/AN, Hispanic, White, Black, and Other. Logistic regression models estimated odds ratios for telehealth use among minoritized groups versus White women, stratified by rurality and adjusted for demographic and health factors.

Results: Telehealth use and access to care varied by race/ethnicity, and geography. Rural patients had 39–43% lower odds of telehealth use than urban patients, with racially minoritized rural patients often faring worse than rural White patients. Compared to White patients, Black and Hispanic patients were less likely to receive no prenatal care but more likely to lack postpartum care. Racially minoritized groups had elevated odds of no postpartum care. Rural residence amplified racial disparities in both telehealth use and care access.

Conclusion: Findings reveal persistent racial/ethnic and rural disparities in hybrid perinatal care access, especially pronounced postpartum. Also, racialized minorities in rural areas faced increased odds of no care. Results emphasize need for policies and rural health infrastructure improvements to address perinatal care gaps.

Perinatal & Pediatric

Examining Sleep Problems as a Mediator Linking Prenatal Phthalate Exposure to Executive Function in Middle Childhood Joana Amankwaa* Joana Amankwaa Stephanie Engel Amanda Ramos

Prenatal phthalate exposure has been linked to poorer executive function (EF) skills in children. However, mechanisms underlying these associations remain unclear. Sleep is a biologically plausible pathway as evidence suggests that phthalates may disrupt hormonal systems involved in sleep regulation which could contribute to sleep disruption and, in turn, poorer EF. Using data from the Mount Sinai Children's Environmental Health Study, we examined whether child sleep mediates the relationship between prenatal phthalate exposure and EF in middle childhood.

This sample includes 404 mother–child dyads with the analytic sample including 87 children with complete data on phthalate exposure, sleep, and EF. Prenatal exposure was assessed using maternal spot urine samples collected between 25 and 40 weeks' gestation and composite log scores were created for low molecular weight (LMW) and high molecular weight (HMW) phthalates. Child sleep at age 4 was assessed using caregiver-reported Pediatric Sleep Questionnaire items. EF was measured between ages 6-9 using the Behavior Rating Inventory of Executive Function (BRIEF). For children with EF data at multiple waves, the oldest available BRIEF assessment was used, resulting in a single EF score per child. Analyses controlled for creatinine, race, sex, marital status, gestational age, smoking during pregnancy, education, and bedroom sharing.

Across separate LMW and HMW models, prenatal phthalate exposures were not associated with sleep duration (LMW ß = 0.01, 95% CI [−0.17, 0.18]; HMW ß = 0.03, 95% CI [−0.16, 0.21]) or daytime sleepiness (LMW ß = 0.01, 95% CI [−0.04, 0.05]; HMW ß = −0.02, 95% CI [−0.06, 0.02]). Only daytime sleepiness was associated with poorer EF in the LMW and HMW models (β = 9.60, 95% CI [2.93, 16.46] and β = 9.40, 95% CI [2.72, 16.40], respectively). Finally, no significant indirect effects were found.

Overall, prenatal phthalate exposure was not associated with child sleep problems, and sleep problems did not mediate associations between phthalates and EF. However, the association of daytime sleepiness with poorer EF underscores a potentially important indicator of neurodevelopmental vulnerability. Further investigation will look to identify specific EF domains that might be more strongly impacted compared to the global composite.

Perinatal & Pediatric

Ethnic Enclaves and Gestational Diabetes Risk Across Asian American Ethnic Groups: A Population-Based Study Clara Voong* Clara Voong Yeyi Zhu Rana Chehab Barbara Laraia Salma Shariff-Marco Amanda Ngo Assiamira Ferrara Liwei Chen

Background: Asian American (AA) individuals experience the highest rate of gestational diabetes (GDM) with substantial variation across ethnic groups. Ethnic enclaves, areas concentrated with residents sharing an ethnic background, reflect social influences on health, yet their role in GDM risk among diverse AA groups is unclear.

Objective: We examined the association of pre-pregnancy ethnic enclave residence and mobility with GDM risk among AA individuals overall and across five groups.

Methods: We conducted a population-based study of 82,609 pregnant AA individuals at Kaiser Permanente Northern California from 2011 to 2022. In the year before pregnancy, enclave residence was assessed using the census-tract level AA Ethnic Enclave Index linked to the longest-held address, while enclave mobility based on full residential history was categorized as non-enclave only, enclave-exit, enclave-entry, and enclave only. Using Poisson generalized estimating equations, we estimated adjusted relative risks (aRR) and 95% CI for GDM in association with AA enclave residence and mobility. Models were adjusted for sociodemographic and clinical covariates and stratified by ethnic group.

Results: Overall, 15% were diagnosed with GDM and 79% lived in AA enclaves. Enclave residence was associated with higher GDM risk (aRR 1.18; 95% CI 1.07-1.30). Chinese (1.17; 1.06-1.29) and Filipino (1.08; 1.00-1.16) enclave residents had higher GDM risk compared to non-residents, with no differences among Vietnamese, Indian, or Other groups. Compared to non-enclave only residents, enclave only residents had a higher GDM risk (1.19; 1.07-1.32), whereas enclave-exit and enclave-entry groups were not associated with GDM.

Conclusions: Among AA populations, enclave residents had higher GDM risk with variation across ethnic groups. Findings point to the potential importance of structural and contextual factors shaping GDM risk among AA communities and inform neighborhood-focused prevention strategies.

Perinatal & Pediatric

Being aWARE: engaging the community in development of a Web-based tool for Autism Research Anisha Singh* Anisha Singh Cindy P. Lawler Astrid C. Haugen Amanda E. Garton Vickie R. Walker Robyn Blain Katherine E. Pelch Anthony Hannani Andrea Chiger Jeremy Frye Wren Tracy Andrew A. Rooney

Background: The breadth and diversity of studies examining the role of nongenetic factors in autism spectrum disorder (ASD) resulted in a large and heterogeneous body of research. This motivated development of **a W**eb-based tool for **A**utism **R**esearch and the **E**nvironment (aWARE) to promote understanding of the state of science.

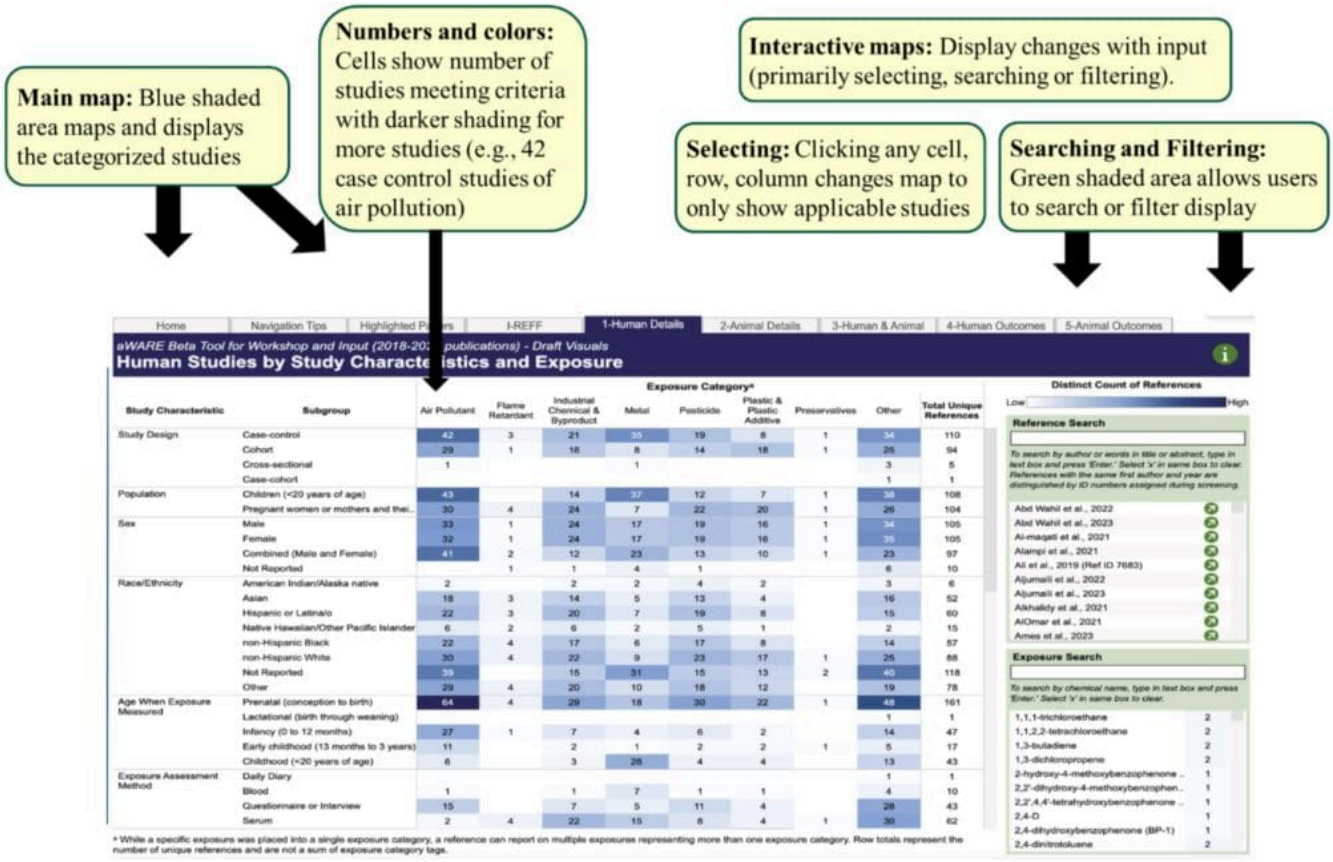
Objective: To identify and characterize published scientific research on early life environmental chemical and physical exposures and their association with ASD using a systematic evidence map (SEM) approach and interactive visualizations to make the information more findable and accessible. This project actively engages the broad autism community to shape relevance and uptake, representing a novel approach to community-informed evidence synthesis.

Methods: SEMs use the rigor and transparency of systematic review methodology to identify, categorize, and display data in an interactive visual format to aid synthesis and support evidence-based decisions. We searched PubMed, Scopus and Web of Science for studies of ASD-relevant outcomes and environmental exposures through September 2025. We engaged the wide autism community to inform our approach, including autistic individuals and families, advocacy groups, clinicians, and researchers through listening sessions, and a focused workshop to test the beta version of aWARE. We also conducted a qualitative analysis of community input.

Results: Over 150,003 studies were screened for relevance using DistillerSR software, and 1065 studies were included. Data were extracted with Dextr into aWARE's interactive evidence maps (figure 1) hosted on Tableau Public. Community engagement identified key themes, one of which highlighted the need for plain-language summaries to improve accessibility of existing evidence.

Conclusion: The aWARE tool is one of a kind in merging community engagement with evidence synthesis approaches, thus creating a valuable resource resonating with diverse perspectives.

Figure 1: An interactive evidence map from the aWARE tool displaying human studies by study characteristics and exposures



Perinatal & Pediatric

Comparing temporal trends and racial differences in child maltreatment identified in child protective services reports and hospital administrative data in California, 2005–2019 Sophia Horiuchi* Sophia Horiuchi Kriszta Farkas Susan Mason Jennifer Ahern Saron Goitom Corinne Riddell

Child maltreatment is often measured using Child Protective Services (CPS) reports, despite the potential for racial biases in reporting and changes in CPS policies and practices to spuriously influence demographic and temporal patterns. Hospitalizations and emergency department visits for injuries suggestive of maltreatment offer a complementary data source on serious health outcomes of maltreatment. We compared rates of child physical abuse and neglect identified in hospital data with CPS reports among children aged <5 years in California from 2005 to 2019.

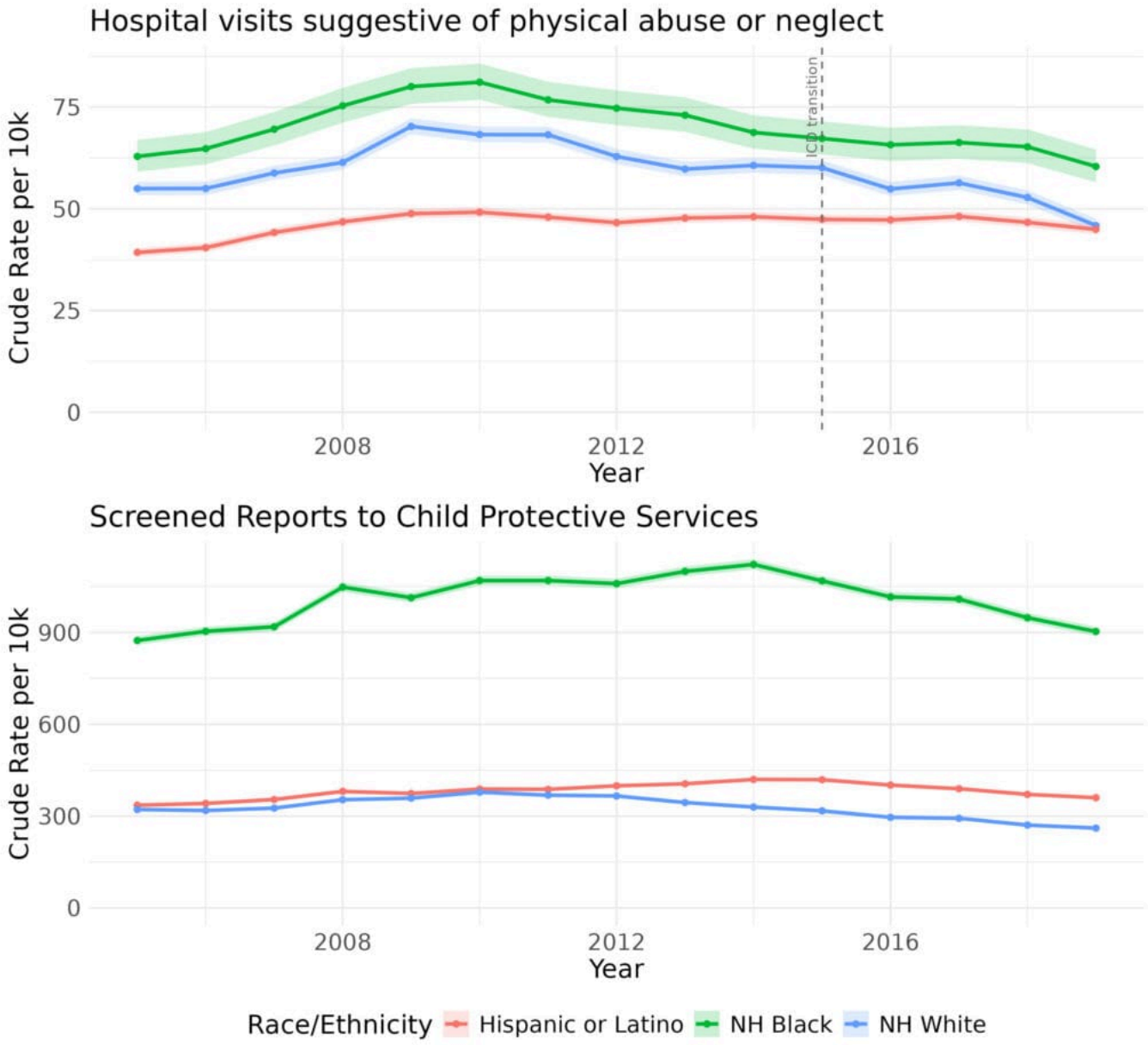
Hospital visits suggestive of physical abuse and neglect were identified using validated diagnosis codes in statewide hospital data from the California Department of Health Care Access and Information. CPS reports of physical abuse and neglect were obtained from the National Child Abuse and Neglect Data System. Annual statewide rates of physical abuse and neglect, separately and combined, were calculated using population estimates from the Surveillance, Epidemiology, and End Results Program. Patterns by race/ethnicity and time were compared across the two data sources.

Across both data sources, combined physical abuse and neglect rates (per 10,000 children) increased and then declined over time, with a later peak in CPS than hospital data. Hospital injury rates rose from 48.5 in 2005 to a peak of 58.8 in 2009, while CPS reporting rates increased from 368.7 in 2005 to a peak of 431.3 in 2014. Non-Hispanic Black children had higher rates than Non-Hispanic White children in both data sources, but with a much larger relative difference in CPS data.

Temporal and demographic maltreatment patterns differ when measured using CPS and hospital data, likely reflecting differences in the severity of cases and in how cases are identified. In addition to CPS outcomes, studies evaluating policies to prevent child maltreatment should examine effects on maltreatment-related injuries captured in hospital data.

Figure 1. Trends in physical abuse and neglect rates among children aged <5 years in California by data source and race/ethnicity, 2005–2019

Shaded areas indicate 95% confidence intervals



LATEBREAKER

Perinatal & Pediatric

Lamotrigine and Ventricular Arrhythmia among Children and Youth: A Target Trial Emulation Using National Claims Data from the United States Jiaxun Zhao* Jiaxun Zhao Jiaxun Zhao Kristen Lloyd Stephen Crystal Mark Olfson Eyal Shemesh Tobias Gerhard Brian L. Strom Benjamin Lentzner Greta Bushnell Daniel B. Horton

Lamotrigine (LTG), widely used for epilepsy and mental health disorders, acquired a cardiac safety warning from the US FDA in 2020 due to theoretical concerns for inducing ventricular arrhythmia (VA) in patients with cardiac disease, based primarily on in vitro studies. Recent epidemiologic evidence in adults suggests no increased risk of VA with LTG, but whether these findings extend to children and youth is unclear.

We emulated a hypothetical pragmatic trial using US national claims data (Jan 2001-Feb 2020). We included children and youth (2-24y) newly initiating LTG or oxcarbazepine (OXC) and followed them from drug initiation to the earliest of VA outcome (adapted from validated algorithm in children, PPV 95%), disenrollment, treatment discontinuation, comparator drug initiation, or Feb 29, 2020. We applied propensity score-based inverse probability of treatment weighting to adjust for 80 baseline covariates and used weighted Cox regression to estimate the adjusted HR with 95% CI.

We identified 515,065 LTG vs. 440,511 OXC new users. For LTG, depression was the most common indication (prior 30-day diagnosis) (26.7%), followed by bipolar disorder (22.9%), anxiety (16.6%), attention-deficit/hyperactivity disorder (ADHD) (15.5%), and epilepsy (10.0%). For OXC, it was ADHD (25.5%), followed by depression (17.1%), conduct disorder (16.4%), bipolar disorder (15.7%), and epilepsy (14.3%). During follow-up, 34 and 18 patients in the LTG vs. OXC group had VA (weighted incidence rate per 100,000 PY: 11.4 vs. 7.9; RD: 3.5; 95% CI, -2.7, 9.7). LTG showed a numerically higher rate of VA compared to OXC (HR: 1.41; 95% CI, 0.74, 2.69). Among those with cardiac disease, the estimated association was close to the null (HR: 0.95; 0.36, 2.49).

We did not see a clear increased risk of VA with LTG compared to OXC in children and youth, especially in those with pre-existing cardiac disease. Regardless, the absolute risk difference appears to be small overall for this rare outcome.


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Pharmacoepidemiology

Neighborhood Socioeconomic deprivation and Opioid Prescribing Trends Among Medicare Part D Clinicians: A Five-Year Longitudinal Analysis (2019–2023) Ashel Chelsea Dsouza* Ashel Dsouza Jill Goslinga Yim Sang Yu Simran Sandhu Anju Edasseri Lee A. Tan

Background: Geographic and socioeconomic disparities often drive variations in healthcare delivery. However, it remains unclear if neighborhood-level deprivation independently influences high-risk opioid prescribing among clinicians in pain-related specialties.

Objectives: To determine if the Area Deprivation Index (ADI) is associated with opioid prescribing rates and long-acting (LA) opioid use, and to evaluate if prescribing declines from 2019 to 2023 were uniform across socioeconomic gradients. To assess whether high opioid prescribing clusters with other high-risk drug classes across the ADI gradient.

Methods: A repeated cross-sectional analysis was conducted using 2019–2023 Medicare Part D prescriber data for clinicians (N=140,519) in pain-related specialties (orthopedics, pain medicine, physical medicine and rehabilitation, and primary care). Residential or practice addresses were geocoded using the U.S. Census Geocoder, with records successfully matched at the census block-group level linked to the Area Deprivation Index (ADI) via 11-digit block-group FIPS codes; addresses without valid block-group assignments or with ambiguous geocodes were excluded. Outcomes included overall opioid prescribing rates and the proportion of beneficiaries receiving long-acting opioid formulations. Models adjusted for beneficiary age, sex, race, disability, dual-eligibility, risk score, and urbanicity. High opioid prescribers were defined as those in the top quartile of opioid volume for a given year, and were compared with respect to high prescribing of antibiotics and antipsychotics.

Results: Adjusted opioid prescribing rates declined steadily from 2019 to 2023; compared with 2019, rates were 4.1% lower in 2020, 4.6% lower in 2021, 10.8% lower in 2022, and 14.5% lower in 2023, with no statistically significant difference in the magnitude of decline across ADI quintiles (p for interaction = 0.09).

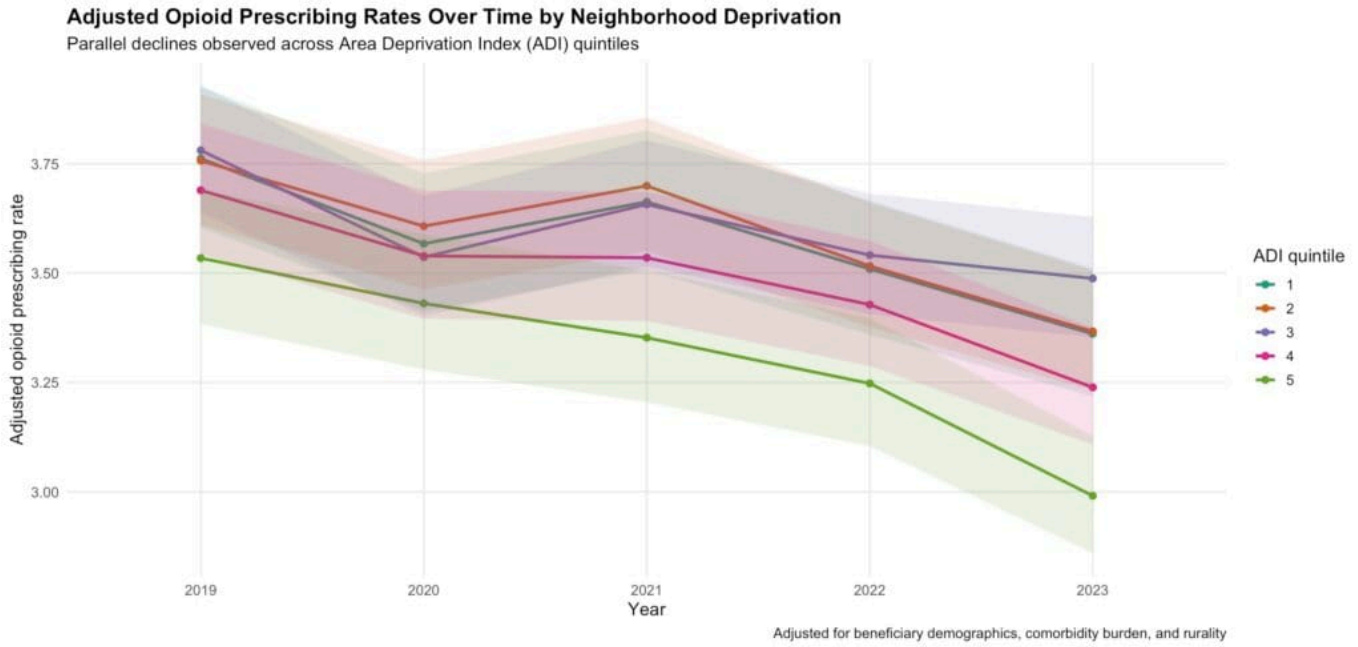
Across all years, higher neighborhood deprivation was associated with slightly lower opioid prescribing. A 10-point increase in ADI was associated with a 1.24% decrease in opioid prescribing rate (95% CI, 1.86%–0.62% decrease; $p<0.001$). The adjusted proportion of beneficiaries receiving long-acting opioids declined from 7.28% at the 10th percentile of ADI to 5.56% at the 90th percentile (1.72 percentage-point absolute and ~24% relative reduction; $p<0.001$ across the ADI gradient).

Within individual specialties, ADI associations were attenuated and not statistically significant, consistent with reduced power and control for between-specialty practice differences.

High opioid prescribers were more likely to also be high prescribers of antibiotics (27.6% vs 20.3%) and antipsychotics (21.9% vs 9.9%), with clustering most pronounced in deprived neighborhoods; in the highest ADI quintile, the adjusted probability of high antipsychotic prescribing among high opioid prescribers was 34.8% versus 12.5% among other prescribers (p for interaction<0.001).

Conclusions: Among Medicare Part D clinicians in pain-related specialties higher neighborhood deprivation was associated with lower rates of long-acting opioid prescribing, suggesting

under-treatment or access barriers in deprived areas rather than excess high-risk opioid prescribing, while concentrated multi-drug high-risk prescribing in these neighborhoods highlights priority targets for intervention.



LATEBREAKER

Pharmacoepidemiology

Externally-derived algorithms to impute missing data may be biased even under MCAR

Amarnath Marthi* Amarnath Marthi Michele Jonsson Funk Jess Edwards Paul N Zivich

Administrative claims data often lack key information (e.g. laboratory results) needed for pharmacoepidemiologic analysis. Linkage to other data sources (e.g. electronic health records), can address this limitation but introduces data that may be missing not at random (MNAR). Alternatively, claims-based prediction models developed in external data can be used to 'impute' missing variables. We sought to evaluate the assumptions of these approaches with a Monte Carlo simulation.

A continuous variable, Y, was generated using two binary variables W (observed) and U (unobserved) in both primary (M) and external (N) datasets under the same data generating process. A linear model for Y using only W was fit in the external data and applied to the primary data to obtain fused predictions via G-computation. We induced 30% missingness for Y in the primary data: (1) randomly (i.e., MCAR); (2) dependent on W (i.e., MAR); and (3) dependent on U and W (i.e., MNAR). To examine the effect of population differences we varied the distributions of W and U across the primary and external datasets. We compared the complete case analysis means and fused means to the true mean across mechanisms. Bias, empirical standard error and root mean squared error were assessed.

When the primary and external data sets are fully exchangeable, the fused mean was unbiased under MCAR, MAR and MNAR. This is preserved when the data sources differ only on observed W. Where data sources differ by unobserved predictors, fused means were biased under all three missingness mechanisms.

External data fusion can mitigate bias due to MNAR, under alternative assumptions of (conditional) exchangeability of primary and external data on observed predictors. Externally-derived algorithms can introduce bias if these assumptions are not met or with model misspecification. These transportability assumptions are implicitly made when using externally-derived algorithms to impute missing data in epidemiology studies.

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Pharmacoepidemiology

Psychiatric Co-prescribing and Prescribing Characteristics of Older Adults Initiated on Sertraline, Citalopram, or Mirtazapine in Clinical Practice Research Datalink Aurum: Descriptive Analyses to Inform a Causal Study Design Aaron Jun Yi Yap* Aaron Jun Yi Yap Aws Sadik Dheeraj Rai Eleanor Sanderson Deborah McCahon Paul Madley-Dowd

Antidepressants, antipsychotics, benzodiazepines and Z-hypnotics are commonly prescribed to treat depression and anxiety; however, polypharmacy of these medications have been associated with increase risks of falls, fractures and cardiovascular events in older adults. Challenges of designing pharmacoepidemiological observational studies examining safety of polypharmacy using electronic health records are (1) specifying sufficiently-well defined interventions where switching and combination use are prevalent, (2) identifying suitable time (grace) periods to apply methodological approaches to reduce time-related biases, and (3) understanding the completeness of indication-based sampling. We aimed to describe in detail prescription and co-prescribing characteristics of adults aged 50 years and above who are initiated on Sertraline, Citalopram or Mirtazapine in GP surgery practices in England registered with Clinical Practice Research Datalink Aurum between 1 January 2010 to 31 March 2023. The outcomes are: (1) proportion of prevalent and new users of Sertraline, Citalopram and Mirtazapine, (2) time to first prescription of a second antidepressant, (3) proportion with coded evidence of depression and/or anxiety, (4) starting dose of Sertraline, Citalopram and Mirtazapine and time to first increase in dose, (5) proportion with co-prescriptions of antidepressants, antipsychotics, benzodiazepines and Z-hypnotics, and (6) average initiation gap and treatment duration of combination therapy for each drug-class pair. Data analysis is underway and will enhance understanding of the feasibility of studying drug combinations. We anticipate discussing applications of findings to the target trial framework.

Pharmacoepidemiology

National Trends and Correlates of National Trends in Psychoactive Prescription Medication Misuse, 2021–2023 Oluwapelumi Odubunmi* Oluwapelumi Odubunmi Adedapo Ogunlewe Barnabas Odeyemi Munachimso Emesobum

Background: Surveillance of prescription drug misuse in the United States has primarily focused on opioids, despite widespread prescribing and misuse potential of other psychoactive medications such as stimulants, benzodiazepines, and sedatives. Whether misuse of these medications shifted in the post-COVID period, and whether patterns align more closely with behavioral risk or healthcare access mechanisms, remains unclear.

Methods: We analyzed pooled 2021–2023 National Survey on Drug Use and Health (NSDUH) data (N=173,808). Past-year misuse of prescription stimulants, benzodiazepines, sedatives, and pain relievers was defined as nonmedical use. Survey-weighted prevalence estimates and multivariable survey logistic regression models assessed associations with time (continuous year), age (12–17, 18–25, ≥26), sex, race/ethnicity, and insurance status, accounting for survey design.

Results: Prevalence of misuse was 1.41% for stimulants, 1.46% for benzodiazepines, 0.33% for sedatives, and 3.02% for pain relievers. From 2021–2023, stimulant misuse declined modestly (OR=0.82; 95% CI: 0.67–1.02) and benzodiazepine misuse trended downward (OR=0.69; 95% CI: 0.47–1.01), while sedative (OR=1.14; 95% CI: 0.67–1.96) and pain reliever misuse (OR=0.99; 95% CI: 0.86–1.14) remained stable. Misuse was strongly patterned by age, with substantially lower odds among adolescents and young adults compared with older adults ($p<0.01$ across outcomes). Variations by race/ethnicity and insurance status were observed, suggesting access-driven rather than purely behavioral mechanisms.

Conclusions: Misuse of psychoactive prescription medications remained stable in the United States during 2021–2023, despite heightened attention to mental health and medication use in the post-COVID period. Age and insurance gradients indicate that misuse may reflect prescribing opportunity and healthcare access. Integrating non-opioid psychoactive medications into pharmacoepidemiologic surveillance frameworks may improve prevention, equity monitoring, and behavioral health policy assessment.

Reproductive

Menstrual and reproductive outcomes in women whose mothers were exposed in utero to diethylstilbestrol (DES): An updated report from the National Cancer Institute (NCI) DES Third Generation Study Stephanie Ho* Stephanie Ho Paloma Mitra Linda Titus Kimberly Bertrand Shaoqi Fan Marianne Hyer Dezheng Huo William Strohsnitter Kjersti Aagaard Ruth Pfeiffer Rebecca Troisi Gretchen Gierach

Background

Diethylstilbestrol (DES), a human carcinogen, was used from the 1940s-70s for women at risk of miscarriage. Adverse health effects have been well documented in women who were given DES during pregnancy and their exposed children. Within the NCI DES Third Generation Study, we followed daughters of prenatally exposed and unexposed women to study menstrual and reproductive outcomes in the third generation.

Methods

In 2000, daughters of women who were prenatally exposed or unexposed to DES in the U.S. were identified through their mothers' parity records; daughters were eligible for study enrollment at age 18. Baseline (n=964 exposed, 529 unexposed) and up to 2 follow-up questionnaires (n=839 exposed, 585 unexposed) were administered from 2001-2019. We estimated prevalence ratios (PRs) and 95% CIs for menstrual and reproductive outcomes associated with DES exposure by age groups (18-<20;20-<30;30-<40;40-<50;50-59), using log-binomial regression models. Repeated questionnaires from the same woman were accommodated via a robust variance estimate.

Results

Compared with daughters of unexposed women, daughters of prenatally DES-exposed women had increased prevalence of irregular menstrual cycles, notably at age 18-<20 (PR=1.82, 95% CI:1.05-3.15). Among women age 20-<30, DES exposure was associated with decreased prevalence of ever being pregnant (PR=0.81, 95% CI:0.67-0.99). Among women age 30-<40, DES exposure was related to increased prevalence of amenorrhea, defined as lack of menstruation for >6 weeks (PR=1.29, 95% CI:1.03-1.61).

Conclusions

Continued follow-up of women whose mothers were prenatally exposed to DES suggests they may be at an increased risk for adverse menstrual outcomes. Decreased pregnancy prevalence in exposed women may signal an effect of DES on infertility; analyses with more direct measures of infertility are ongoing. We plan to study the association of DES and menopause and whether effects differ by DES dose.

Respiratory

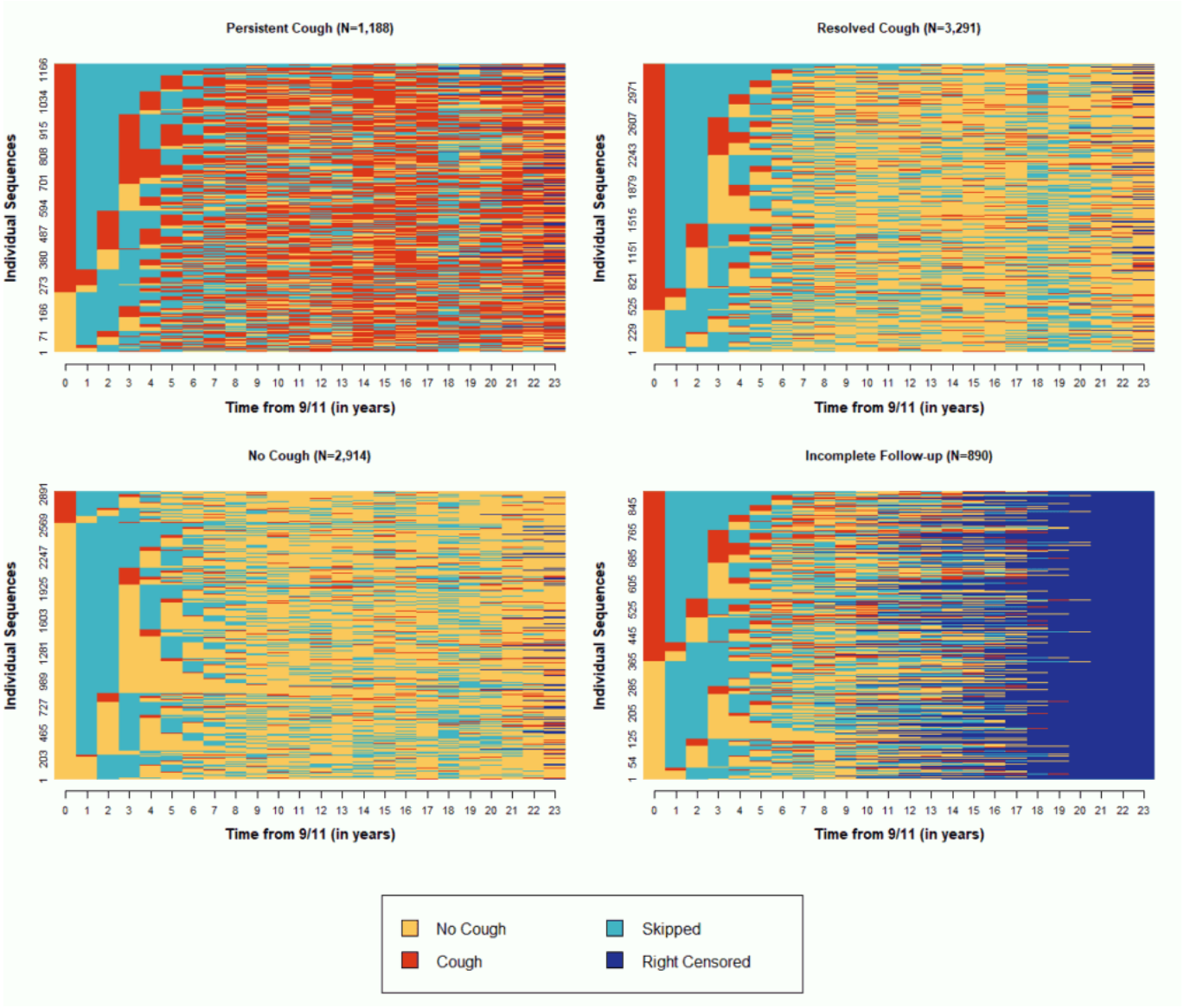
Heterogeneity in World Trade Center-related cough: a 24-year sequence analysis approach
Alexandra Mueller* Alexandra Mueller Rachel Zeig-Owens David Goldfarb David Prezant

Introduction: Nearly 25 years after the World Trade Center (WTC) disaster on 9/11/2001, WTC Cough directly following seems to mostly resolve within a few years. Based on 2024 reports, cough point prevalence is ~8%. However, analyzing this group as a whole may obscure heterogeneity in the timing or persistence of cough outcomes. We characterized underlying patterns of cough trajectories in New York City Fire Department (FDNY) WTC-exposed rescue/recovery workers over 24 years.

Methods: We studied FDNY WTC-exposed responders who completed ≥5 health surveys between 10/2001-9/10/2025, with the first occurring within 1 year of 9/11. Participants answered if they had a cough (present/absent) in the past year unrelated to illness. Sequence analysis characterized longitudinal sequences of cough trajectories. Missing responses were retained. Hierarchical cluster analysis grouped participants with similar trajectories. We measured forced expiratory volume in 1 second % predicted (FEV1%). Diagnoses were obtained from medical records.

Results: In 8,283 people, we identified that 4 distinct clusters best fit the data: Persistent Cough (PC) (14%), Resolved Cough (RC) (40%), No Cough (NC) (35%), and Incomplete Follow-up (IFU) (11%). PC reported cough frequently throughout the study period; RC reported cough at their first exams in 2001-2002 but not often later; NC rarely reported cough; IFU was characterized by shorter follow-up time. 82% of PC had gastroesophageal reflux disease (GERD) compared with 62% of RC and 53% of NC. PC and RC had similar FEV1%, WTC arrival times, BMI, smoking status, and age.

Conclusion: Sequence analysis revealed four distinct cough trajectories over 23 years. While most had no or resolved cough, 14% had persistent cough. Similar WTC exposure timing, smoking, BMI, and, importantly, FEV1% across PC and RC clusters suggest that persistent cough in this cohort may be more related to comorbidities, including GERD which has a known association with chronic cough.


Persistent Cough (N=1,188)
Resolved Cough (N=3,291)
No Cough (N=2,914)
Incomplete Follow-up (N=890)
Individual Sequences
Time from 9/11 (in years)
No Cough
Cough
Skipped
Right Censored

Respiratory

The impact of early childhood growth trajectories on the subsequent risk of developing tuberculosis disease Alick Sixpence* Alick Sixpence Liz Goddard Maresa Botha Mark Nicol Lesley Workman Heather Zar Leonardo Martinez

Background

Undernutrition, measured through low body mass index, is a well-established risk factor for tuberculosis in adults. Whether undernourished children are also at greater risk of tuberculosis is unknown.

Methods

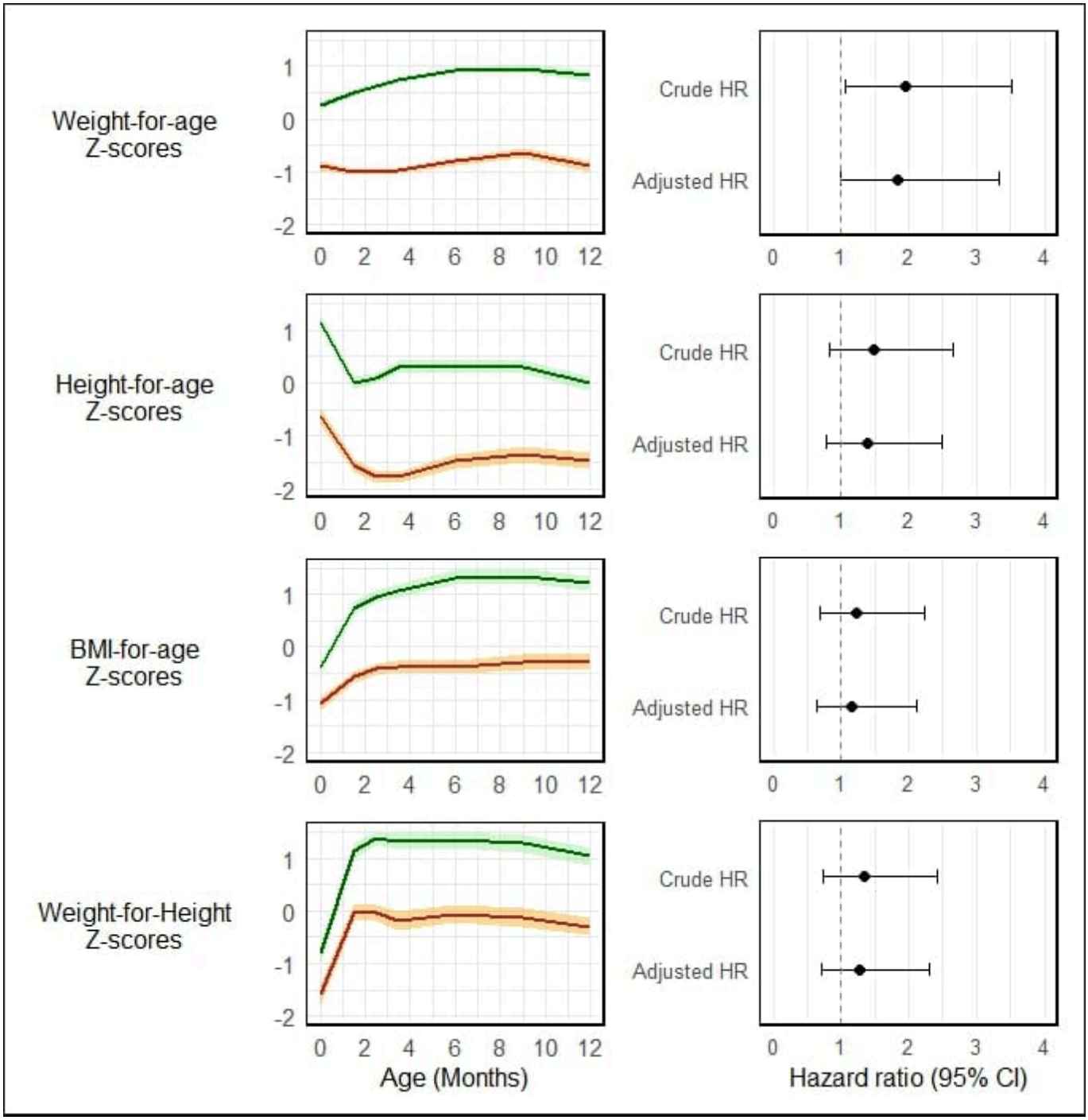
We followed HIV-uninfected children from birth to age 10 years in the Drakenstein Child Health Study, a South African birth cohort. Anthropometric measurements were collected at birth, 6, 10 and 14 weeks, and at 6, 9 and 12 months. Using WHO child growth standards, we calculated Z-scores for weight-for-age (WAZ), height-for-age (HAZ), body-mass-index-for-age (BMIZ), and weight-for-height (WFHZ). We used group-based trajectory modelling to classify growth trajectory groups for children with >2 measurements. The outcome was time to tuberculosis diagnosis between ages 1 to 10 years. Cox proportional hazards regression models were used to estimate hazard ratios comparing tuberculosis risk between children in differing growth trajectory groups.

Results

Among 940 children included, 12-month trajectories found two distinct groups for each anthropometric measure (Figure), characterized by ‘high’ (healthy growth) and ‘low’ (poor growth) longitudinal patterns. There were 46 tuberculosis events from 1–10 years, an incidence of 617 cases per 100,000 person-years. Children were at increased tuberculosis risk if they were in lower WAZ (HR, 1.94; 95% CI, 1.07 – 3.53) or HAZ (1.48; 0.83 – 2.66) trajectory groups. There was no differential tuberculosis risk in relation to early-life BMIZ and WFHZ growth. There was no modification of risk by sex although we were limited by statistical power. Altering trajectories to the first 14 weeks of life demonstrated broadly similar results.

Conclusion

Early growth deficits in WAZ were strongly associated with increased tuberculosis risk.


Weight-for-age Z-scores
Height-for-age Z-scores
BMI-for-age Z-scores
Weight-for-Height Z-scores
Crude HR
Adjusted HR
1
0
-1
-2
0 2 4 6 8 10 12
0 1 2 3 4
Age (Months)
Hazard ratio (95% CI)

Screening

Addressing the immigrant screening gap: A systematic review on interventions to increase colorectal cancer screening among immigrants in the United States Ethan Cohen* Taylor McCready Audrey Renson

Introduction

Interventions to increase colorectal cancer (CRC) screening among US immigrants are increasing, but a rigorous systematic review has not been conducted. Definitions of immigrant and screening outcomes vary widely, limiting synthesis and transportability.

Methods
We searched English-language peer-reviewed and grey literature (January 1, 2000 and April 30, 2025) in PubMed, Cochrane Library, CINAHL (EBSCO), ClinicalTrials.gov, Embase, Scopus, and Web of Science. Two reviewers independently screened and extracted data in Covidence. Risk of bias was assessed using the Risk of Bias 2 (ROB2) tool for randomized controlled trials, and the Risk of Bias in Non-Randomized Studies of Interventions (ROBINS-I) tool for other study designs. Quantitative synthesis was restricted to studies explicitly defining immigrants in the analytic population (PROSPERO: CRD42023488183).

Results
The primary outcome was CRC screening completion. Of 1,824 unique records, 45 studies were included (39 randomized trials, 6 non-randomized), totaling > 21,000 participants. Individualized education (n=12), navigation-based interventions (n=17; including patient navigation alone and navigation plus culturally targeted materials), and non-individualized educational campaigns (n=7) were the most evaluated strategies, alongside mailed and telephone outreach with fecal tests (n=4). Among trials reporting screening outcomes in intervention and control arms (n=19), interventions increased screening by an average of 20% versus control, with culturally tailored navigation-based approaches generally yielding the largest gains. Heterogeneity in immigrant definitions, settings, and outcomes limited cross-population comparisons and precluded a meta-analysis.

Conclusion
Tailored navigation is the most consistently effective approach, but inconsistent measurement of immigrant status and screening outcomes limit transportable inference; standardization is a priority for future trials and evidence synthesis.

Social

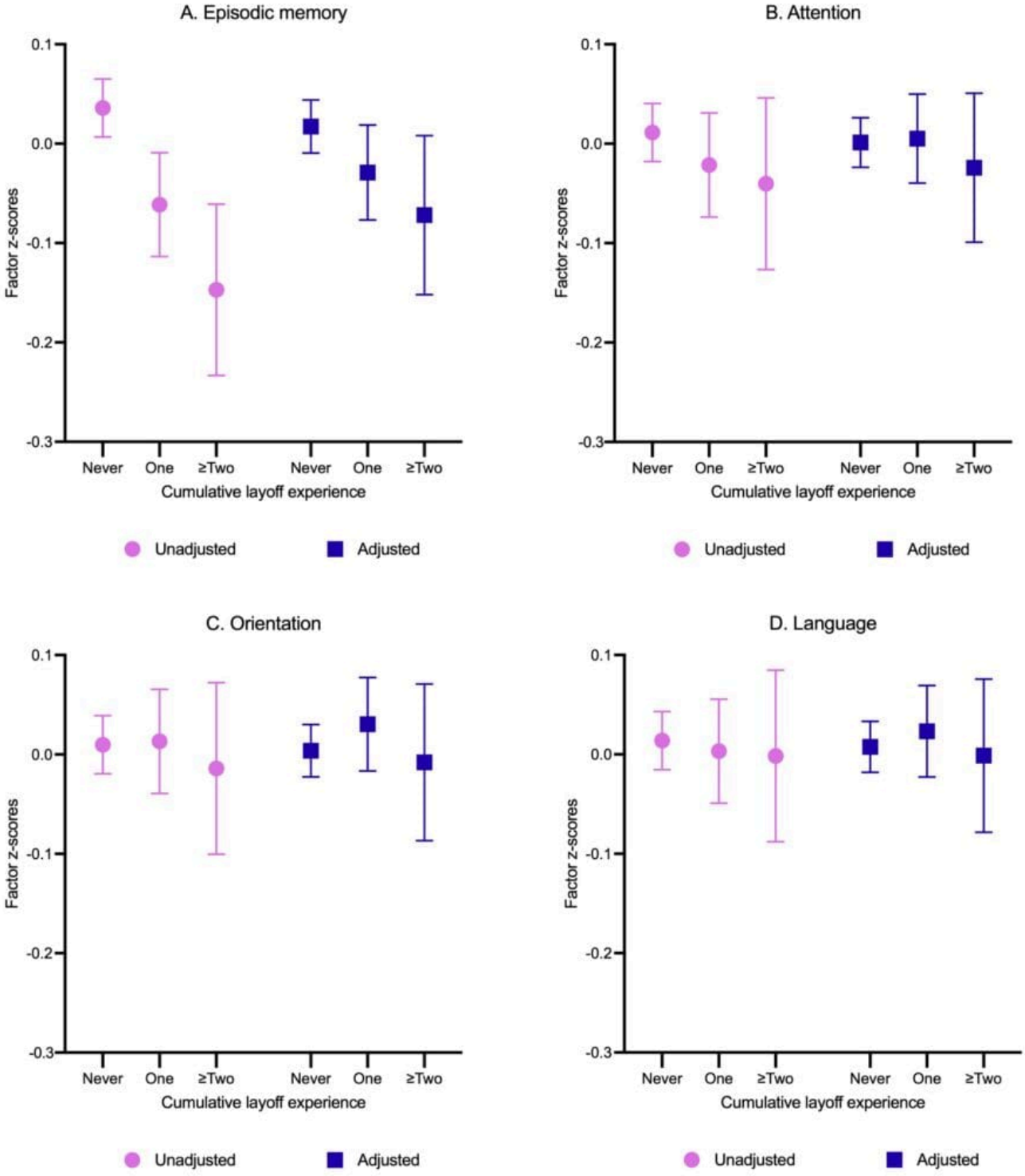
Cumulative layoffs in adulthood and cognitive function in mid-to-later life among US working-age adults, 1979-2020 Xuexin Yu* Xuexin Yu Katrina L Kezios Antonio J Bustillo Martine Elbejjani Allison E. Aiello Adina Zeki Al Hazzouri

OBJECTIVE As one of the most disruptive life events, layoffs are pervasive in the US labor market, while little is known about the neurological consequences of cumulative layoff experience across adulthood. We examined the association between cumulative layoff experience spanning up to 41 years of adulthood and subsequent cognitive function in mid-to-later life.

METHODS Data were from 6,421 adults in the US National Longitudinal Survey of Youth 1979. Cumulative layoff experience, defined as the number of jobs ending in a layoff from 1979 to 2020 (age 15-63), was categorized as never (n = 4,503), one layoff (n = 1,402), and ≥two layoffs (n = 516). Latent factor scores in episodic memory, attention, orientation, and language domains in 2020 (age 56-63) were estimated using confirmatory factor analysis. Multivariable-adjusted linear regression models were used to estimate associations of interest.

RESULTS Mean age at baseline was 20 years (SD=2.8), and 53% were women. A higher frequency of layoffs was associated with lower latent factor scores in episodic memory (β = -0.046, 95% CI: -0.101 to 0.009, one layoff vs. never; β = -0.089, 95% CI: -0.174 to -0.004, ≥two layoffs vs. never; P trend = 0.030), but not in attention, orientation, or language domains. The observed association did not vary by timing of layoff exposure, sex/gender, or race/ethnicity.

CONCLUSION Given its ubiquity in the US labor market, layoffs may represent an important and understudied risk factor for episodic memory function among US adults.


A. Episodic memory
B. Attention
C. Orientation
D. Language
Factor z-scores
0.1
0.0
-0.1
-0.2
-0.3
Never
One
≥Two
Never
One
≥Two
Cumulative layoff experience
Unadjusted
Adjusted

Social

Library Use and Functional Disability, Dementia, and Mortality Among Older Adults in Japan: An Instrumental Variable Analysis Qiuyi Liu* Qiuyi Liu Koryu Sato Daisuke Takagi Yuina Saiga Masamichi Hanazato Yoko Matsuoka Hiroshi Habu Naoki Kondo

Background

Cultural participation has been increasingly recognized as a determinant of health in later life, yet causal evidence remains relatively limited, in part due to self-selection and unmeasured confounding. Libraries represent widely accessible cultural facilities that support reading, learning, and social engagement, but their potential health effects have rarely been evaluated using causal inference methods.

Objective

To estimate the causal effect of library use on the incidence of dementia, functional disability, and mortality among older adults in Japan.

Methods

We conducted a prospective cohort study using data from the Japan Gerontological Evaluation Study (JAGES) 2019–2022, including101,815community-dwelling adults aged 65 years and older without baseline functional disability or dementia. Frequency of library use was self-reported at baseline and converted into an approximate monthly visit measure. Incident functional disability, dementia, and all-cause mortality were ascertained through linkage with national long-term care insurance and resident registries. To address endogeneity in library use, we applied an instrumental variable approach using network-based geographic distance from each participant’s residence to the nearest library as the instrument. We applied the two-stage residual inclusion (2SRI) instrumental-variable framework to Cox proportional hazards models and Aalen’s additive hazards models. All models were adjusted for age, gender, educational background, marital status, household income, employment status, and population density.

Results

We observed 11,412 (11.20%) functional disability, 5,164 (5.07%) dementia, and 5,540 (5.44%) deaths. In the IV Cox model, each additional monthly visit to the library was associated with a 0.56 times risk of dementia (HR = 0.56, 95%CI: 0.34-0.90). In the additive hazards model, the hazard difference was −0.015 per person-year (95% CI: −0.023 to −0.006), corresponding to 150 fewer cases per 10,000 person-years. Point estimates indicated the association of library use with decreased risks of functional disability and mortality, but their confidence intervals were wide.

Conclusions

Using geographic accessibility to libraries as an instrument, this study provides causal evidence that engagement with libraries may contribute to healthier aging among older adults, particularly by reducing dementia risk. Libraries may function as community-level cultural resources with potential relevance for population aging and health policy.

Social

Social Isolation and Mortality in the UK Biobank: The Modifying Role of Transportation Mode Hiroshi Mamiya* Emily Hum Hiroshi Mamiya Jill Baumgartner Kevin Manaugh

Background: Social isolation is an established risk factor for chronic disease and mortality and has reached epidemic levels in many high-income countries. Daily transportation modes (e.g., active and public transport, car use) may mitigate the harmful impacts of social isolation by facilitating social interaction. This study aimed to assess the role of transportation mode as an effect modifier in the association between social isolation and mortality among adults using the UK Biobank.

Methods: We analyzed cohort data from 450,032 UK Biobank participants aged 40-69 years, followed from 2006 to 2022. Baseline social isolation was derived from a three-item index and dichotomized. We used Cox models to estimate the associations between social isolation and mortality outcomes (all-cause and cause-specific), adjusting for socioeconomic factors, health behaviours, and comorbidities. Effect modification by participants' primary mode of transportation was assessed using interaction terms.

Results: Social isolation was associated with increased hazard of all-cause (Hazard ratio [HR] = 1.33, 95% CI: 1.30-1.36), cardiovascular (HR = 1.45, CI: 1.37-1.53), and cancer mortality (HR = 1.22, CI: 1.17-1.27). Associations with all-cause and cardiovascular mortality were stronger among participants who only used public transport compared with those who only used a car (interaction HR = 1.08, CI: 1.00-1.18; interaction HR = 1.22, CI: 1.03-1.45, respectively). In contrast, using a car alongside active or public transport, compared to using a car alone, attenuated the association between social isolation and all-cause mortality (interaction HR = 0.92, CI: 0.87-0.99).

Conclusions: This is the first study to investigate the modifying role of transportation mode to reduce the harms of social isolation. Our findings motivate further exploration of public health strategies that support social connectivity by reducing motor vehicle dependency and improving public transport infrastructure.

Social

Examining Resilience Factors, Discrimination, and Comorbidity Severity Among Older Adults in the United States Isabella Tullio* Isabella Tullio Jee Won Park Aditya Chandel Yendelela Cuffee Jennifer Moss

Background: Discrimination contributes to a greater comorbidity burden among older adults. Resilience resources may buffer these effects and support adaptation to health challenges.

Objective: To examine associations between resilience factors and comorbidity burden, measured by the Charleston Comorbidity Index (CCI), among middle-aged and older adults, and to assess whether this relationship differed by experiences of age-, gender-, or race-based discrimination.

Methods: A total of 2,926 adults aged ≥50 years from seven mid-Atlantic states completed an online cross-sectional survey. Exposures included resilience (Brief Resilience Scale), self-efficacy, social support, trust in the medical profession, and social cohesion (high/moderate versus low). CCI was categorized as low (no/mild) or high (moderate/severe). Adjusted logistic regression models estimated the odds of high versus low CCI, and product terms assessed effect modification by discrimination type.

Results: Negative relationships between higher versus lower self-efficacy (adjusted OR = 0.91, 95% CI: 0.70–1.17), social support (0.89, 0.70–1.11), and resilience (0.79, 0.51–1.22), and higher CCI were most compatible with the data. Positive relationships were observed for trust in medical professions (1.13, 0.90-1.42) and social cohesion (1.15, 0.92-1.44). Our assessment for effect modification showed that race-based discrimination modified the association between self-efficacy and CCI (p = 0.003). Among those reporting race-based discrimination, high self-efficacy was associated with lower odds of high CCI (0.30, 0.14–0.65) while a null relationship among those with no race-based discrimination was most compatible (1.03, 0.78-1.35).

Conclusion: Our findings were mixed. However, self-efficacy may be beneficial among those experiencing race-based discrimination. Prospective studies on the role of resilience in mitigating negative impacts of discrimination in shaping health outcomes among older adults are needed.

Social

Multilevel Resilience Factors, Discrimination, and Physical and Mental Health Among Older Adults. Aditya Chandel* Aditya Chandel Yendelela Cuffee Isabella Tullio Jennifer Moss Jee Won Park

Background: Resilience factors at multiple levels (e.g., self-efficacy, social support) may reduce the negative physical and emotional effects of discrimination and enhance health and well-being among older adults. We examined associations between multilevel resilience factors and health-related quality of life, measured by Physical and Mental Component Summary (PCS, MCS) scores, and assessed effect measure modification (EMM) by type of discrimination (age-, race-, or gender-based).

Methods: Adults aged ≥50 from 7 mid-Atlantic states completed an online cross-sectional survey. Adjusted linear regression models estimated associations between resilience factors (Brief Resilience Scale [BRS], self-care self-efficacy, social support, trust in the medical profession, and social cohesion), categorized as high/moderate versus low, and continuous PCS/MCS scores. EMM by discrimination type was also assessed.

Results: Among 2,407 adults (median age: 67; 57.3% female; 79.4% non-Hispanic White), higher BRS scores were positively associated with PCS (b=4.33, 95% CL:2.80, 5.85) and MCS (b=13.14, 95% CL:11.76, 14.52). Similarly, positive relationships between self-efficacy and both outcomes were most compatible with the data. Weak positive associations were most compatible for social support, trust in the medical profession, and social cohesion with MCS; however, the reverse relationships were observed for PCS. There was some evidence for EMM by discrimination. For instance, a positive association between social cohesion and PCS was most compatible with the data among those experiencing gender discrimination (b=1.60, 95% CL:-0.53, 3.73), but a negative association was most compatible among others (b=-0.86, 95% CL:-1.69, -0.03; p=0.03).

Conclusion: We found positive relationships between individual-level resilience factors and better physical and mental health. Self-care self-efficacy and social cohesion may help improve physical health in older adults facing gender discrimination.

LATEBREAKER

Social

Food Insecurity and Health Outcomes Among College Students: A Cross-Sectional Study in a Health Professions Population Zheng Li* Zheng Li

Objectives:
This study aimed to 1) investigate the prevalence of food insecurity and its association with health outcomes among college students enrolled in the College of Nursing and Health Professions (CONHP), and 2) inform strategies to improve utilization and sustainability of the on-campus CONHP Little Free Pantry.

Methods:
A cross-sectional survey of all students enrolled in CONHP was conducted during the Spring 2025. Food insecurity was assessed using the USDA Six-Item Short Form Food Security Survey Module. Food security status was categorized as high/marginal (raw score 0–1), low (2–4), or very low (5–6). Self-reported demographic characteristics and health indicators—including general health, mental health, sleep disturbance, and quality of life—were collected. Bivariate analyses were conducted to examine differences in health outcomes by food security status.

Results:
Among 128 respondents, 88 (68.8%) had high or marginal food security, 28 (21.9%) had low food security, and 12 (9.4%) had very low food security. Among students classified as having low or very low food security, 12 (30%) reported utilizing the CONHP Little Free Pantry. Students experiencing low or very low food security were significantly more likely to report impaired mental health, sleep disturbance, and lower quality of life compared to food-secure peers (all $p < .05$).

Conclusions:
A substantial proportion of students in health professions programs experience food insecurity, which is associated with adverse mental health and well-being outcomes. These findings underscore the importance of campus-based food access initiatives. A second phase of this study will incorporate qualitative interviews with pantry users to identify barriers, facilitators, and strategies to enhance utilization and long-term sustainability of the CONHP Little Free Pantry.

Spatial Epidemiology

Spatial Distribution of Digestive Disease Diagnoses in Texas Using Outpatient Public Use Data Jasmine Carey* Jasmine Carey

Chronic gastrointestinal (GI) diseases represent a significant global health burden, affecting millions of individuals and straining healthcare systems worldwide. These conditions include inflammatory bowel disease (IBD), irritable bowel syndrome (IBS), chronic liver disease, celiac disease, gastroesophageal reflux disease (GERD), and chronic pancreatitis. The prevalence continues to rise which is driven by factors such as diet, sedentary lifestyles, environmental exposures, and genetic susceptibility.

The goal was to analyze the spatial distribution of outpatient digestive disease diagnoses across Texas public health regions (PHRs) and counties. Data from the 2024 Texas Outpatient Public Use Data File (PUDF) were used to map the spatial distribution. The ICD-10 codes related to digestive diseases were isolated and applied in the mapping. Results indicate that the highest percentages of outpatient digestive disease diagnoses by PHR occurred in Regions 3, 6, and 8, while Kendall and Comal counties showed the highest percentages at the county level.

This analysis provides an important initial look at the geographic patterns of digestive diseases across Texas. The identification of distinct clusters highlights areas where disease burdens may be disproportionately high. These findings underscore the need for further investigation into the demographic, environmental, and healthcare-access factors that may be driving these spatial trends, ultimately supporting efforts to improve targeted public health strategies for Texans living with chronic GI conditions.

Structural

The direct and indirect association between residential Latinx-White segregation and depressive symptoms through neighborhood features in the Multi-Ethnic Study of Atherosclerosis Sarah Valentina Diaz* Sarah Diaz Dr. Theresa Osypuk

Background: Extensive research documents the negative health effects of residential racial segregation among African Americans. However, the impacts of residential segregation on mental health of Latinxs, and pathways, are understudied. Given the demographic growth of Latinxs, the persistence of residential segregation, and that mental health is a leading disabling disorder worldwide, understanding residential segregation effects on mental health of Latinxs is important for population health.

Methods: The Latinx sample from the Multi-ethnic Study of Atherosclerosis (n=796) and inverse odds ratio weighting were used to model the associations and mediators between residential Latinx-White segregation (continuous) and depressive symptoms(continuous), through mechanisms including neighborhood social cohesion (NSC) and, separately, neighborhood problems (NP) at the individual and neighborhood level. Final models were adjusted for age, gender, gross household income, nativity status, country of heritage, and neighborhood-level socio-economic disadvantage. Data from two timepoints were used: 2004-2005 and 2010-2012.

Results: We found a statistically significant direct and indirect association between residential segregation and depressive symptoms through NP at the neighborhood level, but no significant associations through NSC. For example, residential segregation at one standard deviation above the mean was indirectly associated with a 0.37 (95%CI = 0.04, 0.68) increase in depressive symptoms among MESA Latinxs through NP.

Conclusion: Residential segregation and neighborhood problems are important for depressive symptoms, but social cohesion is not, highlighting variability in which factors are important for Latinx health.

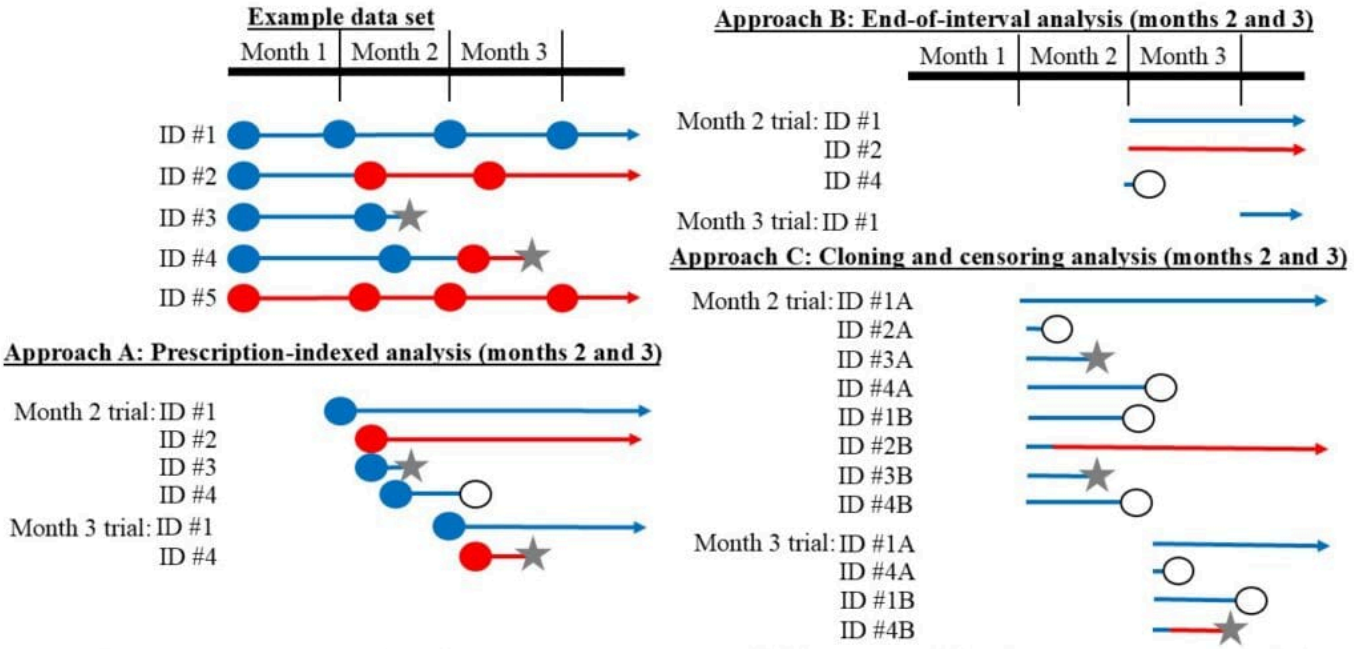
Study Design

Strategies to Avoid Immortal Time when Emulating Sequential Trial Designs Using Observational Data Michael Webster-Clark* Michael Webster-Clark Meng Pan Qoua Her Rachael Ross

Emulating hypothetical randomized trials is an increasingly popular framework for non-experimental studies. In longitudinal data, emulating a series (or sequence) of randomized trials and pooling results may be more efficient than emulating one randomized trial. The prevalent new-user design, for example, emulates a series of trials where individuals initiate a new treatment strategy or continue on an old treatment (comparator). When trials are separated based on time intervals (e.g., switch in month 1, switch in month 2, switch in month 3), immortal time can be introduced if individuals cannot be assigned to one group prior to the end of the interval.

We propose three solutions with unique implications for the target trial under study **(Figure 1)**: A) start follow-up on index events that occur within intervals (e.g., dates of prescriptions for the treatment of interest or comparator in a prevalent new-user study); B) assign treatment group among interval survivors and start follow-up at the end of the interval, or C) clone, censor, and weight each hypothetical trial. We also evaluated a solution D) that started follow-up at the beginning of the interval and looked into the future to assign exposure group. In a simulation study with a null treatment effect, solutions A, B, and C estimated a null 1-year risk difference comparing the two treatments; D did not.

Each approach has limitations. Clear index events (A) may not always exist (e.g., when the “comparator” involves no intervention). Starting follow-up at the end of intervals (B) separates treatment assignment, exposure, and the start of follow-up. Cloning and censoring (C) estimates “naturalistic” effects conditional on the population and pooling trials further complicates interpretation. Both (B) and (C) become more problematic as time interval become longer. Regardless, researchers should try to avoid introducing immortal time when analyzing observational data as a series or sequence of trials.



Legend: How we might construct the 2nd and 3rd sequential trial when comparing initiating treatment B (in red) vs continuing on treatment A (in blue) using each method for avoiding immortal time. Colored circles represent prescriptions for each drug and gray stars represent deaths. Empty circles represent censoring events. In the cloning and censoring analysis, "ID #1A" refers to the clone of individual 1 assigned to continue using A indefinitely, while "ID #1B" refers to the clone of individual 1 assigned to start B during the interval and continue to use it indefinitely.

Study Design

Revisiting Methods to Addressing Selection Bias in the Presence of Missing Data: A Simulation Study Mina Habib* Mina Habib Yulin Gong Roch A Nianogo

Researchers in epidemiology often encounter both missing covariate data and differential loss to follow-up. It is common practice to use multiple imputation for baseline covariates and inverse probability of censoring weights (IPCW) for the outcome. However, many analytical methods are possible, and their performance remains understudied. This study aimed to evaluate the performance of several analytical methods for simultaneously addressing missing covariate data and loss to follow-up within a simulation framework. We simulated 500 datasets for each combination of sample size (300, 600, 1,200, 5,000, and 10,000), missingness proportions (10%, 25%, and 50%), and three common missing data mechanisms: missing completely at random (MCAR), missing at random (MAR), and missing not at random (MNAR). We compared conditional estimates across five strategies: conditional adjustment of covariates related to the selection and missing data process via complete case analysis; inverse probability weighting (IPW) of both covariate and outcome; IPW for the covariate and multiple imputation (MI) for the outcome; MI for the covariate and IPW for the outcome; and MI for both covariate and outcome. Evaluation metrics included bias, variance, root mean squared error (RMSE), confidence interval (CI) coverage, and CI width. Across all mechanisms and methods, bias and CI width increased with higher missingness and decreased with larger sample sizes. The MI/IPW for the outcome approach exhibited the poorest CI coverage across scenarios; however, coverage improved after adjusting for standard error estimation. Despite coverage limitations, this approach consistently produced the narrowest CIs and lowest RMSE. Epidemiologists must balance the complexity of advanced methods against their performance when addressing missing data. No single approach consistently outperformed others. Sample size and missingness proportion had a greater impact on accuracy and precision than the choice of method.

Figure. Selected analysis metrics comparing different missing data handling approaches in the context of missing covariate and selection bias across varying sample sizes with 25% missingness.



Substance Use

Revisiting the Protective Association of Moderate Alcohol Use: A Positive Control Analysis

Anna Shchetinina* Anna Shchetinina Sebastien Haneuse Christina Chambers Andrea Lynne Roberts Henning Tiemeier Natalie Slopen

Introduction

Whether moderate alcohol consumption confers protective health effects has been extensively debated. This study is motivated by the hypothesis that frequently observed inverse associations between moderate alcohol use and health outcomes primarily reflect bias that is not fully addressed by conventional adjustment strategies.

Methods

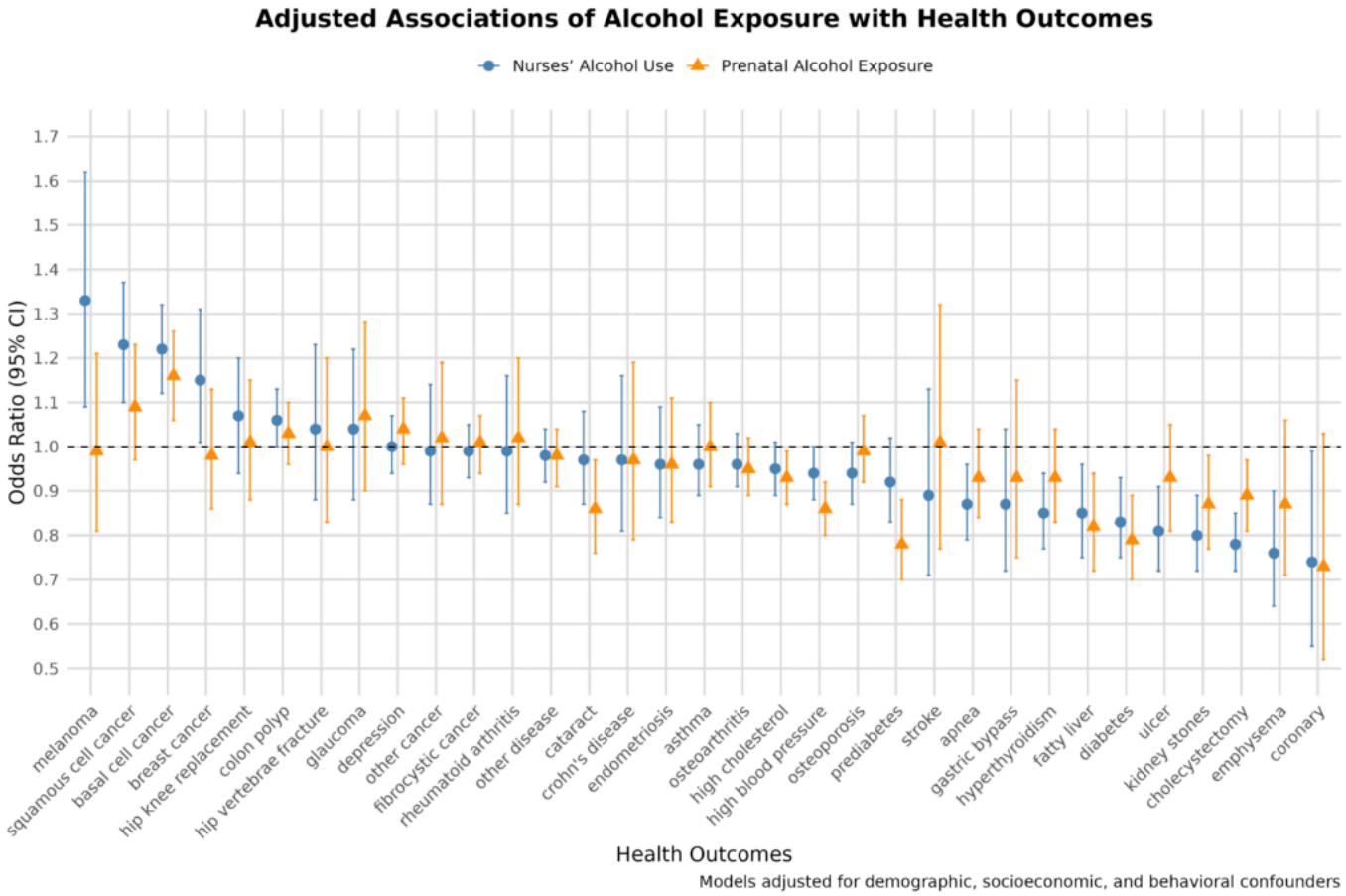
Using the Nurses' Health Study II, we utilized a positive control design leveraging prenatal alcohol exposure (PAE) reported by mothers of nurse-participants. PAE is a well-established teratogen with no plausible protective health effects. We compared associations of adult light-to-moderate alcohol use and PAE with cancers and tumors, cardiometabolic, respiratory, and other chronic conditions later in life. E-values quantified the minimum strength of unmeasured confounding required to fully explain observed associations.

Results

Analytic sample included 21,106 nurse-participants, of whom 62% reported light or moderate alcohol use. Participants who engaged in drinking had slightly higher prevalences of cancers and tumors, while most other conditions were more prevalent among non-drinkers. In positive control analyses, PAE exhibited patterns of association that closely paralleled those observed for adult alcohol use across a wide range of health outcomes. Specifically, PAE was associated with modestly elevated odds of selected cancers, whereas most cardiometabolic, gastrointestinal, endocrine, and other chronic conditions showed inverse associations. E-values indicated that modest unmeasured confounding (generally<2) could explain the observed associations.

Conclusions

Inverse associations commonly interpreted as protective effects of moderate alcohol use were also observed for a known harmful exposure, providing strong evidence that these findings are likely driven by shared residual confounding rather than causal effects. These results underscore caution against interpreting moderate alcohol consumption as health-promoting.


Adjusted Associations of Alcohol Exposure with Health Outcomes
Nurses' Alcohol Use
Prenatal Alcohol Exposure
Odds Ratio (95% CI)
1.7
1.6
1.5
1.4
1.3
1.2
1.1
1.0
0.9
0.8
0.7
0.6
0.5
melanoma
squamous cell cancer
basal cell cancer
breast cancer
hip knee replacement
colon polyp
hip vertebrae fracture
glaucoma
depression
other cancer
fibrocystic cancer
rheumatoid arthritis
other disease
cataract
crohn's disease
endometriosis
asthma
osteoarthritis
high cholesterol
high blood pressure
osteoporosis
prediabetes
stroke
apnea
gastric bypass
hyperthyroidism
fatty liver
diabetes
ulcer
kidney stones
cholecystectomy
emphysema
coronary
Health Outcomes
Models adjusted for demographic, socioeconomic, and behavioral confounders

Substance Use

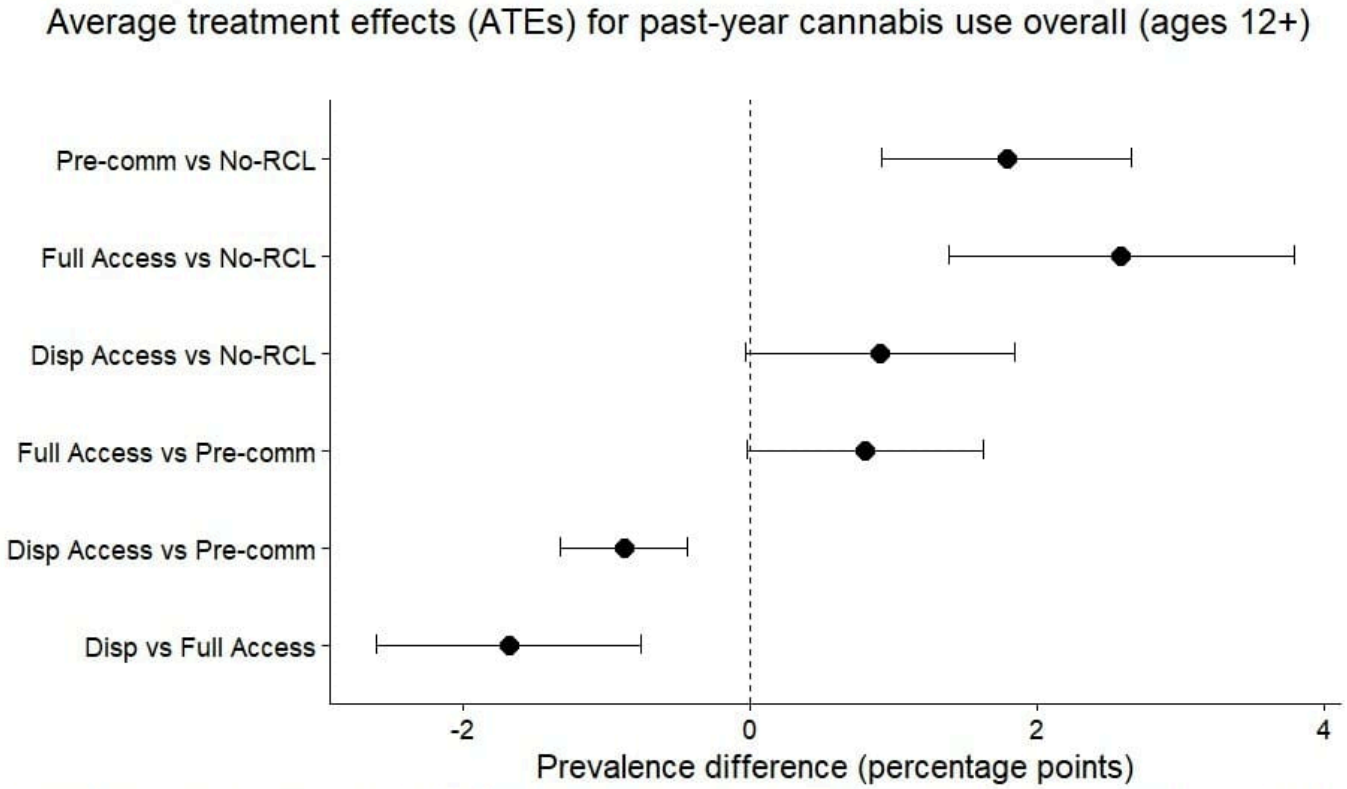
Not all legalization is equal: exploring how recreational cannabis regulatory approaches shape cannabis use and risk perceptions in US states and DC Ariadne Rivera-Aguirre* Ariadne Rivera-Aguirre Ellicott C Matthay Iván Díaz Álvaro Castillo-Carniglia Silvia S. Martins Magdalena Cerdá

Recreational cannabis laws (RCLs) in the US vary widely. However, most evaluations treat legalization as a binary exposure or use aggregate scores, obscuring how specific policy combinations influence public health. We examined the effect of distinct RCL approaches on cannabis use and risk perceptions overall (ages 12+) and across adolescents (12-17), young adults (18-25), and adults (26+).

Using latent class analysis (LCA) on 2019-2022 cannabis policy data from the Alcohol Policy Information System, we identified four RCL models: No RCL, Pre-commercial (minimal regulation, no retail framework); Full Access (retail sales, home delivery, and on-site retail use); and Dispensary Access (retail sales for off-site use only and prohibiting public use). Linking these to the 2022–2023 National Survey on Drug Use and Health, we estimated effects on past-year, past-month cannabis use and perceived risk of frequent cannabis use using Longitudinal Targeted Minimum Loss-based Estimation (LTMLE) with Super Learner to account for time-varying confounding. We estimated average treatment effects via pairwise contrasts and evaluated hypothetical shifts between Full Access and Dispensary Access models.

Relative to No RCL, all RCL models were associated with higher cannabis use and lower perceived risk, with the largest prevalence differences (PD) among young adults and adults. However, the magnitude of the differences depended on the regulatory approach, particularly among adults (Dispensary Access vs. Pre-commercial: PD=-3.09; 95%CI: -3.66, -2.52). Effects among adolescents were generally small or null. Hypothetical shifts from Full to Dispensary Access yielded small and directionally consistent reductions in use (CIs included the null).

While RCLs are generally associated with increased adult use and decreased risk perceptions, RCL approaches that restrict where cannabis can be consumed and limit on-site cannabis consumption may prevent wider prevalence differences in cannabis use.



Estimates compare four RCL approaches: No RCL, Pre-comm (Pre-commercial), Full Access, and Disp Access (Dispensary Access) with 95% confidence intervals.

Substance Use

Recovery Capital Outcomes Associated with an Access to Recovery Program Terry Bunn*
Terry Bunn Amber Kizewski Robin Thompson Madison Ashworth Candace Brancato Kelsey Carter Ernest Fletcher

Introduction: State Access to Recovery (ATR) programs provide client choice among substance use disorder treatment and recovery support service (RSS) providers, increase access and linkage to treatment and recovery support options, and increase SUD recovery support capacity. The effectiveness of the Kentucky ATR (KATR) program was assessed in building recovery capital over time through participant utilization of RSSs.

Methods: ATR study participant data was collected at four time points: 1) intake (0 months); 2) KATR service completion (~3-6 months); 3) 3 months after service completion (~5-8 months); and 4) 12 months after study intake. Mixed random effects regression models examined the impact of RSSs utilization on key outcomes including recovery capital as measured by the Brief Assessment of Recovery Capital (BARC-10), stable housing, employment, and resumption of substance use.

Results: There were 440 participants recruited to the study. BARC-10 scores ($p<0.01$), and rate of employment ($p<0.001$) were significantly higher for participants who used recovery housing compared to participants who did not use recovery housing at all follow-up time points. After controlling for the effects of other recovery support service utilizations, those who used basic needs services had lower BARC-10 scores ($p<0.05$) compared to those who did not utilize basic needs. Participants who used transportation supports had higher BARC-10 scores ($p<0.05$), rates of employment ($p<0.01$) and steady housing ($p<0.05$), and lower resumption of use ($p<0.05$) at follow-up time points than participants that did not use transportation services.

Conclusion: The KATR program was successful in establishing recovery from opioid and stimulant use disorder among persons in treatment or early recovery. This study shows that a self-selected voucher-based RSS program that meets basic needs and provides linkage to recovery housing, and other RSSs facilitate an individual’s journey to long-term recovery.

Substance Use

Chronic pain, PTSD, smoking and opioid misuse: An interaction analysis Ananya Dhanya*
Ananya Dhanya Julia Sisti Jennifer Brite James E Cone

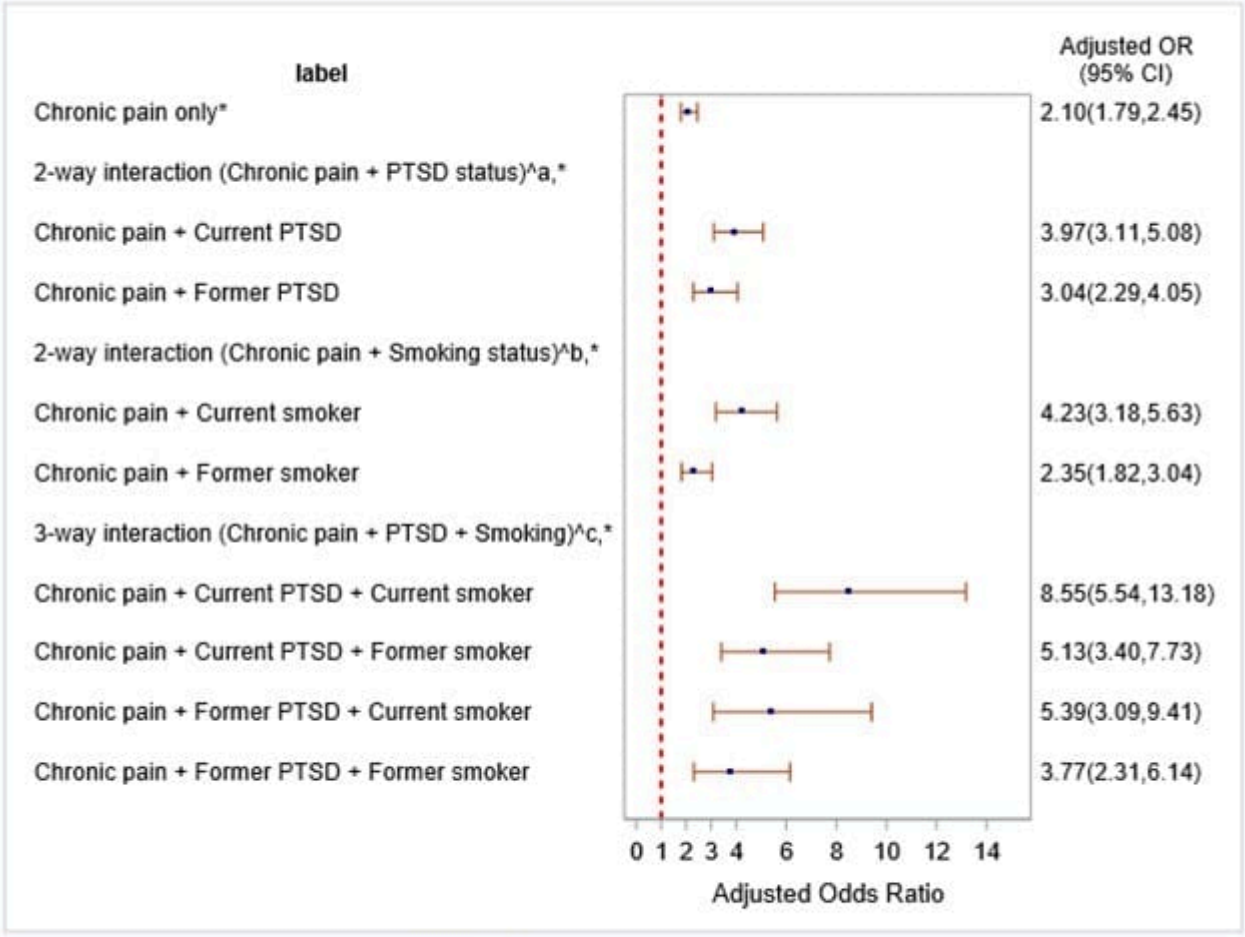
Introduction: This study examined whether chronic pain was associated with opioid misuse and modified by smoking or posttraumatic stress disorder (PTSD) or both, among 9/11-exposed individuals.

Methods: Longitudinal survey data was obtained from 23,714 World Trade Center Health Registry enrollees; 4.18% reported opioid misuse in 2020-21. Opioid misuse was defined as taking more than the recommended dose or using opioids not prescribed in the last 12 months. The exposure was self-reported physician-diagnosed post-9/11 chronic pain. Potential effect modifiers were symptoms of probable 9/11-related PTSD (current, former, never) and cigarette or e-cigarette smoking history (current, former, never). Multivariable logistic regression estimated associations of chronic pain with opioid misuse. Two-way interaction between chronic pain and each modifier was assessed on multiplicative (interaction terms) and additive [Relative Excess Risk due to Interaction (RERI)] scales. Three-way interaction between chronic pain, PTSD, and smoking status was also assessed.

Results: Chronic pain was independently associated with opioid misuse [adjusted OR (aOR)=2.10, 95% CI: 1.79-2.45]. While chronic pain, current PTSD, and current smoking were each independently associated with opioid misuse, evidence of effect modification on the additive scale was not observed (RERI=1.69, 95% CI: -1.78, 5.16). Similarly, though stratified analyses showed stronger associations of opioid misuse with chronic pain among current smokers [aOR=4.23, 95% CI: 3.18-5.63], those with current PTSD [aOR=3.97, 95% CI: 3.11-5.08], and among enrollees with chronic pain, current PTSD, and current smoking [aOR=8.55, 95% CI: 5.54-13.18], two (Psmoking*pain=0.06; PPTSD*pain=0.12)- and three (Psmoking*PTSD*pain=0.31)-way interaction terms were not significant.

Conclusion: Pathways linking chronic pain to opioid use are complex and may require integrated approaches to care that address mental health and behavioral factors.

Adjusted OR for Prescription Pain Reliever (Opioids) Misuse in the World Trade Center Health Registry Cohort



a Reference group was No chronic pain, Never post-9/11 PTSD
b Reference group was No chronic pain, No smoking
c Reference group was No chronic pain, Never post-9/11 PTSD, No smoking
* Adjusted for modifier (smoking or PTSD (2-way only)), sociodemographic covariates (age, sex, race, educational, income, marital status), 9/11-related exposure, rescue/recovery worker status, and alcohol drinking status.

Substance Use

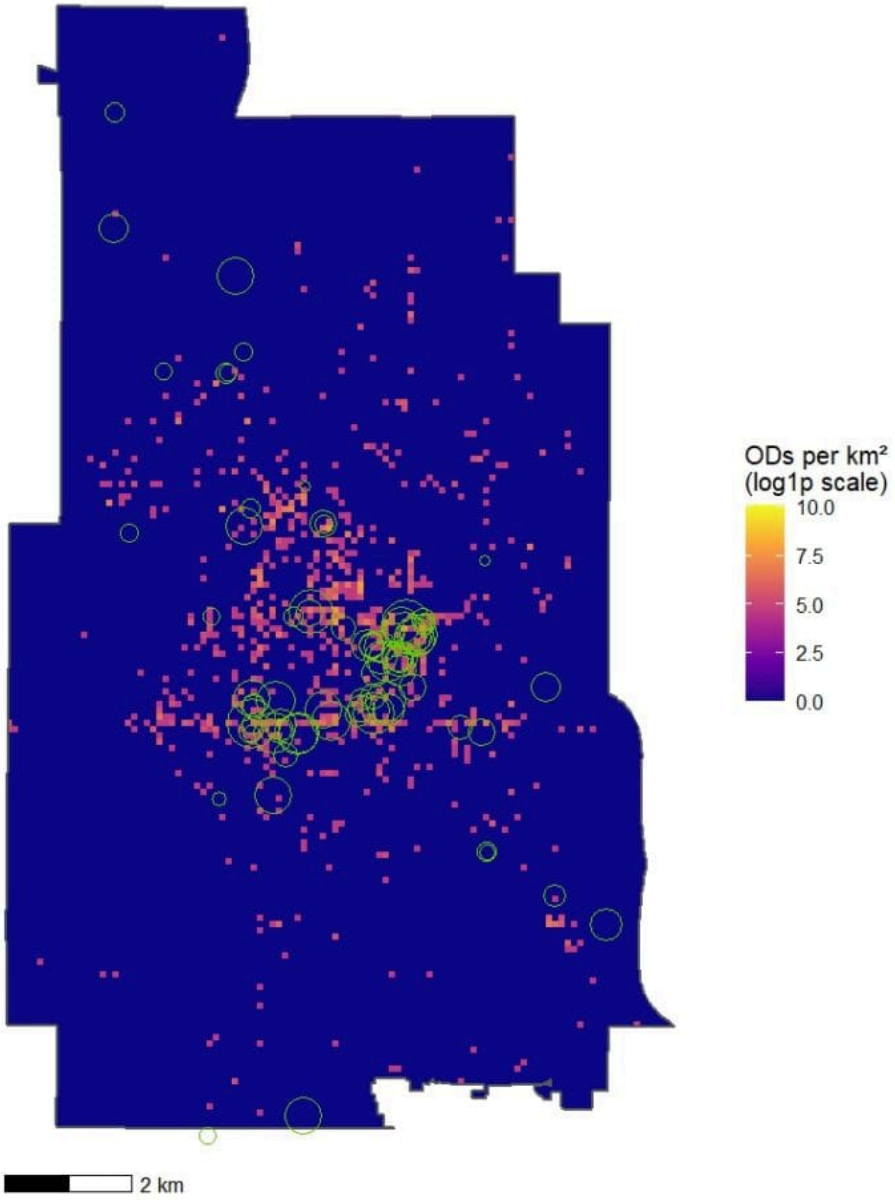
The health impacts of displacement: modelling community spread of overdose following homeless encampment sweeps Kumi Smith* Kumi Smith Sarah Jane Keaveny Josh Leopold Madeleine Possehl Jamie Humphrey Brad Ray Jonathan P Leider

Background: People experiencing homelessness (PEH) have extraordinarily elevated risk of opioid overdose compared to the general population. This population sometimes form encampments, or informal, collectively organized living areas that provide safety and opportunities for resource sharing. Much debate centers on the potential impact of forced displacement of PEH by public agencies (e.g. parks, transit, public works) on overdose risk, whether due to stress driven drug use, community fragmentation, and disruption of drug supply.

Methods: The study used a citizen-science approach to collect information on agency-led forced displacements in Minneapolis, Minnesota, in which community members (PEH, service providers) reported displacement events during monthly meetings. This data was validated against city records. Point level data of non-fatal opioid overdose events were obtained from emergency medical services records, and census tract-level social determinants of health (SDOH) were obtained from multiple sources. Endemic-epidemic spatiotemporal regression models were then used to estimate the impact of SDOH on the background rate of non-fatal opioid overdose events (endemic) and the degree to which forced displacements trigger future overdose events (epidemic).

Results: A total of 1431 non-fatal overdoses and 87 displacement events were reported between March 2024 and April 2025 (Fig 1). Exposure to a displacement event had a significant and positive effect on the future risk of overdose. A displacement event that occurred within 400 meters and 3 days of an overdose event increased the risk of a new non-fatal overdose by 1.58 (rate ratio=1.58, 95% CI, 1.09-2.31). Similar spatiotemporal patterns were observed across all other spatiotemporal bandwidths.

Conclusions: Results demonstrate that public agency-led encampment displacements are significantly associated with increased local risk of opioid overdoses after adjusting for community-level SDOH. Alternative strategies, like encampment resolution or specialized displacement service providers, may not only connect PEH to stable housing and services but also mitigate excess overdose. This study further demonstrates the feasibility of community-engaged approaches to involving PEH in research on their well-being.


ODs per km²
(log1p scale)
10.0
7.5
5.0
2.5
0.0
2 km

Substance Use

Opioid-Stimulant Co-Use and Treatment Decisions: Evidence from 2023 U.S. First-Time Substance Use Treatment Admissions Patrico Tyrell* Patrico Tyrell Thomas O'Grady

Background: Polysubstance use involving opioids and stimulants is increasing and complicates treatment decisions. Prior research suggests that stimulant co-use is associated with lower medication for opioid use disorder (MOUD) initiation and poorer treatment retention. However, it remains unclear whether opioid-stimulant co-use affects treatment allocation at admission in national data. This study examined whether co-use was associated with MOUD receipt and placement into intensive 24-hour treatment settings at admission.

Methods: Data were analyzed from the 2023 Treatment Episode Data Set-Admissions (TEDS-A), including 391,697 first-time admissions (aged ≥12 years) with opioid use across all 50 states, DC, and Puerto Rico. Opioid-stimulant co-use was defined as reporting at least one opioid and one stimulant at admission. Outcomes were MOUD receipt and 24-hour treatment placement (detoxification, inpatient, or residential care). Logistic regression estimated adjusted odds ratios (aORs) and 95% confidence intervals (CIs), controlling for age, sex, race/ethnicity, and psychiatric comorbidity.

Results: Among the sample, 8.8% (n=34,415) reported opioid-stimulant co-use. Co-use was associated with substantially higher odds of MOUD receipt (aOR=3.97, 95% CI: 3.86–4.10) and 24-hour treatment placement (aOR=1.82, 95% CI: 1.77–1.87) compared to opioid use alone. Patterns remained consistent when stratified by sex.

Conclusions: Opioid-stimulant co-use is associated with more intensive treatment at admission, contradicting prior concerns that stimulant co-use leads to withholding of MOUD at admission and suggesting the treatment system recognizes co-use as a severity marker. This pattern may reflect triage practices in publicly funded treatment systems rather than longer-term engagement or retention. However, longitudinal studies are needed to determine whether this intensive approach improves patient outcomes. These findings have direct implications for treatment access, program planning, and retention strategies in publicly funded systems.

LATEBREAKER

Substance Use

Innovating during crisis: A virtual public health detailing campaign on cocaine use amid the COVID-19 pandemic in New York City Jessica A. Kattan* Carla Foster Emily Winklestein Ellenie Tuazon Hillary V. Kunins

Background: In 2019, cocaine was involved in over half of New York City (NYC) overdose deaths, often with fentanyl. During COVID-19, substance use–related morbidity and mortality persisted amid increased isolation and stress. Public health detailing previously conducted in-person required rapid adaptation to virtual delivery to continue provider education.

Objective: To implement and evaluate NYC Department of Health and Mental Hygiene's (DOHMH) first virtual detailing campaign to educate healthcare providers about cocaine risks, fentanyl in the drug supply, and harm reduction strategies.

Methods: From September–November 2020, DOHMH conducted an 8-week campaign targeting prescribers in areas with high cocaine-related mortality across all five NYC boroughs. Four core messages were delivered via remote one-on-one video detailing, supported by action kits with tools and educational materials for providers and people seeking care. Detailers were trained in person-centered, non-stigmatizing, equity-focused communication. Evaluation used pre- and post-visit surveys of knowledge, attitudes, and intended practice changes.

Results: Despite pandemic-related logistical barriers, the campaign reached 671 providers (84% of target). Among providers completing both surveys (n=186), knowledge of fentanyl in the drug supply increased from 75% pre-visit to 95% post-visit. Intent to provide harm reduction information rose from 63% to 91%. Over 80% found materials useful and planned to incorporate recommendations.

Conclusions: DOHMH successfully transitioned detailing to a virtual format during a public health crisis, preserving overdose prevention education and improving provider knowledge and intent to adopt harm reduction practices. This replicable approach can help maintain critical public health interventions during emergencies and underscores the importance of flexible, innovative, equity-centered responses to substance use.

LATEBREAKER

Substance Use

Mobile Health Interventions for Cessation and Reduction Among Adults who use both Cigarettes and E-Cigarettes: A Scoping Review Olatokunbo Osibogun* Olatokunbo Osibogun Fahima Nasrin Eva

Background: Dual use of combustible cigarettes and e-cigarettes is increasingly prevalent among adults, yet most mobile health (mHealth) interventions have been designed for exclusive cigarette smoking. Evidence on the effectiveness of mHealth cessation tools for adults who use both cigarettes and e-cigarettes remains limited. This scoping review aims to synthesize published evidence on mHealth interventions evaluated among adults who use both cigarettes and e-cigarettes and identify gaps to inform tailored digital cessation strategies.

Methods: A systematic literature search was conducted in PubMed, Embase, Web of Science, and CINAHL from inception through January 2026. Peer reviewed studies were eligible if they evaluated phone- or mobile-based interventions among adults who use both cigarettes and e-cigarettes. Titles, abstracts and full texts were screened using predefined criteria. Two reviewers independently screened all records in Covidence, and the review follows the PRISMA-ScR guidelines.

Results: The search yielded 1,611 records and 511 duplicates were removed. Of 1,100 titles and abstracts screened, 1,080 were excluded. Twenty studies met criteria for full-text review. Full text screening is ongoing to determine final eligibility and extract data on study designs, mHealth intervention types and components and reported cessation or reduction outcomes for cigarette and e-cigarette use.

Conclusion: This scoping review will synthesize the current evidence on mHealth interventions for adults who use both cigarettes and e-cigarettes to identify gaps in intervention design, tailoring and outcome reporting. Findings will inform the development of tailored digital cessation strategies that address the unique needs of these adults and highlight priority areas for future research.

LATEBREAKER

Translational & Implementation Science

The effectiveness of healthy lifestyle training in migrant domestic helpers in Hong Kong: a quasi-experimental study Jie V Zhao* Jie V Zhao Chen Bing Michael Magtoto Manio

Background: Migrant domestic helpers are vulnerable to obesity and mental disorders, yet few interventions target this population. To address the research gap, we designed healthy lifestyle intervention tailored to this population and evaluated its effectiveness on healthy behaviors and mental well-being among Filipino domestic helpers in Hong Kong.

Methods: The intervention included dietary education and yoga practice, delivered onsite or online. Questionnaire surveys were conducted at baseline, immediately post-intervention, and four weeks post-intervention. Healthy Eating Vital Sign (HEVS) assessed dietary behvior, and PHQ-4 assessed mental health. Linear mixed-effects models were used to assess the changes in dietary behaviors and mental health.

Results: Of 318 participants (271 onsite), over 95% reported willingness to improve diet and lifestyle, and recommend the program to employer families. Four weeks post-intervention, participants showed statistically significant improvements in dietary behavior (HEVS score: -0.55; 95% confidence interval (CI): -0.92 to -0.18) and mental health (PHQ-4 score: -0.30; 95% CI: -0.57 to -0.02), with greater benefits among those with poorer baseline diet (HEVS: -1.90; 95% CI: -2.50 to -1.29) or higher mental stress (PHQ-4: -0.71; 95% CI: -1.16 to -0.27). Improvements included vegetable and fruit intake, breakfast frequency, and reduced depressive symptoms.

Conclusions: This healthy lifestyle intervention was well-accepted and brought improvements in dietary behavior and mental health among migrant domestic helpers, particularly those at higher risk. These findings contribute to an under-researched area and highlight the potential of integrating such low-cost, accessible interventions into community health initiatives to reduce health disparities in this vulnerable population.

Women’s Health

SARS-CoV-2 Infection and Asthma Exacerbations Among Pregnant Women with Asthma in South Carolina, 2020-2021 Aisha* Aisha Alkandari Jihong Liu Nandita Perumal Jiajia Zhang Vanessa Murphy

Background: The association between SARS-CoV-2 infection during pregnancy and asthma exacerbations among pregnant women with asthma is unclear. We evaluated this association and examined heterogeneity by race/ethnicity and residence.

Methods: We conducted a cohort study of 6,005 pregnancies (5,876 women) using the South Carolina COVID-19 Cohort Pregnancy Database (March 2020-December 2021). Asthma exacerbation was defined as an emergency department visit, intensive care unit admission, or inpatient hospitalization with an ICD-10 asthma diagnosis during pregnancy. We fit a trimester piecewise Cox model with race/ethnicity-specific baseline hazards, adjusting for maternal age, modified obstetric comorbidity index, education, pre-pregnancy body mass index, insurance, and calendar time, using a natural cubic spline to capture COVID-19 pandemic changes. Robust standard errors were used to account for multiple pregnancies per woman.

Results: Overall, 1,818 (30.3%) experienced asthma exacerbation. SARS-CoV-2 infection was not associated with asthma exacerbation overall (adjusted hazard ratio [aHR] 1.19, 95% CI 0.91-1.55), but the association varied by trimester (p=0.042). First trimester infection was associated with higher risk (aHR 2.57, 95% CI 1.09-6.05) compared with no infection, with no associations in later trimesters. Race/ethnicity modified the association (p=0.065). Within-group trimester-specific aHRs were higher in trimester 1 for White (aHR 3.28,95% CI 1.37-7.84) and Hispanic pregnancies (aHR 5.38,95% CI 1.83-15.84) and in trimester 2 for Hispanic pregnancies (aHR 2.91,95% CI 1.12-7.54), compared with uninfected in the same trimester and group.

Conclusion: Among pregnancies with asthma, SARS-CoV-2 infection early in gestation was associated with increased hazard of asthma exacerbation, with evidence of heterogeneity by race/ethnicity. Results may inform risk assessment during respiratory virus surges and point to early gestation as a key vulnerable window.

Women’s Health

Disparities in Prenatal Depression Treatment Engagement by Nativity, Race, and Ethnicity
Kendria Kelly-Taylor* Kendria Kelly-Taylor Sara Aghaee Joshua Nugent Nina Oberman Ai Kubo Charles Quesenberry Kathryn Ridout Mibhali Bhalala Lyndsay Avalos

Depression severity may play a key role in understanding racial, ethnic, and nativity related disparities in prenatal depression treatment. This study examines differences in treatment initiation and type by maternal nativity (US-born vs. non-US-born) among a diverse cohort of pregnant individuals universally screened for depression. We conducted a retrospective cross-sectional analysis (2013-2019) of Kaiser Permanente Northern California members who were newly diagnosed with depression between the first day of LMP to the day before a live birth (n=27,044). Race and ethnicity, and nativity were obtained from birth records. Treatment initiation (any vs. none), type (antidepressant medication vs. psychotherapy), and covariates (e.g., maternal age, Medicaid, anxiety, parity, substance use, depression severity via Patient Health Questionarrie-9) were extracted from electronic health records. Modified Poisson regression models (one with depression severity included and one without) estimated the adjusted relative risk (aRR); analysis was stratified by race/ethnicity. In the models excluding depression severity, US-born Hispanic and White individuals were significantly less likely to initiate treatment than their non–US-born counterparts (aRR:0.78;95%CI:0.67-0.92, aRR:0.81;95%CI:0.71-0.91, respectively). These associations attenuated and became non- significant after adjusting for depression severity. No significant differences were observed between US-born and non–US-born Black or Asian individuals. Treatment type did not significantly differ by nativity across racial and ethnic groups. Findings suggest depression severity may mediate the relationship between maternal nativity and treatment initiation; further analysis is warranted. In addition, examining this relationship across race, ethnicity, and nativity incorporates an intersectional lens to better understand disparities in perinatal treatment engagement.

Women’s Health

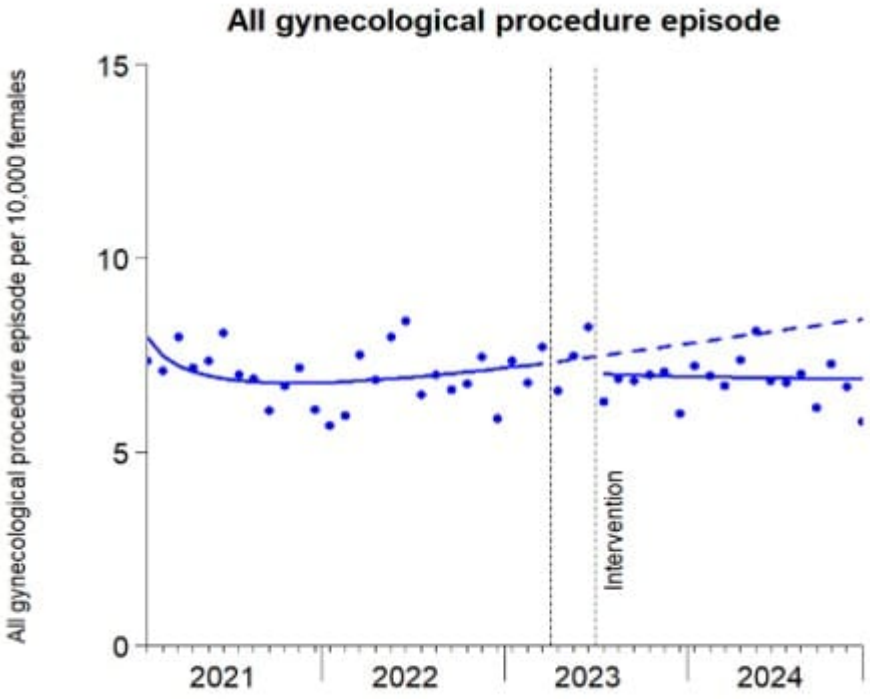
Effect of universal, no-cost contraception coverage on gynecological procedure volume: a population-based interrupted time series analysis Laura Schummers* Laura Schummers Andrea Stucchi Lucy Cheng Wendy V Norman Erin Brennand Regina-Maria Renner Michael R Law

Background: Long-acting reversible contraception (LARC, e.g., intrauterine devices), may reduce the need for gynecological procedures for abnormal uterine bleeding or permanent contraception. In Canada, physician visits and procedures are covered through public insurance; prescription medications/devices are generally covered through a mix of public and private insurance or out-of-pocket by patients. In 2023, British Columbia introduced universal no-cost prescription contraception coverage. This policy substantially increased LARC use, though impacts on gynecological procedure volumes remain unknown.

Methods: Using population-based linked health administrative data, we used physician billing, hospitalization, and emergency department records to identify endometrial ablation, hysterectomy, salpingectomy, and tubal ligation procedures in a cohort of provincially insured female BC residents from 2017-2024. We excluded events with a recent cancer or uterine prolapse diagnosis. We used an interrupted time-series analysis to estimate level and trend changes in monthly procedure rates (per 10,000 females) and compared observed to expected (counterfactual) rates as of December 2024.

Results: We identified **101,686 gynecological procedures** from 2017-2024. Pre-policy, there were 8 (CI 7, 9) procedures per 10,000 females/month, increasing by **0.08** (CI 0.03, 0.12) **per month**. After the policy change, there was an immediate nonsignificant reduction in the procedure rate (**-0.41;** CI −0.83, 0.02), followed by a **significant decline in the trend** (**-0.06; CI -0.11, -0.02 per 10,000 females**/month). By December 2024, there were 1.6 fewer procedures per 10,000 females/month than expected without the policy change, amounting to an 18% volume reduction.

Conclusion: Universal no-cost contraception coverage reduced gynecological procedure volume. Expanded contraceptive access may reduce downstream demand for resource-intensive procedures for permanent contraception or abnormal uterine bleeding.


All gynecological procedure episode
All gynecological procedure episode per 10,000 females
15
10
5
0
Intervention
2021
2022
2023
2024

LATEBREAKER

Women’s Health

Finding Barriers to Breast and Cervical Cancer Screening Adherence among low resourced population in Eastern Virginia: Prevention Matters Prachi P Chavan* Prachi Chavan Fang Fang

Breast and cervical cancers are the most prevalent cancers affecting women in Virginia, with disproportionately high mortality rates among underserved and low-resource populations, particularly, African American females. Recent data from the American Cancer Society indicate a rising incidence of cancer among women <50 years of age, with breast and cervical cancers being the most common in women <65 years. While U.S. Preventive Services Task Force provides clear screening recommendations, its adherence remains suboptimal. Programs such as ‘Every Woman’s Life’ initiatives by the Virginia Department of Health have improved screening access, yet disparities persist. In this study we conducted a systematic review of the community health needs assessment (CHNA) reports by a local urban trauma center and oncology center in Eastern Virginia to assess the needs of the community related to cancer. The goal of this study was to conduct a systematic review of the reports from CHNA conducted by Oncology Affiliates such as the Medical Center, Regional Center, General Hospital and Recovery Center, and others. Data from reports of 12 hospitals from 2019 to 2025 were reviewed using ‘Covidence’, an evidence based practice software for systematic review, and an AI powered tool ‘Rayyan’ to identify factors that affect the rate of cancer screenings and to identify emerging themes from 9 other surgery centers which helped discover barriers related to cancer screening behavior. Using the practice based software (Covidence) we imported citations from reference managers and filtered irrelevant studies using machine learning techniques, whereas the AI powered tool (Rayyan) was used for deduplication of studies applying research framework of PICO and generating flow diagrams using PRISMA. This systematic review of the reports from 2019 to 2025 provided a holistic approach in identifying health indicators and other factors related to breast and cervical cancer screenings. These insights will inform the development of targeted, community-based interventions aimed at increasing awareness, improving access, and ultimately reducing morbidity and mortality associated with breast and cervical cancer in women.

Women’s Health

Metabolomic markers associated with antenatal depression Priscilla Kay Clayton* Priscilla Clayton Kathy Trang Sixto E. Sanchez Guisong Wang Marta B. Rondon Michelle A. Williams Zhen Chen Amy Deik Clary Clish Bizu Gelaye

Background: Maternal depression affects up to 20% of pregnancies and is associated with adverse maternal and offspring outcomes. Several studies link antenatal depression to alterations in metabolites such as amino acids, lipids, and energy metabolism. However, few studies have examined these patterns during pregnancy.

Methods: We leveraged samples from the Pregnancy Outcomes, Maternal and Infant Study (PrOMIS) to examine metabolomic differences in 298 pregnant women. We assessed depression using the Patient Health Questionnaire-9 (score ≥10) and conducted targeted metabolomic profiling using liquid chromatography–mass spectrometry. We randomly partitioned the dataset into a training set (n=198) and an independent testing set (n=100). In the training set, we screened candidate metabolites using univariate logistic regression ($p<0.05$), followed by Elastic Net regularized logistic regression for the best model. We constructed receiver operating characteristic (ROC) curves to evaluate predictive performance.

Results: A total of 43 metabolites were significantly associated with depression ($p<0.05$), of which 17 were retained in the final model. Five metabolites were negatively associated (alloisoleucine, glutathione, pyruvic acid, PC P-34:0, palmitoyl-EA), while 12 were positively associated (R-3-hydroxy myristic acid, carnosine, PC O-38:5, glutamine, tridecylic acid, threonine, CAR 8:0; OH, N1,N8-diacetylspermidine, methionine, 3R-hydroxypalmitic acid, 2-aminoheptanoic acid, CAR DC6:0). ROC analyses yielded area under the curve (AUC) values of 0.81 (training), 0.73 (testing), and 0.78 (overall), adjusting for maternal age, pre-pregnancy BMI, gestational age, parity, and access to basic needs.

Conclusion: We identified metabolic signatures associated with antenatal depression, highlighting potential biomarkers and pathways such as amino acid, nitrogen, and anabolic metabolism. Future research should validate these findings in larger samples to establish clinical utility and potential for risk stratification.

Women’s Health

Emergency Contraceptive Pills Usage and Its Associated Factors Among Female Tertiary Students in Ghana Michael Fosu Ofori* Michael Ofori David Ngmenbelle Antoinette Ama Aidoo Emmanuel Kweku Nakua

The fear of unwanted pregnancy and sexually transmitted infections cause many to use emergency contraception pills (ECPs) also called morning-after pills. ECPs have become part of our community. The problem is that females who use ECPs are not aware of their side effects, how they work, their availability, and the general education about these pills. This study sought to assess the prevalence and factors associated with emergency contraceptive pill usage. The design for this study was a cross-sectional study targeting female students at Kumasi Technical University. A structured questionnaire was used to obtain information from 517 respondents. The result revealed that the prevalence rate of emergency contraceptive pills use among female students is 62% with about 98% awareness level. There is a statistically significant association between ECPs usage and sexually transmitted infections (STIs) contraction in the past, marital status, age at first sex, ever been pregnant, the number of lifetime sex partners, religion, and awareness levels. The logistic regression found marital status, ever-pregnant, lifetime sex partners, awareness of ECPs, and ever-contracted STI as factors that significantly affect ECPs usage among female tertiary students. There should be continuous education among female students regarding the use, function, and effects of ECPs.

Keywords: emergency contraceptive pills, prevalence, knowledge, sexually transmitted infections

Women’s Health

Maternal and Neonatal Outcomes by Birth Setting: Planned Home Births vs. Hospital Births Carissa Rodriguez* Carissa Rodriguez

Background: Home births have increased in the U.S. over the past two decades, partly due to low intervention rates and patient perceptions of birth safety. This analysis compares maternal and neonatal outcomes for planned home vs. hospital births.

Methods: Using Tennessee birth certificate data (2012–2022) and linked birth-death certificate data (2012–2021), we excluded unplanned home births, births whose status regarding intention was unknown, and births in other settings. Hospital births excluded transfers. Analyses included in-state residents, singletons, and term births (≥37 weeks). Chi-square and Fisher’s exact tests were used to assess birth outcomes.

Results: Among 673,193 births, 1.27% were planned home births. Home births had fewer interventions, including induction (0.63% vs. 39.50%), augmentation (1.16% vs. 22.65%), and perineal lacerations (0.32% vs. 1.06%), and more vaginal deliveries (99.89% vs. 67.58%; $p < .0001$ for all). Neonatal outcomes varied: Apgar <7 (1.63% vs. 1.33%, $p=.02$), seizures (0.09% vs. 0.02%, $p<.0001$), and ventilation (3.75% vs. 3.21%, $p=.01$) were higher for home births, while NICU admissions were lower (1.25% vs. 3.83%, $p<.0001$). No significant differences in early neonatal or neonatal deaths; infant deaths were slightly lower for home births (0.16% vs. 0.29%, $p=.05$).

Conclusions: Planned home births show fewer maternal interventions but mixed neonatal outcomes. Several factors contribute to favorable home birth outcomes, including reliable access to safe and timely transportation to hospitals. To ensure that newborn screening is conducted promptly for home births, the Tennessee Department of Health added home birth tracking to its Newborn Screening Dashboard. Additionally, the state is enhancing its perinatal regionalization guidelines to include standards for neonatal resuscitation training and has funding for three years of statewide perinatal telehealth projects to develop or expand telehealth services.

Women’s Health

An assessment of antibiotic treatment failure burden among lactational mastitis patients by initial antibiotic prescription and demographic characteristics Ruchir Raman* Ruchir Raman Christina Ludema Molly Rosenberg Patrick Quinn Indrakshi Roy Beate Henschel

Background and Justification: Lactational mastitis is an inflammatory breast disease associated with significant maternal morbidity. Its incidence varies from 2.5-20% in breastfeeding mothers, however these rates are generally thought to be underestimated. Antibiotics have been recommended for treatment of lactational mastitis, particularly in cases where infection is persistent and unable to self-resolve. However, there is a lack of comparative effectiveness studies of the different types of antibiotics prescribed for lactational mastitis treatment. To this purpose, we aim to assess treatment failure burden among lactational mastitis patients by the type of antibiotic first prescribed and by other demographic factors.

Methods: We used data from the Merative MarketScan database from January 1, 2016 – December 31, 2023 for our analysis. All patients < 49 years old with an incident diagnosis of lactational mastitis identified by ICD-10 codes N61.0 (mastitis without abscess), O91.1x (abscess of breast associated with pregnancy, puerperium or lactation) and O91.2x (nonpurulent mastitis associated with pregnancy, puerperium or lactation) and a documented care encounter with a physician in an outpatient setting were included. Treatment failure was defined as a binary outcome when a patient initiated a second prescription that was different the initial prescription. We assessed treatment failure on two time scales, within 72 hours and within . Antibiotic prescription and demographic covariate details were obtained from MarketScan.

Results: We found 65,243 lactational mastitis patients, of which 51,231 (78.5%) were prescribed an antibiotic. In patients with > 1 prescription, the median time between initial and next prescription fill was 8 days (IQR: 3-15 days). A comprehensive analysis of the antibiotic prescription, treatment failure burden, and other demographic characteristics of lactational mastitis patients is currently underway.